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Catherine Lefay, Yohann Guillaneuf. Recyclable/degradable materials via the insertion of labile/cleavable bonds using a comonomer approach. *Progress in Polymer Science*, 2023, 147, pp.101764. 10.1016/j.progpolymsci.2023.101764 . hal-04734437

HAL Id: hal-04734437

<https://hal.science/hal-04734437v1>

Submitted on 14 Oct 2024

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Recyclable/Degradable Materials via the Insertion of Labile/Cleavable Bonds using a Comonomer Approach

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Abstract

Polymers have many advantages such as low weight, low cost, and, importantly, stability under thermal, chemical, and mechanical stress. This stability, on the other hand, leads to criticism for causing environmental pollution on a macro-scale and via long-lasting microscopic plastic fragments (microplastics). Since it is very difficult but also very expensive to design brand-new materials that could both have the desired properties (mechanical, thermal, solvent resistance, etc.) and that are in the same time either recyclable and/or biodegradable, transforming already known materials to make them biodegradable/recyclable is more interesting. This approach relies on the introduction of labile/cleavable bonds onto the polymer backbone. The degradation could thus occur from these weak bonds leading to oligomers that could be easily recyclable and/or bioassimilable. This approach is currently applied to all polymerization techniques and led to interesting alternatives to numerous polymers ranging from polyolefins (polyethylene, polypropylene, ...), polyethylene oxide, polyesters, polyamides, vinyl polymers, thermosets, etc. This review thus aimed at giving a comprehensive overview of the chemistries/monomers that could be used for the different polymerization processes but also described the alternatives to common polymers whatever the polymerization process. An emphasis will be put on the degradation/biodegradation/recycling properties of the new materials.

Keywords

cyclic monomers; degradation; recycling; weak bond insertion; cleavable/labile bond; copolymer; radical ring-opening polymerization; oligomers; biodegradation; End of Life;

Abbreviation list

A	frequency factor
AA	acrylic acid
AAm	acrylamide
ACE	active chain end mechanism
ADMET	acyclic diene metathesis polymerization
AIBN	2,2'-azobisisobutyronitrile
AM	activated monomer mechanism
AN	acrylonitrile
AoC	<i>Aspergillus oryzae</i> cutinase
APH	1-acetyl-2- phenylhydrazine
AROMP	alternating ring-opening metathesis polymerization
ATRP	atom transfer radical polymerization
BASP	brush-arm star polymers
BCOE	[4.2.0]bicyclooctene
BDE	bond dissociation energy
BDO	1,4-butanediol
BIT	benzothiazolinone
BMDO	5,6-benzo-2-methylene-1,3-dioxepane
CC	β -cyclocitral
BzA	benzaldehyde
<i>m</i> CPBA	<i>meta</i> -chloroperbenzoic acid
CEMP	cascade enyne metathesis polymerization
CEVE	chloroethyl vinyl ether
cinA	cinnamaldehyde
CKA	cyclic ketene acetal
CKHE	cyclic ketene hemiacetal ester
CMOS	complementary metal-oxide-semiconductor
COD	1,5-cyclooctadiene
CTA	chain transfer agent
CuAAC	copper-catalyzed azide-alkyne cycloaddition
CVD	chemical vapor deposition
<i>D</i>	dispersity

DABCO	diazabicyclo[2.2.2]octane
DBT	3,3-dimethyl-2,3-dihydro-5Hbenzo[e][1,4]dioxepine-5-thione
DCOIT	4,5-dichloro-2-octylisothiazolone
DEAAm	<i>N,N</i> -diethylacrylamide
DEAEA	2-(diethylamino)ethyl acrylate
DEAEMA	2-(diethylamino)ethyl methacrylate
DFT	density functional theory
DHF	2,3-dihydrofuran
DIPEA	<i>N,N</i> -diisopropylethylamine
DLP	digital light processing
DLW	direct laser writing
DMA	<i>N,N</i> -dimethylacrylamide
DMDL	4,4-dimethyl-2-methylene-1,3-dioxolan-5-one
DMF	dimethylformamide
DMPA	2,2-bis(hydroxymethyl) propionic acid
DMSO	dimethylsulfoxide
DOL	1,3-dioxolane
DOLO	1,3-dioxolan-4-ones
DOP	1,3-dioxepane
DOSY	diffusion ordered spectroscopy
DOT	dibenzo[c,e]oxepane-5-thione
DOX	1,3-dioxane
DP_n	number-average degree of polymerization
DPP	diphenyl phosphate
DP_w	weight-average degree of polymerization
DTA	differential thermal analysis
DVB	divinylbenzene
E_a	activation energy
EA	ethyl acrylate
ECH	epichlorohydrin
EG	ethylene glycol
ENB	5-ethylidene-2-norbornene
EO	ethylene oxide
EoL	end of life

EVEB	ethyl 4-[2-(vinylloxy)ethoxy]benzoate
EVEP	2-ethylene glycol vinyl ether-1,3,2-dioxaphospholane 2-oxide
f	molar fraction of comonomer
F	copolymer composition
FCA	2,5-furandicarboxaldehyde
FLDA	9,9-di-n-octylfluorene-2,7-dicarboxaldehyde
FRP	free radical polymerization
GA	galactose
GIII	Grubbs third generation catalyst
GFP	green fluorescent protein
GL	glucose
GMA	glycidyl methacrylate
HBVE	4-hydroxybutyl vinyl ether
HDPE	high density polyethylene
HEA	2-hydroxyethyl acrylate
HiC	<i>Humicola insolens</i> cutinase
HMDA	hexamethylenediamine
HPA	2-hydroxypropanoic acid
HPLC	high performance liquid chromatography
IBO	isobutylene oxide
IBVE	isobutyl vinyl ether
IRRAS	infrared reflection absorption spectroscopy
k_p	propagation rate constant
k_{MC}	kinetic MonteCarlo simulation
KPS	potassium persulfate
LA	lactide
LCST	low critical solution temperature
LDPE	low density polyethylene
LLDPE	linear low density polyethylene
M	monomer
MA	methyl acrylate
MAA	methacrylic acid
MANa	sodium methacrylate
MBDO	2-methylene-4H-benzo[d][1,3]dioxin-4-one

MCA	methyl α -chloroacrylate
MDOL	2-methyl-1,3-dioxolane
MePEGA	poly(ethylene glycol) methyl ether acrylate
MePEGMA	poly(ethylene glycol) methyl ether methacrylate
MDO	2-methylene-1,3-dioxepane
MDOP	2-methyl-1,3-dioxepane
MEO	methylene ethylene oxide
MGA	methyl glycidyl acetate
MMA	methyl methacrylate
M_n	number-average molar mass
M_w	weight-average molar mass
MMD	molar mass distribution
MPDL	2-methylene-4-phenyl-1,3-dioxolane
MPO	myeloperoxidase
MTC	2-methylene-1,3,6-trioxocane
NB	Norbornene
<i>n</i> BA	<i>n</i> -butyl acrylate
NBOEG	2-(oligo ethylene glycol)-3a,4,7,7a-tetrahydro-1H-4,7-methanoisoindole-1,3(2H)-dione
NIPAm	<i>N</i> -isopropyl acrylamide
NMP	nitroxide-mediated polymerization
NP	nanoparticle
NMR	nuclear magnetic resonance
NTA	<i>N</i> -thiocarboxyanhydride
NVP	<i>N</i> -vinyl pyrrolidone
OFET	organic field-effect transistor
PA	(<i>S</i>)-(-)-perillaldehyde
PAA	poly(acrylic acid)
PAN	polyacrylonitrile
PBS	phosphate-buffered saline
PBT	poly(b-thioester)
PBSA	poly(butylene succinate-adipate)
PCL	polycaprolactone
PDEAAm	poly(<i>N,N</i> -diethylacrylamide)

PDHF	poly(2,3-dihydrofuran)
PDMAAm	poly(dimethyl acrylamide)
PEA	poly(ethyl acrylate)
PEG	poly(ethylene glycol)
PEO	poly(ethylene oxide)
PBAT	poly(butylene adipate-co-terephthalate)
PCET	proton coupled electron transfer
PET	poly(ethylene terephthalate)
PET-RAFT	proton electron transfer – reversible addition fragmentation chain transfer
pMeSt	<i>para</i> -methylstyrene
PETA	pentaerythritol tetraacrylate
PETIA	pentaerythritol triacrylate
PHA	poly(hydroxyalkanoate)
PHB	poly(hydroxybutyrate)
PHBV	poly(hydroxybutyrate - <i>co</i> -3-hydroxyvalerate)
PhDL	5-methyl-2-methylene-5-phenyl-1,3-dioxolan-4-one
PhP	1-phenyl-3-pyrazolidone
poly(DCPD)	poly(dicyclopentadiene)
PISA	polymerization induced self-assembly
PLA	polylactide
PLBA	poly(lactide- <i>co</i> -glycolide)
PMMA	poly(methyl methacrylate)
<i>Pn</i> BA	poly(<i>n</i> -butyl acrylate)
PNIPAAm	poly(<i>N</i> -isopropylacrylamide)
PP	polypropylene
PS	polystyrene
PTDO	2-phenoxy-1,3,4,7-tetrahydro-1,3,2-diazaphosphepine 2-oxide
PU	polyurethane
PVC	poly(vinyl chloride)
<i>Pt</i> BA	poly(<i>tert</i> -butyl acrylate)
QCM-D	quartz crystal microbalance with dissipation
RAFT	reversible addition-fragmentation transfer
RDRP	reversible deactivation radical polymerization

REACH	registration, evaluation, authorisation and restriction of chemicals
ROMP	ring-opening metathesis polymerization
ROP	ring-opening polymerization
ROS	reactive oxygen species
rROP	radical ring-opening polymerization
rROPISA	radical ring-opening polymerization induced self-assembly
S	styrene
SCC	strand-cleaving crosslinker
SCM	sulfide cyclic methacrylate
SEC	size exclusion chromatography
SEM	scanning electron microscopy
SET	single electron transfer
SPC	self-polishing copolymer
SS	sodium 4-styrenesulfonate
SSDR	specific surface degradation rate
t	time
T_g	glass temperature
T_m	melting temperature
<i>t</i> BA	<i>tert</i> -butyl acrylate
TBAF	tetra- <i>n</i> -butylammonium fluoride
TBC	<i>tert</i> -butyl catechol
TBD	1,5,7-Triazabicyclo 4.4.0 dec-5-ene
<i>t</i> -BuP4	1- <i>tert</i> -butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)-phosphoranylideneamino]-2 Λ 5, Λ 5-catenadi(phosphazene
TBSM	tributyl silyl methacrylate
TEM	transmission electron microscopy
TFA	trifluoroacetic acid
TGA	thermogravimetric analysis
TGMVE	tri(ethylene glycol) methyl vinyl ether
thCL	ϵ -thionocaprolactone
thDL	decathionolactone
THF	tetrahydrofuran
THP	tetrahydropyran
TIL	<i>Thermomyces lanuginosus</i> lipase

TLD	thionolactide
TMBQ	trimethyl-locked benzoquinone
TMC	trimethylene carbonate
UCST	upper critical transition temperature
UV	ultra violet
UV-Vis	ultra violet-visible
VAc	vinyl acetate
VCHO	4-vinyl-1,2-epoxycyclohexane
VE	vinyl ether
VOEM	diethyl [2-(vinyloxy)ethyl]malonate
WAXS	wide-angle X-ray scattering

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1 Introduction

1.1 Context

Since the beginning of the 20th century, plastics have emerged as materials that replace traditional ones due to their diverse properties, including lightness, low thermal and electrical conductivity, corrosion resistance, oxygen and water barrier properties, and, notably, stability under thermal, chemical, and mechanical stress. All these features, combined with their low production cost, make polymers valuable for a wide range of applications, including biomedical devices, textiles, construction, agriculture, automotive, household items, packaging, and more.[1] In our societies, it is now impossible to avoid the use of plastics. Over the past few decades, the environmental pollution caused by plastics in various forms at a macro-scale has become evident, as seen through images of overloaded landfills and the improper disposal of waste into rivers and oceans.[2]

More recently, the concern about environmental pollution via long-lasting microscopic plastic fragments (microplastics)[3-5] is likely more important since the amount of such microparticles is estimated to be close to 250 Mt in 2025.[6] Such microplastics have been reported everywhere in nature, from ice in the Arctic Sea[7] to the deepest floor of the oceans,[8] but also in the air, water, and food we eat.[9] The potential of such micro/nano-particles to induce inflammation, genotoxicity, and oxidative stress has been reported[9], even if their impact in the environment with the background of numerous natural particles requires more studies due to the high complexity of the system.[10] Nevertheless, limiting their spread in the environment is strongly encouraged and will be soon regulated.

There are two main scenarios for end-of-life (EOL) of polymers. There are two main scenarios for the end-of-life (EOL) of polymers. The first and strongly encouraged option is recycling,

which simultaneously helps conserve energy and reduce the consumption of natural or fossil resources required for plastic production.[11, 12] This sustainable approach is known as the ‘circular plastic economy’.[13-16] However, recycling has not been the primary end-of-life option for plastics. For instance, in 2018, only 33% of the plastic waste collected in Europe was recycled.[17] The importance of recycling will increase over time but this will require important changes in waste management infrastructure, societal attitudes, and new policies. Among the various methods, mechanical recycling is difficult due to the key challenges of waste separation according to polymer type and the presence of additives.[18] Increasingly, plastic producers are developing techniques for chemical and enzymatic recycling of commodity and specialty polymers, in which a polymer is converted to its original feedstock.[12, 19] The best example is the enzyme-based recycling approach developed for poly(ethylene terephthalate) (PET)[20, 21] or the thermal depolymerization of poly(methyl methacrylate).[22-25] However, this approach is highly specific to the polymer to be recycled and waste separation is a key issue to isolate only one kind of polymer.

There are scenarios where it is not possible to recycle or reuse plastic waste, such as short-term and single-use applications (food packaging or single-use items), or when plastics are impossible to collect after use, such as water-soluble polymers, agricultural films, and fishing tool items. The alternative is thus to use specially designed biodegradable polymers that can undergo bio-assimilation and mineralization by microorganisms under natural environment (soil, ocean) or in controlled conditions such as composting facilities.[16] Composting results in a complete breakdown of a compound to biomass and either fully oxidized or reduced simple molecules (such as carbon dioxide, nitrate/ ammonium, and water), which can be further utilized as a valuable soil amendment (organic recycling).[26-28] Current research in that field primarily focuses on aliphatic and aliphatic–aromatic polyesters such as poly(hydroxyalkanoate) (PHA)[29] and poly(butylene adipate-*co*-terephthalate) (PBAT).[30-

33] Nevertheless, such kind of polymer cannot have a wide range of properties (mechanical, thermal, barrier, etc.) to cover all the applications of commodity and specialty plastics.

The challenge for polymer chemists is to produce plastics that are completely and rapidly both biodegradable and/or recyclable while retaining the excellent mechanical and functional properties of commodity polymers during service life. In the last two decades, biobased/biosourced materials have been envisioned as a solution. Chen and coworkers[34] recently reviewed this topic and noticed that only performance advantaged bio-based polymers could be an answer to this technical challenge. Since it will be very complex but also very expensive (cost for new monomer syntheses, costs of tests to perform REACH registration,[35] etc.) to design brand-new materials that could both have the desired properties (mechanical, thermal, solvent resistance, etc.) and that are in the same time either recyclable and/or biodegradable, transforming already known materials to make them biodegradable/recyclable is more interesting. This approach relies on the introduction of labile bonds onto the polymer backbone. The degradation could thus occur from these weak bonds leading to oligomers that could be easily recyclable and/or bioassimilable (Fig. 1).

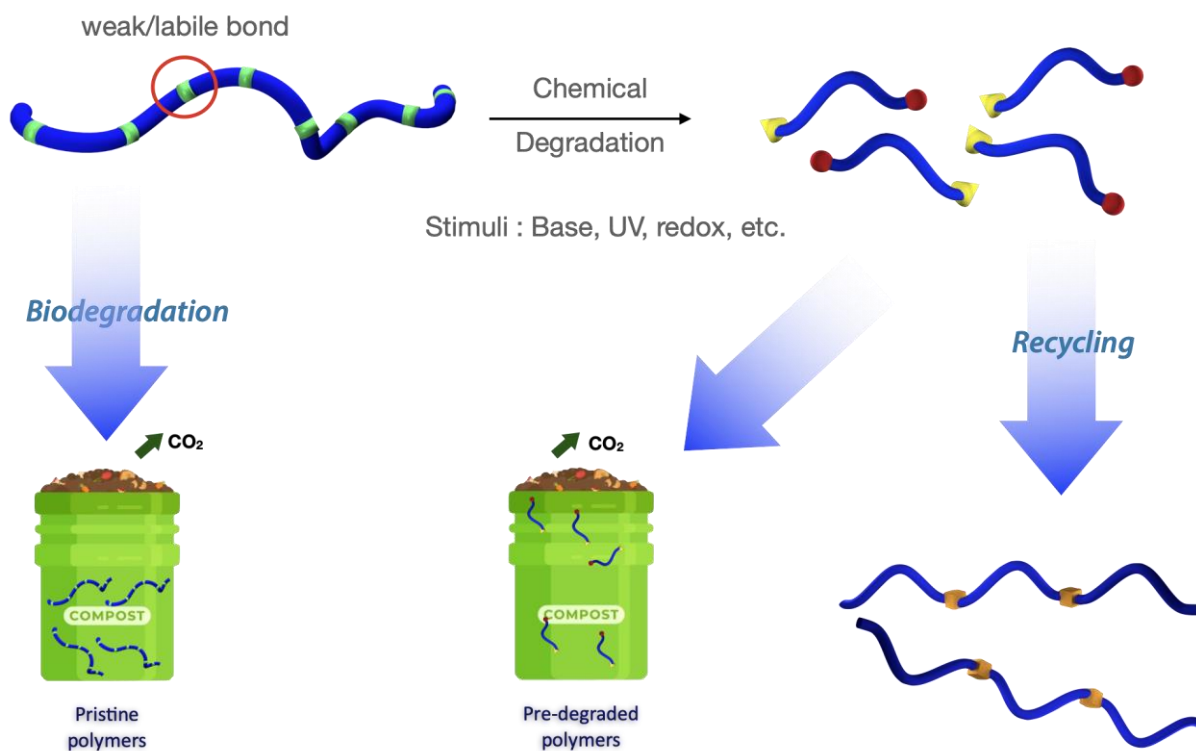


Fig. 1. Insertion of weak/labile bonds onto polymer materials via the comonomer approach and their EoL, *i.e* recycling or biodegradation.

This approach is currently applied to all polymerization techniques (radical polymerization via the radical ring-opening polymerization (rROP), ring-opening polymerization (ROP), ring-opening metathesis polymerization (ROMP), etc.) and led to interesting alternatives to numerous polymers ranging from polyolefins (polyethylene, polypropylene, etc.), polyethylene oxide, polyesters, polyamides, thermosets, etc. This review thus aimed at giving a comprehensive overview of the chemistries/monomers that could be used for the different polymerization processes but also described the alternatives to common polymers whatever the polymerization process (degradable polyethylene-like materials could be obtained by polycondensation or via ROMP for example). An emphasis will be put on the degradation/biodegradation/recycling properties of the new materials.

1.2 The case of oxo-degradable materials

The insertion of labile/cleavable bonds into the polymer backbone will lead to the fragmentation of the materials to induce either biodegradation or recycling. Such approach is often wrongly perceived as similar to the oxo-degradable materials that is also considered to fragmentate polymeric materials. A detailed description of the oxo-degradable approach is thus important to compare the two approaches.

Intensive research was carried out to increase the biotic degradation of polymers and especially the degradation of polyolefins (polyethylene, polypropylene) that is a crucial material in various fields such as packaging, agriculture and construction that cause the major leakage of plastic in the environment.[36] The approach that was developed consists in polyolefins that is designed to undergo an oxidative degradation using catalysts to cause the breakdown of the polymer backbone into small fragments that could be bio-assimilated. Polyolefins are thus additivated with pro-oxidant molecules (between 1 to 5% by weight) composed mainly of metallic salts of iron, magnesium, nickel and cobalt.[37] This additive catalyzes the oxidation of the polymer and causes polymer chain breaks, which induces a macroscopic decomposition of the material (Fig. 2). The mechanism consists of the oxidation of the polymer chains, triggered by UV light and/or heat, followed by fragmentation. In a second step, once the abiotic degradation led to smaller fragments, the classic biotic degradation could occur.

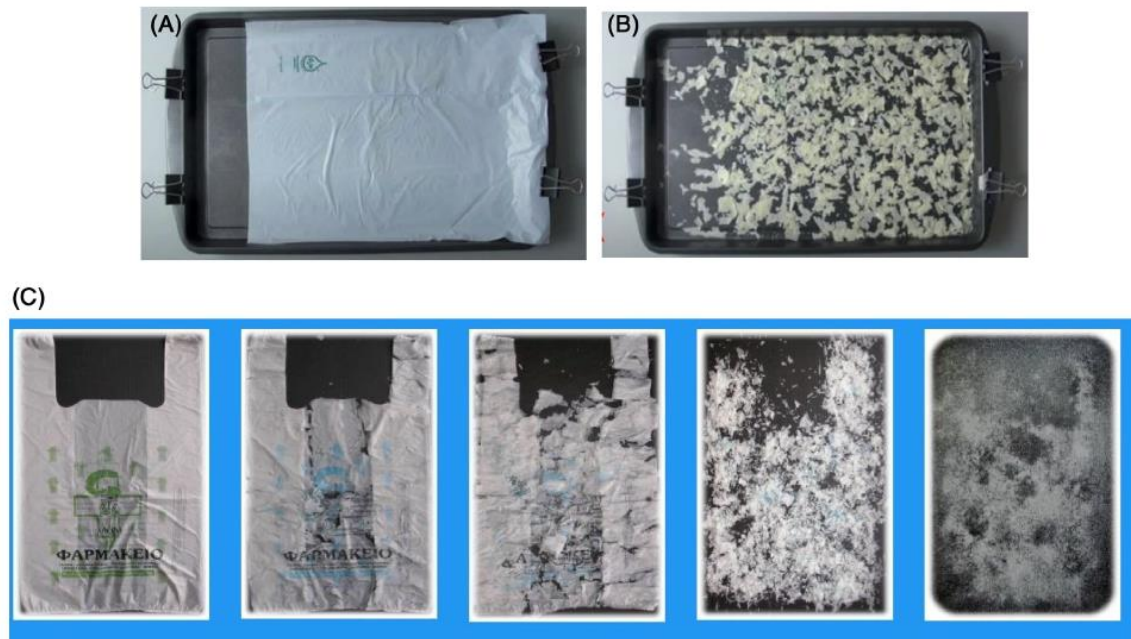


Fig. 2. Degradation of oxo-degradable materials. (A) oxo-degradable plastic bag at time zero, (B) oxo-degradable bag after 24 months. (C) Degradation of the single-use bag from Revert. Adapted from ref. [38] with permission.

The average molecular weight of oxidized polyolefin should be under $5,000 \text{ g.mol}^{-1}$ to ensure a significant biodegradation in a reasonable time. The biodegradation of such materials is complex with numerous publications showing either good biodegradation profile or showing only moderate degradation and questioning about the biodegradation. The review from Mustafa *et al.*[38] presented in details such debate. The addition of potentially toxic catalysts that can escape into the surrounding environment[39] as well as the only partial degradation of the polymer chains have led to the partial banning of these materials.[40] Indeed, photo-oxidation occurs preferentially at the surface of the material and is favored in the amorphous regions of the polymers, which leads to fragmentation of the plastics and leads to the accelerated production of microplastics whose final biodegradation is not assured. The only partial

degradation of the bulk material and the heterogeneity of the degraded products are the main difference between oxo-degradable materials and materials that are incorporated labile/cleavable bonds into their backbone.

2 Concept

2.1 Linear Polymer

For the popular press, there is no or little degradation of plastics in the environment. Even if the field of polymer degradation is very prolific, we could find easily various estimation of the degradation time for a plastic bag that could range from 10 to 1000 years.[41] A key point in the analysis of polymer degradation is the shape and size of the sample. Indeed, as shown by Suh and coworkers[42] degradation of a thin film, cylinder or a hard sphere of the same mass led to drastic different conclusion for the time to complete degradation (Fig. 3). Starting from a thin film mimicking a plastic bag, the same mass but presented as a hard sphere increases the time to complete decomposition from 2 years to 700 years. The same authors then recently compared in their perspective the degradation rate of plastics according to the environment.[42] The results are gathered in Fig. 4 with data for plastics type 7 (“others”) includes the biodegradable plastics PLA, polyhydroxybutyrate (PHB), poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV), Mater-Bi and polycaprolactone (PCL).

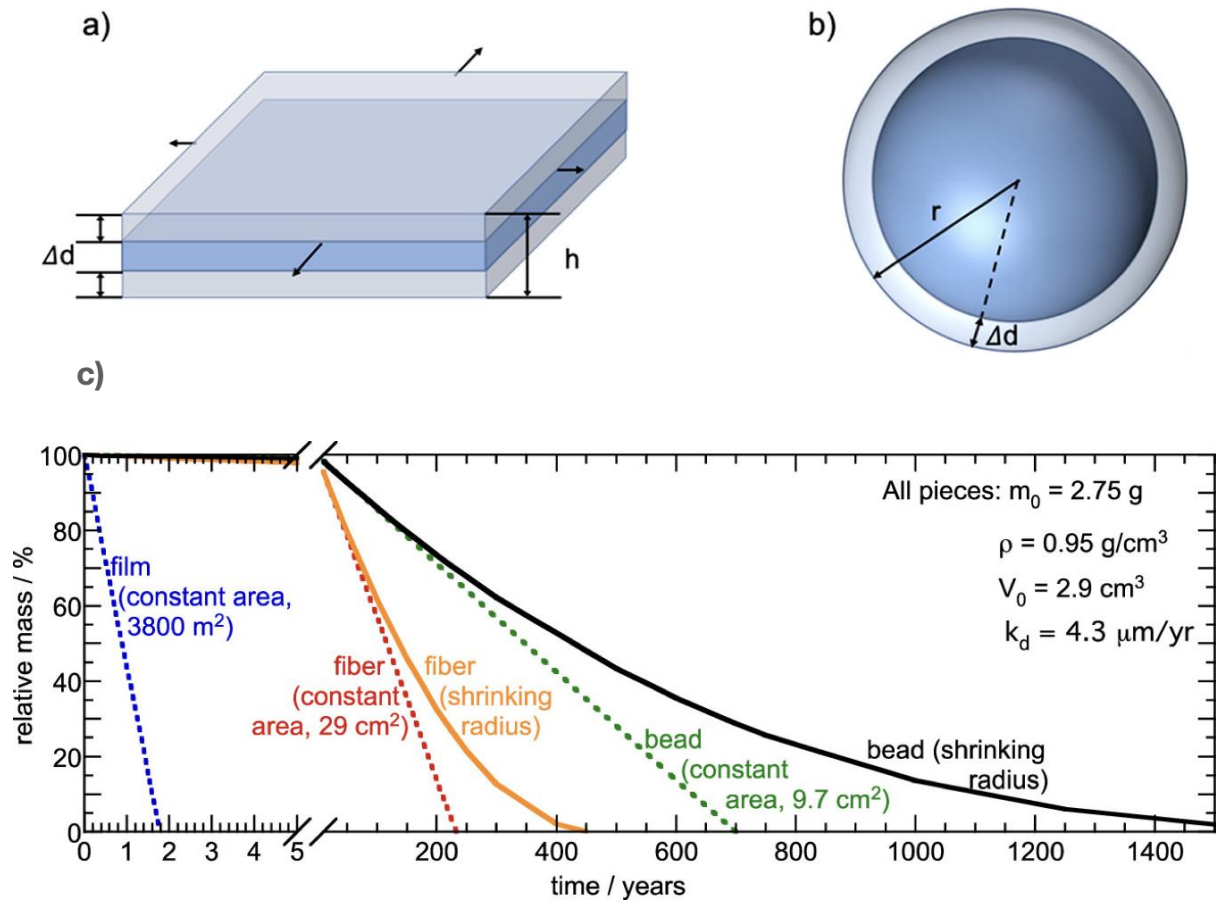


Fig. 3. Representative structures for (a) a section of a flat produce bag with total thickness h and (b) a sphere of radius r . The specific surface degradation rate (SSDR) is defined as the volume of material lost by removal of a layer of thickness Δd in a specified time. c) Comparison of predicted degradation profiles for HDPE pieces with the same mass, density, and SSDR but different shapes (thin film, fiber, and bead). The dashed lines correspond to extrapolations assuming constant surface area; the solid lines correspond to a model which assumes the radius, and therefore the surface area, decrease over time. Reproduced from Reference [42] with permission.

PS and PVC presented the lowest degradation rate that are far lower than the polyolefins. Indeed, LDPE has a quite high rate of degradation due to low crystallinity combined with the presence of branched point and a moderate sensitivity to oxidation. Even if biodegradable materials (PHB/PLA) show the higher degradation rate in compost and landfill conditions (59

and 21 $\mu\text{m}/\text{year}$), their degradation in marine environments is similar to the degradation rates of the polyolefins. Although PLA and other polyesters are expected to be fully degradable, the low water temperature and the hydrophobicity of the backbone led to such phenomenon. In soil conditions, however, the degradation rate of PLA is higher than the corresponding values for polyolefins. These results showed that depending of the environment it could be beneficial to increase the degradation profile of all kinds of polymers to limit the long lifetime of plastic waste.

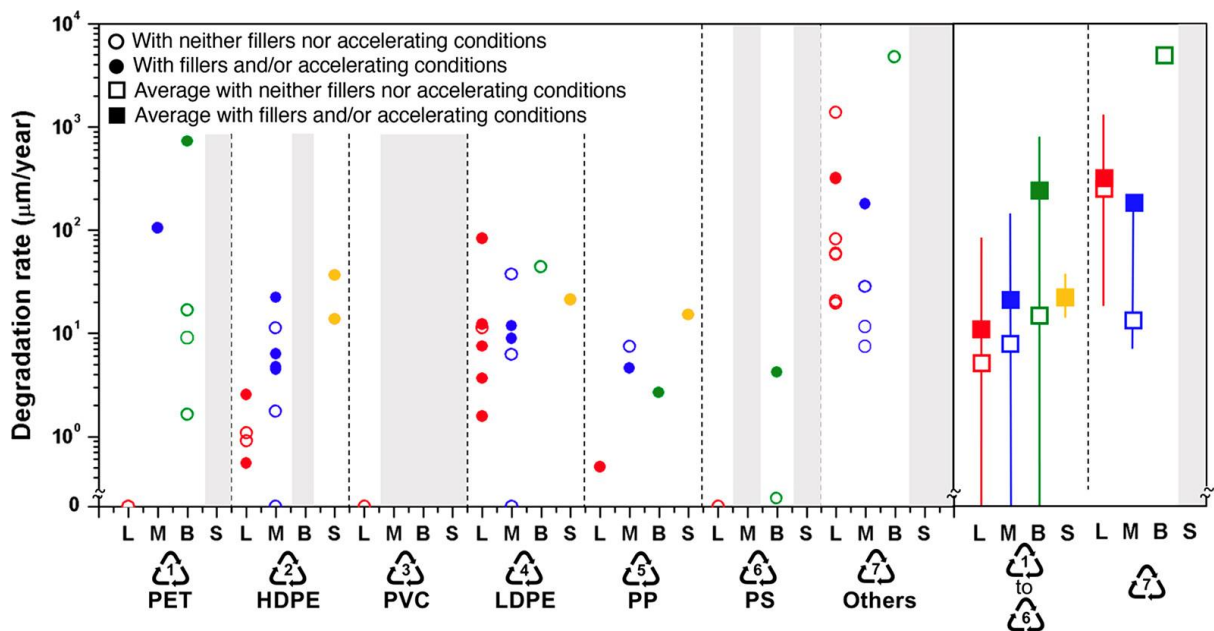


Fig. 4. Specific surface degradation rates for various plastics, in $\mu\text{m year}^{-1}$. Vertical columns represent different environmental conditions (L, landfill/compost/soil; M, marine; B, biological; S, sunlight) and plastics types (represented by their resin identification codes). Plastics type 7, “others”, corresponds to various nominally biodegradable plastics. The range and average value for plastics types 1–6 are shown on the right as lines and squares, respectively, as well as for biodegradable “others”. Data points representing degradation rates that were unmeasurably slow are shown on the x-axis. Gray columns represent combinations for which no data were found. Reproduced from Reference [42] with permission.

To increase the rate of degradation of common polymers, several routes could be used (Fig. 5). The first one is to introduce a more labile functionality into the polymer backbone. The best example is the introduction of hydrolysable bonds into a C-C backbone. The most common group inserted is the ester group that could be degraded by various pathways that are hydrolysis (catalyzed in acidic and/or basic pH), enzymatic processes, microbial degradation, etc. Others functional groups were also widely used such as silyl or acetal moieties that could allow more specific degradation conditions to be applied. Recently other triggers such as light (ortho nitrobenzyl ester) could be used to have a temporal and special control of the degradations. Table 1 gathers different groups that impart the cleavage of the macromolecules. In all these examples, the cleavage is directly linked to the insertion of cleavable unit in the main chain. Recently other functional groups have been used to insert in the main chains some units that will induce such cleavage once activated. The best example is the production on demand of radicals into (meth)acrylate chains that will induce the depolymerization/degradation of the chains (Fig. 5). Such approach is presented in detail in part 3.2.3. The various groups are also gathered in Table 1.

Lastly it is now well established that the rate of degradation of various polymers are strongly correlated with the physical properties of the polymers such as crystallinity, glass transition temperature and mainly hydrophobicity.[43] Mathers *et al.*[44] recently used large database, various molecular descriptors and machine learning to describe the impact of the different polymer properties on degradation in marine conditions. The introduction of comonomer impacting these parameters will directly increase the rate of degradation. Indeed, hydrophobic polymers exhibit limited water diffusion into the bulk materials. A good example of such approach is the copolymerization of 1,3-dioxolan-4-one with D,L lactide to prepare PLA based

materials that will become marine degradable[45] (Fig. 5). This approach is less universal than the first one since it could only be performed on polymer that are already degradable but with a very slow rate of degradation in certain condition. Nevertheless, such approach could also be combined with the introduction of labile groups to enhance the degradability. For example, the introduction of ester bond into vinyl-based polymers by CKA radical copolymerization with common vinyl monomers allowed for a good chemical accelerated degradation but the rate of hydrolysis is very slow. The modification of the CKA monomer from the hydrophobic MDO to MTC that led to the production of an ester coupled with a hydrophilic ether bond increased the rate of degradation of similar vinyl based polymers in PBS at 37 C.[46]

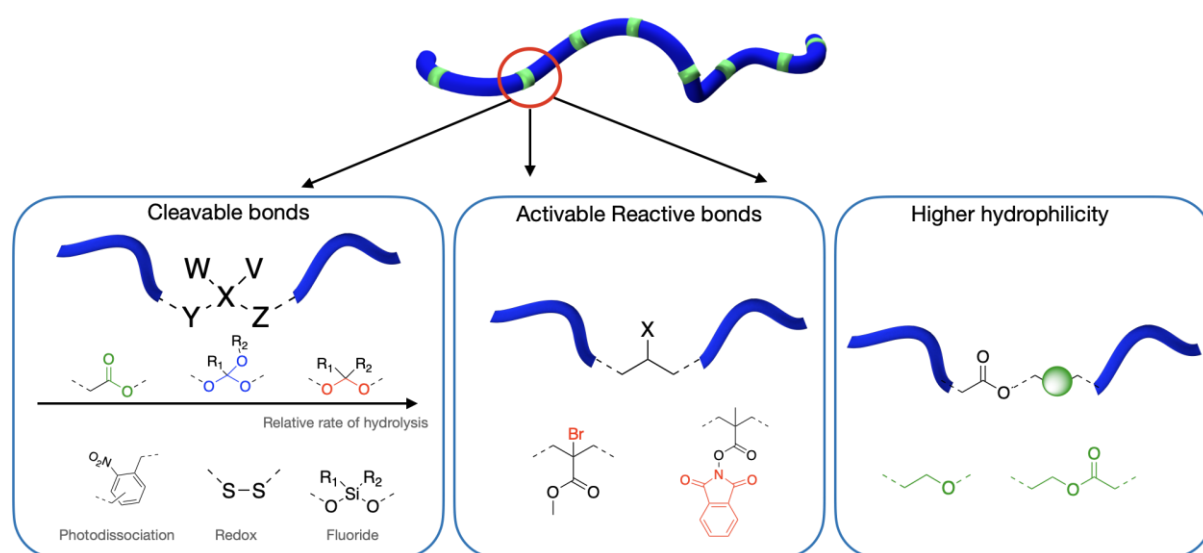
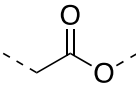
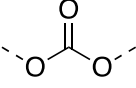
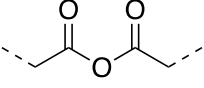
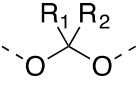
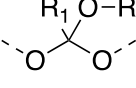
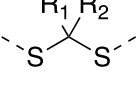
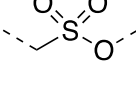


Fig. 5. The different methodologies that were used to induce/enhance the degradation of polymer chains.

Table 1.

Cleavable bonds	ADMET	ROMP	Radical Polymerization	Cationic polymerization	Anionic Polymerization	Polycondensation	Conjugated polymers	Coordination polymerization
	✓	✓	✓	✓	✓	✓		
		✓						
	✓							
	✓	✓		✓	✓	✓		
		✓						
		✓						
	✓							

		✓		✓				
	✓	✓						
	✓	✓						
		✓	✓					✓
		✓						
		✓	✓	✓				
			✓					
			✓					

							✓	
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2.2 Cross-linked polymers

Besides linear polymers, thermosets, that are cross—linked polymeric materials is becoming more and more important in the world annual plastic production due to their advanced properties (permanent shape, chemical and thermal resistance, etc.). Nevertheless, their intrinsic cross-linked structure avoids any reprocessing, recycling or degradability. Since then and due to the increasing demand for degradable/recyclable thermosets solutions were found by the use of dynamic covalent bonds, the so-called vitrimers that allow the reprocessing or recycling of thermoset at high temperature.[47-49] Another solution is the use of specifically designed monomers that embed a degradable core between the multi-functional linking group. Such approach has been recently reviewed.[50] In the latter case, this implies the design of *de novo* monomers with degradable ability but produces materials with material properties that could differ from already known thermosets. In other words, degradability and the resin properties are not decorrelated. Johnson *et al.*[51] in 2020 hypothesized that the location of labile bonds inside the thermoset may impact the degradation profile. They compared the degradability and potential recyclability of thermosets with labile bonds inside the backbone of the network at low co-monomer loadings, with the analogous network that was prepared via the addition of cleavable crosslinks. They theoretically derived a reverse gel-point model based on the Miller–Macosko and Flory–Stockmayer theories to quantify the amount of labile bonds x needed to degrade networks of strands with f cross-linkable functional groups and c crosslinks into soluble products (Equation 1).

$$x > \frac{c(2f - 1) - f}{c + f} \quad (1)$$

Such relationship then implied that when $f \gg c$, degradation should occur when x is greater than $2c$. If $f \approx c$, then degradation to soluble products should occur for $x > c-1$. This could be described more qualitatively by: the degradation of thermoset into soluble part should be possible for networks having cleavable bonds in the order of magnitude to the number of crosslinks. This is summarized in Fig. 6.

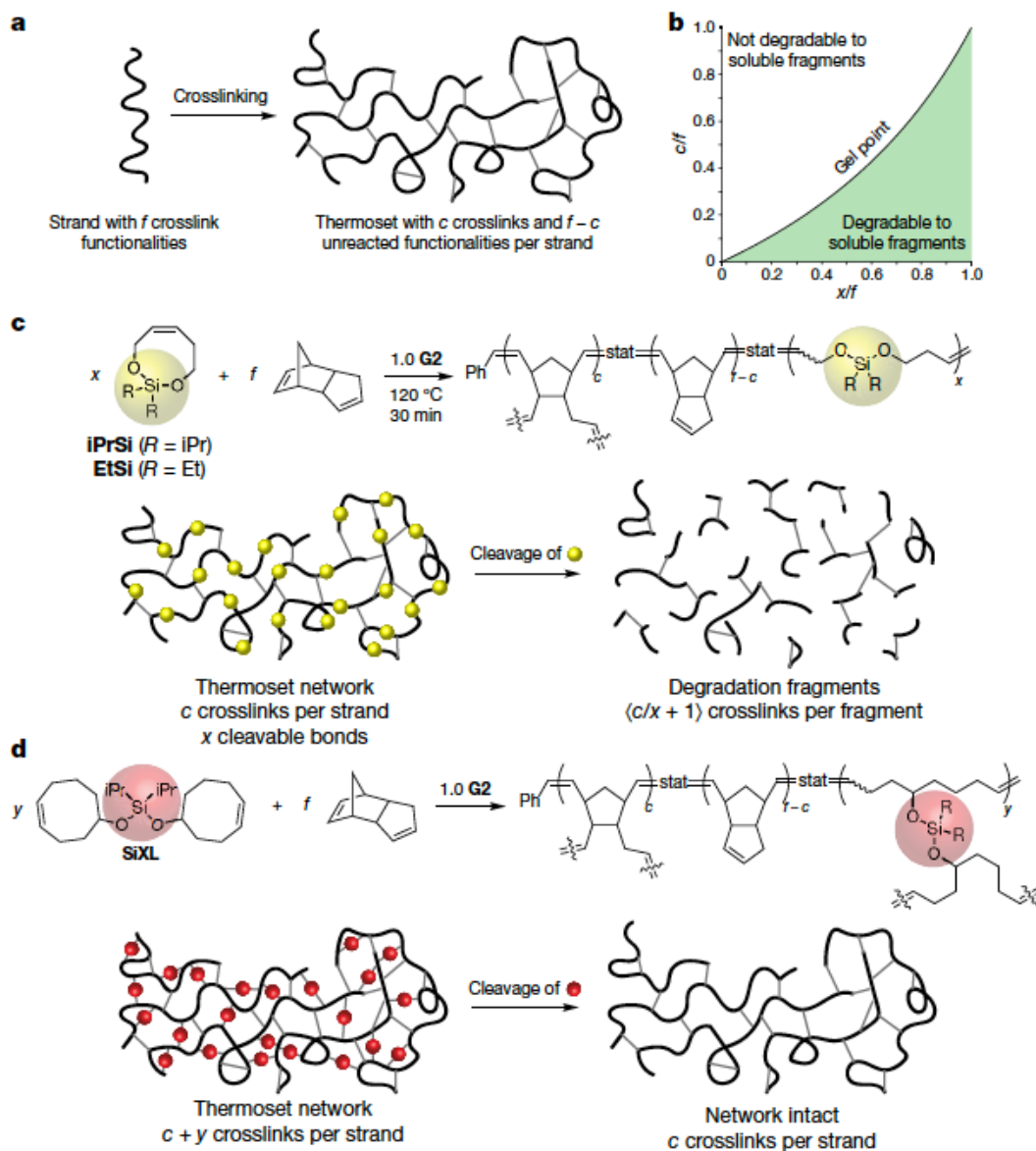


Fig. 6. a) Thermosets are often synthesized from the crosslinking of linear prepolymers with f crosslink functionalities. The resulting materials can have outstanding properties, but they often have unknown numbers of crosslinks (c) and they are typically non-degradable/non-reprocessable. b) Theoretical model describing the amount of cleavable monomer (x) relative

to non-cleavable crosslinks (c) that will result in degradation of materials composed of strands of functionality $f = 3,000$ into soluble products. c) The silyl ether-based monomer $iPrSi$ copolymerizes efficiently with norbornenes through ROMP, which introduces cleavable silyl ether sites within the polynorbornene strands of poly(DCPD). The introduction of x cleavable bonds within the strands of poly(DCPD) with c crosslinks provides degradation fragments with $\langle c/(x + 1) \rangle$ crosslinks per strand. d) The silyl ether crosslinker $SiXL$ copolymerizes with norbornenes through ROMP, but introduces cleavable silyl ether sites between polynorbornene strands (that is, in crosslinks). The introduction of y cleavable crosslinks produces poly(DCPD) with $c + y$ crosslinks. Thus, soluble products can only be generated when $y \gg c$, suggesting that complete material degradation at low cleavable crosslinker loadings will be difficult. Reproduced from Reference [51] with permission.

This model is still ideal and implies that the cleavable bonds are randomly distributed along strands, that equivalent functional groups have equal and independent reactivity and that there are no intramolecular reactions. Moreover, the presence of loops may further lower the number of degradable bonds needed to achieve degradation.

Roth and coworkers[52] recently revisited such study in the case of a radical polymerization in the presence of a divinyl monomer as a crosslinker. With this condition, $f \gg c$ and thus equation (1) could be summarized by:[52]

$$x > Dc - 1 \quad (2)$$

where D is the dispersity of the degraded fragment.

For a statistical insertion of weak bonds into a Flory-Schutz distribution, we could expect that ($D = 2$) and thus this relation is equals to $x > 2c - 1$. However, experimental SEC data obtained by this author on polyacrylate derivatives containing thioester units showed that dispersity of the fragment is more depicted by $D \approx 5$, implying that degradation would occur at $x > 4$ mol%.[52] This is in good agreement with the experimental data obtained in the same study and other data on the same system in the literature.

2.3 Importance of reactivity ratios on degradability

To obtain a homogeneous degradation of the chains and thus avoid the production of long fragments stable in the environment, a necessary condition is that the cleavable elements are homogeneously distributed along the chain. In the case of copolymerization between a vinyl monomer (non-degradable) and a cyclic monomer (introducing the cleavable function), the homogeneity of insertion of the cleavable moieties is governed by the reactivity ratios of the two monomers (Fig. 7a).

In parallel with experimental research, the use of computer simulations is increasingly improving the detailed characterization of polymers. Most often, to reduce the computational time, one approach is to model only the (statistical) moments of each distribution, although a significant amount of information is then lost. Recently, a stochastic approach based on (reaction) probabilities is more and more used. This technique is called matrix-based kinetic Monte Carlo (*kMC*) simulation and allows to model the precise location of monomer units in a polymer chain and to model a large number of polymer chains, representative of the material. [53, 54] A visualization of the chains in a stretched format can be achieved (Fig. 7b), with each line representing a polymer chain and each colored dot a monomer unit with a colored background. Such approach has been used to drive/characterize the preparation of sequence-

controlled polymers.[55-57] This methodology has also been used to finely tune the experimental conditions of large scale synthesis of polyacrylate derivatives when temperature and feed control are important parameter for properties and safety of the polymerization.[58, 59]

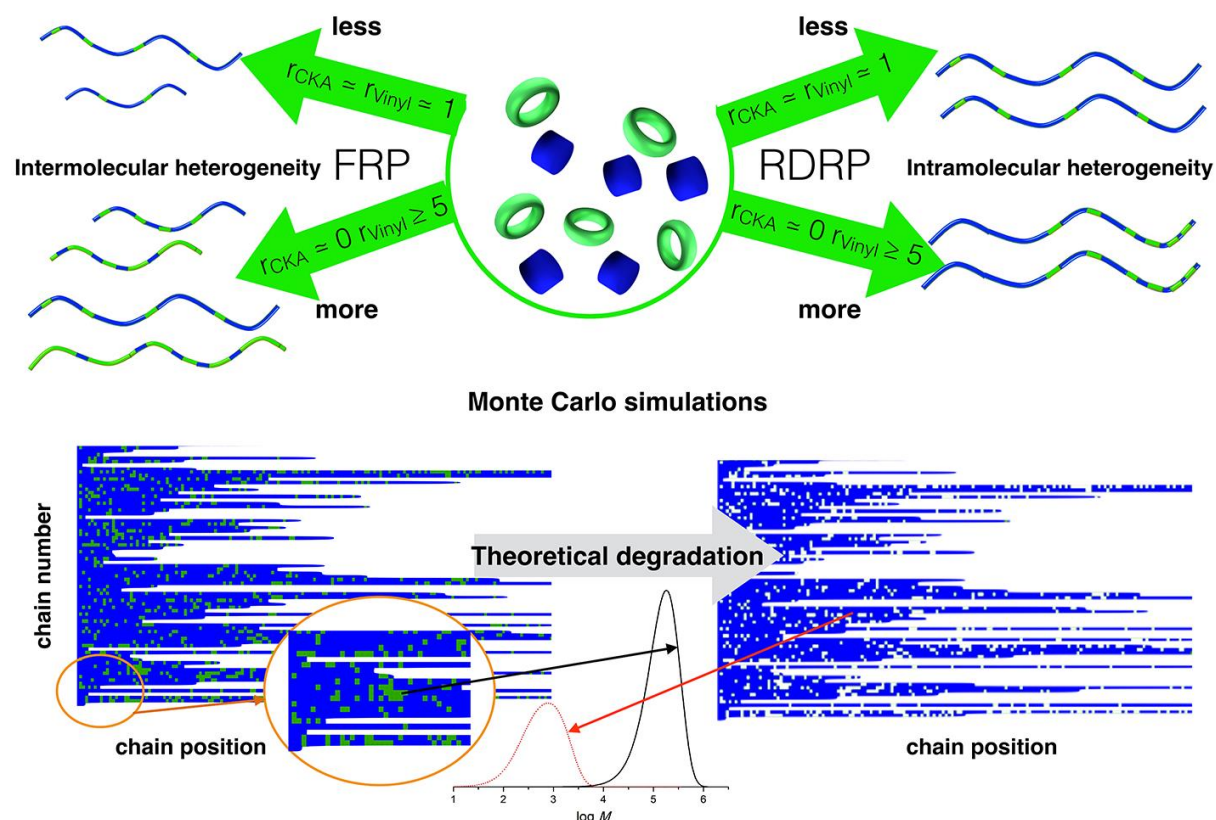


Fig. 7. a) Influence of the reactivity ratios r_{vinyl} and r_{CKA} on the copolymer structure, i.e. intra or intermolecular heterogeneity. blue: vinyl monomer – green CKA monomer 2-methylene-1,3-dioxepane (MDO) b) Simulation of the degradation of the individual chains, as obtained by kinetic Monte Carlo simulations and the corresponding computed SEC traces for both pristine and degraded chains. Reproduced from Reference [60] with permission.

Theoretical studies based *k*MC simulations have thus studied the relationship between the molecular composition of the chains and their degradation products, chain by chain. Indeed, with the precise localization of the different monomers, it is possible to theoretically degrade the polymer chains and thus study the distribution of molar masses before and after degradation (Figure 7b). The first study was then performed by D’Hooge and Lefay[60] that studied the impact of various reactivity ratios that modeled the CKA/Vinyl monomer pairs on the ester insertion profile into the polymer backbone. Cases with similar (MDO and Vinyl ether) and highly different (MDO and styrene) reactivity ratios were modeled using both free radical polymerization and reversible deactivation radical polymerization (RDRP). Indeed, the level of heterogeneity is different since intermolecular heterogeneity is expected with conversion in case of free radical polymerization whereas intramolecular heterogeneity is expected due to the gradient/tapered nature of the living polymer chain. For this study, the same cumulative copolymer composition in vinyl monomer units $F_{\text{vinyl}} = 0.8$ was targeted. When similar reactivity ratios were modeled, only one experimental condition was used but for highly different reactivity ratios, various experimental conditions could be modelled that will target different monomer conversions and thus will produce moderate or high compositional drift (Fig. 8). The *k*MC simulations first showed that in all cases the radical technique of polymerization does not influence the material properties after degradation since similar degradation profiles were obtained. The main parameters are the reactivity ratios and the compositional drift that strongly impact the degradation profile.[60] For example, Fig. 8c compared the degraded oligomers coming from the RDRP of a S/MDO system with a strong composition drift (63 % conv. from an initial feed ratio $[S]_0:[MDO]_0 = 50:50$) with the RDRP of a VE/MDO (55 % conv. from an initial feed ratio $[VE]_0:[MDO]_0 = 75:25$). The weight average degree of polymerization of the two pristine copolymers were between 111 and 103 and the ones of the degraded oligomers were strongly different (DP_w of 124 and 7 respectively).

The strength of the compositional drift also influenced the dispersity and length of the degraded oligomers. Figure 8c compared the degradation profile of two S/MDO polymerization where the initial feed ratios were modified to obtain the desired $F_{\text{vinyl}} = 0.8$. In the case of an initial feed ratio of $[S]_0:[MDO]_0 = 50:50$, 63% of conversion is necessary to reach $F_{\text{vinyl}} = 0.8$, whereas with an initial feed ratio of $[S]_0:[MDO]_0 = 25:75$, $F_{\text{vinyl}} = 0.8$ is reached at 26 % of conversion (Fig. 8a). The lower compositional drift furnished the lower DP_w from after degradation (124 to 42, Fig. 8c).[60]

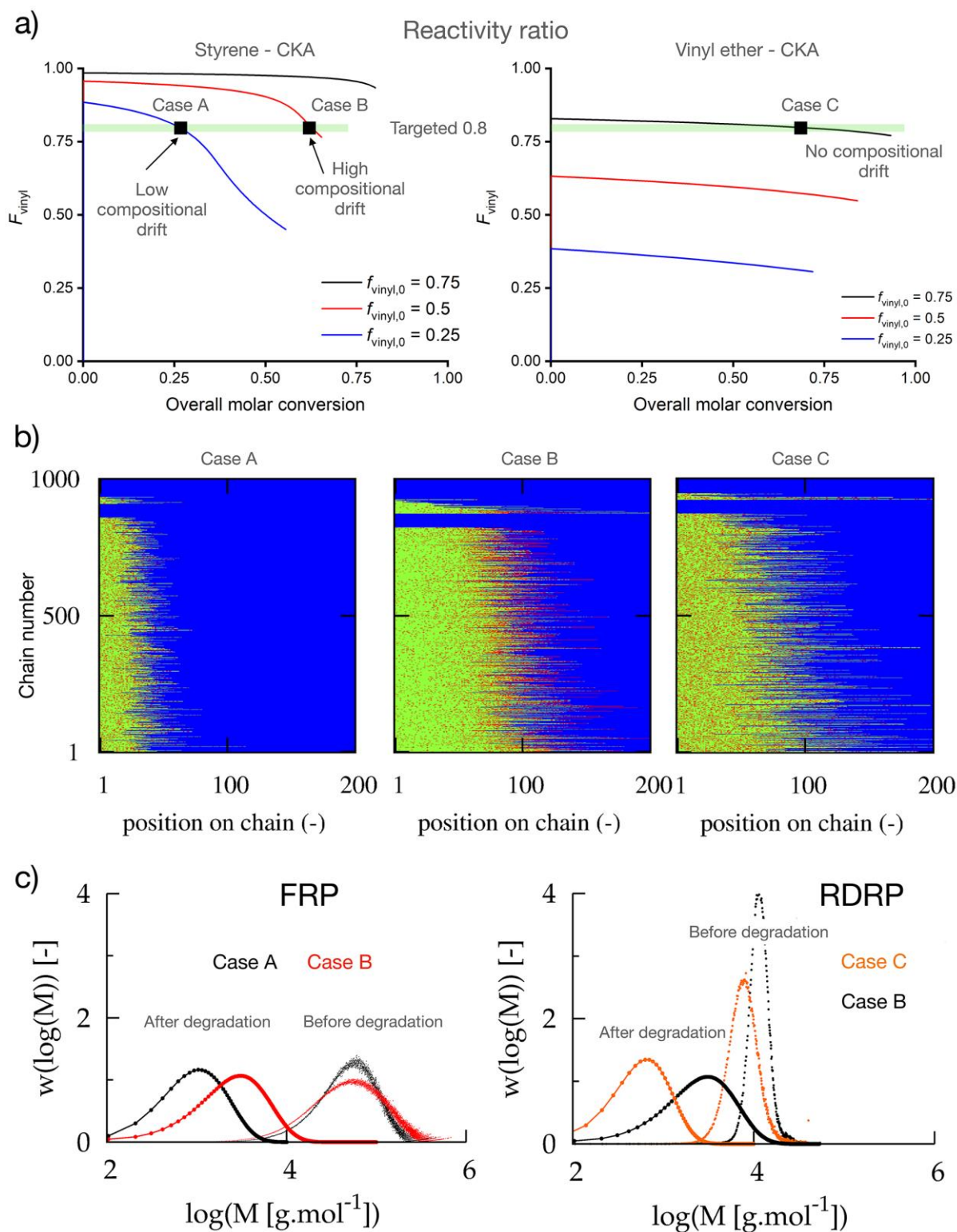


Fig. 8. a) Evolution of the cumulative (average) mole fraction of vinyl units in the polymer F_{vinyl} as a function of the overall molar conversion at different initial feed ratio $f_{\text{vinyl},0}$ for Styrene – CKA pair and Vinyl ether derivatives – CKA pair. b) Visualization of individual chains (red CKA monomer unit – green vinyl monomer unit - blue: absence of monomer) before hydrolysis

at $F_{\text{vinyl}} = 0.8$. c) SEC trace before and after hydrolysis of copolymers according to various parameters. Adapted from Reference [60] with permission.

Following this study, D'Hooge and coworkers[61] investigated in more details the copolymerization of MMA and MDO to illustrate how *kMC* could be useful to develop circular economy. In this study, the authors focused first on the compositional drift that occurs during such system. This was highlighted by the determination of the instantaneous copolymer composition ($F_{\text{MMA,inst}}$: left axis; $F_{\text{MDO,inst}}$: right axis, Fig. 9) and also by the *kMC* representation of copolymer chains that was plotted chronologically during the *kMC* simulation of the radical copolymerization. In the first moment of the polymerization, polymer chains with long PMMA sequences were obtained, thus the length of monomer sequence inverted to polymer chains without any PMMA. The authors thus recommend to avoid reaching high conversion (80 %) to stay in a regime where PMMA with weak bond is still obtained.[61]

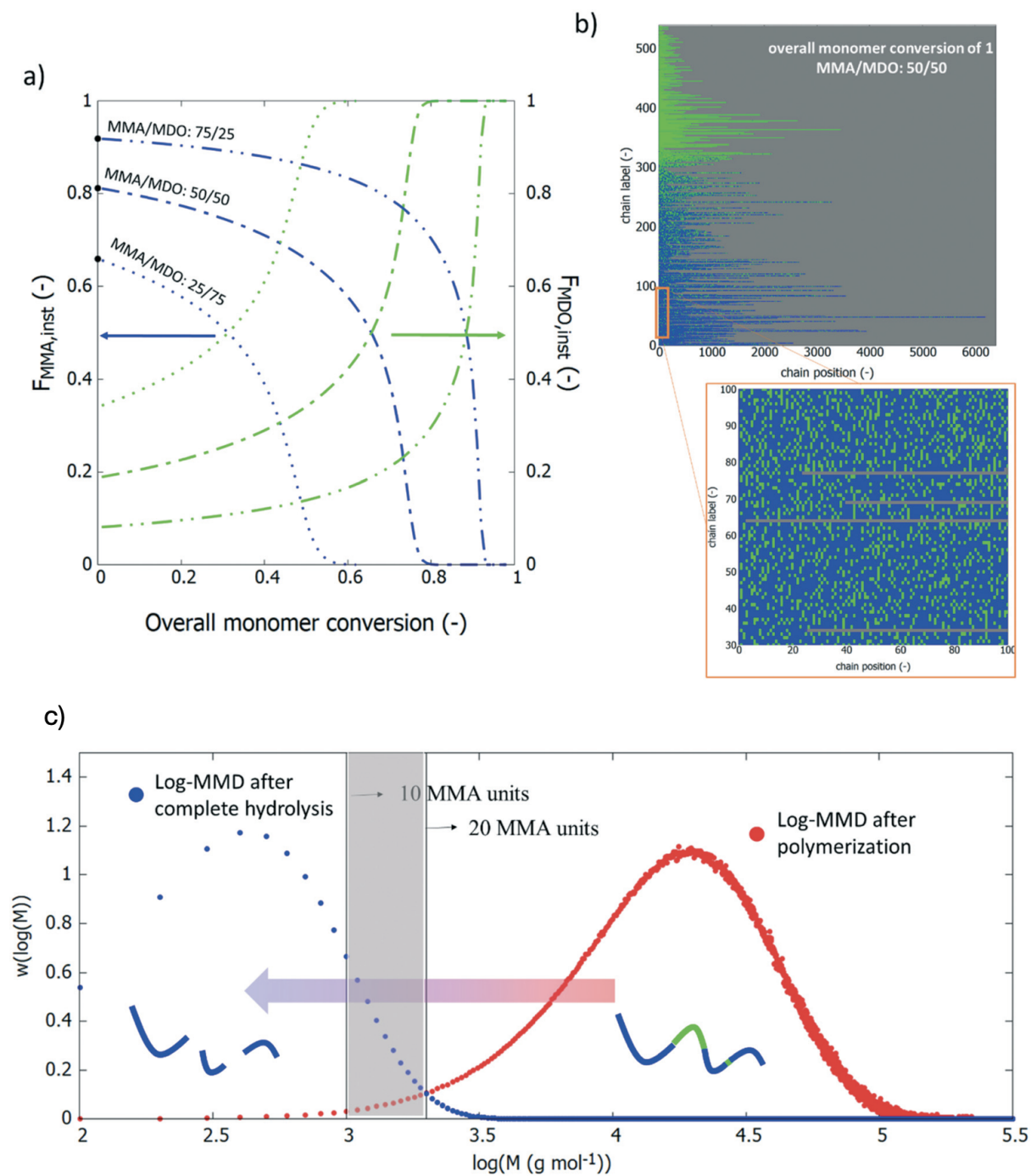


Fig. 9. (a) Simulated instantaneous (average/overall) copolymer compositions (F values) as a function of overall monomer conversion for batch radical copolymerization of MMA and MDO at 343 K; green lines (right axis): $F_{\text{MDO,inst}}$; blue lines (left axis): $F_{\text{MMA,inst}}$. Initial feed fractions ($f_{\text{MMA},0}/f_{\text{MDO},0}$) of 0.75/0.25; 0.50/0.50; 0.25/0.75; (b) explicit visualization of monomer sequences for a selection of copolymer chains at the end for $f_{\text{MMA},0} = 0.50 = f_{\text{MDO}}$ with

blue/green being a MMA/MDO unit; 2 mol% AIBN initially; black spheres in (a) highlight terminal Mayo–Lewis values (eqn (1)); in (b), the chains depicted at the bottom are formed at lower overall monomer conversion and those at the top at higher overall monomer conversion due to a regulated sampling of a representative number of chains out of a total chain population of 10^7 chains. c) Red line: simulated log-molar mass distribution (log-MMD) for poly(MMA–MDO); blue line: corresponding long-MMD after complete hydrolysis; the black demarcation lines indicate the molar masses of chains with 10 and 20 MMA units. Adapted from Reference [61] with permission.

The same authors thus used a similar methodology than previously to present the molar mass distribution of the degraded oligomers. They also added a grey zone that corresponds to their own limit of chain-length (10-20 MMA units) that will be better not to exceed in order to have a possibility to be biodegradable (Fig. 9).

Lastly, Van Herk *et al.*[62] compared the *k*MC simulation approach to determine the length of the oligomers after degradation with a more easily accessible analytical solution (noted AS in Fig. 10) that allows to determine the sequence length distribution. They established the following equations to give the average sequence length distribution:

$$x_i = p_{11}^{i-1} (1 - p_{11}) \quad (3)$$

with p the probability of a specific chain end radical reacting with a specific monomer. p_{11} could be expressed using reactivity ratio and feed ratio following the equation (4).

$$p_{11} = \frac{f_1}{(f_1 + (\frac{f_2}{r_1}))} \quad (4)$$

By integration it is also possible to obtain the average sequence length:

$$\bar{i}_n = \sum_{i=1}^{\infty} x_i i = \frac{1}{1 - p_{11}} = r_1 \frac{M_1}{M_2} + 1 \quad (5)$$

They showed[62] that in case of small oligomers such approach is a straightforward approach to obtain the length of the oligomers. The analytical solution does not consider the impact of termination that occurs in the polymerization. To take into account the termination event during a sequence, the authors introduced a correction, the probability that the chain propagates. With this additional term they showed that both the *k*MC simulations and the analytical solutions were in good agreement whatever the comonomer pair with moderate and high difference in reactivity ratios and also whatever the composition of the initial monomer feed (Fig. 10a).

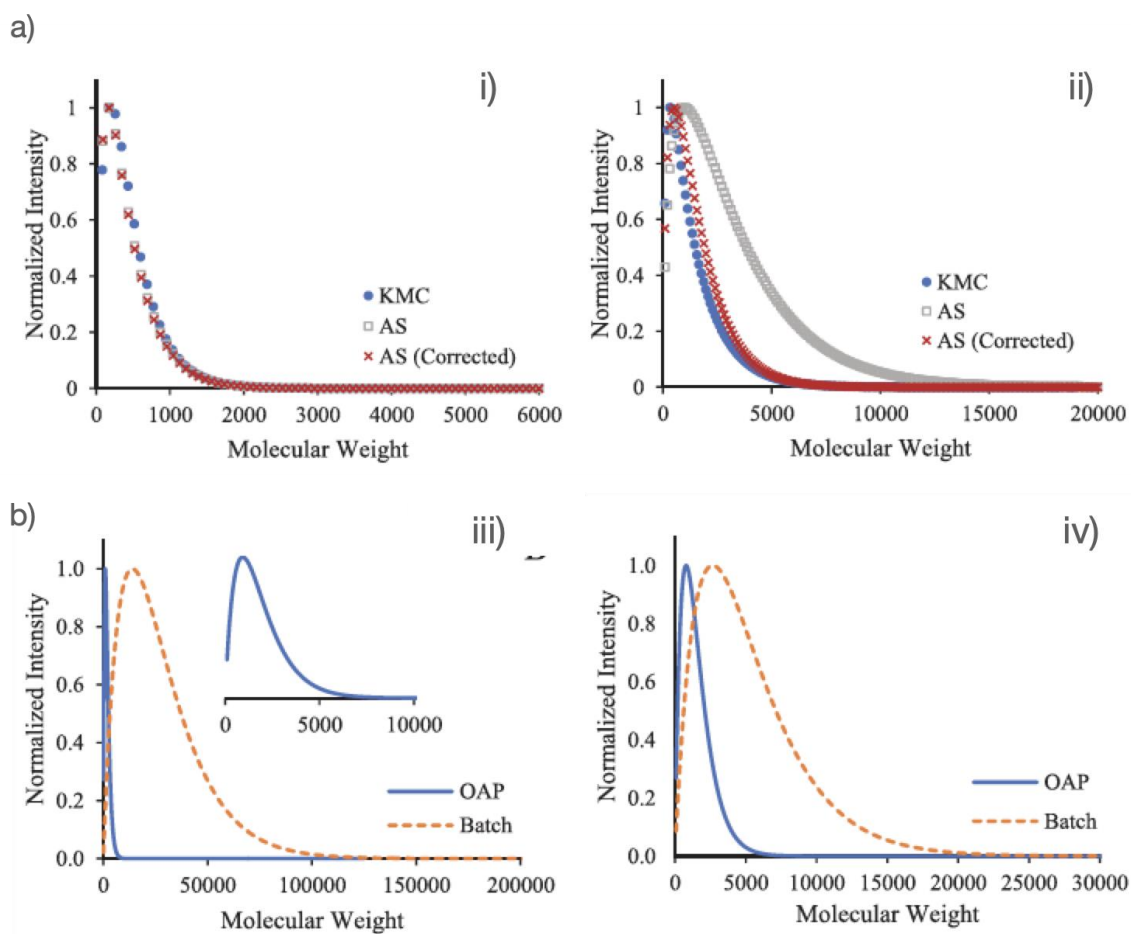


Fig. 10. a) Sequence distributions of *k*MC (\circ) versus analytical solution (AS) (corrected) (\times) and AS without correction for termination (\square), for MA–MDO (i) and S–MDO (ii) at equimolar ratio and at conversions of 72% and 55.5%, respectively. b) Comparison of oligomer length for S–MDO, 9:1 mol (i) and MA–MDO, 9:1 mol (ii) synthesized with batch (—) versus optimal addition profile (OAP) (—) process. Adapted from Reference [62] with permission.

In the same study, they also used this approach to compare batch and semi-batch copolymerization. Indeed, in the case of comonomer pairs with moderate to high difference in reactivity ratios, feeding one or two monomers during the copolymerization process allow to compensate the various rate of monomer consumption and thus keep the monomer concentration at a constant value with conversion, leading to homogeneous copolymers. In a

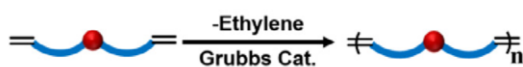
previous study,[63] a semi-batch addition profile was already determined, and the experimental characterization showed better homogeneity of both the copolymer and the degradation product. The theoretical impact of the two processes (batch and semi-batch) was represented on Fig. 10b and are coherent with the experimental data, confirming both the interest of the semi-batch process but also in the theoretical design of copolymers via numerical simulations.[62]

3. The various chemistries & monomer structures

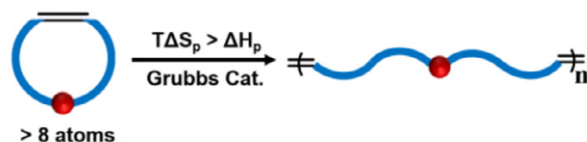
3.1 Ring-Opening and Acyclic Diene Metathesis Polymerization

Polyalkenamers and in particular polypentenamers are a class of polymers whose synthesis and applications are in rapid expansion with the development of the metathesis reaction to the polymerization field.[64, 65] The polymerization is thus based on the formation of a metallocyclobutane intermediate, and construction of a linear double bond-containing chain.[66] Among the various polymerization mechanism, acyclic diene metathesis polymerization (ADMET), entropy-driven ring-opening metathesis polymerization (entropy-driven ROMP), enthalpy-driven ring-opening metathesis polymerization (enthalpy-driven ROMP) and cascade enyne metathesis polymerization (CEMP) were reported (Fig. 11). The development of efficient, highly stable and commercially available catalysts has allowed the preparation of well-defined and functional polyalkenamers that make this technique of polymerization highly popular.[66-68] One of the limitation is related to the degradability of the materials prepared via this technique and thus many new monomers were designed to introduce weak bonds onto the polymer chains. This topics has been recently reviewed by Gianneschi and coworkers (Figure 11)[69] and Hadjichristidis and coworkers.[70]

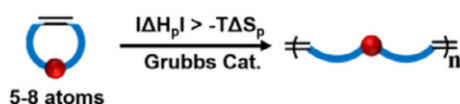
(i) Acyclic Diene Metathesis Polymerization



(ii) Entropy-Driven Ring-Opening Metathesis Polymerization



(iii) Enthalpy-Driven Ring-Opening Metathesis Polymerization



(iv) Cascade Enyne Metathesis Polymerization

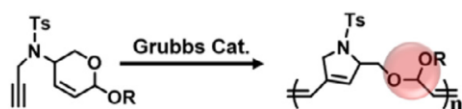


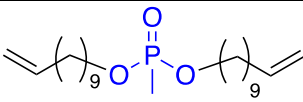
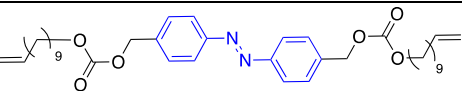
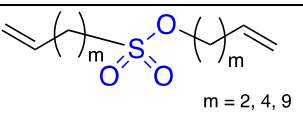
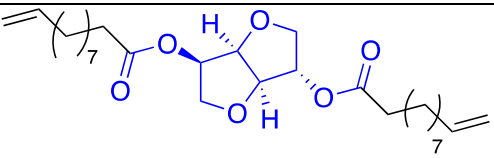
Fig. 11. Synthetic approaches to degradable polymers via olefin metathesis polymerization. (i) acyclic diene metathesis polymerization (ADMET); (ii) entropy-driven ring-opening metathesis polymerization (entropy-driven ROMP); (iii) strain-induced or enthalpy-driven ring-opening metathesis polymerization (enthalpy-driven ROMP); and (iv) cascade enyne metathesis polymerization (CEMP). Reproduced from Reference [69] with permission.

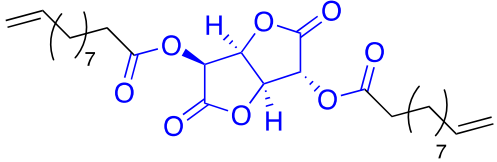
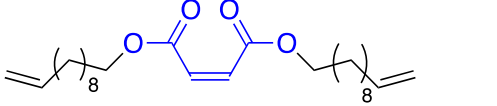
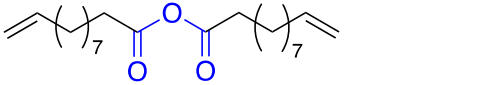
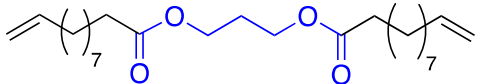
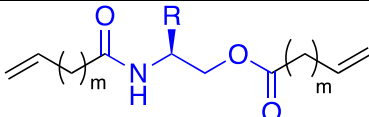
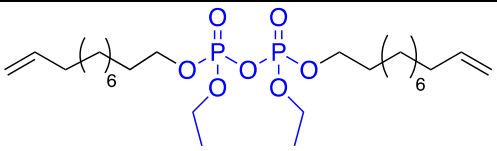
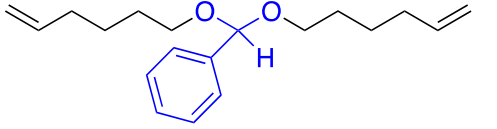
3.1.1 ADMET

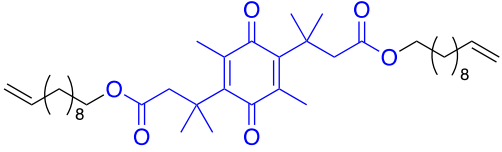
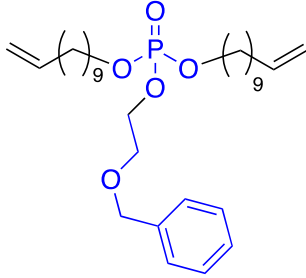
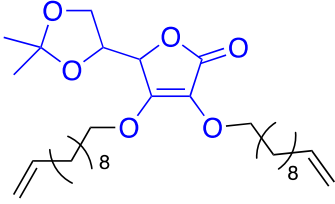
Acyclic diene metathesis polymerization (ADMET) is a polymerization of α,ω - dienes that produces ethylene as a byproduct. The removal of ethylene under vacuum is the driving force of the polymerization. Because of the step-growth nature of ADMET, the polymerization

reactions require highly pure monomer and quantitative conversion to reach high molecular weight. Early ADMET polymerization research focused primarily on the polymerization of all aliphatic symmetric, α,ω - dienes, resulting in alkylene copolymers with a precise control of the location of the double bond. The scope of ADMET polymerization has recently been expanded to new α,ω -diene monomers containing heteroatoms that can undergo ADMET to form a diverse library of degradable polymers. The obtained copolymers are thus polyethylene mimics with a functional group precisely localized between the double bonds that could be later hydrogenated. The main structures are reported in Table 2.

Table 2. ADMET Monomers

Monomer	Ref.
 <p>ADMET1</p>	[71]
 <p>ADMET2</p>	[72]
 <p>ADMET3</p>	[73]
 <p>ADMET4</p>	[74]

 <p>ADMET5</p>	[74]
 <p>ADMET6</p>	[75]
 <p>ADMET7</p>	[76]
 <p>ADMET8</p>	[76]
 <p> $m = 2 \text{ R} = \text{CH}(\text{CH}_3)_2$ $m = 2 \text{ R} = \text{CH}_2\text{CH}(\text{CH}_3)_2$ $m = 3 \text{ R} = \text{CH}_2\text{CH}(\text{CH}_3)_2$ $m = 8 \text{ R} = \text{CH}(\text{CH}_3)_2$ $m = 8 \text{ R} = \text{CH}_2\text{CH}(\text{CH}_3)_2$ </p> <p>ADMET9</p>	[77]
 <p>ADMET10</p>	[78]
 <p>ADMET11</p>	[79]

 <p>ADMET12</p>	[80]
 <p>ADMET13</p>	[81]
 <p>ADMET14</p>	[82]

The structures reported in Table 2 presented various chemical functions that are esters, anhydride, amide/peptide, acetal, sulfonate ester, phosphonate, pyrophosphate, and azobenzene. The main difference between these polymers is the stimuli that could be used to trigger the decomposition. For the ester series, when **ADMET4** and **ADMET5** were used, the lower hydrolytic stability (i.e. higher hydrophilicity) of the glucarodilactone group compared to isosorbide led to basic degradation (0.25 M of NaOH in water) when this monomer unit was inserted whereas the isosorbide ester was not degraded.[74] The use of maleate group as a source of ester functionality was realized by Li and coworkers. [75] They use the activated double bond to post-functionalize the polymer via thiol-Michael addition. The introduction of amino groups pendant to the polymer backbone enhances the thermal decomposition of the polymer in the solid state via an intramolecular cyclisation that led to lactam derivatives. When

the nucleophilicity of the amino group is decreased or if the mobility of the amine is lowered, the polymer presented a higher stability (Fig. 12). Via the protonation of the amine, the authors modulated the reactivity of the amine and they were able to delay the polymer degradation up to 80-100 °C via the removal of TFA. Besides basic degradation, Barner-Kowollik and coworkers[80] introduced a trimethyl-locked benzoquinone (TMBQ) group into an ADMET monomer to impart redox-responsive ability of the obtained materials. The obtained polymer is easily degraded in presence of $\text{Na}_2\text{S}_2\text{O}_4$ in THF/ H_2O solution and it was possible to recover the TMBQ unit, that enables the recycling of this chemical group.

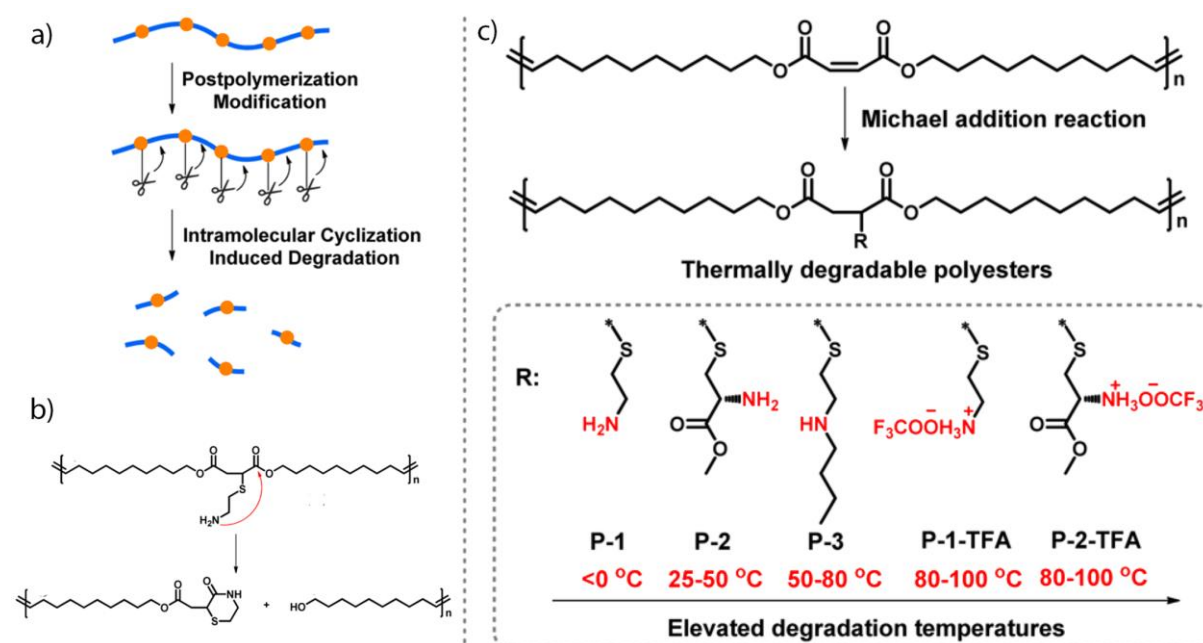


Fig. 12. a) Preparation of thermally degradable polyesters via postpolymerization modification using Michael addition. b) Mechanism of the intramolecular cyclisation reaction that degrade the polymer. c) influence of the amine group on the degradation temperature. Reproduced from Reference [75] with permission.

Bioactive moieties were also inserted into polyolefins via ADMET. Landesfer et al.[82] reported the preparation of a polyethylene mimics containing vitamin C units by the polymerization of **ADMET14**. The vitamin C act as a defect and is thus expelled from the crystal lattice. The antioxidant properties of vitamin C embedded in the polymer are preserved that make them a good candidate for biomedical applications. Moreover, treatment by NaOH led to complete decomposition even in the crystal state with the disappearance of the ascorbic acid ring signal.

More polar groups were also inserted into polyolefin backbone via ADMET polymerization. Wurm and coworkers[71] prepared for example a α,ω -diene presenting a phosphonate group and polymerize it by ADMET. The resulting polymer was hydrogenated to obtain a polyethylene mimic. Since the results of biodegradation were not satisfying (< 3% after 30 days), the same author prepared a second-generation monomer where a pyrophosphate was inserted instead of a phosphonate (**ADMET10**).[78] After ADMET and hydrogenation, polymers films were obtained. When films were submerged in water, the pyrophosphate groups displayed rapid hydrolysis despite their hydrophobicity and water insolubility, leading to polymer breakdown. Furthermore, bacteria subsequently biodegraded the hydrolyzed fragments, leading to an efficient biodegradation.[78]

To obtain a good biodegradation profile, Barner-Kowollik and coworkers[72] have introduced an azobenzene group (**ADMET2**) as a core of a α,ω -diene monomer. Such azo-benzene motif is known to be degraded by specific enzymes,[83] among which are azoreductases and glycosidases that are present and active both in the gut microflora and mammalian tissues.[84] Nevertheless, a polymer with this group onto the backbone does not show a quick degradation profile in the presence of enzyme azoreductase (also known as DT-diaphorase) in the presence of the coenzyme NADPH because of the low accessibility of the azobenzene group. To solve

this problem, the authors thus prepared an ABA amphiphilic copolymer with PEG hydrophilic group by using a chain transfer agent. With this modification, efficient enzymatic degradation was monitored.

Lastly, Wurm and coworkers[81] inserted a phosphoester with an ethoxy hydroxyl side chain into polyethylene-mimics via ADMET followed by hydrogenation (**ADMET13**). This side chain mimicked the 2'-OH group of ribose and was capable of intramolecular transesterification with the main chain in a similar manner to RNA hydrolysis. In comparison to structurally comparable polyphosphoesters without pendant ethoxy hydroxyl groups, polymer films submerged in aqueous solutions at various pH levels shown a faster degradation. While the polymer was stable at a physiological pH of 7.4, polymer degradation occurred in artificial seawater at pH=8. NMR spectroscopy proved selective hydrolysis via the intramolecular transesterification and was also supported by DFT calculations (Fig. 13). The "RNA-inspired" degradation of polymers could significantly contribute to speeding up the hydrolysis of plastics and polymers in natural conditions, such as seawater.

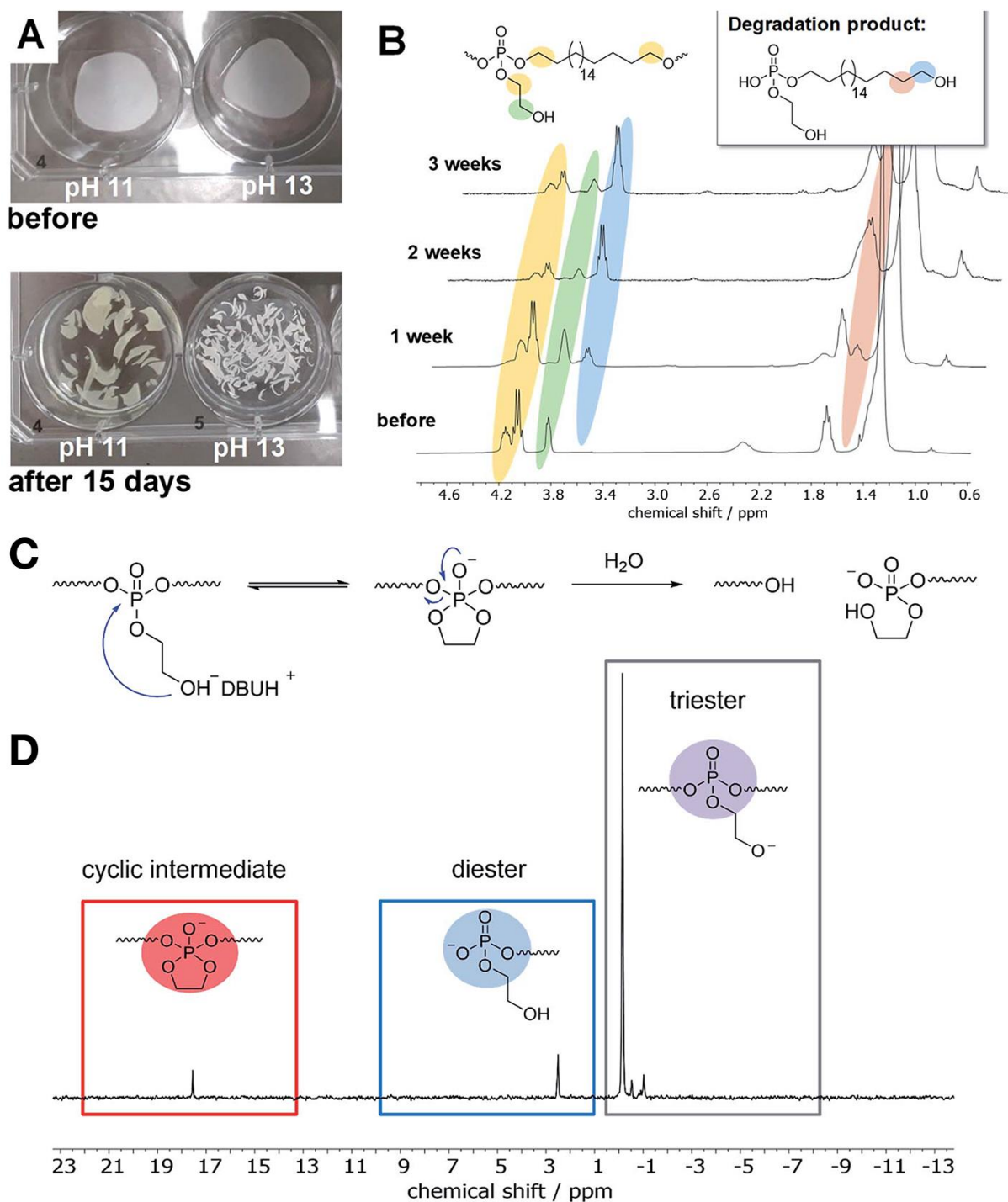




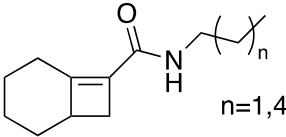
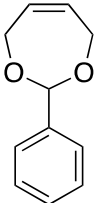

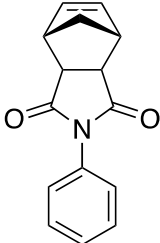
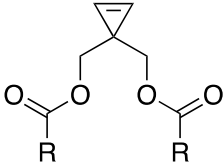
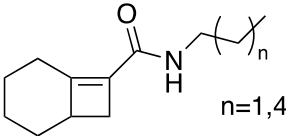
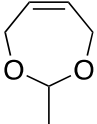
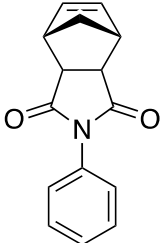
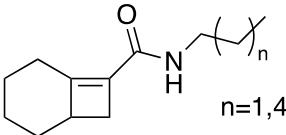
Fig. 13. a) (A) Films of poly-1H before and after 15 days immersing in different buffer solutions at 37 C. Diameter of films is ca. 2 cm. (B) ^1H NMR (300 MHz, CDCl_3) overlay of poly-1H after degradation at pH 11.1. (C) Indication of the major degradation pathway by the intramolecular attack of the pendant OH-groups on the phosphate groups with subsequent

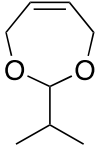
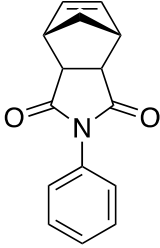
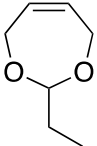
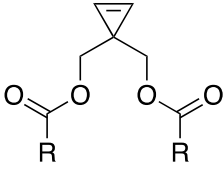
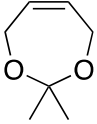
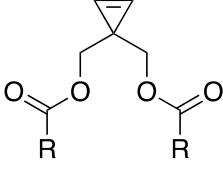
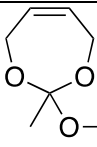
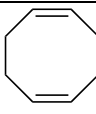
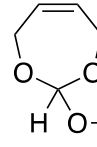
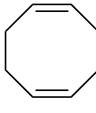
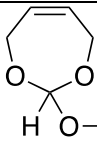
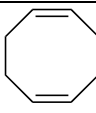
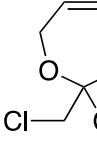
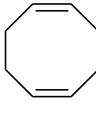
main-chain cleavage. (D) ^{31}P NMR (121 MHz, CDCl_3) spectrum of poly-1H after addition of DBU showing the cyclic intermediate due to the RNA-inspired degradation pathway. Reproduced from Reference [81] with permission.



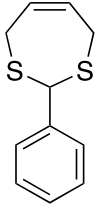
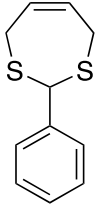
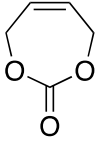
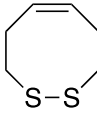
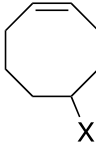
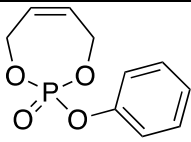
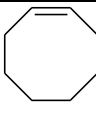
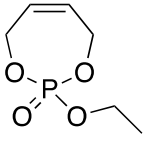
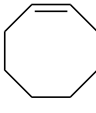
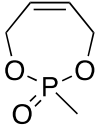
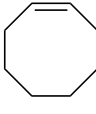
3.1.2 Ring-Opening Metathesis Polymerization (ROMP)

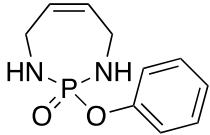
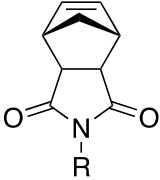
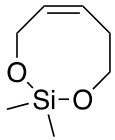
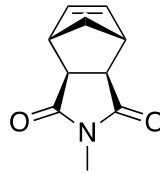
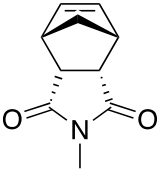
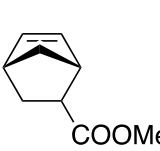
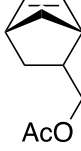
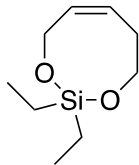
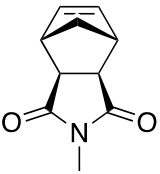
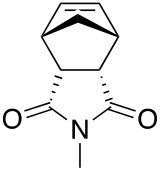
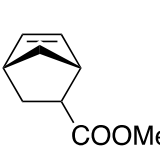
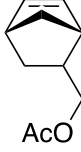
Contrary to ADMET that is a step-growth polymerization, Ring-Opening Metathesis Polymerization is a chain-growth polymerization process and this feature allow to obtain higher molecular weight and less dispersed polymers. Two categories of ROMP can be distinguished based on the type of thermodynamic driving force: (i) entropy-driven ROMP and (ii) enthalpy-driven ROMP. Entropy driven ROMP used macrocycles that are already constituted of heteroatoms and will not be covered by this review. On the contrary, enthalpy-driven ROMP is based on the simultaneous release of strain and ring opening of low-molecular-mass cyclic alkene monomers. ROMP has gained huge attention since many (functional) cyclic monomers are available and the chain-growth mechanism of ROMP is compatible with a living-like character that nevertheless requires specific catalysts and optimization of the reaction conditions. Due to its high strain, norbornenes are the most common monomers used for ROMP even if cyclopropane, cyclobutene, cis-cyclooctene and cyclooctadiene are also used. Many different structures were then prepared to impart (bio)degradability into polymers prepared by ROMP and are gathered in Table 3.

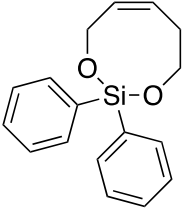
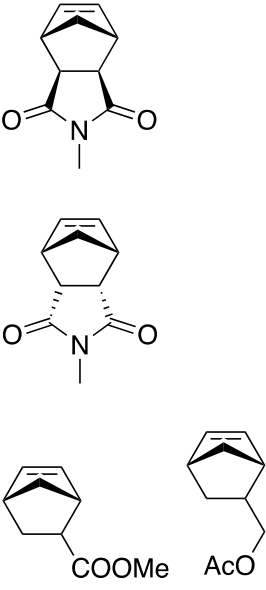
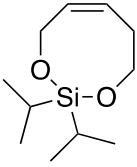
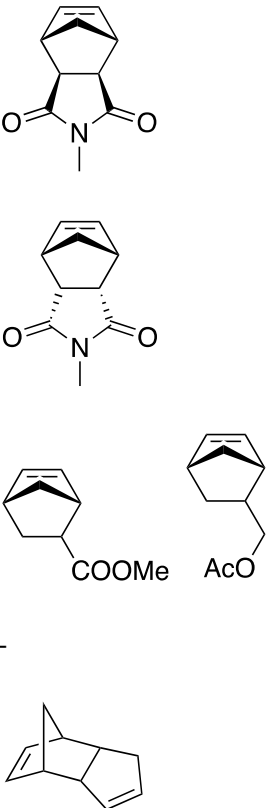
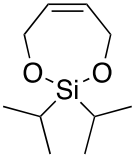
Degradable ROMP monomer	Main chain ROMP monomer if used	Reference

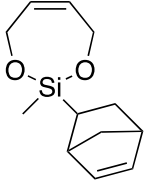
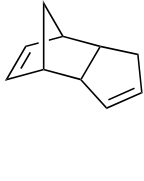
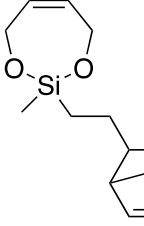
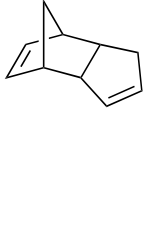
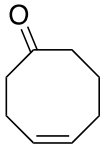
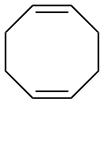
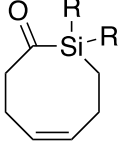
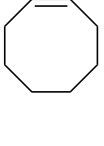
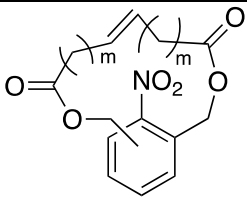
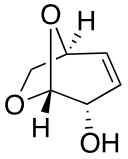
 <p>ROMP1</p>	 	<p>[85]</p> <p>[86]</p>
 <p>ROMP2</p>	   	<p>[85]</p> <p>[87],[88]</p> <p>[89]</p> <p>[86]</p>
 <p>ROMP3</p>	 	<p>[88]</p> <p>[86]</p>

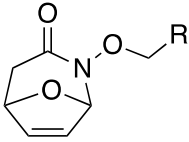
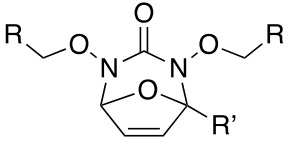
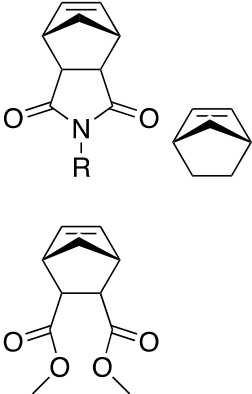

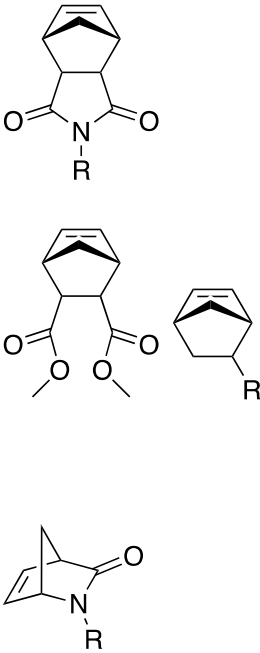
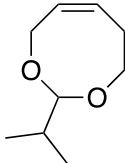
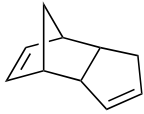
 ROMP4		[87],[88]
 ROMP5		[89]
 ROMP6		[89]
 ROMP7		[90]
 ROMP8		[90]
 ROMP9		[90]
 ROMP10		[90]

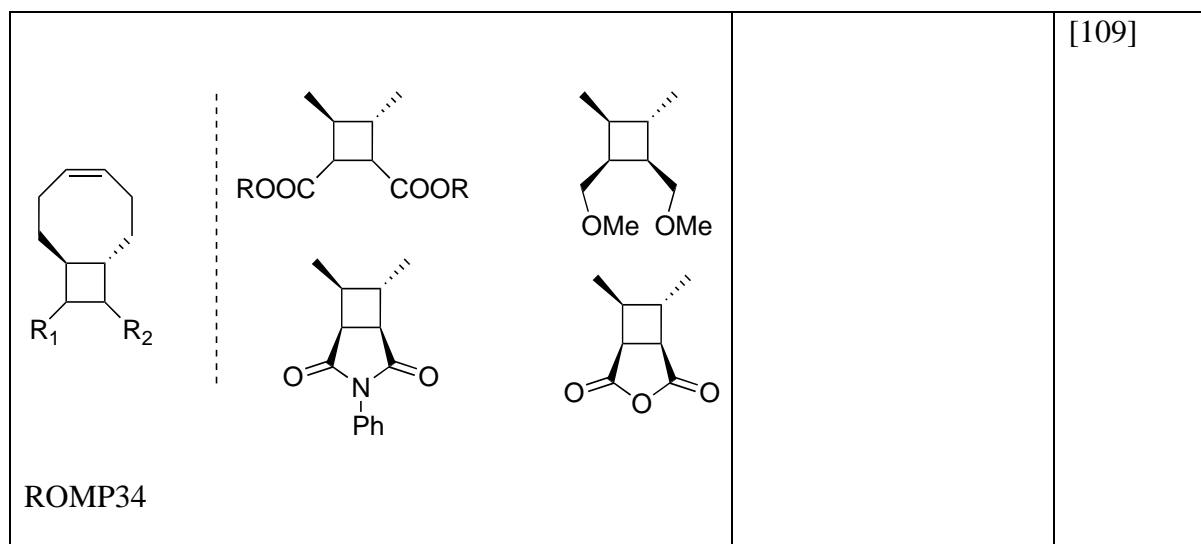
 <p>ROMP11</p>		[91]
 <p>ROMP12</p>		[91]
 <p>ROMP13</p>	-	[92]
 <p>ROMP14</p>		[93]
 <p>ROMP15</p>		[93], [94]
 <p>ROMP16</p>		[94]
 <p>ROMP17</p>		[71]

 <p>ROMP18</p>		[95]
 <p>ROMP19</p>	   	[96]
 <p>ROMP20</p>	   	[96]

 <p>ROMP21</p>		[96]
 <p>ROMP22</p>		[96] [97] [51]
 <p>ROMP23</p>	-	[97]

 <p>ROMP24</p>		[98]
 <p>ROMP25</p>		[98]
 <p>ROMP26</p>		
 <p>ROMP27</p>		[99]
 <p>ROMP28</p>	-	[100]
 <p>ROMP29</p>	-	[101]

 <p>ROMP30</p>	-	[102, 103]
 <p>ROMP31</p>		[104]
 <p>ROMP32</p>	<p>-</p> 	[105] [106] [107]
 <p>ROMP33</p>		[108]



Cis-4,7-dihydro-1,3-dioxepin derivatives were the first structures reported to introduce a weak/cleavable bond into polymers prepared by ROMP. Various derivatives were prepared depending on the acetal moiety. While homopolymerization of **ROMP2** was unsuccessful, the polymerization of **ROMP1** produced a polyacetal with a broad molecular weight distribution using first-generation Grubbs catalyst G1.[85] The same authors[85] then successfully performed the copolymerization of **ROMP1** and **ROMP2** with cyclooctadiene (COD). Despite the creation of high molecular weight copolymers, a significant amount **ROMP1** and **ROMP2** was unreacted, resulting in a low acetal moieties incorporation between 4% and 30%, depending on the feed ratio. The acetal groups were then cleaved in acidic condition to led to 1,4-hydroxytelechelic polybutadiene. The benzylidene acetal was more easily cleaved than the methylene acetal that require a two steps process, *i.e.* a pretreatment with trifluoroacetic anhydride and acetic acid followed by the addition of NaOMe in methanol.[85] Grubbs et Kilbinger[87, 88] extended this study to the preparation of sacrificial block to insert hydroxy functionality and exemplify such approach with the copolymerization of dioxepin derivatives (**ROMP2**, **ROMP3**, **ROMP4**) with a polymer of *exo-N*-Phenyl-2,3-norbornene dicarboximide that is known to have a living character. The same group also shifted from dioxepins to dithiepinines (**ROMP11-ROMP12**) bearing thioacetal functions to prepare thiol-functionalized

polynorbornene via the sacrificial block method.[91] In that method only **ROMP12** gave satisfactory results.[91]

Wurm *et al.*[90] latter extended the use of dioxepins to the orthoester derivatives by preparing monomers **ROMP7** to **ROMP10**. Polyorthoesters were prepared *via* their copolymerization with 1,5-cyclooctadiene (COD) followed by thorough hydrogenation. As already observed previously with acetal-based monomers, the incorporated ratio of orthoester is lower than in the feed, confirming the higher reactivity of COD compared to **ROMP7-ROMP10**. It is then possible to regulate the amount of methylene groups between two orthoester units by varying the comonomer ratio and the rate of hydrolysis by the nature of different orthoester substituents. The rate of degradation (in d-THF with TFA in D₂O) was governed by the nature of the orthoester group. The polymer bearing the highest electron-deficient moiety (R = -CH₂Cl, $t_{1/2}$ = 111 h) was found to be more stable than the orthoformate (R = H, $t_{1/2}$ = 10 h), which was also more stable than electron-rich orthoacetates (R = Me, $t_{1/2}$ = 3 min).

The alternating copolymerization of dioxepins and 1,1-disubstituted cyclopropenes (CPEs) was recently reported by Xia and colleagues.[89] They previously showed that by a careful selection of the ring strain and steric hindrance of the pendant group, it is possible to design disubstituted cyclopropenes that selectively underwent single monomer addition in ROMP but exhibit an alternating ROMP (called AROMP) with low-strain cyclic olefins in a live manner.[110] Via the copolymerization with **ROMP2**, **ROMP5-ROMP6**, they produced polyacetals with limited dispersity and controlled molecular weights under ideal AROMP conditions. The alternating structure of the copolymers led to small molecules as degraded products. The kinetics of degradation (1 vol% TFA in THF) is governed by the structure of the acetal group with copolymer containing **ROMP6** being totally degraded in less than 1h whereas copolymer containing **ROMP5** required more than 9h to present partial

degradation.[89] In parallel, Sampson and coworkers[86] also developed alternating ROMP copolymer by copolymerizing **ROMP1**, **ROMP2** and **ROMP3** with bicyclo[4.2.0]oct-1(8)-ene-8-carboxamides. In aqueous TFA solution, degradation was obtained, exhibiting the same substituent-dependent hydrolysis kinetics as previously described.

Besides acetal functionality, other weak bonds were inserted into cycloalkene monomers. Buchard *et al.*[92] focused on carbonate functionality and prepared **ROMP13** from the biosourced erythritol. The interest of such monomer is its dual polymerization mode (either ROP of carbonate or ROMP of cyclooctene) that lead to two distinct polymers varying by the stereochemistry of the remaining C=C double bond. By ROMP, a soft amorphous polymer ($T_g = -22$ °C) is obtained with high trans-stereoregularity (95%) whereas by ROP, a hard semicrystalline polymer ($T_m = 115$ °C) is produced with a pure cis-stereoconfiguration of the olefin. Disulfide based polyolefins were also prepared by ROMP of **ROMP14** with others cyclooctene monomers.[93] Up to 30 mol% of disulfide were readily inserted that impart redox responsiveness to the copolymers. Degradations were performed in the presence of mild-reducing agent such as tri-*n*-butyl phosphine or 1-dodecanthiol. A radical photodegradation mechanism was also demonstrated that rely on the irradiation of the copolymer with 2,2-dimethoxy-2-phenylacetophenone. Other heteroatoms were also inserted into cis-cycloalkene monomers. Polyphosphoesters were first reported by Wurm *et coll.*[94] in 2013 via the preparation of **ROMP15-ROMP16**. The authors showed that the Grubbs third generation catalyst (GIII) produces polymers with M_n up to 5000 g.mol⁻¹, showing its limitation for the homopolymerization due to side-reactions. Moreover, copolymerization with cis-cyclooctene was successful, leading to M_n about 50 000 g.mol⁻¹, and the ratios of the monomers could be adjusted even if the control is moderate. Acidic hydrolysis of the copolymer resulted in a complete degradation, indicating that the phosphate monomers were randomly incorporated into the poly(cyclooctene) backbone and that the phosphate bonds along the backbone may

have degraded. At the same time, Emrick *et al.*[93] also developed the phosphoester **ROMP15** that was copolymerized with **ROMP13** to produce copolymer with orthogonally degradation behavior. Wurm[71] then extended such monomers to phosphonate (**ROMP17**) and recently Gianneschi and coworkers[95] to phosphoramidate (**ROMP18**). The latter authors found that the polymerization could achieve high conversion and high M_n only at 2 °C in the presence of GIII catalyst. This finding is consistent with the thermodynamic principle for enthalpy-driven ROMP of low strain cyclic monomers, such as cyclopentene, which states that lower reaction temperatures encourage the change of equilibrium toward polymerization and also limit side reaction such as backbiting. In acidic DMSO, the resultant polyphosphoramidate entirely decomposed in 240 hours into phosphoric acid and 1,4-diamino-2-butene. Also, the authors used a copolymerization technique to show that approximately 50% of **ROMP18** could be incorporated into polynorbornenes (Fig. 14), which caused either total or partial backbone degradation. Whatever the norbornene comonomer, **ROMP18** conversion was higher than in homopolymerization but its insertion into the copolymer backbone was a bit lower than the incorporation of the norbornene derivative. **ROMP18** was utilized to copolymerize norbornene with pendant oligoethylene glycol (NBOEG), and the resulting NBOEG-**ROMP18** copolymers were amphiphilic and successfully self-assembled into micellar degradable nanoparticles.

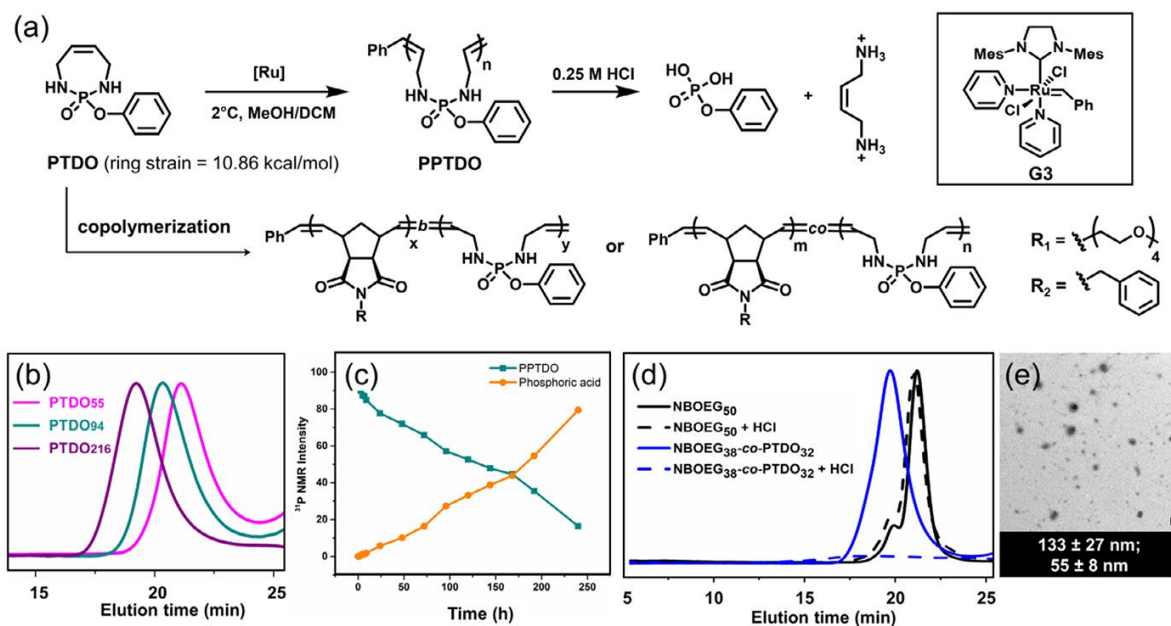


Fig. 14. Degradable polyphosphoramidate via low temperature ROMP. (a) Schematic of PTDO polymerization and degradation. (b) SEC traces of PPTDO of different degrees of polymerization (DP = 55, 94, 216). (c) Degradation of PPTDO and production of phosphoric acid monitored by ³¹P NMR. Condition: 0.25 M HCl in DMSO-*d*₆ at room temperature. (d) SEC traces of NBOEG homopolymer and NBOEG-PTDO random copolymer before and after acid treatment. (e) Transmission electron microscopy (TEM) image of micellar nanoparticles assembled from NBOEG-PTDO random copolymer. Scale bar: 100 nm. Reproduced from Ref. [69] with permission.

The last heteroatom that is inserted via ROMP into the polymer backbone is Silicon. Johnson et al.[96] thus developed silyl ether cyclic olefin **ROMP19-ROMP22** that differ by the alkyl moiety carried by the Si atom. These monomers are unlikely to homopolymerize since their strained energy is less than 8 kcal/mol, according to computer estimates. Nevertheless, these authors[96] demonstrated that when the molar ratio of norbornenes to cyclic silyl ether was 1:1, these cyclic silyl ether monomers were capable of efficiently copolymerizing with norbornenes to produce well-defined copolymers. The scope and limitations of these systems

were thoroughly investigated. The authors showed that the 8-membered cyclic silyl ether **ROMP22** had the best balance between statistical copolymerization efficiency and synthetic accessibility when compared to the 7- and 9-membered counterparts through a screening of monomers with varying ring sizes. The nature of the norbornene (Fig. 15) was also studied and they showed that the copolymerization efficiency is correlated with a low ROMP reactivity with NB4 being the best norbornene derivative. Reactivity ratios of 0.61 for NB4 and 0.72 for **ROMP22** was determined. In a solution of dioxane and water, the resultant silyl ether-norbornene copolymer hydrolyzed entirely into low molar mass species. Changing the substituents carried on the Si atom allowed for different degradation rates. With the use of norbornene-based macromonomers, degradable materials with a range of topologies, including linear, bottlebrush, and brush-arm star polymers (BASPs), were produced (Fig. 15).[96] **ROMP22** was also used as additive to prepare degradable thermoset via the copolymerization with dicyclopentadiene (see the network part).[51] Specific silyl ether cyclic olefin derivatives bearing a norbornene group in the Si atom were also prepared to improve the mechanical properties of these degradable thermosets (**ROMP24-ROMP25**).[98] Since the alkyl moieties carried on the Si atom of the silyl ether cyclic olefin derivatives is a key parameter for the degradation and hundreds of combinations could be prepared, Johnson et al.[111] recently used machine learning to find the best derivatives to obtain a degradable thermoset with predictable properties (see the network part). A thorough analysis of the ROMP of **ROMP22** and **ROMP23** highlight that their low strain impede their homopolymerization in common enthalpy-driven ROMP but homo **PROMP22** was obtained by entropy -driven ROMP, playing with concentration and temperature.[97]

Photosensitive groups were also inserted into cyclic olefins. The pioneering work was performed by Matson and coworkers that prepared **ROMP26** carried on a ketone functionality.

By copolymerizing **ROMP26** with COD as a soft middle segment and ROP of lactide (LA) as two hard segments via ROP, Matson and colleagues created a photodegradable thermoplastic elastomer. After being exposed to a weathering chamber (UVC fluorescence bulb) for 30 minutes, the triblock polymer containing 9 mol% ketone groups lost 23% of its modulus and completely lost its mechanical integrity after 2h of irradiation.

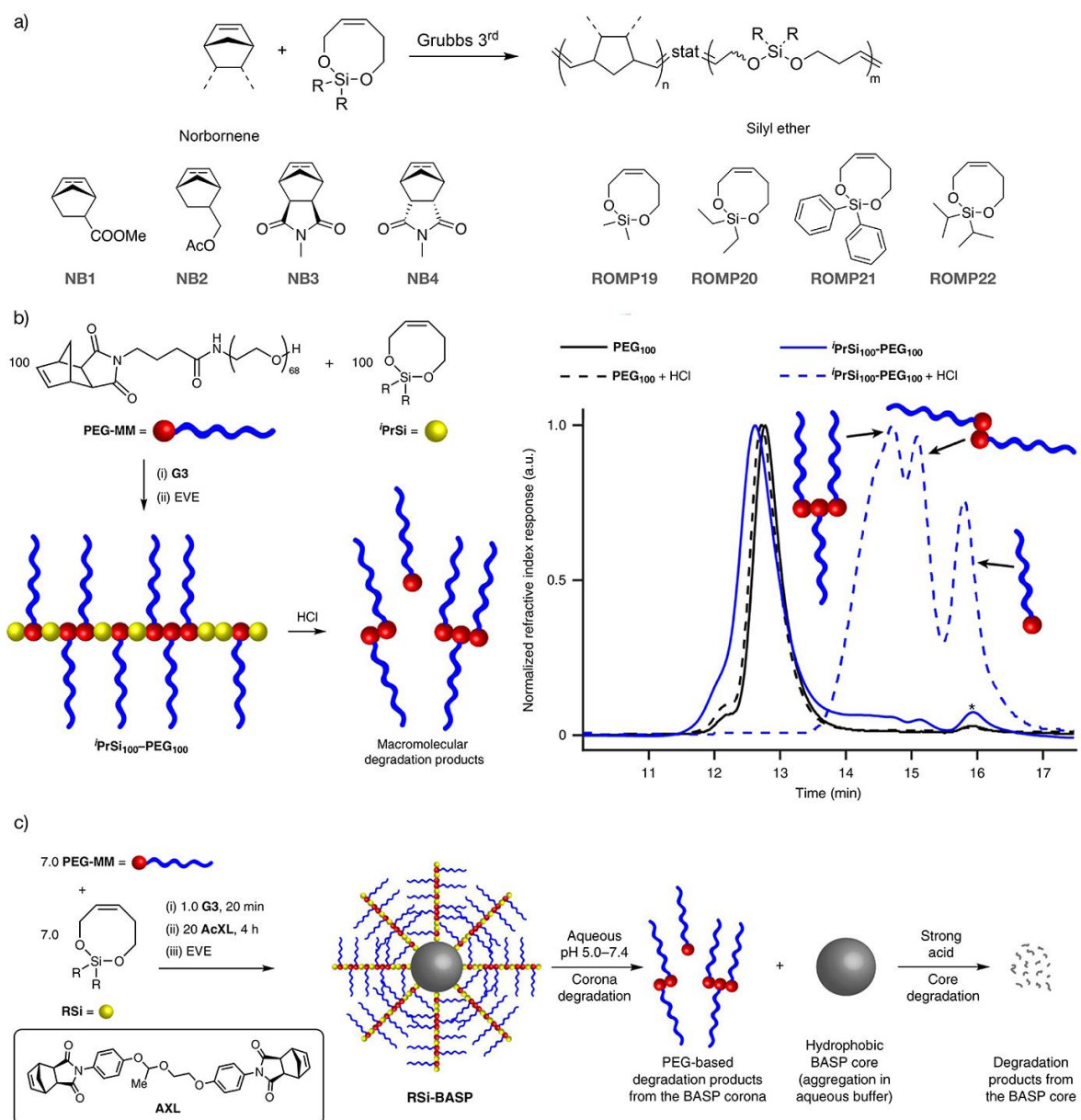


Fig. 15. a) Copolymerization of cyclic silyl ether olefin with norbornenes to prepare degradable copolymers. b) Preparation of degradable bottlebrush, and c) brush-arm star polymers. Adapted from Ref. [96] with permission.

Toste and coworkers[99] chose acylsilane as photolabile group to introduce in polyalkenamers. Due to its cleavage mechanism and long wavelength UV-absorption profile (350–420 nm), acylsilanes are appealing for such photolabile polymers. **ROMP27** was thus prepared and showed an efficient copolymerization with common ROMP monomers. The degradation in solution or in bulk occurred efficiently under 390 nm irradiation (Fig. 16).

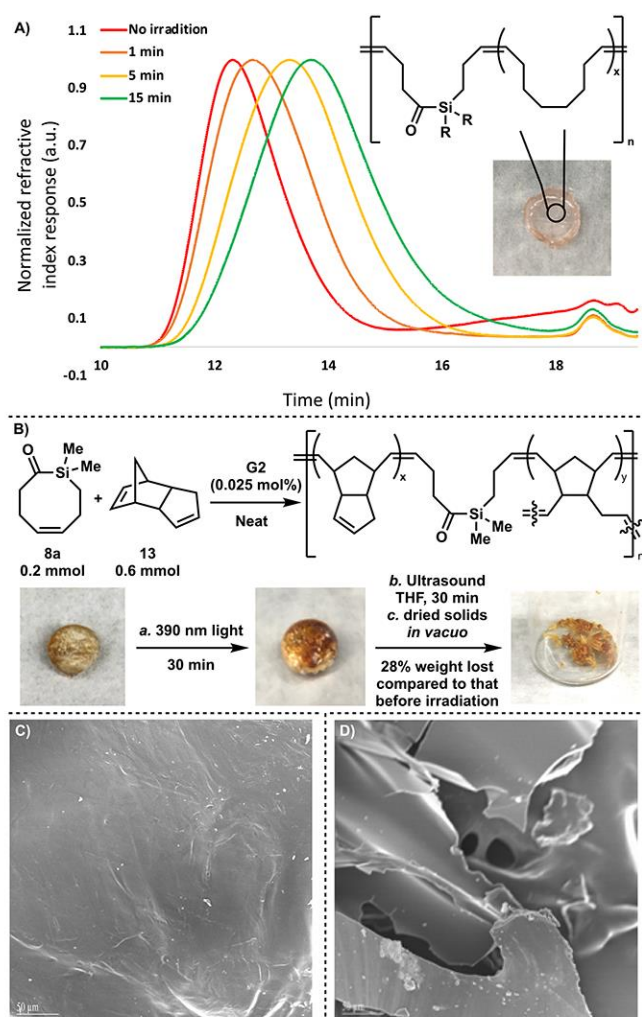


Fig. 16. Photodegradation of acylsilane copolymers in the solid state; all irradiation studies were conducted with a 52 W Kessil PR160L-390 nm LED lamp: A) Irradiation studies of polymer films and GPC traces in THF; B) Irradiation studies of polydicyclopentadiene containing acylsilane; C) SEM image of the copolymer sample before irradiation showed smooth surface; D) Holes and cracks emerged from the surface as shown by SEM image of the copolymer sample after 30 min irradiation. Reproduced from Reference [99] with permission.

Ortho-nitrobenzyl ester is one of the most representative photoresponsive moiety and thus was also inserted into a cyclic olefin. Kim and coworkers[100] recently reported the preparation of a library of trans cyclic olefins whose ortho-nitrobenzyl ester are inserted in ortho, meta, and para position towards the cycle (**ROMP28**). Even though macrocycles with low ring strain were prepared, the polymerization was completed within 30 minutes at room temperature but produced polymers with similar molecular weight whatever the monomer-to-initiator ratios. Degradation was observed under UVA irradiation but required a more complete study to be fully understood.

Besides cyclic olefins, bicyclic monomers were also studied. By reducing levoglucosenone, a substance obtained by the pyrolysis of cellulose, the biomass-derived levoglucosenol **ROMP29** was easily produced.[101] Using derivatives of second-generation Grubbs catalysts, successful polymerization of levoglucosenol was accomplished in 24 hours at room temperature with around 60% monomer conversion, producing high molar mass polyacetals ($M_n > 100,000 \text{ g}\cdot\text{mol}^{-1}$). The polymerization is however non-living. Concerning the degradation, the polyacetals completely degraded in acidic 1,4-dioxane in 40 days at room temperature.[101] Another bicyclic olefin monomer (**ROMP30**) was designed by Kiessling and coworkers[103] that leads to the creation of degradable polyoxazinones by ROMP. Aza-

[4 + 3] cycloaddition was used to create the bicyclic oxazinone-based monomers, which have a moderate ring strain (13.4 kcal/mol) similar to trans-cyclooctene and can be polymerized under ROMP conditions. The polyoxazinone was stable in a THF and MeOH mixture for 18 h at a neutral pH. but fast degradation was noticed at pH < 1 or greater than 13. A wide library of compounds could be prepared via various hydroxamic ester substituent.[103] Among the various functionalities, the introduction of an acetophenone group is of particular interest since it was reported very effective post-polymerization modification via oxime linkage by reacting alkoxyamine-based reagents (Figure 17).[102]

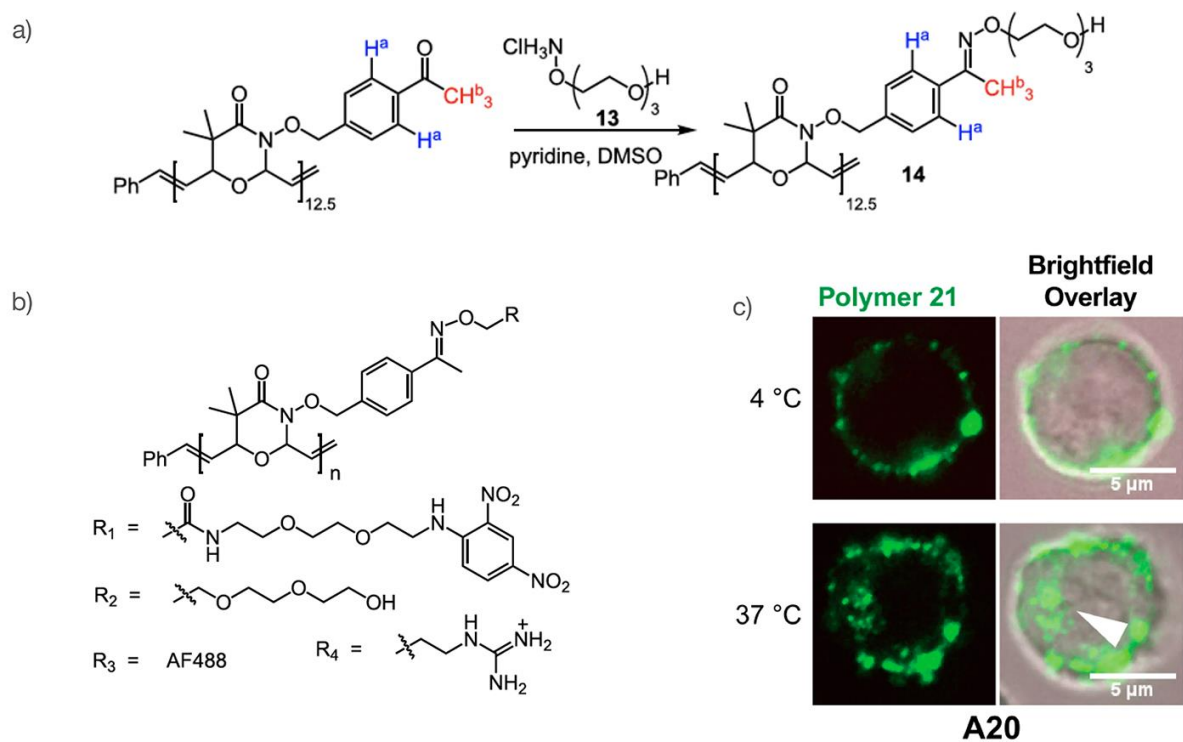


Figure 17. a) Preparation of polyoxazinones bearing an acetophenone moiety and its further postmodification via oxime linkage. b) Various post-modification possible based on the polyoxazinones backbone. c) Internalization of polyoxazinones bearing guanidinium side groups in A20 cells at 37 °C but not at 4 °C. Adapted from Ref. [102] with permission.

Later, Liu and colleagues[104] showed that ROMP of a structurally related monomer called oxadiazabicyclooctenone (**ROMP31**) could be used to create pH-sensitive polymers. Nevertheless, adding additional heteroatoms to the monomer structure strengthen the coordination with the metallocarbene and, as a result, make the control of the polymerization more difficult. As a result, in the presence of G3 and G2 catalysts, the polymerization of bicyclic dioxazinones was less controlled than that of bicyclic oxazinones. The use of G1 catalyst surprisingly improved the control of the polymerization and afford the polymer with a low dispersity. The resulting poly(oxadiazinone)s degraded quickly in acidic or basic environments. Such polymer has thus a unique degradation profile since it is stable at neutral pH but labile in acidic or basic environments. Random copolymerizations of oxadiazinones and norbornenes/oxanorbornene were performed. The molecular weight and the incorporation of dioxazinone in the copolymer was dependant of the structure of the norbornene derivative.

Vinyl ethers have long been thought of as ROMP terminating agents due to the formation of a Fisher carbene, which is thermodynamically stable. However, 2,3-dihydrofuran (DHF or **ROMP32**), a commercially available cyclic enol ether, recently underwent a successful enthalpy-driven ROMP that produced poly(enol ether) with molar masses ranging from 6.0 to 130 kDa.[105] Very high initial DHF concentration (neat monomer) are necessary to perform the polymerization. After 4 hours at room temperature, the polymerization equilibrated and attained a monomer conversion of around 80%. The authors[105] determined the thermodynamic parameters for the ROMP of DHF using the Van't Hoff equation, ($\Delta H = 5.0$ kcal/mol and $\Delta S = 19.4$ cal/mol \cdot K). They are similar to the one of cyclopentene. The molecular weight could be regulated by the monomer to catalyst ratio and the catalyst could be removed by treatment with oxygen peroxide. The PDHF degraded into 4-hydroxybutanal and its furan isomer after being treated with acidic THF (Fig. 18a). The authors[105] also showed

that in situ ring-closing metathesis may depolymerize PDHF back to the cyclic enol ether (Fig. 18b). This work shows the promise of this platform in chemically recyclable materials because it is the one of the few examples in ROMP to provide both a degradable and a depolymerizable polymeric backbone. In a similar approach Wang et al.[109] prepared a fused ring cyclopentadiene to lower the ring strain and thus impart depolymerization when the polymer prepared by **ROMP34** were put in presence of the G2 catalyst.

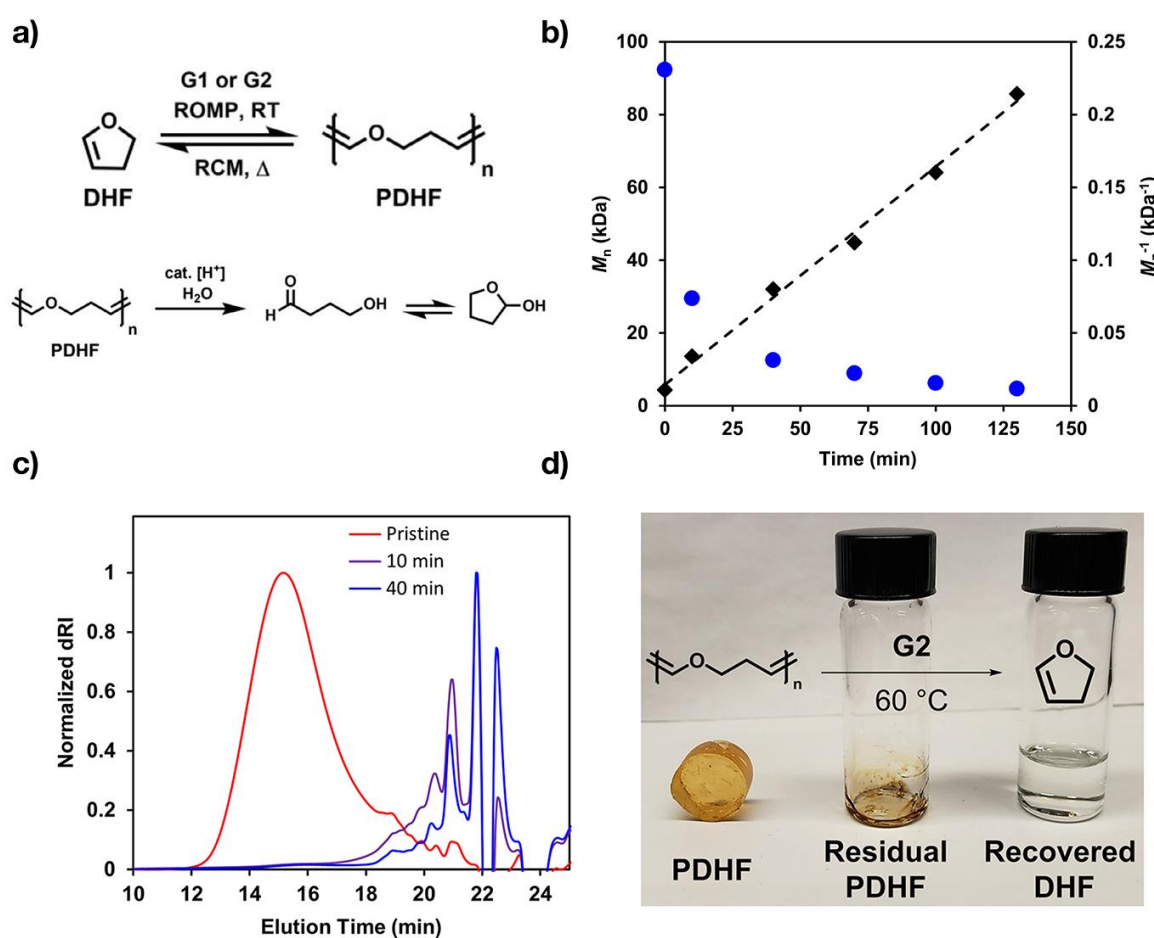


Fig. 18. a) ROMP of DHF and its degradation mechanism. b) Molecular weight (blue dot) and inverse molecular weight (black square) of PDHF during TFA triggered hydrolysis. c) GPC analysis of PDHF hydrolysis in THF with 135 mM water and 25 mM HCl d) PDHF depolymerization and monomer recovered via ring-closing metathesis at 60 °C. Adapted from Ref [105] with permission.

The copolymerization of cyclic olefins and DHF was then investigated. Kilbinger et al.[107] reported the copolymerization of DHF and (1R,4S)-2-azabicyclo[2.2.1]hept-5-en-3-one, which is often termed Vince lactam and its derivatives. The copolymerization was well controlled, and the livingness was assessed by the preparation of block copolymers and even a triblock from a POE divinyl ether as macroinitiator. The degradation was observed in the presence of dilute HCl in less than one hour. It has to be noted that the ROMP conditions was chosen to use only a catalytic amount of Ru (500 fold less than common ROMP) by using chain transfer agents.[107] Xia and coworkers[106] investigated the copolymerization of DHF with various norbornene derivatives (water-soluble, functionalizable and/or crosslinkable). The homopolymerization of norbornene derivatives was suppressed by the rapid reaction of the electron-rich enol ethers, allowing a random distribution of DHF along the polymer chain that will lead to an efficient degradation under mild acidic conditions.[106] The commercial availability of DHF and its efficient copolymerization with a wide range of norbornene derivatives make this system very interesting for many applications. Xia and Moore[112] for example used DHF with dicyclopentadiene to prepare thermoset by frontal polymerization (see network section).

The presence of cleavable functional groups, such as esters, acetals, and silyl ethers, which may be broken down under the right circumstances, is usually what makes a polymer degradable. While cleavable groups facilitate degradation, they may also be sparked by non-desired factors, making the polymer unstable when handled, stored, and used. A new approach to this problem was recently proposed: "locking" the degradability during polymer storage and usage and "unlocking" it when degradation is required. By including a locking moiety (Fig. 19a), the cleavable group is locked within a cyclic structure in this design. This maintains the

polymer backbone intact even if the cleavable group is broken. Restoring the original functionality is made possible by adding a reversibly cleavable group, which is challenging to do with traditional degradable polymers. On the other hand, the locking moiety may be released by mechanical pressure when degradation is required, creating a backbone-degradable polymer (Fig. 19a).

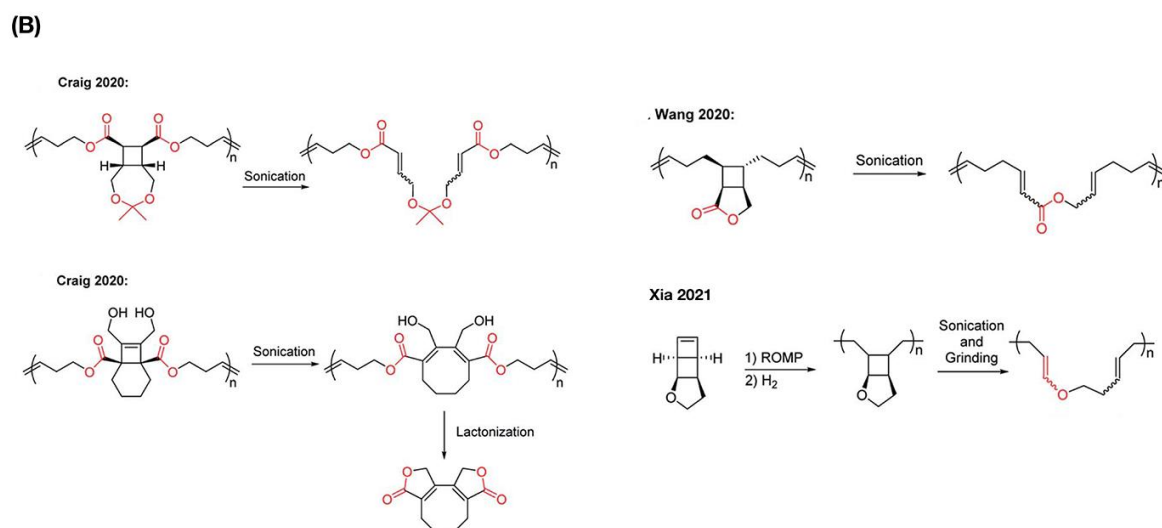
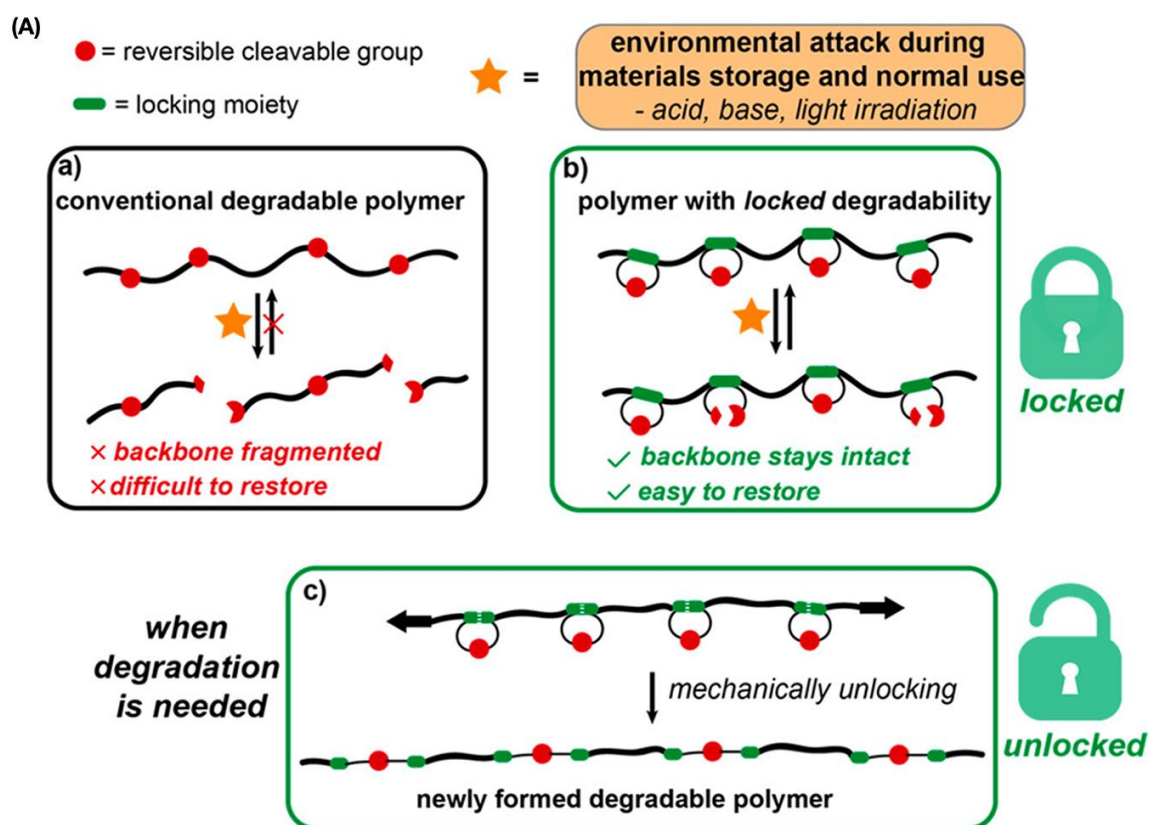


Fig. 19. (A) a) Schematic comparison between a conventional degradable polymer and a polymer with locked degradability. (a) The cleavable groups on a conventional degradable polymer can be attacked, causing polymer fragmentation, which is difficult to undo. (b) In a polymer with locked degradability, the locking moiety keeps the polymer backbone intact under conditions that break the cleavable groups, and the cleavage can be readily undone if the cleavable group is reversible. (c) When the polymer needs to be degraded, the locking moiety can be mechanically unlocked, forming a new degradable polymer. (B) Design of polymers that can mechanochemically generate degradable backbone linkages. Adapted from Ref [113] and Ref [114] with permission.

This locking moiety must be a stable scissile mechanophore under thermal, radiative, acidic, and basic conditions to play its role. For the degradability to remain latent, the mechanophore must also be stable under common stress that is applied to the polymer during its serving use. Because of its great stabilities under stimuli including heat, acid, base, and redox conditions, as well as exposure to light, cyclobutane is the best mechanophore group to fulfill all these requirements.[115] The Craig[116] and Wang[113] groups in parallel present a methodology to mechanically "unlocking" polymer degradability by coupling cyclobutane mechanophores with cleavable lactone and acetal links in the polymer backbone (Fig. 19B). These hydrolysable moieties were inserted into the backbone once cyclobutane's rings are opened via sonication, allowing the mechanochemically activated polymers to be hydrolyzed.

In both cases, after the unlocking, the polymer becomes directly degradable via the introduction of a lactone/acetal group. For some applications such as programmed obsolescence, in which a part subjected to early-stage damage events would continue to function until its immediate tasks were completed, a delayed fragmentation response could be worthwhile. To impart a delay in the degradation, Craig and coworkers[117] reported a cleverly designed alternative

mechanophore based on tetrasubstituted [4.2.0]bicyclooctene (BCOE) that, upon mechanochemical ring-opening into 1,3-cyclooctadiene, can spontaneously undergo intramolecular lactonization and result in backbone cleavage (Fig. 20). Once 60 min of sonication was performed, the degradation of the pristine 120 kDa BCOE copolymer via lactonization occurred smoothly for days and led to oligomers of 4.4 kDa, that are ten times smaller than control polymers in which lactonization is blocked.[117]

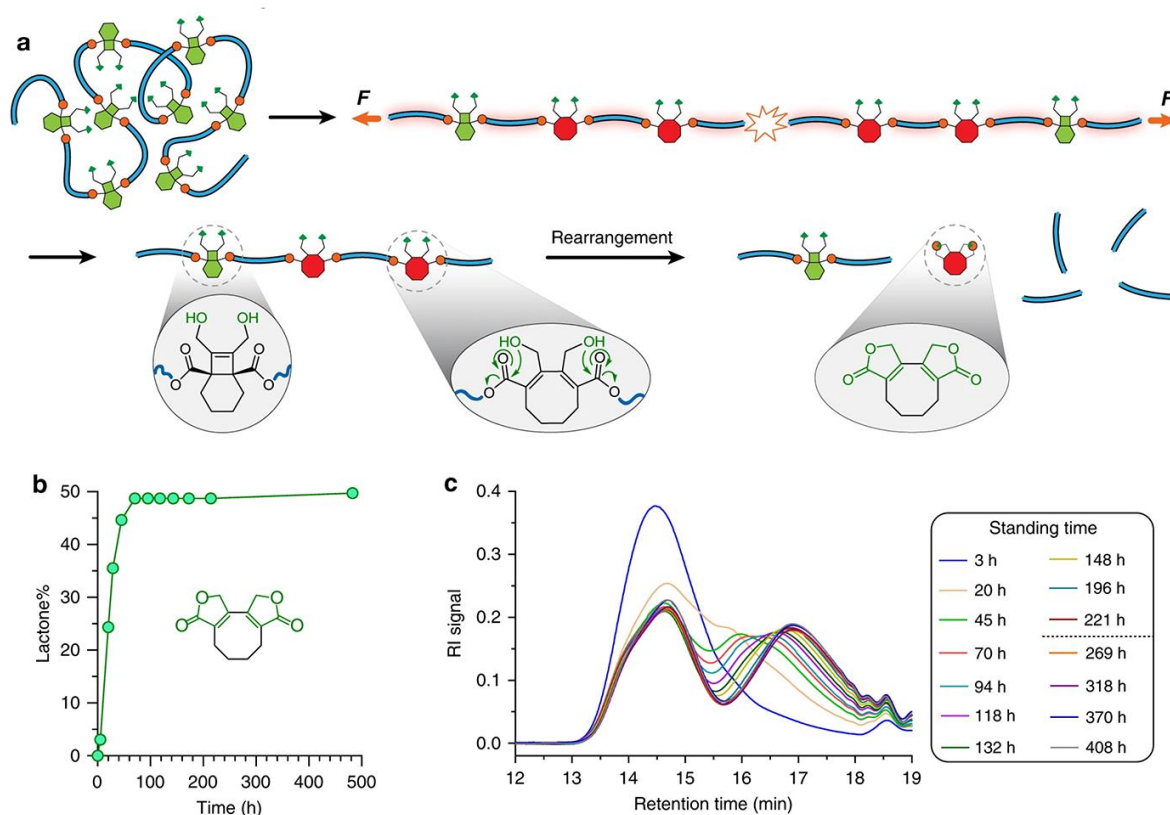


Fig. 20. a) Polymer bearing BCOE mechanophores undergoes mechanically induced forbidden ring opening and subsequent lactonization rearrangement, leading to enhanced degradation. b) ^1H NMR quantification of lactone formation over standing time in a polymer post 60 min sonication. c) GPC trace evolution of the polymer after 60 min sonication over various standing time in THF. Adapted from Ref. [117] with permission.

Lastly, Wang and coworkers[118] combined the concept of mechanochemically triggered modification of polyalkenamers with the preparation of efficient depolymerizable polymers. The authors prepared a locked poly(DHF) by preparing the an unsaturated polyether containing cyclobutane-fused THF in each repeat unit (Fig. 19B). Upon force-induced cycloreversion of cyclobutane, each repeat unit is converted into repeat units of PDHF. As already discussed below, the PDHF undergoes quantitative depolymerization to give back the pure DHF in the presence of Ruthenium catalyst. In a similar manner, Xia et coll.[114] reported the preparation of a cyclic ether fused bicyclohexene (Fig19B). This monomer underwent an efficient ROMP polymerization using G3 catalyst and required the hydrogenation of the double bonds to be thermally stable up to 400 °C. Once mechano-activated via sonification, the the cyclobutene led to an enol ether that could be degraded under acidic condition. Copolymerization of this monomer with functionalized norbornene were also successfully performed and a solid stage degradation by grinding 10 min of the polymer in a mortar in the presence of TFA led to a consequent degradation.

3.1.3 Cascade Metathesis Polymerization

The vast majority of cyclic olefin monomers with degradable moieties have little to no ring strain. Due to this feature, ROMP of such monomers could exhibit a thermodynamic equilibrium or non-negligible secondary metathesis events, making difficult the control and/or the livingness of the polymerization. Choi and coworkers[119] developed in 2012 the concept of tandem ring-opening/ring-closing metathesis polymerization from two rather unreactive functional groups: cyclohexene and a terminal alkyne. Many cascade-based metathesis systems were then developed.[120, 121] Since this seminal study, Gutekunst and Hawker[122] explore

this methodology to prepare sequence-controlled polymers. They first prepared a polymerization trigger via a three-steps synthesis based on commercial artificial sweetener saccharin (Fig. 21). The trigger could then be cyclized with various α -amino, ω -acid derivatives including a well-defined sequence glycolate, lactate, phenyl-lactate and β -alanine (Fig. 21).[122] The polymerization using G3 catalyst was well-controlled and led the corresponding sequence-controlled polyester whose decomposition occurred in 30s in the presence of 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD). This approach has been exemplified with a short ester-based sequence, but this could be applied to other sequences such as peptides or to introduce orthogonal cleavable bonds.

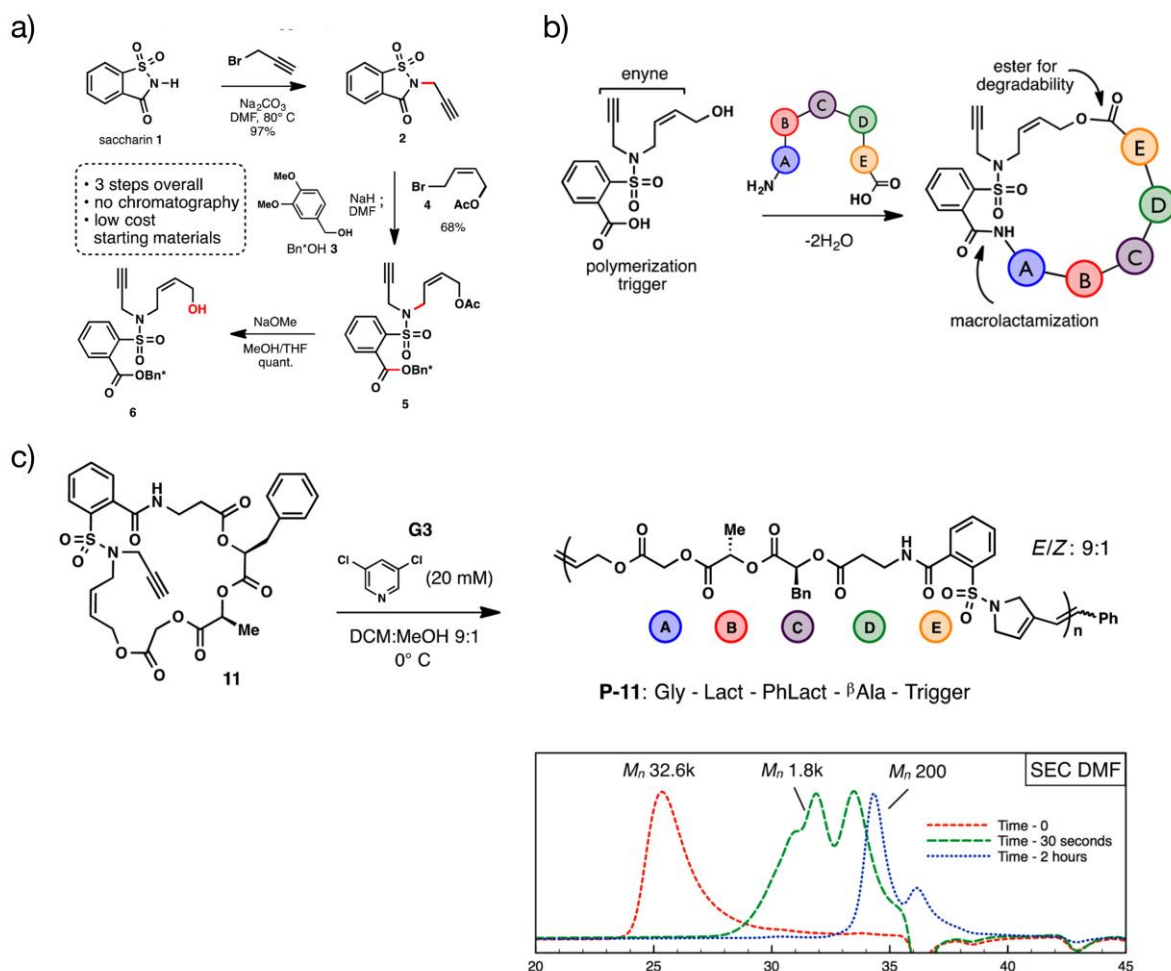


Fig. 21. a) Preparation of the polymerization trigger b) general strategy for polymerization of macrocyclic sequences. c) Preparation of a macrocyclic polyester sequence (Gly-Lact-PhLact- β Ala-Trigger) $_n$ and its degradation using TBD. Adapted from ref. [122] with permission.

Enyne and diyne are another type of monomers that could be prepared using Grubbs catalysts via a cascade approach even if such polymers are less studied than traditional polyalkenamer materials. Due to the high efficiency of cascade metathesis polymerization of enyne monomers, Gutekunst[123] used cyclic enol ether as comonomer to impart degradability to such materials (Fig. 22a). In the presence of cyclic enol ether, controlled and living alternating chain growth polymerization was obtained with close to 90% of alternating diads. The obtained polymers and block copolymers were stable in the solid state and in water but presented a rapid degradation in a water/dichloromethane/TFA solution. Besides enyne monomers, a similar copolymerization approach between used cyclic enol ether and diynes monomers was also reported (Fig. 23b).[124] The homopolymerization of diyne is slower than the one of enyne, allowing a fully alternating copolymer to be obtained. The control and livingness of the copolymerization allow to combine diyne and enyne monomers in a fully degradable block copolymers (Fig. 22b). The degradation properties of diyne and enyne polymers were similar.

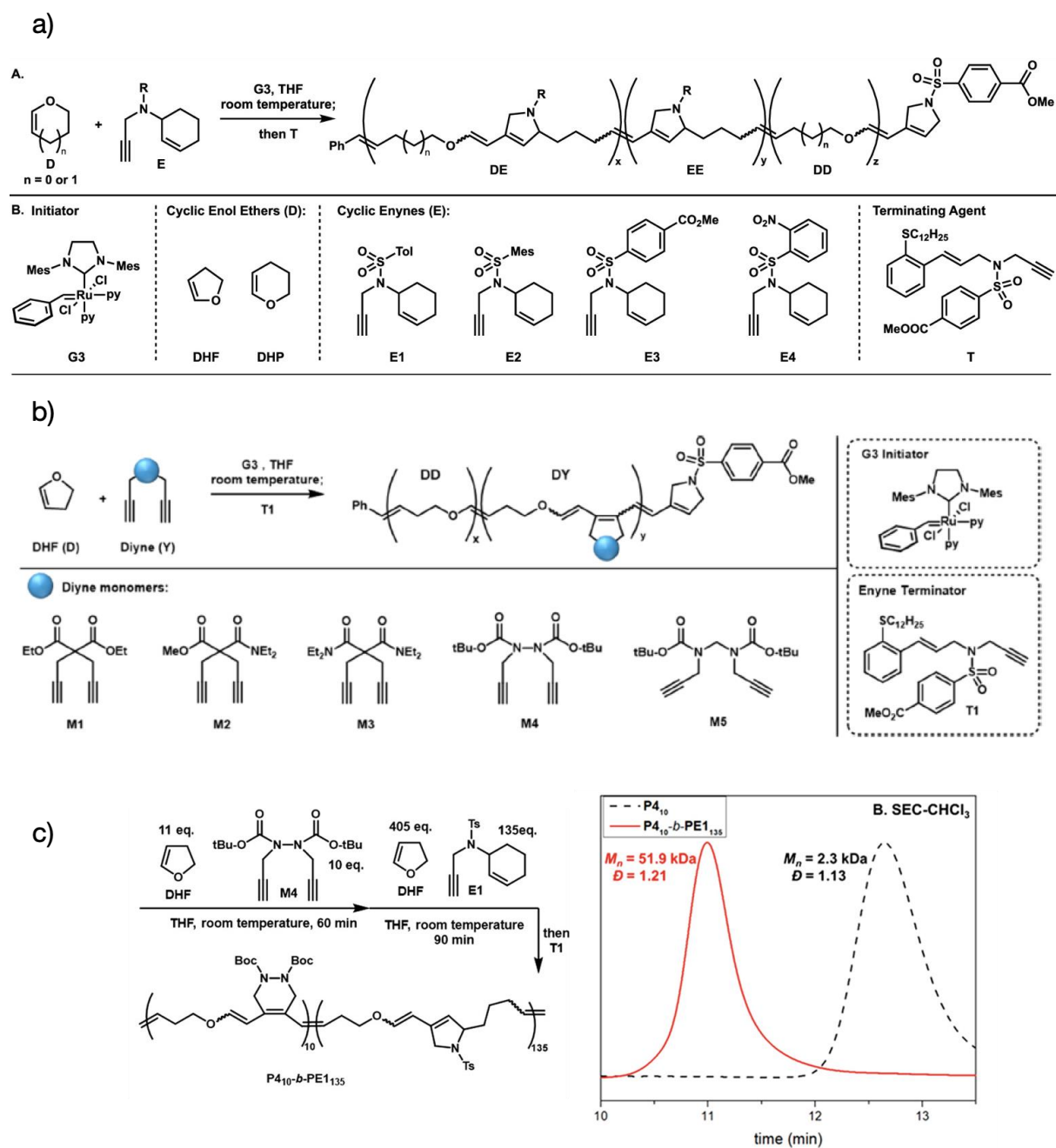


Fig. 22. a) Structures of enynes and cyclic enol ether monomers, initiator, and enyne terminator. b) Range of diene to prepare degradable polymers. c) Synthesis of diblock P410-b-PE1135 through sequential monomer addition and SEC chromatogram of the first block and chain extension. Adapted from Refs. [123, 124] with permission.

Gutekunst[125] and the group of Choi[126, 127] then developed various monomers bearing either a acetal based cyclohexene or enyne monomer that is based on glucose and/or galactose derivatives. In both cases these monomers combine efficient polymerization process, biobased monomers (for sugar-derived monomers) and degradable materials. These monomers have not been used already in copolymerization but have a good potential to be inserted in *via* the copolymerization approach and turn carbon-based copolymers into degradable materials.

3.2 Radical Polymerization

Polymers prepared by radical polymerization accounted almost half of the world production of polymers (e.g., low density polyethylene LDPE, polystyrene PS, polyvinyl chloride PVC, synthetic rubber, polyacrylate derivatives, polymethacrylate derivatives such as poly (methyl methacrylate) PMMA, fluoropolymers, etc.).[128] All these materials are prepared from vinyl monomers, leading to a carbon-based skeleton, and thus are non-degradable. Multiple methods that are described in Fig. 23 have been developed for incorporation of cleavage/labile bonds into the backbone.[22, 129] The first one consists of reversible deactivation radical polymerization that could both control the growth of the polymerization and the nature of the chain-ends. This enables the insertion of one or multiple bonds that could be either cleaved according to their position or reactivated to active radicals and further quenched to oligomers. In this figure the trapping of dormant ATRP chains by nitrones or nitroxides was described as example. Other approaches require the copolymerization with dioxygen to introduce unstable peroxy bonds onto the polymer backbone or the copolymerization with cyclic monomers, whose addition/fragmentation mechanism will lead to the introduction of heteroatoms into the main chain. Finally, the introduction of pro-radical groups was also reported.

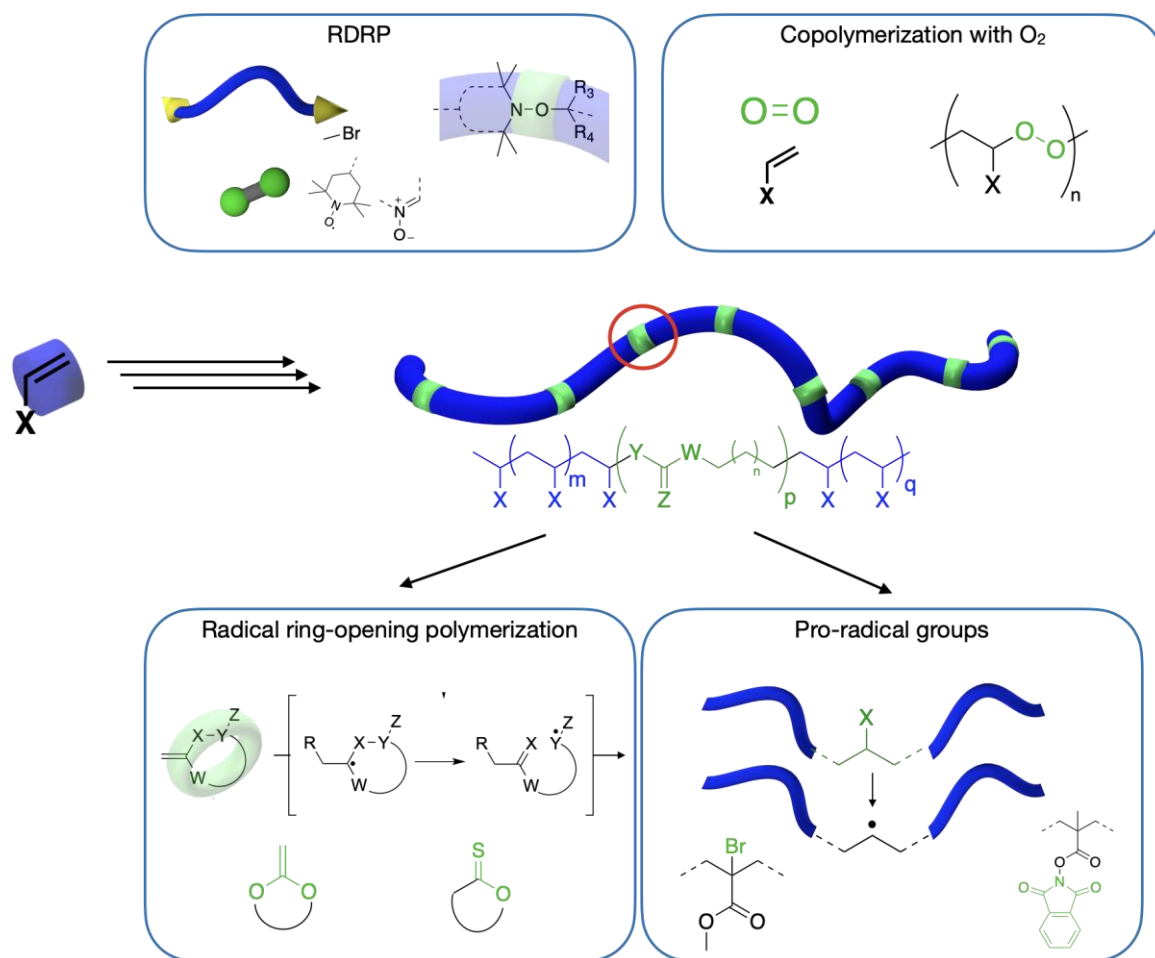


Fig. 23. Different methods to prepare degradable vinyl polymers via a radical process.

3.2.1 Reversible Deactivation Radical Polymerization

The readily available approach to confer degradability to macromolecules is to introduce one labile unit within the polymer backbone. Indeed, a single cleavable unit located in the middle of the chain will lead to a half decrease of the number average molar mass (M_n) after degradation. This could be accomplished using a difunctional initiator in which a cleavable bond joins the two initiating sites.[130] The use of reversible deactivation radical polymerization (RDRP) techniques such as nitroxide-mediated polymerization (NMP),[131] atom-transfer radical polymerization (ATRP),[132] and reversible addition-fragmentation

chain-transfer polymerization (RAFT)[133] allow to prepare polymers via a divergent chain growth. Such approaches have been reviewed by Nicolas and coworkers[129] and by Matyjaszewski and coworkers.[22]

When multiple cleavable units are wanted for increasing the degradation, macromolecular coupling approaches can be used to prepare multi-segmented degradable polymers by using difunctional macromolecular building blocks. In that case a step growth mechanism is used to prepare the final material. The control of chain-end fidelity via RDRP and the straightforward functionalization of the end-chain is a common way to obtain such telechelic building blocks.[22] The preparation of multi-segmented copolymer using non-radical chemistries are detailed in the polycondensation section. One efficient method to polymerize such building blocks is radical cross-coupling.[134] Di-functional precursors prepared by RDRP could be links by difunctional radical scavengers to prepare multi-segmented copolymers. Nicolay et al.[135] followed by Monteiro and coworkers[136] prepared α,ω -dihalogenated polymers by ATRP and reacted them to prepare alkoxyamine-containing multi-segmented polymers (Fig. 24a). Such approach has been also widely used to prepare complex macromolecular architectures[137] or polyalkoxyamines.[138] Multi segmented alkoxyamine-based copolymers were also prepared by an heterodifunctional initiator[139] bearing both a nitroxide and an halogenated compound and also by trapping α,ω -dihalogenated polymers via a nitroso compound.[140] In all cases due to the alkoxyamine linking group, the multi-segmented copolymers could be degraded by heating in presence of radical traps such as monofunctional nitroxide allowing a possible recycling (Fig. 24a). Wang and coworkers[141] extend this concept with the use of ethyl dithiobenzoate as a radical trap (Figure 24b). The multisegmented polymer is then linked by a C-S bond via a step-growth mechanism up to 20 segments. The polymer can be degraded thermally (265-285 °C) in the presence of hydrogen atom donor or

air to prevent self-coupling of polymeric radical during the fragmentation. To confirm that the degradation occurred via the cleavage of the labile C-S bond, the polymer was also treated by *N*-bromosuccinimide in the presence of dimethyl sulfoxide (NBS/DMSO), that is known to deprotect *S,S*-acetals groups, The SEC of the degraded polymers were identical, confirming the location of the labile group.

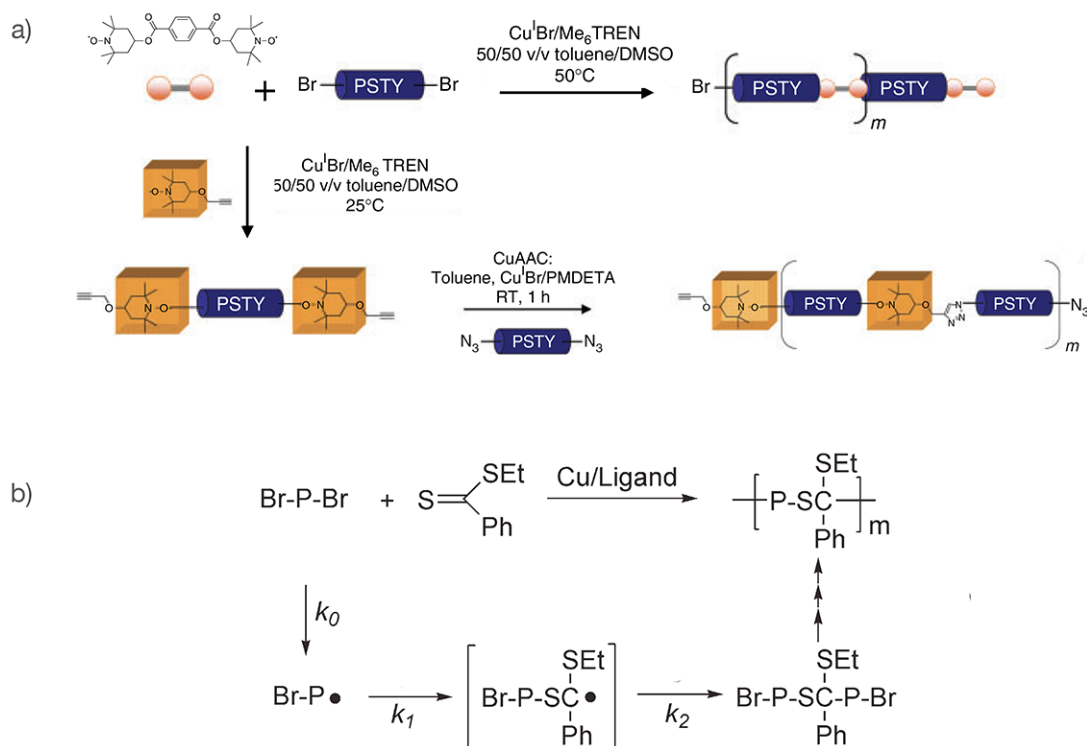


Fig. 24. a) Synthetic strategies for the formation of multiblocks using the SET-NRC reaction, and exchange with functional nitroxides, leading to the formation of multiblocks by a CuAAC reaction. b) Preparation of multiblock copolymer via the trapping of macroradicals using a RAFT agent. Reprint from Ref. [136] and Ref. [141] with permission.

The introduction of multiple RDRP linkages into a polymer backbone was also performed via the polycondensation of a symmetrical trithiocarbonate RAFT agent bearing two carboxylic acid (2,2'-(thiocarbonylbis(sulfanediyl))bis(2-methylpropanoic acid)) with a dihalogenated

compound (1,4-bis(bromomethyl)benzene).[142] The polytrithiocarbonate ($M_n = 7,500 \text{ g.mol}^{-1}$) obtained was used as a polyRAFT agent for the polymerization of styrene that led to a multiblock copolymer of $M_n = 60,000 \text{ g.mol}^{-1}$. The copolymer could be first degraded via aminolysis in solution to PS of M_n close to $10,000 \text{ g.mol}^{-1}$. Due to the photosensitivity of the trithiocarbonate linkage, UV irradiation of film (150 μm thick) of the copolymers led to complete degradation in 745h.[142]

3.2.2 Copolymerization with O_2

Oxygen is usually thought of as a radical scavenger that impedes the radical polymerization of vinyl polymers through the generation of less reactive peroxy radicals. Nevertheless, at excess oxygen pressure (2-4 atm), polyperoxides that are alternating copolymers of vinyl monomer and molecular oxygen could be formed where thermally labile peroxy (-O-O-) bonds are incorporated in the polymer backbone.[143, 144] This process is called oxidative polymerization. The unstable peroxy bonds are prone to degrade in the presence of multiple stimuli such as heat, UV irradiation, acid, base, enzyme, etc.[143, 144] The polyperoxides also show unique exothermic degradation, in contrast to common polymers, which generally undergo endothermic degradation.

Many vinyl monomers were found to copolymerize with O_2 to form polyperoxides.[143] Styrene, MMA, and diene monomers were the more reported comonomers.[144] Copolyperoxides using two vinyl monomers and O_2 could also be prepared.[145] Alkyl sorbates are the main diene monomers used to prepare polyperoxides since it could be produced by the copolymerization with oxygen under mild polymerization conditions, that is, ambient pressure and temperature in the presence of a radical initiator.[146-148] Moreover, the

copolymer has a highly regular chain structure consisting of an exclusive 5,4-unit as the alternating repeating diene unit and generate acetaldehyde and a fumaraldehyde monoalkyl ester as the well-defined degradation products upon degradation (Fig. 25).[148]

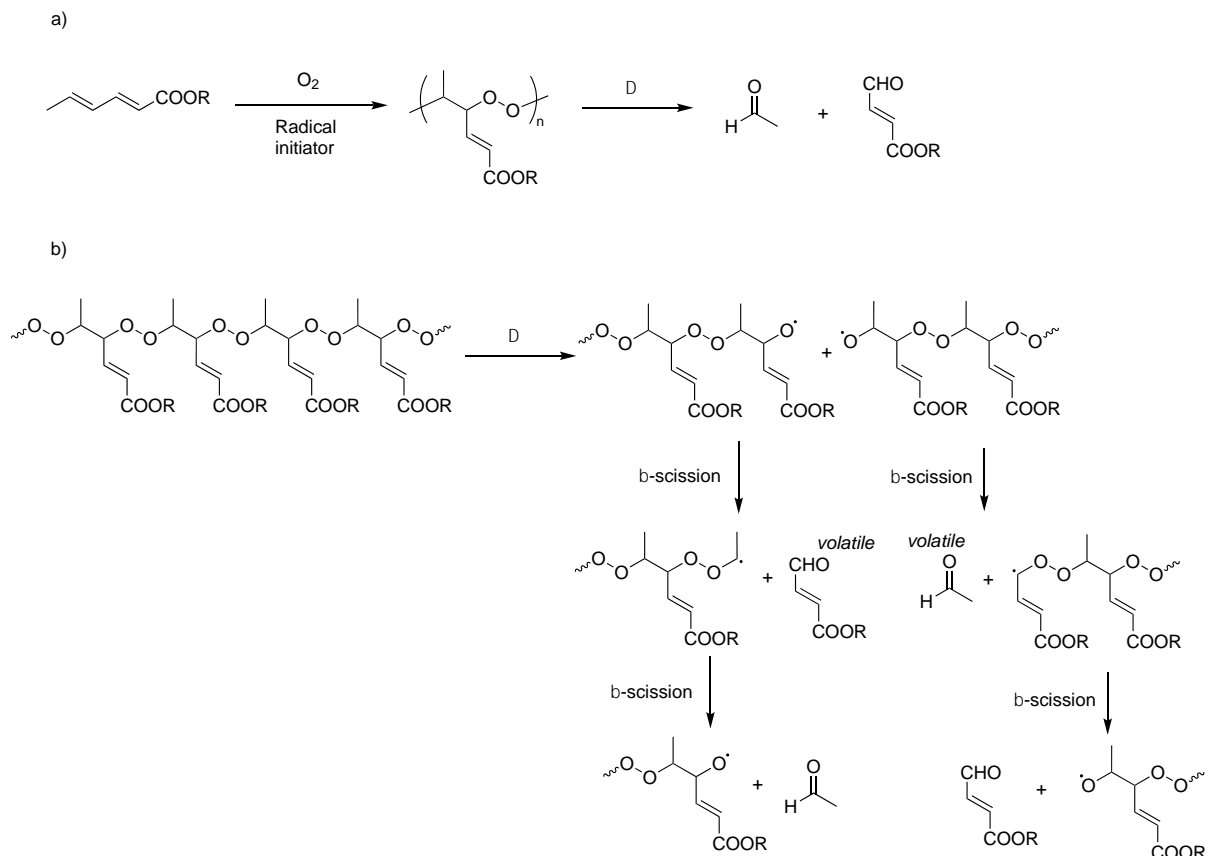


Fig 25. a) Formation of polyperoxides by copolymerization of O₂ and alkyl sorbate. b) Mechanism of degradation.

The selectivity of such copolymerization was explained by DFT calculations.[149] The modification of the ester group to amide led to a lower selectivity due to its lower electron-withdrawing property.[150] The thermal decomposition was studied and differential thermal analysis (DTA) and thermogravimetric analysis (TGA) showed that initial and maximum decomposition temperatures are close to 110 and 150 °C respectively.[146]

One of the drawbacks of the polyperoxides is related to their low mechanical properties (usually highly viscous amorphous materials) because of the flexible peroxy (–O–O–) bonds

in the main chain. To improve such properties, De and coworkers[151] reported the copolymerization of styrenic monomers having fatty acid moieties attached to the phenyl ring with O₂ (100 psi). For fatty acid with 12 carbon atom or longer, crystallinity was observed. The crystalline polyperoxides have a good thermal stability up to 120 °C and are solid powdery materials, making them simple to handle. The melting temperature T_m of crystalline polyperoxides rises regularly as side-chain length increases.[151] The same author modified the pendant group of the phenyl ring by introducing a poly(ethylene glycol) moiety to make polyperoxide water soluble.[152] A similar approach was used by Matsumoto *et al.*[153] that couple oligo(ethylene glycol) onto sorbate group. The produced polyperoxide displayed a phase separation with a lower critical solution temperature (LCST)-type, and this LCST decreased with the amount of the hydrophobic ester group present in the copolymer. Under the LCST, this copolymer created nanoaggregates in water that have diameters between 250 to 370 nm. The polyperoxide suitability as a drug delivery carrier was tested by encapsulating 1-anilinonaphthalene-8-sulfonic acid as a fluorescence probe and epirubicin as an anticancer drug and by measuring their cytotoxicity and cellular absorption. Similar cytotoxicity as other biodegradable polymers and efficient entry into cell via endocytosis was observed.[153]

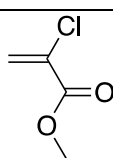
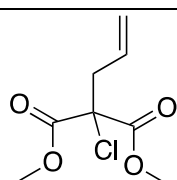
To speed up the degradation process, Matsumoto and coworkers[154] screened different reductants to find additive that do not impact their thermal stability at room temperature. Among different nitrogen -based compounds, they focused on 1-phenyl-3-pyrazolidone (PhP) and 1-acetyl-2- phenylhydrazine (APH) that successfully accelerated the degradation of hydrocarbon diene-based polyperoxides at 100 °C without reducing its stability at 30 °C.[154] Because of its pure 5,4 structure, sorbic ester-based polyperoxides stability in the presence of APH and PhP was not preserved for 12h at 30 °C. Such system is nevertheless very promising for inducing degradation at room temperature.

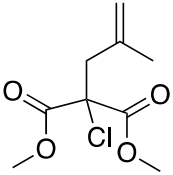
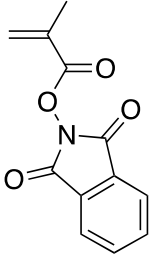
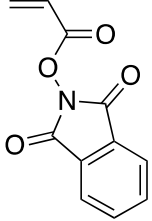
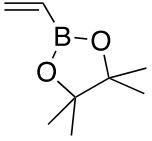
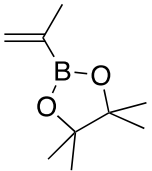
Finally polyperoxides were also used to prepare either brush copolymers[155] by preparing sorbate based macromonomers or degradable gels via the copolymerization of O₂ and vinyl sorbate.[156]

3.2.3 Introduction of pro-radical groups

Apart from introducing labile bonds containing heteroatoms into the polymer backbone, it was recently shown that introducing pro-radical groups onto the polymer backbone is a convenient way to degrade polymer chains. The various structures were gathered in Table 4. Indeed, it is long known that some polymers, especially polymethacrylate derivatives are prone to depolymerize by an unzipping process.[22, 24, 157] Such approach is interesting since various stimuli or triggers could be used to generate such radicals and without them, the polymer is stable and is only degraded on demand.

Table 4.

Structure	Ref
 <p>ProRad1</p>	[158]
 <p>ProRad2</p>	[159]

 <p>ProRad3</p>	[159]
 <p>ProRad4</p>	[160]
 <p>ProRad5</p>	[160]
 <p>ProRad6</p>	[161]
 <p>ProRad7</p>	[161]

Starting from a previous work reporting the depolymerization of polymethacrylate derivatives via the activation of a terminal chlorine bond,[162] Ouchi and coworkers[163] prepared the methyl α -chloroacrylate (MCA or **ProRad1**) that was used as a comonomer for the polymerization of methacrylate derivatives (Fig. 26). The use of such monomer induced chlorine defect into the polymer backbone and trigger for the degradation. Conventional free radical polymerization or RAFT polymerization was used to prepare the copolymer. Due to the difference in reactivity ratios between ProRad1 and MMA ($r_{\text{MMA}} = 0.3$ and $r_{\text{ProRad1}} = 1.2$), more chlorine units were inserted into the polymer chains than in the feed, and conversions of MMA have to be kept below 80% to ensure that chlorine group are still inserted into the backbone. The authors investigated the degradation of the obtained PMMA using a similar protocol they used for depolymerization.[162] Using RuInd complex at 100 °C, they obtained 80% degradation on copolymer without compositional drift. Other degradation conditions were then tested, and it was found first that the combination [polymer]/FeCl₂]/[*n*-Bu₃N] = 10/20/40 mM in tetraglyme led to the best degradation conditions with 95% of degradation. The temperature was also investigated and increasing the temperature from 100 to 140 °C drastically sped up the degradation process since a similar degradation rate was observed after 20 min instead of 24h.[163]

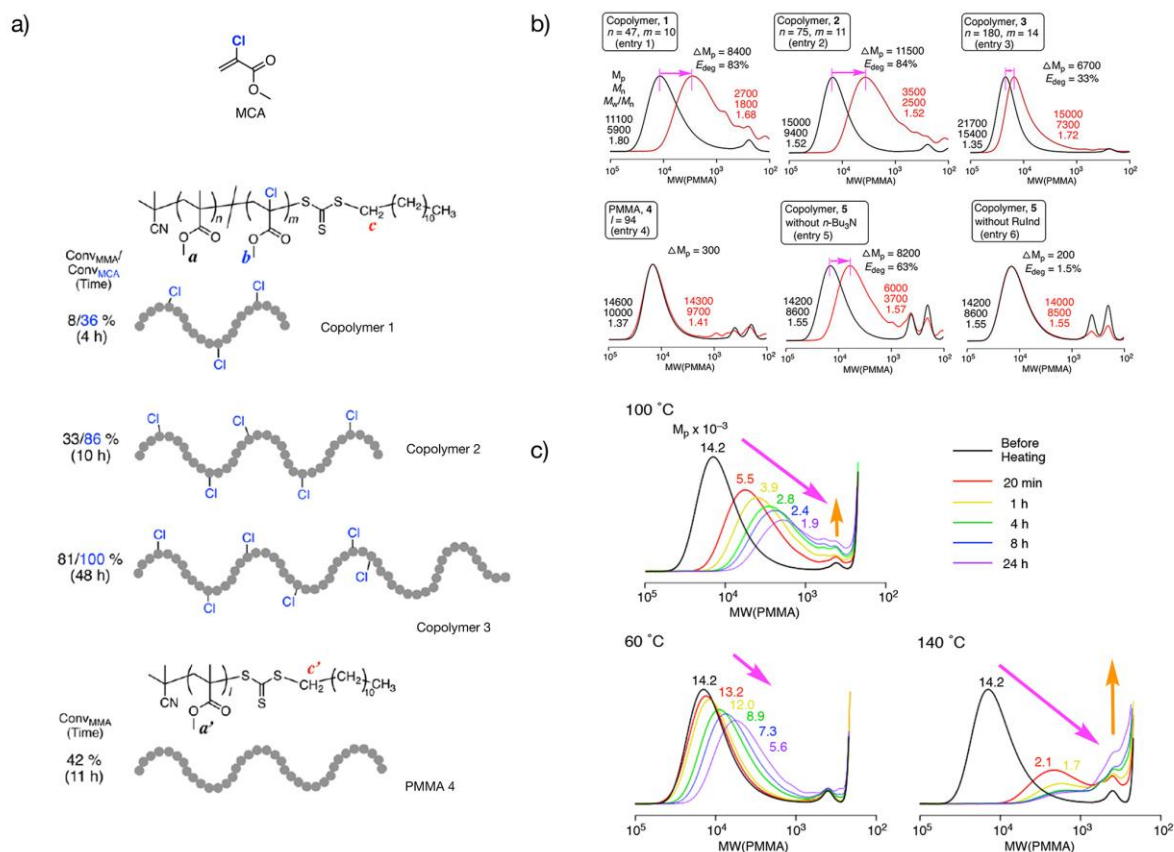


Fig. 26. a) Preparation of copolymer with various conversion and b) SEC curves of copolymers (1–3, 5, similar to copolymer 2) and pure PMMA (4) before and after heating in the presence or absence of catalyst (RuInd) and/or cocatalyst ($n\text{-Bu}_3\text{N}$) in toluene at 100 °C. c) Degradation process monitored by SEC of copolymer similar to copolymer 2 over time at 100 °C, 60 °C, and 140 °C. $[\text{copolymer}]/[\text{FeCl}_2]/[n\text{-Bu}_3\text{N}] = 10/20/40$ mM. Adapted from Ref. [163] with permission.

Sato *et al.*[159] have removed the chlorine atom from the backbone to the pendant group by developing new monomers **ProRad2** and **ProRad3** bearing a chloromalonate group. Due to the low reactivity of the vinyl bond, the incorporation in a polyacrylate chain was not efficient with less than half of the comonomer that was in the feed inserted into the backbone. In the case of polymethacrylate, ProRad2 was marginally more efficient at introducing the chloromalonate group into the main chain than ProRad1. The degradation occurred via an

intramolecular 1,5-shift to give the main-chain radical. β -scission of the main-chain radical took place to result in the scission of backbone (Fig. 27). For the copolymer with MMA, the copolymer did not show a significant decrease in molecular weight, because they do not possess any α -hydrogen atoms for the intramolecular 1,5-shift.

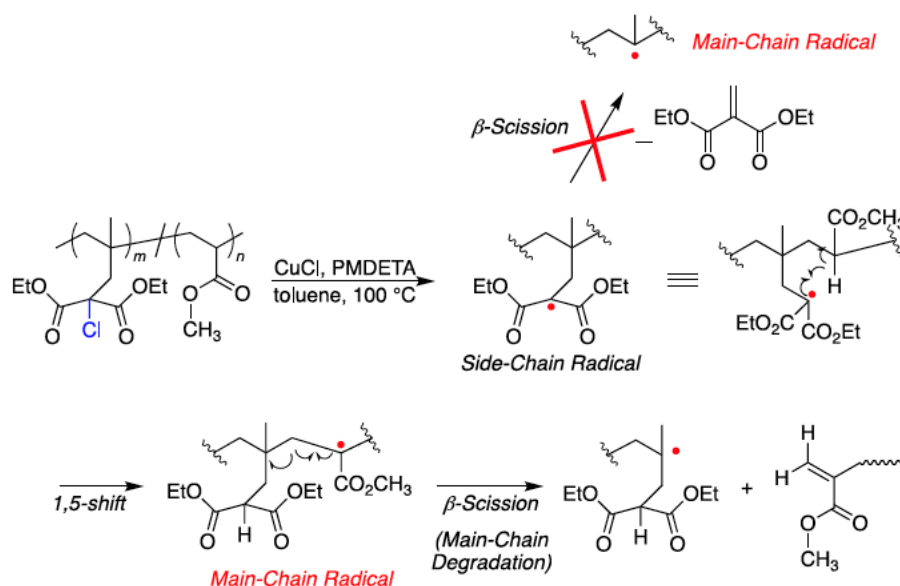


Fig 27. Proposed mechanism for interlocking main-chain degradation of **ProRad2**-based copolymer. Adapted from Ref. [159] with permission.

In a similar approach, Summerlin *et al.*[160] introduced another pro-radical group via the use of N-(acyloxy)phtalimide (meth)acrylate monomers (**ProRad4** and **ProRad5**, Fig. 28) to generate radicals by a Single Electron Transfer (SET) mechanism. He was inspired by the decarboxylative radical cross-coupling reactions that were extensively used in photoredox catalysis and in which N-(acyloxy)phtalimide was widely used.[164-168] The same author[169] and the group of Theato[170, 171] already used similar monomers to prepare polyolefins from poly(meth)acrylate derivatives via the trapping of the produced macroradical by a H-donor. The copolymers were prepared by RAFT polymerization. With 10 mol% of phtalimide unit inserted into PMMA backbone using **ProRad4**, the degradation occurred in

the presence of EosinY/ N,N-diisopropylethylamine (DIPEA) under green light irradiation (Fig. 28) until it was not possible to determine an accurate molecular weight anymore (20h). The degradation is still efficient with a lower amount (1.3 mol%). To see if other copolymers may be rendered degradable by adding either **ProRad4** or its acrylate derivative **ProRad5** as a comonomer, the authors investigate different comonomer combinations. In copolymerization with MMA, ProRad5 led to degradation but with lower efficiency (close to 70%). The reasons for the lower efficiency might be either a better rate of macroradical quenching by a hydrogen atom from DIPEA, or a lower stability of the newly formed macroradical following the β -scission (Fig. 28). A full acrylate backbone was also investigated. Complete decarboxylation was observed by ^1H NMR. However, instead of degradation, the molecular weight increased certainly due to polymer coupling. When **ProRad5** was used in combination with styrene, polymer coupling was obtained due to a low rate of β -scission.[160]

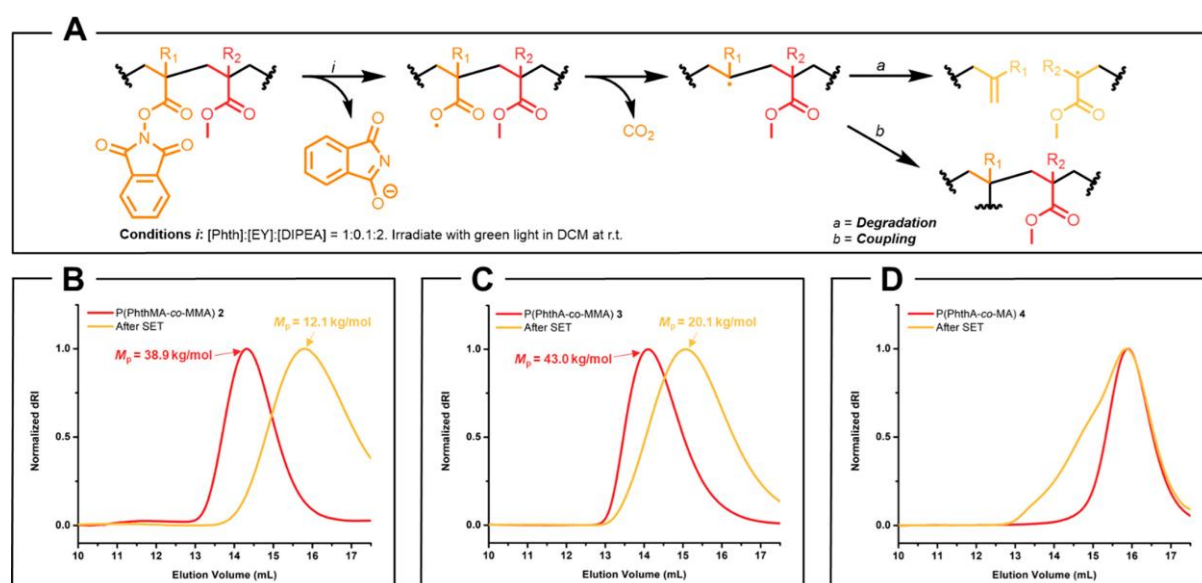


Fig. 28. (A) Reaction scheme for SET to polymers containing redox-active phthalimide ester pendants in the absence of a radical quenching species displaying two potential reaction pathways: degradation and coupling. (B) GPC traces before and after SET to a copolymer 2, revealing polymer degradation. (C) GPC traces before and after SET to copolymer 3, revealing polymer degradation. (D) GPC traces before and after SET to copolymer 4, revealing polymer coupling. Reprinted from Ref [160] with permission.

In a following study, Sumerlin and colleague[172] reported the direct decarboxylation polymer bearing a carboxylic acid to trigger the degradation. Indeed, up to now, specific comonomers have to be introduced to produce radicals in the polymer chains. With this process, acrylic acid, or methacrylic acid are sufficient to induce degradation. The direct decarboxylation is based on a pioneering work from Oda[173] that reported the use of acridine as a photocatalyst to convert carboxylic acid to alkane via a photoinduced proton-coupled electron transfer (PCET) process in the excited state of the acridine-carboxylic acid hydrogen-bond complex. The degradation of polymethacrylate derivatives made by RAFT and containing methacrylic acid was thus tested. It was first shown that due to the similar nature of monomers, there is no compositional drift during the reaction allowing the random insertion of the carboxylic acid in the polymer chain. The degradation by irradiation at 395 nm with mesityl acridine as catalyst was then very efficient and led to complete degradation in 1-2 hours at RT (Fig. 29).

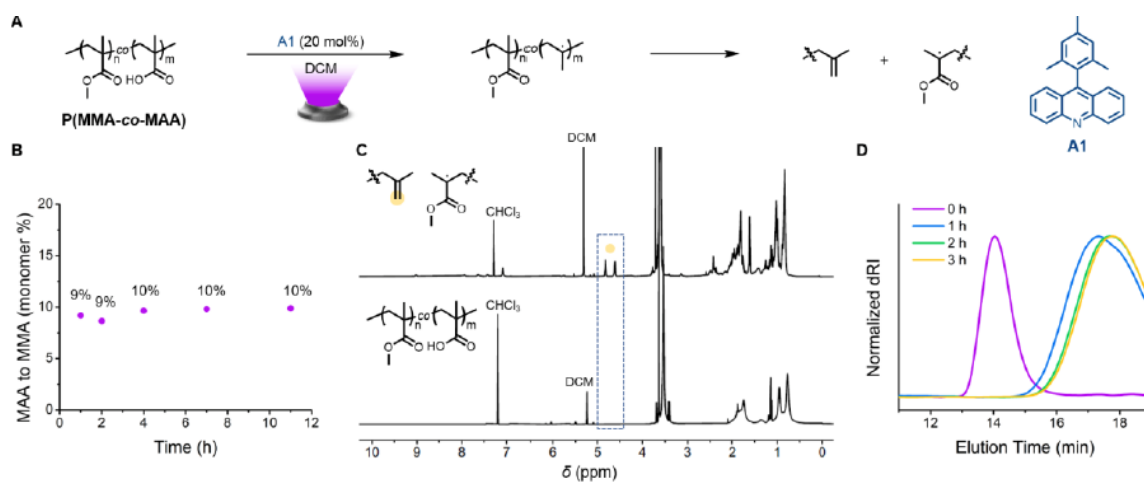


Fig. 29. A) Decarboxylative degradation of P(MMA-co-MAA_{10%}) occurred with A1 under violet light. B) Incorporation of MAA into the copolymer chain during RAFT polymerization indicated a constant comonomer composition. C) ¹H NMR spectra illustrated the appearance of an alkene degradation product. D) GPC traces during decarboxylation demonstrated a significant decrease in molecular weight resulting from release of CO₂ and chain cleavage. Reprint from Ref. [172] with permission.

Ouchi and coworkers[161] recently developed monomers based on boron chemistry due to their unique properties.[174, 175] In particular, boronic acid pinacol ester (Bpin) is frequently used as a protecting group that could be converted to reactive species.[176] The copolymerization of ProRad6 with MMA was performed via RAFT polymerization, and the introduction of boronate ester was lower than in the feed due to the difference in reactivity ratios.[161] The degradation requires the use of manganese acetate Mn(OAc)₃ as an oxidant in conjunction with fluoride ion for activation of the C–B bond (tetra-*n*-butylammonium fluoride TBAF), and 4-tert-butylpyrocatechol (TBC) as ligand. Only 72% of degradation was observed at 120 °C for 24h. The modification of **ProRad6** to **ProRad7** via the addition of a methyl group led to a small increase of the efficiency via the generation of a tertiary macroradical that is more prone to degradation.

Many photoinitiators are carried on ketone groups since this functionality can degrade through Norrish Type I and Type II reactions when exposed to ultraviolet light. Vinyl ketone and their related polymers were thus employed to impart photosensitivity to polymers. The first studies were reported in the 50s[177] and a patent related to styrene-vinyl ketone SVK resin was granted in 1973.[178] Many studies were reported on conventional free radical copolymerization with various comonomers.[179-183] Vinyl ketones are not easily handling materials, thus Priddy et al.[184] reported the preparation of poly(styrene-*co*-vinyl ketone) via the *in situ* dehydrative generation of vinyl ketone from more stable and easily handled β -hydroxyketone. The obtained copolymer was identical to the one prepared via the vinyl ketone, without dealing with the highly toxic and reactive monomer. More recently, the introduction of vinyl ketone into polymers prepared via RDRP was revisited by Konkolewicz.[185, 186] Thermoplastic elastomers with selectively etchable blocks were produced using multiblock copolymers of poly(vinyl ketones) and nondegradable polymers.[187] By using UV light for etching the poly(methyl vinyl ketone) blocks, the modulus of triblock copolymers with a poly(*n*-butyl acrylate) center block and PVK outside blocks dropped. In a similar way after the degradation of the poly(methyl vinyl ketone) block, the morphology of the polystyrene-*b*-poly(methyl vinyl ketone) thin films was altered,[188] confirming the efficiency of the photodegradation and the interest of this method to obtain nanostructured patterns.

3.2.4 Radical Ring-Opening Polymerization (*rROP*)

A straightforward method of randomly incorporating weak bonds into the C-C backbone of the polymer made by radical polymerization is the copolymerization of vinyl monomers with

cyclic monomers via ring-opening radical polymerization (rROP).[189, 190] This method combines the advantages of ring-opening polymerization and those of radical polymerization, i.e., the production of polymers with heteroatoms and/or functional groups in the main chain (to introduce cleavable functions), with the robustness, ease of use and mild polymerization conditions of a radical process. In this approach it is possible to introduce directly the weak point in the polymer chain and to have an easier degradation mechanism (Fig. 30a).

Although the polymerization of traditional vinyl monomers is performed by chain growth with creation of carbon-carbon bonds, some cyclic monomers bearing vinyl/exomethylene groups or equivalent can be polymerized radically by a addition/fragmentation mechanism also called ring-opening mechanism. Polymerization of cyclic monomers bearing a vinyl group leads to polymers with a double bond in the polymer backbone, while polymerization of cyclic compounds with an exomethylene group produces polymers with a dangling double bond. The functionality (e.g., ketone, ester, amide, thioester, etc.) derives from the nature of the W and Z atoms in the α position of the initial C=Y double bond (Fig. 30b).[189]

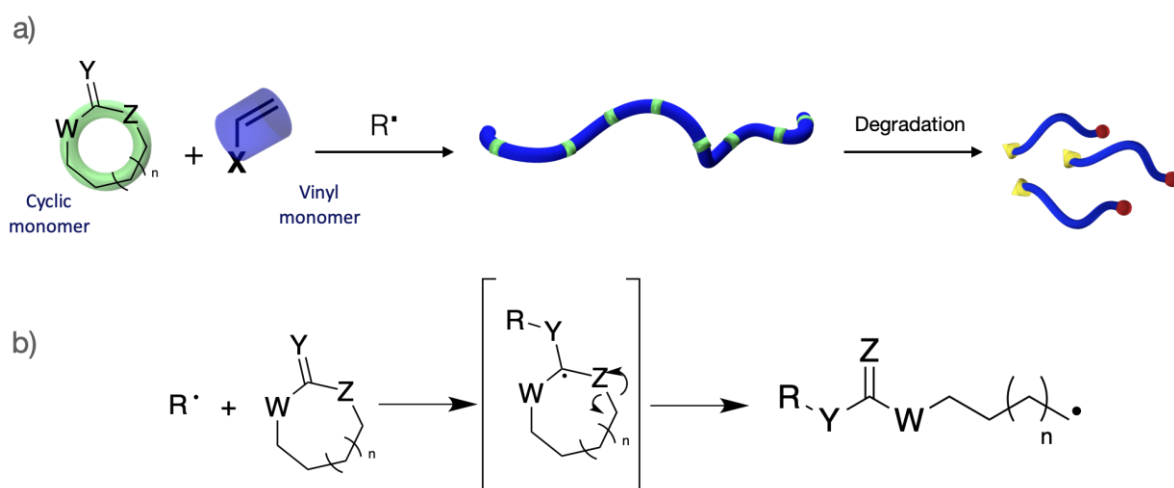


Fig. 30. a) Radical copolymerization between cyclic and vinyl monomers to obtain degradable materials. a) Mechanism of ring-opening radical polymerization.

Since early studies dating back to the 1980s it was thought that certain conditions must be satisfied for a given cyclic monomer to be polymerizable, namely (i) the ring strain must be high (or distortion of the ring structure must occur) to induce ring opening; (ii) the ring opening must be accompanied by an isomerization process forming thermodynamically more favorable functional groups (C=Z in Fig. 30), and (iii) the alkyl radical released after fragmentation must be stabilized.[189] If these conditions are not met or if side reactions occur during the polymerization, competition between the ring-opening and ring-retaining processes can take place, leading to the presence of different monomer units in the polymer backbone (Fig. 31).

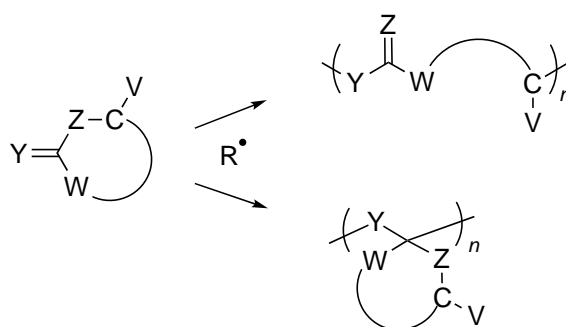


Fig. 31. Competition between ring-opening radical polymerization and ring-retention polymerization for exomethylene monomers.

The presence of ring-retaining units due to classical vinyl-type propagation leads in the case of C=C double bond to an aliphatic, and therefore non-degradable, carbon backbone. Radical polymerization by ring-opening was proposed in the 1960s by Errede,[191] using spiro-di-oxylylene type structures. Since then, many structures belonging to completely different chemical families (e.g., spiro-ortho-carbonates, cyclic acrylates, unsaturated spiro-ortho-esters, etc.) have been tested for their ring-opening ability. Fig. 32 lists the different monomer structures that lead to the introduction of heteroatoms into the main chain and thus can provide degradability properties to materials.

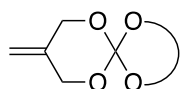
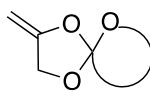
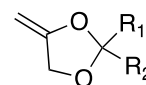
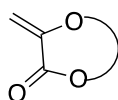
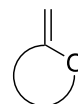
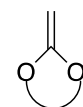
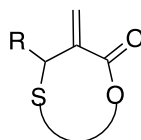
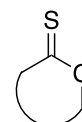
spiro-ortho-carbonate (SOC)**spiro-ortho-ester (SOE)****cyclic vinyl acetal (CVA)****cyclic α -oxyacrylate ($C\alpha OA$)****cyclic vinyl ether (CVE)****cyclic ketene acetal (CKA)****sulfide cyclic methacrylate (SCM)****thionolactone (TL)**

Fig. 32. Structures of the different monomer families that can be polymerized by ring opening radical polymerization (rROP).

Among these structures, cyclic ketene acetals, sulfide cyclic methacrylates and thionolactones are of particular interest and have been the most studied. Their description and characteristics are presented in more detail in the following subparts.

3.2.4.1 Cyclic Ketene Acetals

The principal method for the synthesis of cyclic ketene acetals (CKAs) involves the formation of the ring by acid-catalyzed transacetalization (either p-toluene sulfonic acid pTSA or a DOWEX resin) from the dimethyl chloroacetal and a diol. The methanol formed must be removed to shift the equilibrium to the formation of the cyclic chloromethyl acetal. The second

and final step is the formation of the exomethylene function by deshydrochloration in the presence of a strong base. The most commonly used bases are KOH or potassium *tert*-butanolate (t-BuOK).[189] Because of the strong tendency of CKA monomers to polymerize by a cationic process, they were exclusively purified by distillation under reduced pressure. This synthetic method allowed the preparation of a wide range of CKAs by modifying only the diol structure. Other synthesis methods[192] or optimization of the reaction[193] have also been reported in the literature but are only rarely used.[189]

The essential characteristic of CKA monomers comes from the acetal functionality. Because the doublet of the two oxygen atoms is delocalized on the C=C double bond, the latter is highly polarized and the β -carbon is highly nucleophilic.[194] The nucleophilic character of the CKA double bond explains the instability of these monomers in the presence of protic species.[195] When polymerization is carried out under appropriate conditions, CKAs have the advantage of producing after an addition/fragmentation reaction predominantly aliphatic polyesters, whose structures are close to those of well-known (bio)degradable polyesters such as polycaprolactone (PCL). The properties of these polyesters and their potential applications have already been widely studied and the interest in preparing a polyester by radical route explains why CKAs have been widely studied in the last decades.

The main disadvantage of CKA monomers is related to the possible competition[196] between the ring-opening process (providing a degradable chain) and the unwanted direct vinyl propagation that leads to the undegradable polyacetal (Fig. 33a). Thus, for the majority of CKA monomers, the resulting polymer is a random copolymer of ester and acetal units. A large library of CKA monomers has been reported in the literature to study the influence of different factors on ring-opening, such as experimental conditions and CKA structure. The free radical reactivity (and thus the free radical ring-opening ability) of the most common CKA monomers

is reported in Fig. 33b, which however only gives a trend because a more precise analysis is very difficult to perform. Indeed, these results were obtained using different experimental conditions depending on the choice of temperature, solvent, nature and concentration of the free radical initiator, etc., and using different characterization techniques (e.g. NMR, FTIR, etc.) which can lead to significant differences depending on the case.[196]

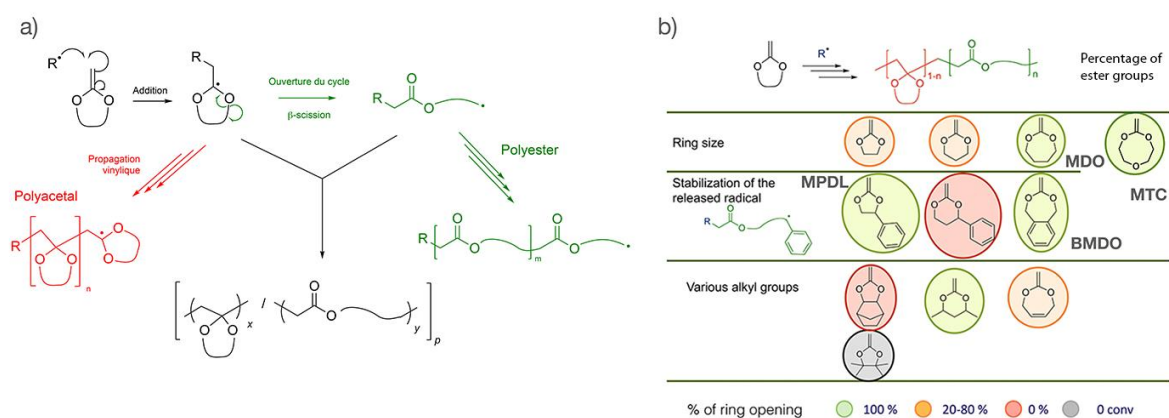


Fig. 33. (a) Competition between ring-opening and vinyl propagation reactions. (b) Percentage ring-opening of the most common CKA monomers. Adapted from Ref. [189] with permission.

From these results, it is very difficult to identify the key parameters that would favor a full opening of the cycle. This explains why the vast majority of studies dealing with CKA monomers and especially those dealing with applications are based only on MDO, BMDO and MPDL (Fig. 33b) which are known to experience complete ring-opening under a wide range of different experimental conditions. CKA with heteroatoms in the ring are not widely used even if they bring interesting properties such as higher hydrophilicity for MTC,[46] and thermo-responsivity for CKA bearing amino groups developed by Gaitzsch et al.[197, 198]

Recently, the reactivity of the CKAs could be modeled by the combination of quantum calculations (DFT density functional theory) which allows to evaluate the rate coefficients of

the addition and fragmentation steps and a numerical simulation which allows to take into account the kinetic competition which takes place during the propagation (Fig. 34).[196] Indeed all the previous theoretical calculations[199] focused only on the ring-opening step that is not enough to describe the competition between the ring-retaining and ring-opening reaction (Fig. 34).

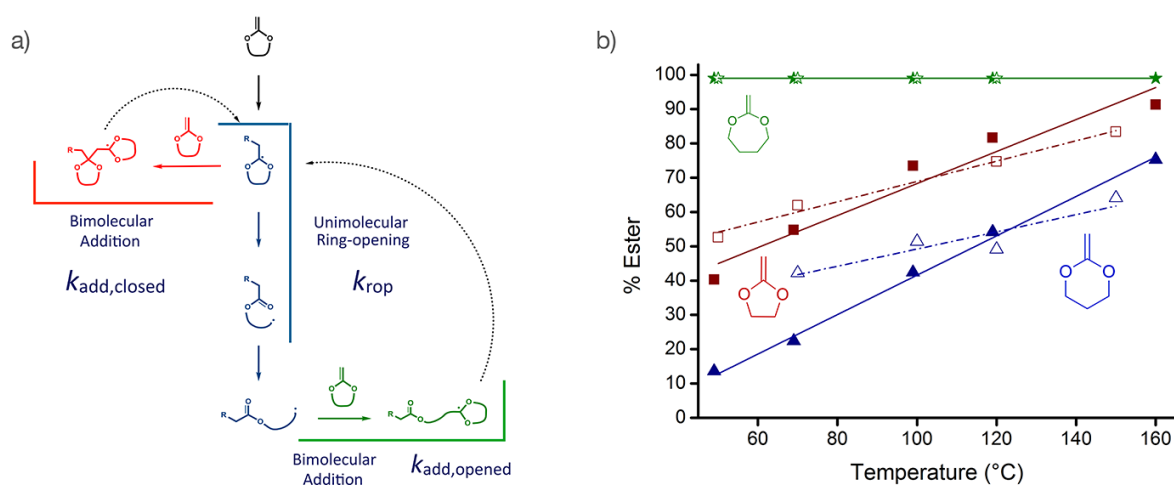


Fig. 34. a) Kinetic competition between vinyl propagation and ring-opening. b) Percent ring opening of 5,6 and 7 chain CKA monomers. Full point experimental data. Empty point theoretical point. Adapted from reference [196] with permission.

Indeed, to incorporate the ester unit into the polymer chain, it is necessary to have the following reaction sequence: addition of a radical on the CKA (bimolecular reaction) followed by fragmentation (unimolecular reaction) and addition of the open radical on another CKA (bimolecular reaction). Using this approach, it is now possible to predict *in silico* the behavior of CKAs and thus to prepare molecules with optimal ring-opening efficiency.[196] DFT calculations were also used by Thoniyot *et al.*[200] to compare radical reactivity of CKA with different ring sizes. They confirmed the better ring-opening efficiency for large ring sizes (7-8 membered) than for lower ring sizes (5-6 membered).

The polymerization of MDO led to a polymer that is structurally similar to polycaprolactone (PCL), but due to the radical mechanism, 1,5 and 1,7 H-transfer could occur that led to intra and intermolecular branching. Such behavior has been shown in detail by Jin and Gonsalves,[201] later by Guillaneuf *et al.*[202] and more recently by the group of Gaitzsch.[203, 204] This feature led to lower or even no crystallinity This was used by Agarwal and coworkers[205] to prepare films of polyester by blending classic PCL and polycaprolactone made by rROP of MDO to tune first the degree of crystallinity of the film and thus modify the degradation kinetics of the films in soil (Fig. 35).

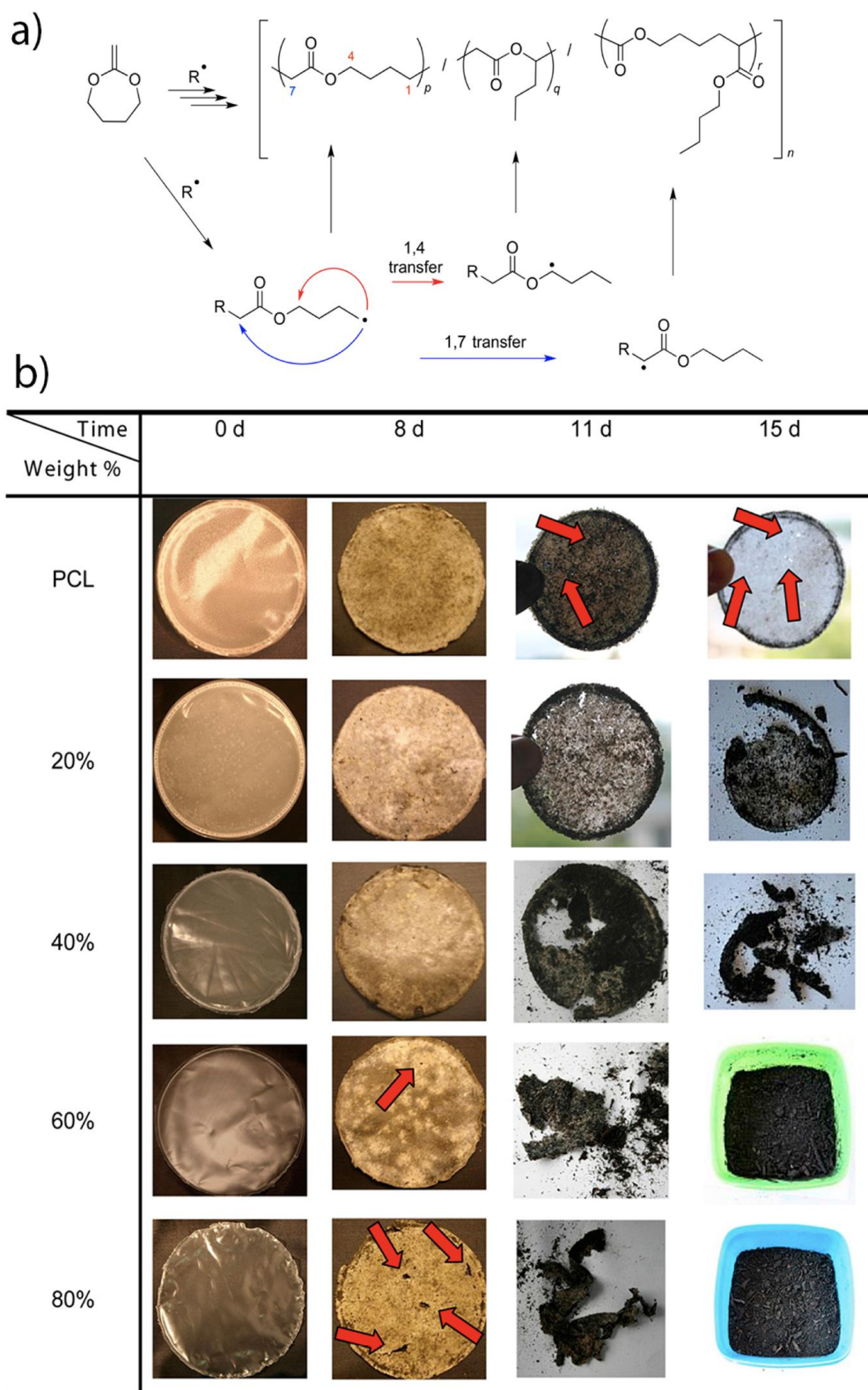


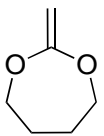
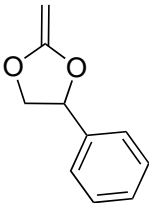
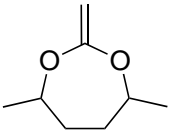
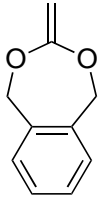
Fig. 35. (a) Mechanism of the intramolecular (backbiting) reaction that occurs during the rROP of MDO. (b) Compostability study performed on blend films (% of amorphous PCL/P(MDO))

and compared to semi crystalline PCL. Films of 5.9 cm of diameter and 80 μm of thickness. Compost at 45 °C. Reproduced with permission from ref. [205]

One of the major interests of radical polymerization lies in the possibility to copolymerize together different monomers to obtain materials with properties varying according to the ratio of monomers incorporated in the chain.[206] Since there is a wide range of commercial vinyl monomers, it seems thus possible to transform many non-degradable vinyl polymers into (bio)fragmentable or even (bio)degradable equivalents by simple copolymerization with a low proportion of CKA. In the case where the proportion of CKA would be the majority, this technique would also allow the easy preparation of functional polyesters by copolymerization of CKA with a low proportion of functional vinyl monomers.

Radical copolymerization of CKAs has been performed with several vinyl monomers. The results of copolymerization with an initial comonomer composition around 50% are presented in Table 5[189] and Table 6 listed the copolymerization pairs. The polymerization times are generally high (24 - 72h) and the incorporation of ester functions into the polymer chains is overall lower than the initial amount of CKA in the reaction mixture. The efficiency of incorporation into the polymer chain of CKAs as a function of vinyl monomer follows the following order: vinyl esters > (meth)acrylate = (meth)acrylamide > styrene. The preparation of degradable polystyrene using CKA monomers is thus difficult without using a large amount of CKA. Thoniyot and van Herk recently revisited the different studies and presented the optimal conditions to prepare degradable PS.[207]

Table 5. Copolymerization of CKA with common vinyl monomers at $[\text{CKA}]_0:[\text{Vinyl Monomer}]_0 = 1:1$.

CKA	Vinyl Monomer	Polymerization conditions	$f_{CKA,0}$ (mol%)	F_{CKA}	References
 MDP/MDO	Styrene	DTBP, 120 °C, 36h	50	23	[208]
	4-vinylanisole	DTBP, 120 °C, 36h	50	19	
	MMA	DTBP, 120 °C, 12h	50	33	
	MMA	AIBN, 50 °C, 48h	50	25	
	VAc	DTBP, 120 °C, 12h	50	49	
	VAc	AIBN, 50 °C, 48h	50	34	
 MPDO/MPDL	Styrène	DTBP, 120 °C, 24h	50	32	[209]
	4-vinylpyridine	DTBP, 110 °C, 12h	50	34	
	MMA	DTBP, 120 °C, 24h	50	40	
	VAc	DTBP, 120 °C, 24h	50	40	
	Styrene	DTBP, 120 °C, 72h	50	27	[210]
	MMA	AIBN, 50 °C, 48h	50	24	
 BMDO	Styrene	DTBP, 120 °C, 42h	50	31	
	4-vinylanisole	DTBP, 120 °C, 42h	50	33	
	MMA	AIBN, 50 °C, 45h	50	13	

Compared to styrene, it seems easier to copolymerize MDO with 2,3,4,5,6-pentafluorostyrene.[211] According to the authors, the enhanced electrophilicity of the pentafluorostyryl radical make the copolymerization with the nucleophilic CKA radical easier

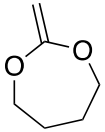
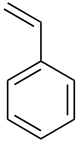
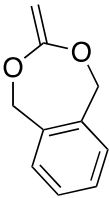
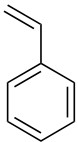
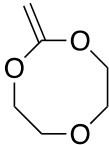
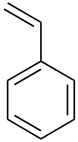
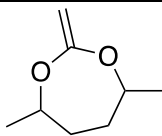
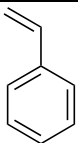
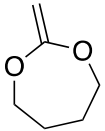
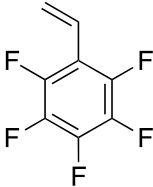
than with the nonfluorinated equivalent.[211] The copolymerization of CKA with some functional monomers is a challenge.

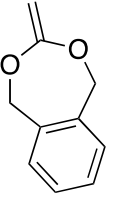
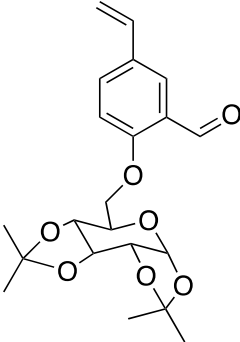
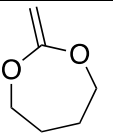
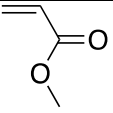
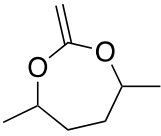
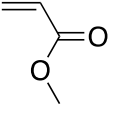
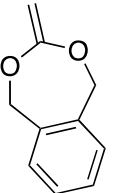
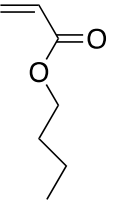
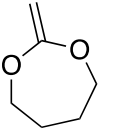
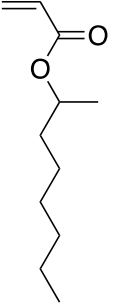
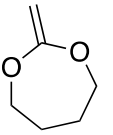
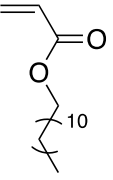
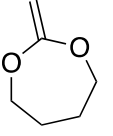
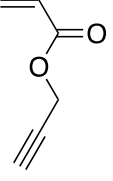
Copolymerization of BMDO with methacrylic acid[212] was for example shown to be impossible due to the undesired reaction of the carboxylic acid function with the nucleophilic double bond of BMDO that consumed the CKA and avoided its radical copolymerization. The use of protected carboxylic acid in the form of tert-butyl ester derivatives followed by mild deprotection was employed by Thoniyot *et al.*[213] to prepare poly(acrylic acid) containing ester groups from MDO. Similarly, when hydroxyl-containing monomers, particularly 2-hydroxyethyl methacrylate (HEMA), were copolymerized with CKA monomers like BMDO, the undesired proton addition to the CKA double bond also consumed the main part of the CKA and thus produced various methacrylate derivatives that were inserted into the polymer backbone.[214] Agarwal and colleagues[214] thus prepared a TMS-protected HEMA that successfully copolymerized with BMDO to add ester units to the PHEMA backbone after a classic KF/TBAF deprotection technique. Kikushi and coworkers[215] reported the copolymerization of hydroxyethyl acrylate and MDO without the need of hydroxy protection by performing the polymerization in DMSO at low temperature (30°C). In that case, the polymerization is faster than the side-reaction.

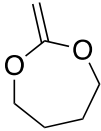
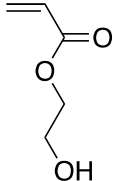
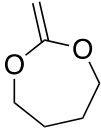
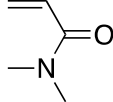
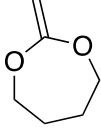
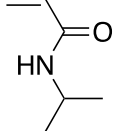
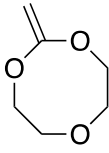
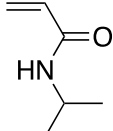
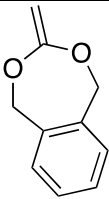
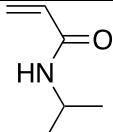
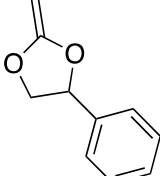
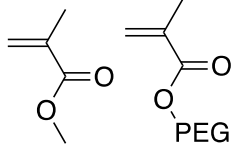
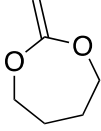
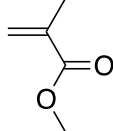
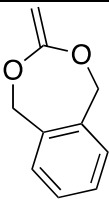
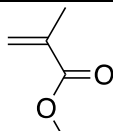
The use of fluorinated structures was also envisioned using (meth)acrylate derivatives. Ouchi and coworkers[158] used 2,3,4,5,6-pentafluorophenyl methacrylate and showed that its copolymerization with BMDO was efficient and led to alternating-rich sequence due a high crossover reaction. Post polymerization the pentafluoro phenyl group could be modified by alcoholysis ou aminolysis to produce functional methacrylate or methacrylamide alternating copolymer. Maynard and Sawamoto[216] demonstrated that the insertion of ester units during the copolymerization of BMDO and PEGMA was enhanced by the addition of a fluorinated

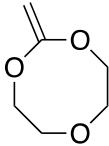
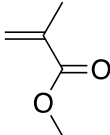
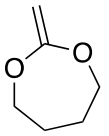
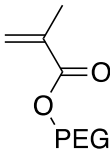
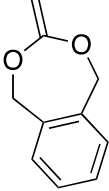
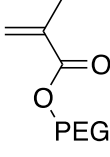
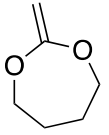
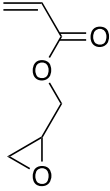
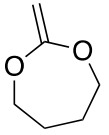
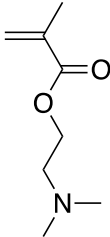
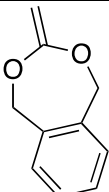
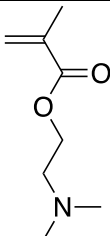
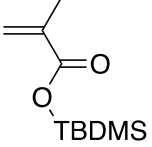
methacrylate. Lastly, it is interesting to notice the preparation of a copolymer bearing both ester unit in the main chain coming from the use of MDO and orthogonal photosensitive o-nitrophenyl group to obtain a dual-stimuli-responsive copolymer.[217]

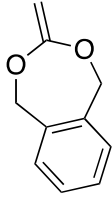
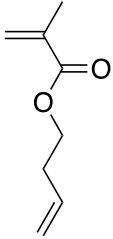
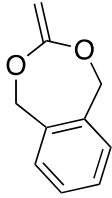
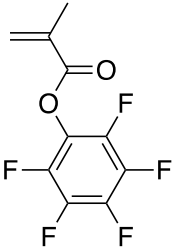
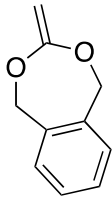
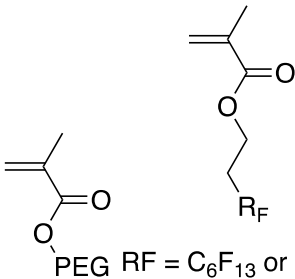
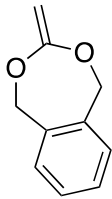
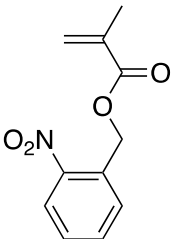
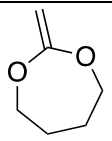
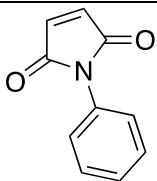
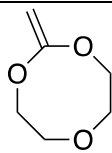
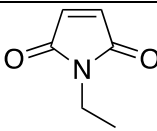
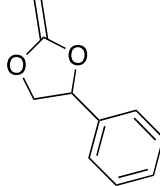
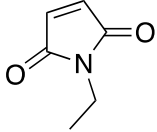
Table 6. Summary of the various CKA vinyl monomer pair.

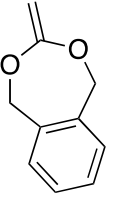
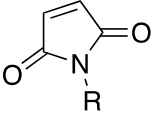
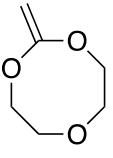
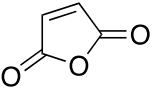
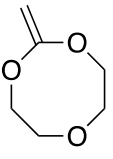
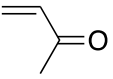
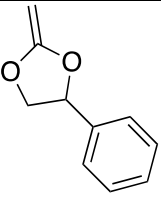

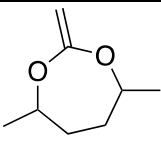

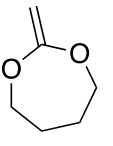

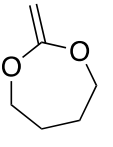
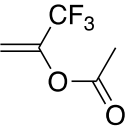
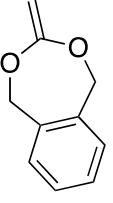
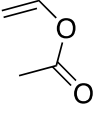
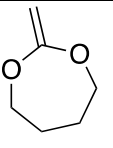
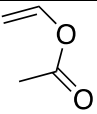
CKA	Co-monomer	Conditions	References
		FRP FRP FRP	[218] [219] [207]
		ATRP	[220]
		FRP	[221]
		ATRP	[222]
		FRP	[211]

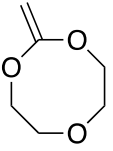
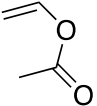
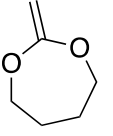
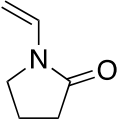
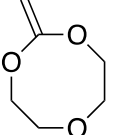
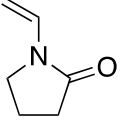
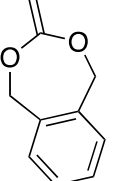
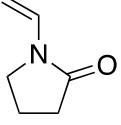
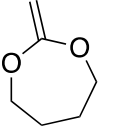
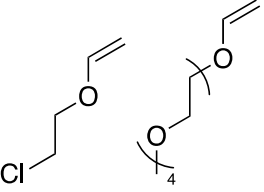
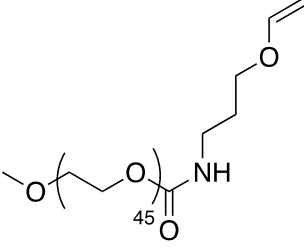
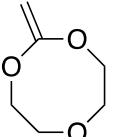
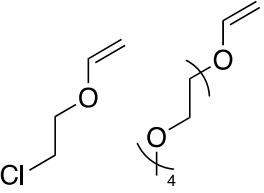
		RAFT	[223]
		FRP	[224]
		ATRP	[222]
		ATRP	[225]
		FRP	[226]
		FRP	[226]
		FRP	[227]

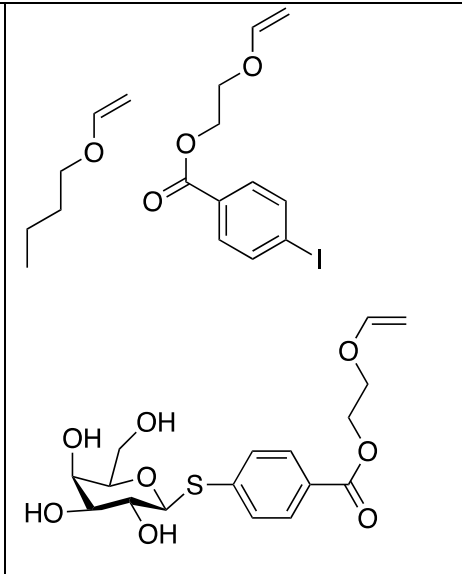
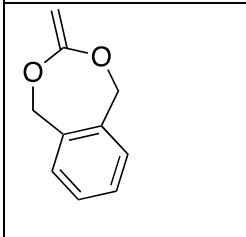
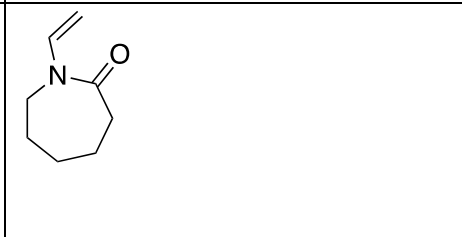
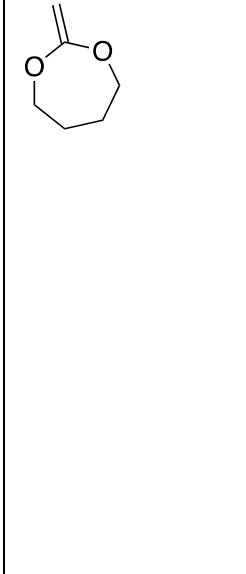
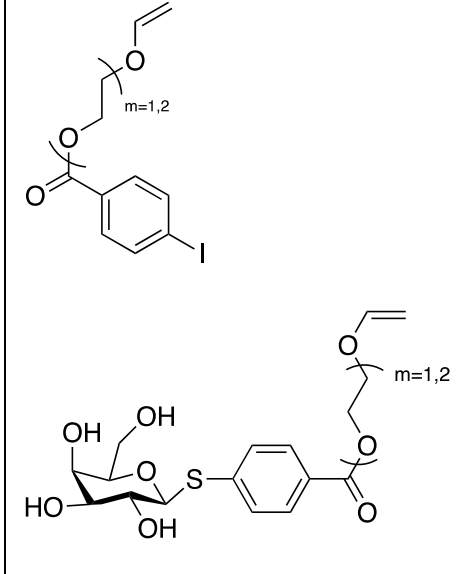
		FRP	[215, 228]
		FRP	[228]
		FRP UV irradiation	[229] [230]
		FRP	[231]
		RAFT/ATRP FRP	[232] [233]
		NMP FRP	[234] [235]
		FRP FRP FRP	[236] [237] [238]
		ATRP	[239]

		FRP	[221]
		FRP	[240]
		ATRP	[241]
		FRP	[242]
		FRP	[243]
		FRP	[244]
		RAFT	[245]
		FRP	[246]
		RAFT	[245]
		FRP	[214]

		RAFT	[247]
		FRP RAFT	[158]
	 PEG RF = C ₆ F ₁₃ or CH ₂ C ₂ F ₅	ATRP (Ru)	[216]
		FRP	[217]
		FRP	[248]
		RAFT	[46]
		RAFT	[249]

	 $R = \text{Et} \quad \text{Benz}$ $\text{C}_6\text{H}_5 \quad (\text{EG})_3$	FRP RAFT	[250]
		FRP	[251]
		FRP	[252]
		FRP	[253]
		ATRP	[222]
		CMRP RAFT	[254] [255]
		FRP	[256]
		RAFT	[257]
		FRP FRP FRP	[258] [259] [208]

		FRP	[221]
		FRP	[260]
		FRP semi-batch FRP	[261] [262]
		FRP semi-batch	[261]
	 	FRP	[263, 264] [264]
		FRP	[46]

			
		RAFT	[265]
		FRP	[266]

The differences in the incorporation of monomers into the copolymer can be explained by differences in reactivity, which can be quantified by determining the reactivity ratios of the vinyl monomer - CKA pair (r_{vinyl} and r_{CKA} the reactivity ratios of vinyl monomer and CKA respectively). In order to obtain materials with homogeneous degradation properties, vinyl monomer - CKA couples with the closest reactivity ratios are preferred to avoid compositional

drift and non-uniform introduction of the different repeating units (and in particular CKA) into the polymer backbone. Literature data[189] show that conventional vinyl monomers (styrene, acrylates, methacrylates, etc.) have higher reactivity ratios than CKAs. It is therefore very important to elucidate the reason of these differences to develop more homogeneous copolymerization systems. Due to the various methods that can be used to determine reactivity ratios, heterogenous data were consequently obtained for monomer pairs that are rather similar. Van Herk[267] reevaluated some of the reactivity ratios determined in the literature with the nonlinear least-squares method, taking into account the error in the ^1H NMR measurements of monomer fractions in copolymers and showed that that reactivity ratios of CKA/vinyl monomers follow a family-like behavior. Secondly, the analyses of polymer microstructures to determine the ratio of the various comonomers into the backbone could be not straightforward and led to some errors. Van Herk and Thoniyot[207] for example revisited the copolymerization and Styrene and MDO and showed that the signals attributed to the ester moiety is strongly dependent of the triads present in the copolymer (Fig. 36), explaining some discrepancies in the literature.

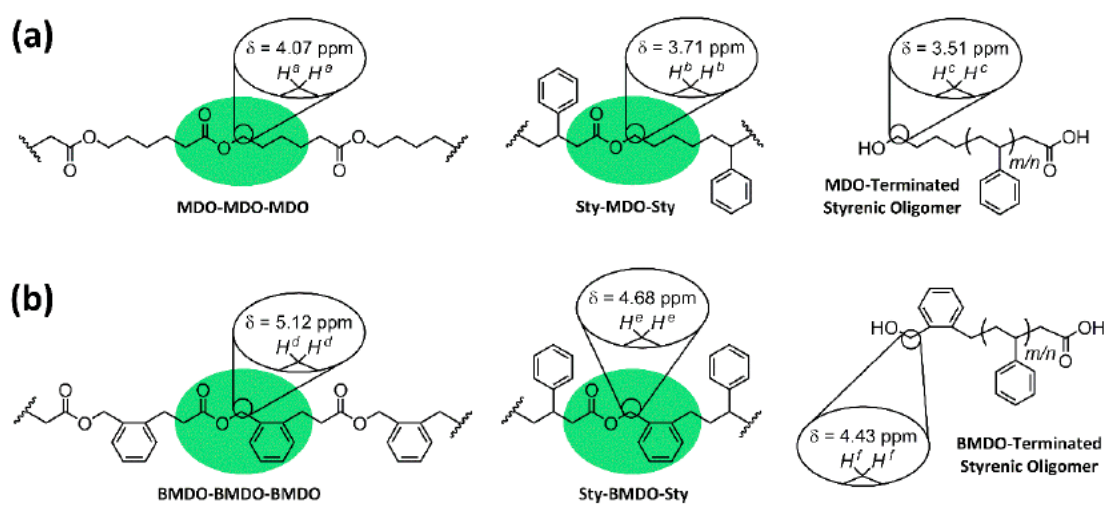


Fig. 36. Key protons utilized for ^1H NMR (CDCl_3) characterization of poly(CKA-co-styrene) copolymers and degraded styrenic oligomers within (a) poly(MDO-co-styrene) copolymers and (b) poly(BMDO-co-styrene) copolymers. Reprint from Ref. [207] with permission.

Using DFT calculations,[256] it was shown that the difference in reactivity between CKAs and common vinyl monomers was not due to the highly nucleophilic nature of CKAs but was mainly due to a very low addition of CKA to itself compared to other additions. Therefore, a vinyl monomer with similar reactivity must be used if a statistical incorporation of both monomers into the polymer backbone is desired. This led to the use of vinyl ether monomers which theoretically and experimentally provided reactivity ratios close to 1 for both monomers.[263] Several authors also showed that copolymerization with maleimide derivatives[249, 250] provided degradable alternating copolymers which can be functionalized using a functional maleimide.[250] Based on DFT calculations, trifluoromethylvinyl acetate was also tested with success to prepare alternating copolymers with CKA.[256]

To improve the homogeneity of monomer (vinyl and CKA) incorporation in the case of very different reactivity ratios, Van Herk *et al.*[63] used a semi-continuous synthesis process by slowly adding a portion of the acrylate derivative to an initial MDO/Acrylate mixture. This process eliminated compositional drift, increased the conversion of MDO (and thus limited its waste) and as a result improved the biodegradability of the synthesized polyacrylate chains (obtaining a better degradation rate and improving the homogeneity of the degraded oligomers). The same authors[268] also investigated the use of a terpolymerization system comprising one CKA and two vinyl monomers to mimic more realistic industrial recipes.

The homopolymerization and copolymerization was also widely performed using RDRP methods.[269]. Nicolas and Guillaneuf focused mainly on the compatibility between rROP and NMP[270-274] whereas Jackson and coworkers[275-277] used RAFT polymerization for macromolecular engineering.

In addition to cyclic ketene acetals, few authors were interested in cyclic ketene hemiacetal ester monomers that contain an extra carbonyl group. Kohsaka et coll.[278] prepared the 2-methylene-4H-benzo[d][1,3]dioxin-4-one (MBDO) that is produced easily from aspirin in two steps (Fig. 37a). This structure is not supposed to ring-open since only a phenyl-type radical will be produced. Both homopolymerization and copolymerization with vinyl acetate were reported and showed the production of polymers with the ring-retained structure. Surprisingly, the produced polymers were hydrolyzed in acidic conditions. The analysis of the degradation products revealed the presence of acetic acid and salicylic acid, which are the components of MBDO. The authors hypothesized that the polymers may be recyclable even if there was no evidence for it.[278]

Goto *et al.*[279] thus prepared the 4,4-dimethyl-2-methylene-1,3-dioxolan-5-one (DMDL) and the 5-methyl-2-methylene-5-phenyl-1,3-dioxolan-4-one (PhDL) (Fig. 37b). After a ring-opening, a tertiary radical with an ester group should be generated, that favors this reaction over the ring-retaining one. Unexpectedly, the DMDL polymerized well at 70°C but led to a polymer backbone with exclusively the ring-retaining unit. The PhDL did not lead to polymers whatever the reaction temperature. The copolymerization with various vinyl monomers was then carried out and led to copolymers in all cases. The reactivity of DMDL was nevertheless similar to the one of CKA: CKHE reactivity lower than the one of vinyl monomers with $r_{\text{vinyl}} = 1 - 5$ and $r_{\text{CKHE}} = 0 - 0.3$. Various modes of degradation were tested. In presence of NaOH, the polymer degraded rapidly and produced only one side-product that is 2-hydroxyisobutyric

acid (HIBA). Goto and coworkers[279] proposed a degradation mechanism that is represented in Fig. 37c.

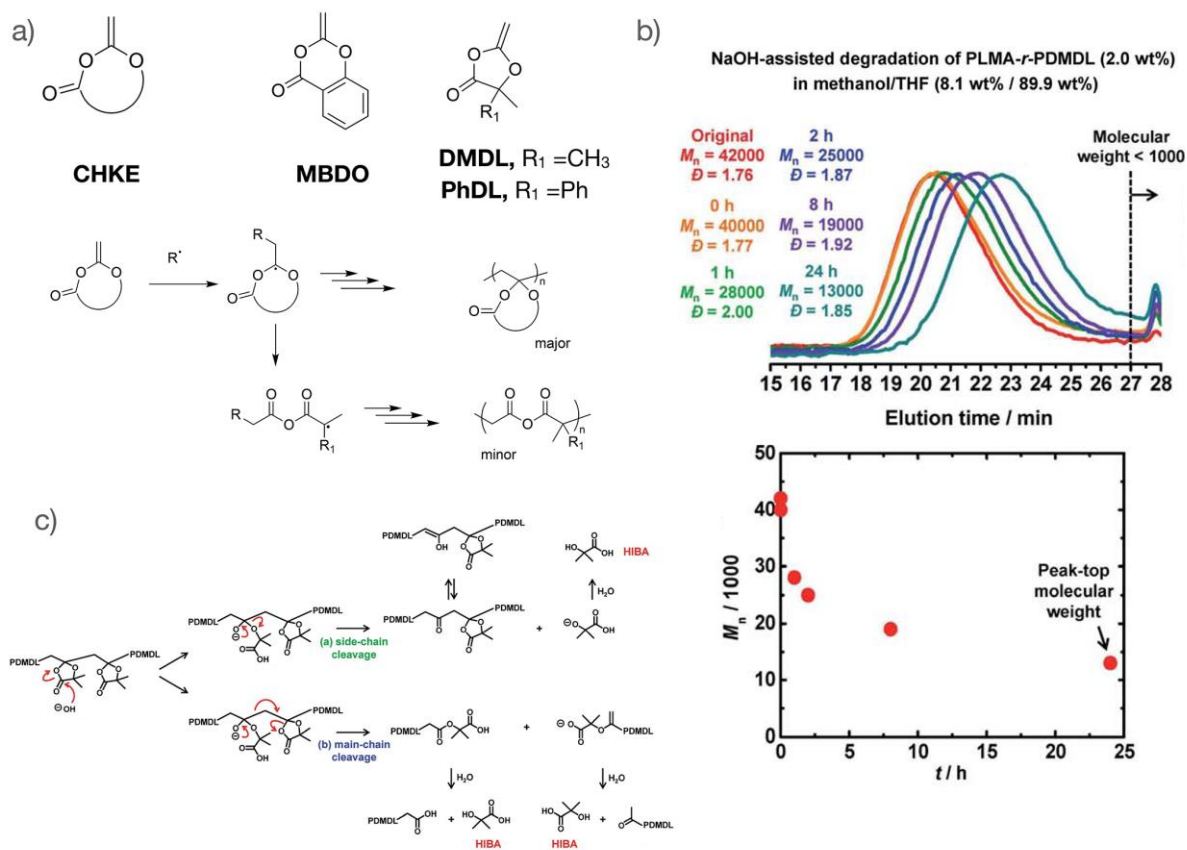


Fig. 37. a) Structures of the CKHE monomers and the corresponding polymers. b) Degradation of PLMA-*r*-PDMDL ($M_n = 42\,000\text{ g}\cdot\text{mol}^{-1}$, $\bar{D} = 1.76$, and $F_{\text{DMDL}} = 16\%$) (1.8 wt%) with 3.5 equiv. of KOH in a mixture of methanol (8.1 wt%) and THF (89.9 wt%) at room temperature; c) supposed mechanism of degradation. Adapted from Ref [279] with permission.

In acidic conditions, the degradation was only partial but also led to HIBA as a side-product. Aminolysis with pentylamine at 65°C was also tested and the homopolymer PDMDL was totally cleaved in 60h. The KOH degradation of poly(lauryl methacrylate) containing DMDL was then monitored in MeOH/THF (Fig. 37b) and a two third decrease of M_n was observed

confirming the interest of CKHE copolymerization for imparting degradation of vinyl monomers.[279]

3.2.4.2 Sulfide Cyclic Methacrylate

In 1994, Rizzardo and co-workers developed a new class of cyclic monomers, namely sulfide cyclic methacrylates also called macrocyclic allyl sulfide.[280-282] The synthesis of these compounds is carried out in several steps, usually starting from 2-bromomethyl acrylic acid and a mercapto alcohol to lead to the functionalized α -carboxy- ω -hydroxy compound. The monomer is then obtained by intramolecular esterification under very dilute conditions (Fig. 38a). An alternative route that allows for the introduction of a phenyl group at α of the double bond involves coupling of benzaldehyde with methyl acrylate via the Morita-Baylis-Hillman reaction.[283] After protecting the hydroxyl group with acetic anhydride, this intermediate can react with the mercaptoester to give a thioether. The α,ω -ester compound is finally cyclized in the presence of diols.

Due to the high lability of the C-S bond, β -scission is favored and leads to the formation of a C=C bond and a thiyl propagating radical. Sulfide cyclic methacrylate monomers were mainly polymerized by a radical ring-opening process but Huang and coworkers [284] showed its interest in anionic polymerization using a thio-Michael reaction. Many monomers have been prepared and their structures are shown in Figure 38b. The first work focused on the **SCM1-SCM4** structures.[280, 281]

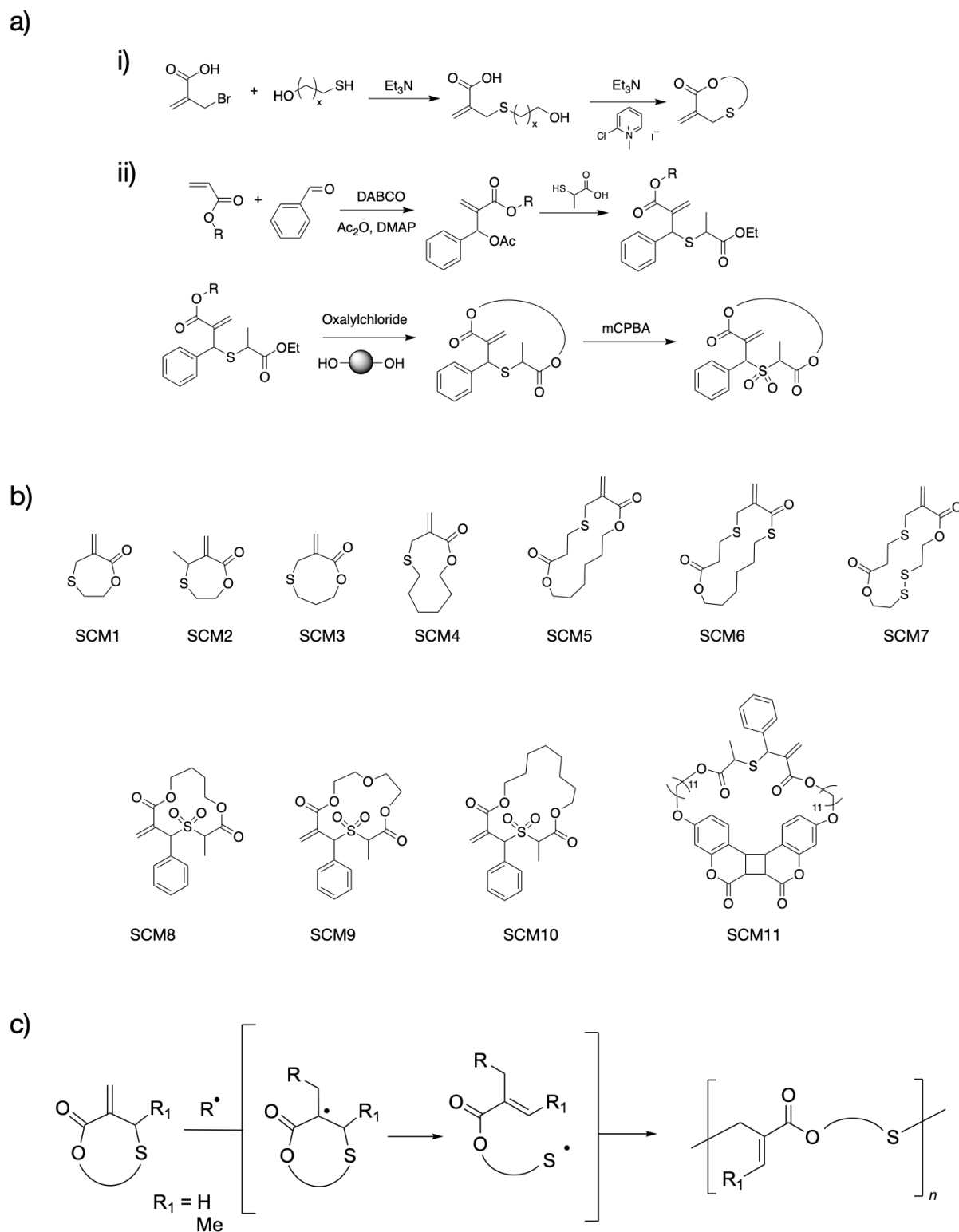


Fig. 38. a) Synthesis of SCM monomers without (i) alkyl groups or with a phenyl group (ii) in alpha position to the double bond. b) Structures of the various SCM monomers c) Mechanism of the rROP of SCM monomers.

These molecules have a high reactivity both in homopolymerization (about 80% conversion in 3h at 70°C) and in copolymerization (quantitative insertion with MMA) but crosslinking was observed for the compound **SCM1** after 20% conversion during homopolymerization.[280] However, this problem was not observed with the compound **SCM2** because the methyl group on the double bond formed after ring-opening prevents radical addition.[280] The polymerization mechanism of sulfurized cyclic methacrylate monomers is described in Figure 45c. Unlike the other types of monomers polymerizing by ring-opening, the propagation is done by a thiyl radical. The study of the polymerization mechanism showed a slight influence of the ring size on the reactivity of the monomer with a slightly higher polymerization rate in the case of large ring size and a decrease in the crosslinking rate with increasing ring size.[285] The first studies showed that these monomers led to copolymers with methacrylate derivatives. In particular, the insertion of SCM monomers into poly(methacrylate) backbones are of the random (or statistical) type, showing close reactivity ratios. Copolymerization with styrene is also possible but with a lower reactivity of the SCM monomer with respect to styrene leading to limited chain degradation.

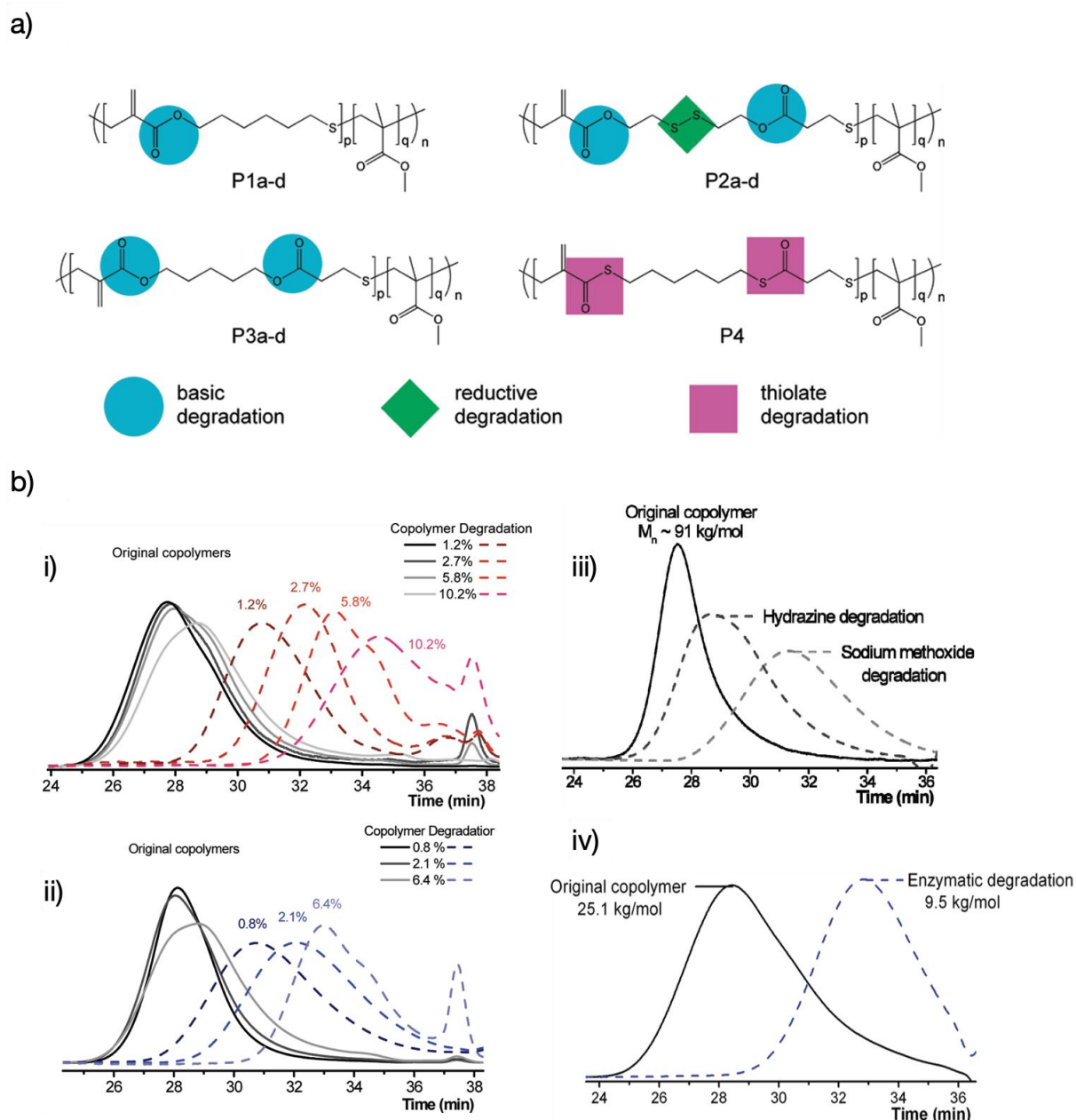


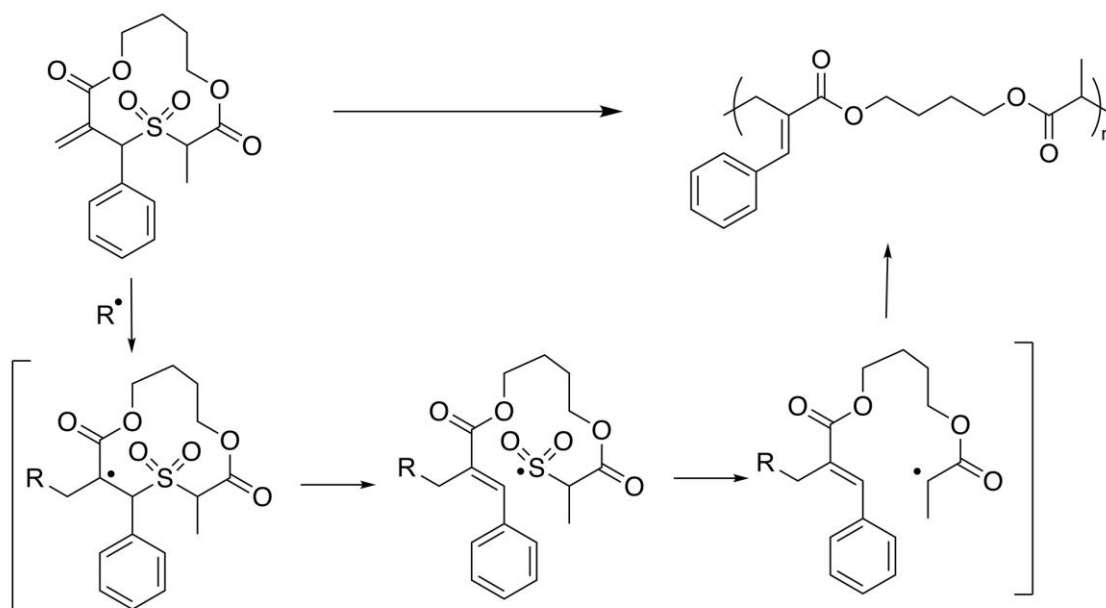
Fig. 39. a) Copolymers based on MMA and cyclic monomers **SCM4** – **SCM7**, respectively, and degradation conditions for specific cyclic allylic monomers. b) SEC traces of copolymers (i) derived from MMA/**SCM4**; (ii) derived from MMA/**SCM7** and their corresponding degradation products (dashed lines). Percentage values indicate molar % of SCM monomer in polymer. (iii) SEC traces of mixed copolymer P(MMA-*co*-**SCM5**-*co*-**SCM7**) and its products after stepwise degradation; (iv) SEC traces of copolymer P(DMAEMA-*co*-**SCM7**) before and after enzymatic degradation. Adapted from Ref. [286] with permission.

Hawker and co-workers[286] then continued this work and extended the study to cyclic monomers with ester, thioester and disulfide functionalities in the side chain (Fig. 39). By copolymerizing in different proportions the **SCM5-SCM7** monomers with methacrylic monomers (methyl methacrylate, 2-hydroxyethyl methacrylate and 2-dimethylaminoethyl methacrylate), copolymers with different degradation modes have been obtained: degradation under alkaline conditions, reductive degradation of the disulfide bond (in the presence of hydrazine or tributylphosphine) or degradation of the thioester groups with sodium thiomethoxide.

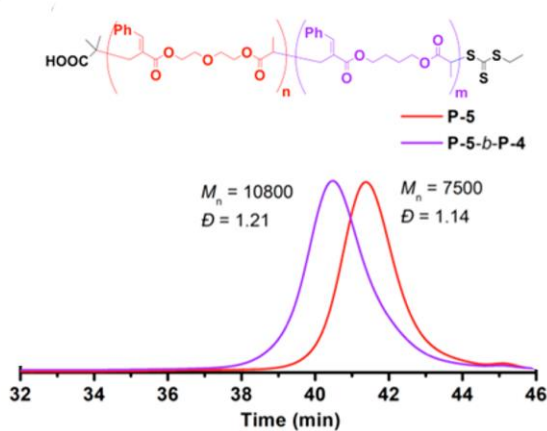
This family has finally seen new advances with the work of Niu *et al.*[283] who oxidized the thioether to a sulfone and modified the side alkyl moiety (**SCM8-SCM10**). In particular, a phenyl moiety is introduced at α of the double bond to avoid crosslinking. In this way, during the ring-opening reaction, a radical cascade can take place, with the formed radical undergoing a SO_2 removal reaction, leading to a stabilized acrylate-type alkyl radical. Since propagation is via an acrylate-type radical (Fig. 40), it then becomes possible to control the polymerization by reversible deactivation polymerization (RDRP). Block copolymer with different MCS was possible (Fig. 40b) as well as its copolymerization with methyl acrylate that led to fast and efficient degradation of this vinyl polymer via the treatment with sodium methoxide (Fig. 40c). A more detailed investigation of the copolymerization of **SCM8** with acrylate highlighted the faster rate of incorporation of SCM compared to acrylates that led to a non-ideal incorporation of the weak bonds into the polymer backbone. To circumvent this drawback, Niu *et al.*[287] showed that reactivity ratios are more favorable at room temperature by carrying out the polymerization using the PET-RAFT photoRDRP process. Using fac-Ir(ppy)_3 as photocatalyst and a trithiocarbonate, they managed to prepare various acrylate and acrylamides derivatives with reactivity ratios close to 1, that thus led to oligomers with a lower M_n and narrower D than

the same recipe polymerized at 70 °C.[287] The same authors[288] also extended this study to styrene and methacrylate derivatives. In this case, reactivity ratios with styrene ($r_{SCM} = 3.02$ and $r_S = 0.35$) or methyl methacrylate ($r_{SCM} = 0.18$ and $r_{MMA} = 5.81$) were determined and this led to the preparation of a wide library of degradable vinyl copolymers that requires various amount of SCM to obtain a good degradation profile and that exhibited tunable thermal properties also correlated with the incorporation of the degradable ester moiety.

a)



b)



c)

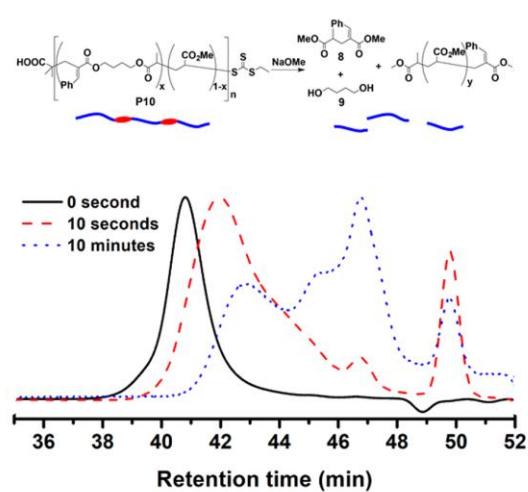


Fig. 40. a) Mechanism of radical cascade triggered ring opening polymerization. b) Preparation of block copolymer **SCM9-*b*-SCM8** by RAFT polymerization. c) Copolymer poly(methyl acrylate -*co* - **SCM8**) and its degradation using sodium methoxide. Adapted from Ref. [283] with permission.

Recently, Frisch et al. used the **SCM8** template that was proposed by Niu[283] to prepare other SCM of interest. They first prepared[289] the structure **SCM11** which has a photolabile moiety coming from the [2+2] photocycloaddition of coumarin derivatives. After polymerization, the polymers can undergo photocycloreversion of coumarin dimers upon UV irradiation, causing polymer degradation within minutes under UVB light or days under sunlight exposure. These polymers should be seen as materials with programming degradability. They then prepared[290] the structure **SCM12** that contains a peptide sequence (Fig. 41), allowing to embedded peptides into a polymer backbone and not only tethering onto the side chain. The SCM method was then totally compatible with the twenty amino acids and deprotection of the peptides was realized without side reaction. Such approach could lead to even more programmed degradability.

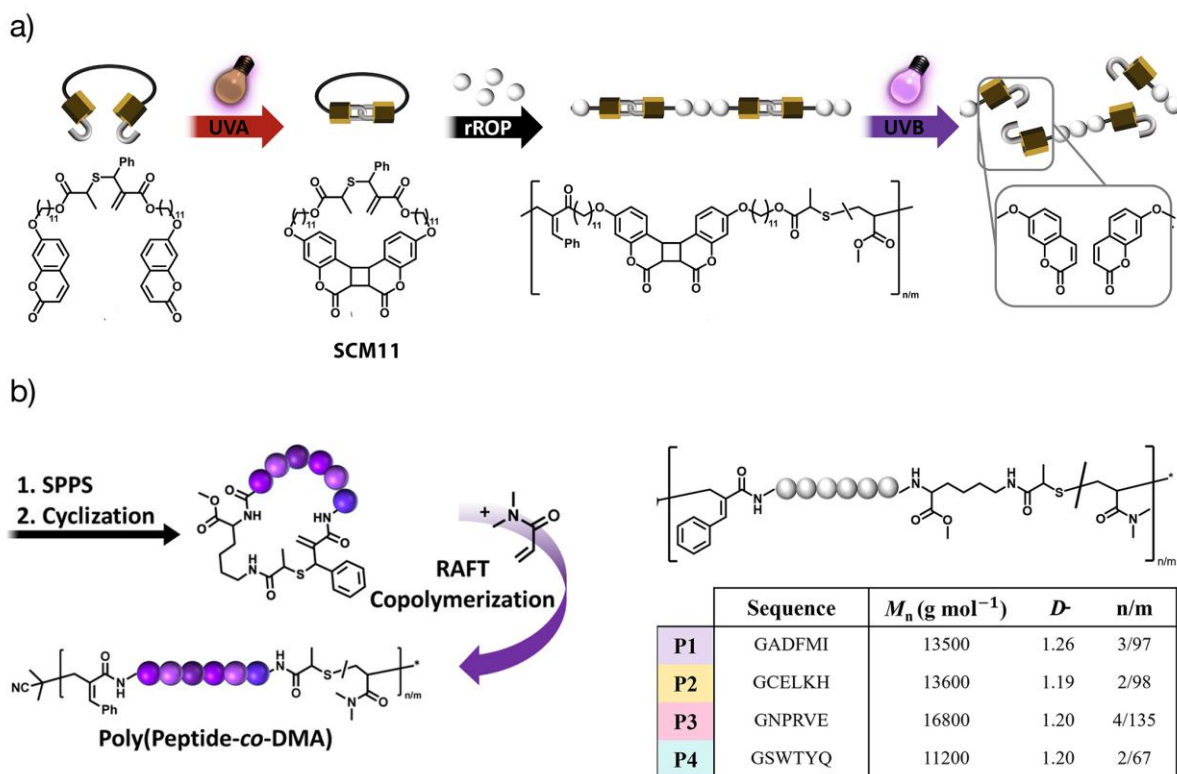


Fig. 41. a) Schematic representation of photodegradable polymer synthesis and its photodegradation: UVA irradiation of allylic sulfide C2 initiates intramolecular [2+2] photocycloaddition of terminal coumarin end groups yielding cyclic allylic sulfide **SCM12**; the radical ring-opening copolymerization between **SCM12** and a vinylic monomer results in the incorporation of coumarin dimers into the main chain of the resulting polymer P1; UVB light exposure initiates the cycloreversion of the imbedded coumarin dimer causing polymer degradation. b) Preparation of embedding peptides into synthetic polymers via rROP of SCM monomers. Adapted from Refs [289, 290] with permission.

Lastly, Niu and coworkers[291] combined a ring-closing and a ring-opening reaction in a cascade process to prepare new degradable materials. This work is based on 1,6-diene-fused allylic sulfide or sulfone that could undergo radical cyclopolymerization (favored by the Torpe-Ingold effect brought by the tosyl group on the nitrogen atom) that is coupled with the generation of radical via the rapid β -elimination of the alkylsulfony radical. After α -scission of

SO₂, a stable ethyl-2-propionate radical is produced that could propagate via addition of new monomers (Fig. 42). Huang et al.[292] extend this work by varying the nature of the linker that is inserted between the tosyl group and the 1,6-diene-fused allylic sulfide. The same author also showed that the homopolymerization of 1,6-diene-fused allylic sulfide monomers could be combined with the RAFT process provided isocyanide compounds (0.8 equiv.) were added.[293] Indeed, the macrothiyl radical isocyanide could be desulfurized *in-situ* to generate the corresponding radical allowing the control of the polymerization.

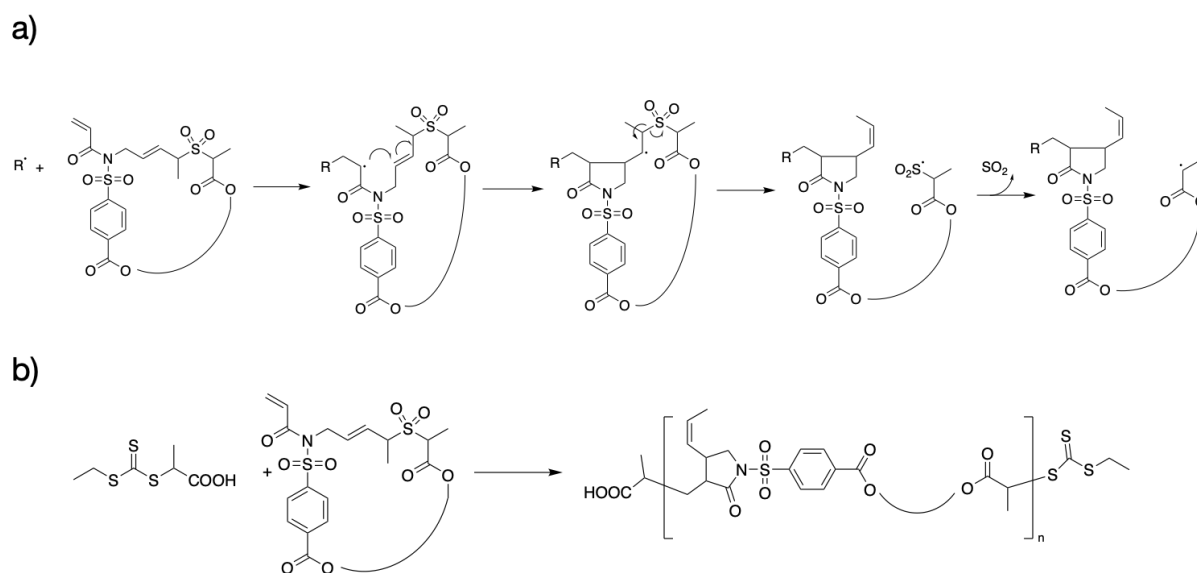


Fig. 42. a) Mechanism of the radical ring-closing/ring-opening polymerization. b) Preparation of degradable materials via the combination of radical ring-closing/ring-opening polymerization and RAFT.

3.2.4.3 Thionolactone

As presented in the previous section, cyclic ketene acetals have been widely used to introduce cleavable functions into the backbone of many polymers produced by radical polymerization. The main limitations of this polymerization process are related to the specific reactivity of

CKAs compared to common vinyl monomers and their sensitivity to hydrolysis. In order to overcome these limitations, Roth[294] and Gutekunst[295] presented at the same time the thionolactones as a new family of interest for rROP. Indeed, it is known that the C=S double bond is one of the most efficient functions to accept radicals (analogy with RAFT-type polymerization). In particular, Rizzardo *et al.*[296] have shown that thionoesters are very good transfer agents and allow the insertion of a thioester functionality at the end of the polymer chain. The first structure of thionolactone monomer is therefore based on a cyclic structure similar to these transfer agents. After addition of a radical on the thionoester function (C=S)-O (yellow coloration), a fragmentation reaction leads to the creation of a thioester function (C=O)-S (colorless) in the polymer backbone (Fig. 43).

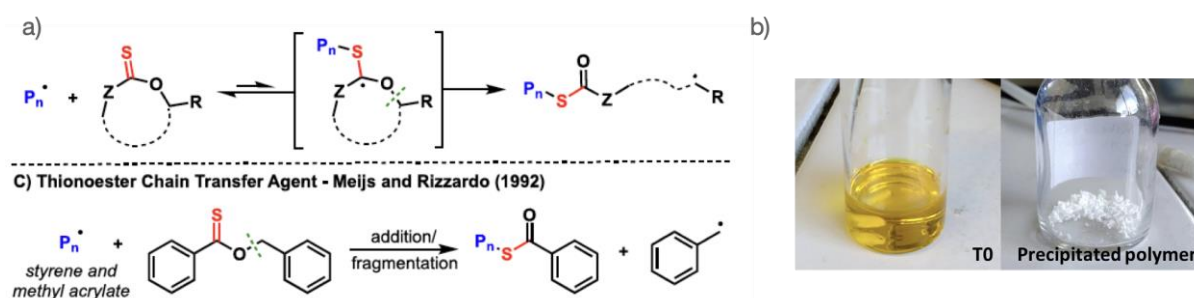


Fig. 43. a) Radical ring-opening polymerization of thionolactone derivatives. b) isomerization of the C=S bond during the polymerization and discoloration of the reaction medium. c) Thionoester as chain transfer agent. Adapted from Refs. [295, 297] with permission.

Thionolactones are prepared by thionation of the corresponding lactones. The operating conditions generally use Lawesson's reagent[294, 295] but efficient thionation from P_4S_{10} and hexamethyldisiloxane (HMDSO) has also been reported.[298] Fig. 44 illustrates the synthesis of thionolactone with the synthesis of dibenzo-[c,e]oxepin-5(7H)-thione (DOT), which is the

most widely used thionolactone in the literature. This topic has been reviewed recently.[299, 300]

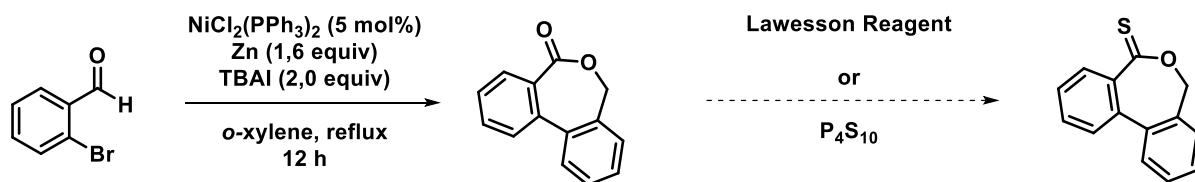
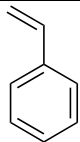

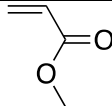
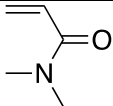
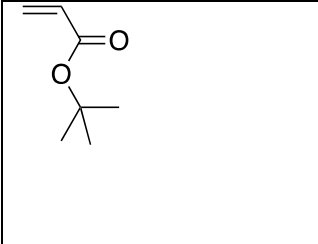
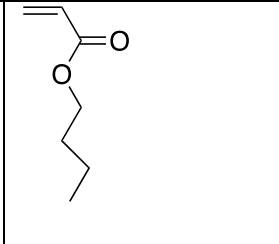
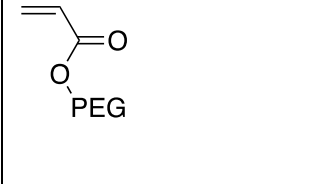
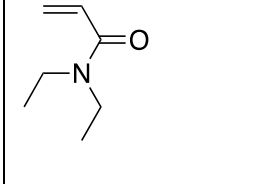
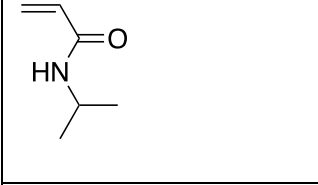
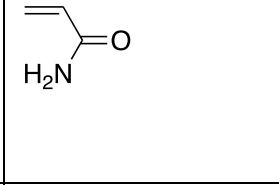
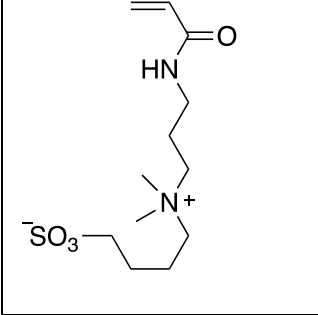
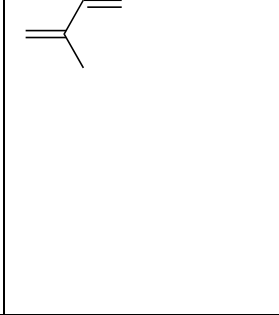
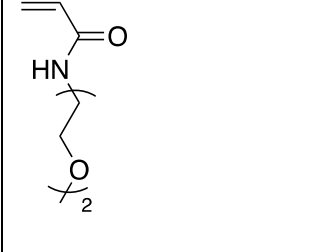
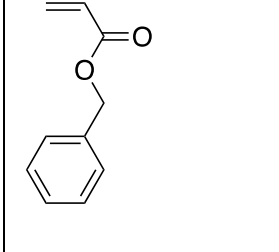
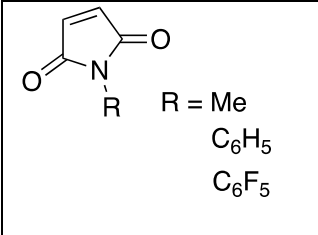


Fig. 44. Synthesis of dibenzo-[c,e]oxepin-5(7H)-thione (**DOT**).

In the first studies on thionolactones,[294] dibenzo[c,e]-oxepane-5-thione (**DOT**) was the only thionolactone among a library of six structures that was found to copolymerize efficiently with mainly acrylate and acrylamide-type derivatives and produced a copolymer with a thioester unit inserted into the backbone. It should be noted that DOT has a faster incorporation rate than acrylate monomers during polymerization, which can lead to compositional drift during polymerizations.[295] The different vinyl monomers that copolymerize with DOT are reported in Table 7.

Table 7. Summary of the various DOT - vinyl monomer pair.

Vinyl monomer	References	Vinyl monomer	References
	[297, 301-304]		[294, 305]
	[294, 306]		[294, 305]

	[295]		[52, 295, 302-304, 306]
	[294, 305-307]		[305]
	[305]		[305]
	[305]		[308]
	[307]		[306]
	[309]		

In their seminal report, Roth *et al.*[294] reported the efficient copolymerization of DOT with methyl acrylate, (oligoethylene glycol)acrylate, acrylonitrile, and *N,N*-dimethylacrylamide. Gutekunst[295] showed similar results that are an efficient copolymerization with tert-butyl acrylate and n-butyl acrylate. DOT was found to inhibit radical polymerizations of vinyl acetate

and *N*-vinylcarbazole and to retard radical polymerizations of styrene without being incorporated.[294] Various other acrylamides such as *N,N*-diethylacrylamide, *N*-isopropylacrylamide, acrylamide, and the charged *N*-3-(*N*-4-sulfobutyl-*N,N*-dimethylammonium)propylacrylamide were also successfully copolymerized with DOT.[305] The alternating copolymerization with maleimide derivatives was also reported.[309]

Guillaneuf and coworkers[297] studied in more details the copolymerization of DOT and styrene and found that DOT was incorporated into the polymer backbone but at a lower extent than in polyacrylate derivatives. Using DFT calculations, they found that the incorporation of DOT in styrene is better at high temperature (Fig. 45) and determine the reactivity ratio to be $r_S = 0.55$ and $r_{DOT} = 1.68$ at 150 °C.[297] High molecular weight polystyrene could be obtained without modifying the mechanical properties but showing good degradation profile.

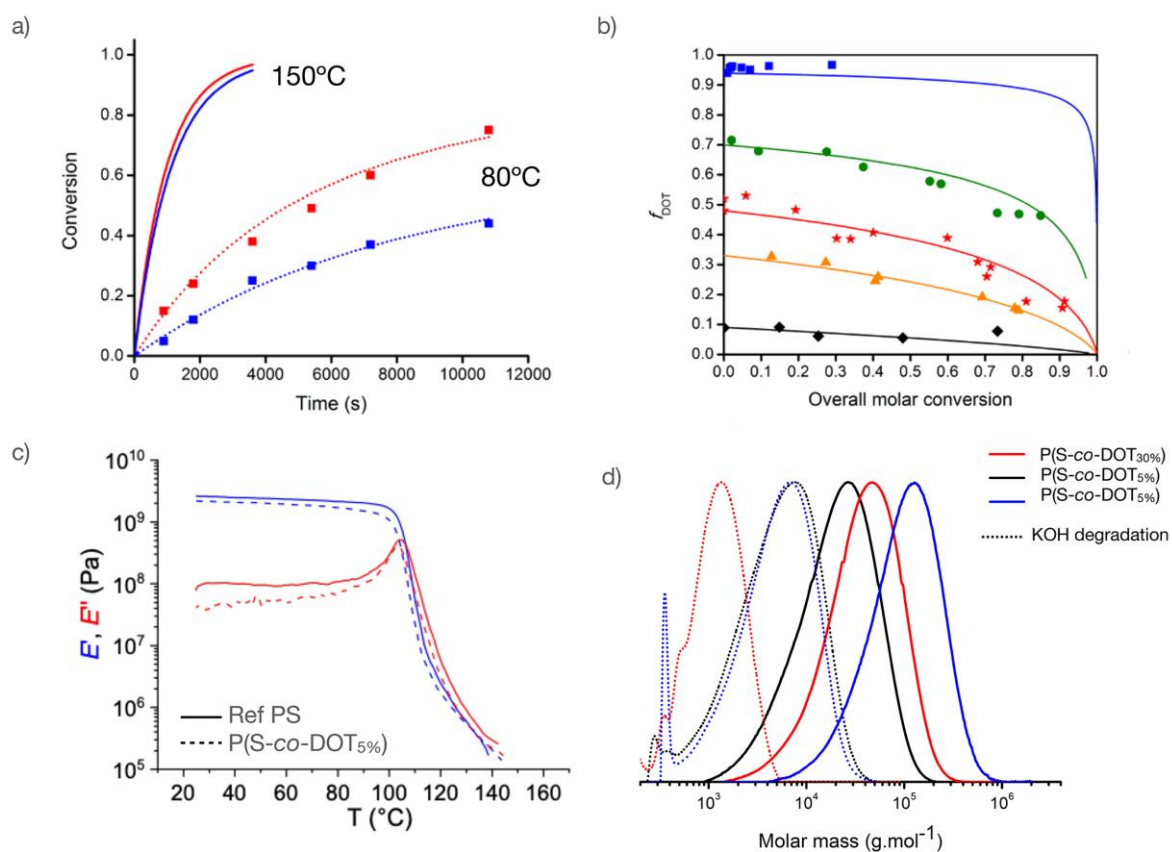


Fig. 45. a) Kinetic plot of the experimental copolymerization of styrene (red squares) and DOT (blue squares) at 80 °C in the presence of anisole (10 mol %) with the feed ratio of $[\text{styrene}]_0/[\text{DOT}]_0 = 95:5$. The dashed lines are the PREDICI fits using $r_S = 2.0$, $r_{\text{DOT}} = 0.36$, and $k_{p,\text{DOT}} = 30 \text{ L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$. The solid lines are the corresponding PREDICI simulations at 150 °C, assuming that the kinetic parameters follow a pseudo-Arrhenius behavior and E_a values are determined by DFT calculations. b) Experimental and theoretical DOT monomer composition versus overall molar conversion with $r_S = 0.55$ and $r_{\text{DOT}} = 1.68$ during the bulk copolymerization of DOT and styrene at 150 °C initiated with 1 mol % of Trigonox 301. c) DMA analysis of Reference PS (solid lines) and P(S-*co*-DOT_{5%}) (dashed lines) at 1 Hz and a heat rate of 3 °C min⁻¹. d) Evolution of the molar mass distribution of the P(S-*co*- DOT) after the degradation process (KOH of 5 wt % in THF/MeOH during 18 h). Reprinted from Ref. [297] with permission.

Similar results were also obtained by Johnson *et al.*[301] that also showed that the incorporation of DOT is solvent dependent. The same authors also prepare DOT derivatives that allow a better solubility of the thionolactone monomer.[301] DOT was also copolymerized with isoprene with reactivity ratios of $r_{\text{DOT}} = 4.29$ and $r_I = 0.14$, confirming preferential incorporation of DOT in comparison to isoprene.[308] The preliminary studies of Roth[294] and Gutekunst[295] combined thionolactone and RAFT polymerization. Later, Guillaneuf[297] and Johnson[301] showed that DOT copolymerization is also compatible with NMP. Roth tried to combine ATRP and DOT.[306] He observed a very efficient degradation of DOT to the lactone derivative due to Cu(I)-catalyzed dethionation. This impedes the use of DOT at concentration higher than 15 mol% and led to the insertion of only half of the DOT

that was put in the feed. By a carefully analysis, the authors showed that the oxygen source for the dethionation was adventitious water and by performing the polymerization in complete anhydrous medium, efficient ATRP of acrylate with DOT was obtained.[306]

Several authors have attempted to expand the range of structures capable of efficient polymerization via an rROP mechanism. The different structures are shown in Fig. 46.

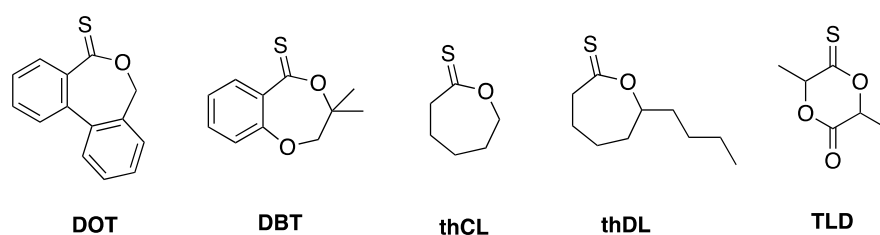


Fig. 46. Structures of the various thionolactones used in rROP.

3,3-dimethyl-2,3-dihydro-5Hbenzo[e][1,4]dioxepine-5-thione (DBT)[310] is capable of copolymerizing with styrene and methacrylate derivatives. Nevertheless, the copolymerization with styrene is not ideal with a tendency to polymerize DBT in a first step and styrene in a second step. In the case of methacrylate derivatives, the results are opposite with the incorporation of DBT only at the end of the polymerization.[310] In parallel, Satoh[311] and Destarac[312] also developed thionolactide (TLD) that copolymerized with styrene and acrylate derivatives, but with a competition of ring opening and retention mechanisms. This secondary reaction, although not leading to the desired thioester, can nevertheless under certain conditions such as treatment with AgNO_3 lead to the degradation of the polymer chain (Fig. 47). Nevertheless, these monomers are still not compatible with less activated monomers.

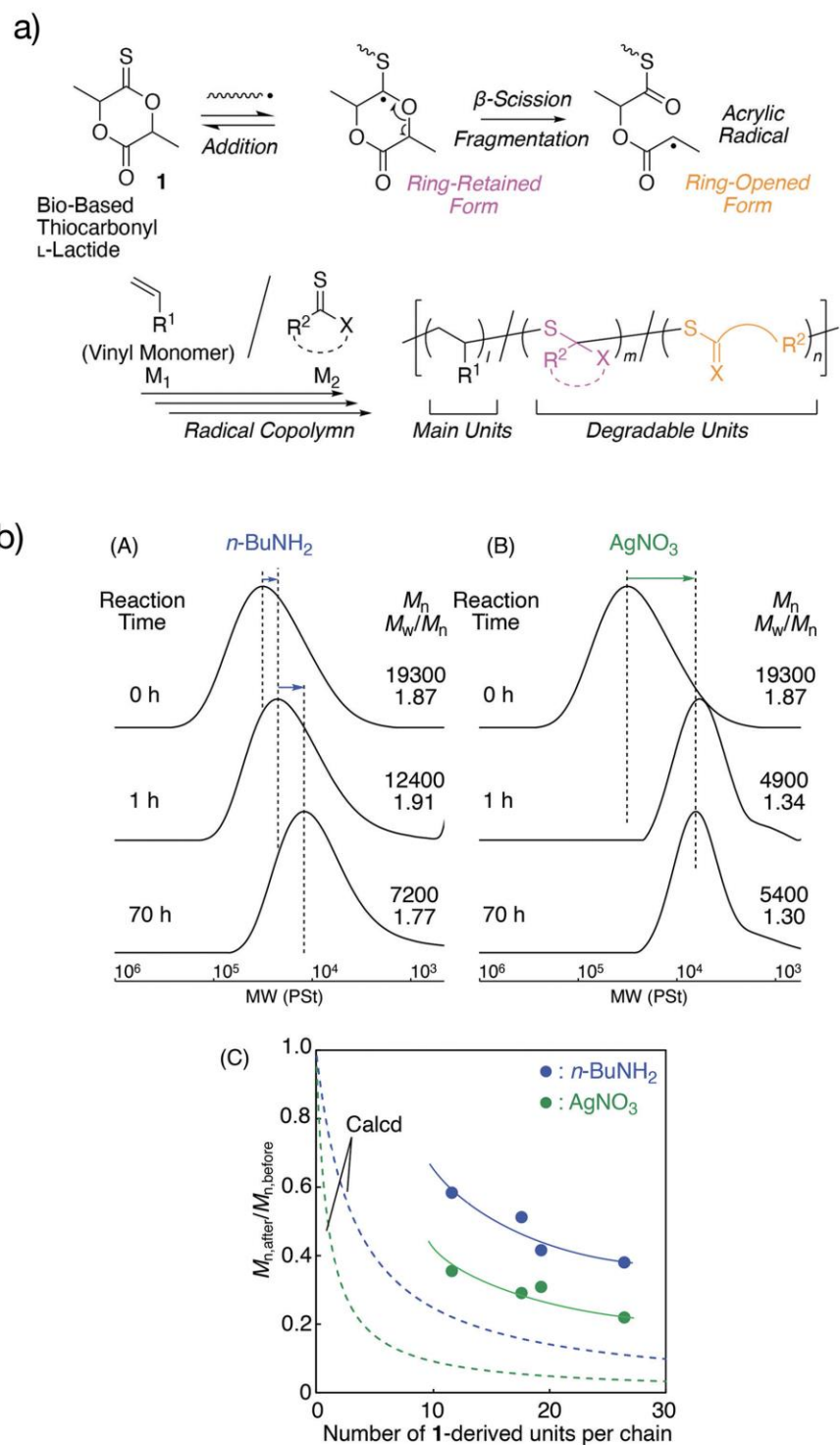


Fig. 47. a) Radical copolymerization of TLD with vinyl comonomers. b). Degradation of poly(MA-co-TDL) with $n\text{-BuNH}_2$ or AgNO_3 at 40 °C: A) SEC curves with $n\text{-BuNH}_2$; $[-\text{SC}(=\text{O})-]_0/[n\text{-BuNH}_2]_0 = 1/100$ in CHCl_3 , B) SEC curves with AgNO_3 ; $[\text{S}]_0/[\text{AgNO}_3]_0 = 1/20$ in $\text{THF}/\text{H}_2\text{O}$ (19/1), and C) $M_{n,\text{after}}/M_{n,\text{before}}$ as a function of the number of TLD-derived units

per chain. Dashed lines denote the calculated values where $M_{n,after}/M_{n,before} = 1/(1 + \text{Number of degradable units})$. Reprinted from Ref. [311] with permission.

According to the literature, the replacement of aryl groups by alkyl groups decreases the transfer constant of the RAFT agent and thus allows to control the polymerization of less activated monomers.[133] By analogy, one would expect that the preparation of a thionolactone without the presence of the phenyl group in alpha position to the C=S double bond would lead to an effective rROP monomer compatible with less activated monomers, such as vinyl ester derivatives. Based on this hypothesis, Destarac[313] and Guillaneuf[298] showed for example at the same time that it was possible to copolymerize ϵ -thionocaprolactone (thCL) and decathionolactone (thDL) with vinyl acetate and its derivatives. However, both authors observed a higher incorporation rate of thionolactones than vinyl esters, leading to a compositional drift during polymerization. In this copolymerization process, the presence of ring-retaining units was reported in case of bulk copolymerization, [313] whereas only opened units were observed when the polymerization was performed in solution.[298]

The introduction of a thioester function in the polymer backbone allows the use of different degradation modes. The simplest degradation is the accelerated basic degradation in the presence of KOH. The thioester functions are also sensitive to aminolysis at room temperature.[294, 295] This mode of degradation has been shown to be effective in the case of polyacrylates and polyacrylamides but is significantly less effective in the case of polystyrene. More drastic operating conditions (increase of concentration and temperature) have nevertheless made it possible to degrade polystyrene by aminolysis (Fig. 48a).[297, 301] Recently it has also been shown that thioester functions can also be degraded under oxidizing

conditions (bleach,[312] oxone[305]) and in the presence of thiols (cysteine, *N*-acetylcysteine, glutathione).[307]

Roth *et al.* [307] demonstrated that under mimicked intracellular conditions (PBS, 10 mM glutathione, pH 7.2), efficient degradation is effective for PEG acrylate and di(ethylene glycol) acrylamide-based copolymers at concentration lower than 1 g/L. Moreover, amphiphilic diblock copolymer micelles containing Nile Red as a model for a hydrophobic drug was shown to disintegrate upon addition of glutathione, suggesting a very promising application in drug delivery materials. To confirm this interest, the same authors investigated the cytotoxicity of the copolymers containing thioester units and their cysteinolytic degradation products. They found that both samples were nontoxic toward human pancreatic adenocarcinoma cells at concentrations up to 1 g/L. [307]

Besides classic basic KOH solution (5 wt% in THF/MeOH), and aminolysis, the use of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) at 1.25 wt % in THF as a base was shown to degrade the thioester units very quickly.[297] The kinetics of degradation was investigated using an *in situ* rheology experiment using a Couette cell and concentrated polymer solutions. The specific viscosity that is representative of the molecular weight was monitored after the TBD addition. The drop of the viscosity after few minutes confirmed the efficiency of the degradation that reached 90% in less than 20 min (Fig. 48b). Following this experiment, the same group thus prepared a photolabile TBD to trigger on demand the degradation (Fig 48c). A solution of polystyrene containing thioesters units was then mixed in THF with the photolabile base and no degradation was observed up to 120h. After irradiation (10 times 2.5 min with hand shaking between the irradiation) and 1h at room temperature, the SEC analysis confirmed the degradation. Such approach paves the way to new materials to both keep the usage material

properties of a product but in the same time could enhance the degradation after use by a selective irradiation.

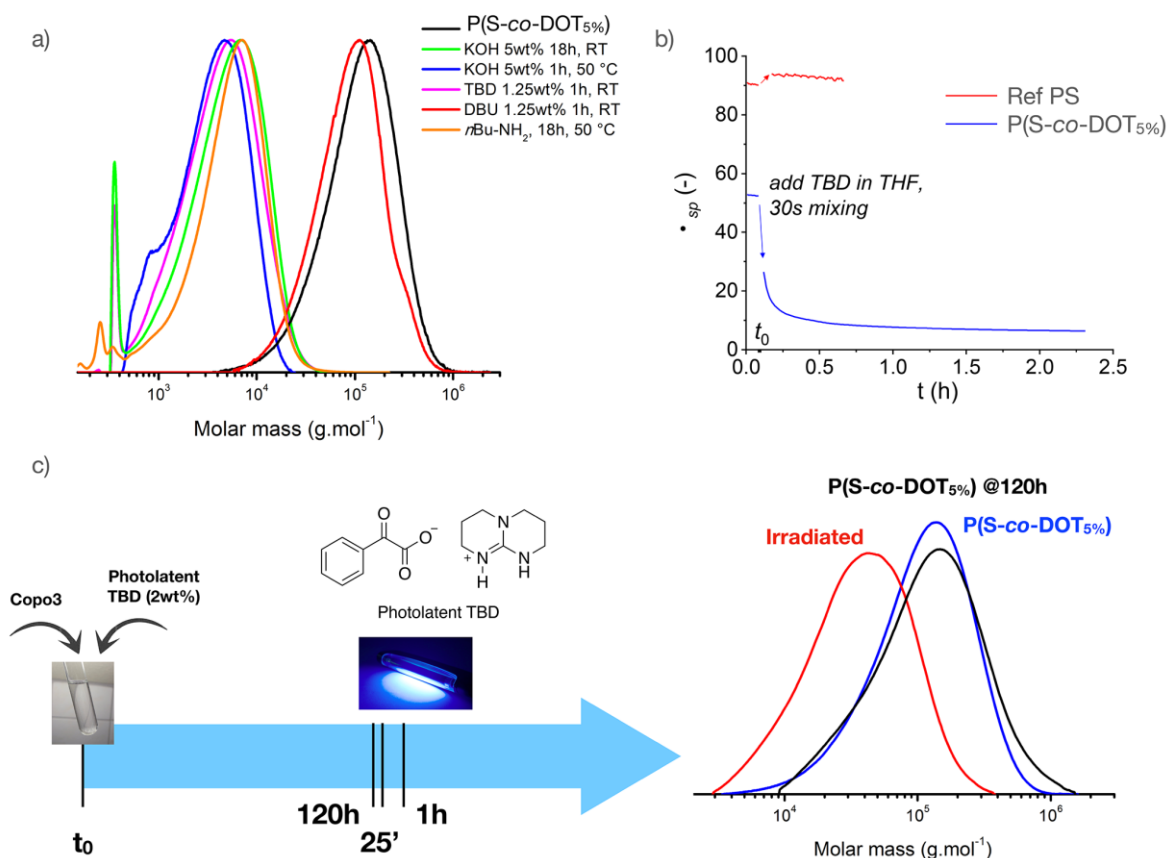


Fig. 48. a) Evolution of the molar mass distribution of P(S-co-DOT) during the degradation process: P(S-co-DOT_{5%}) before degradation (black), after 1 h of degradation at RT using DBU in THF (red), after 18 h of degradation at RT using 5 wt % KOH (green), after 1 h of degradation at 50 °C using 5 wt % KOH (blue), after 18 h of degradation at 50 °C in pure *n*Bu-NH₂ (orange), and after 1 h of degradation using TBD at RT in THF (purple). b) Evolution of specific viscosity of solutions of Reference PS and P(S-co-DOT_{5%}) in THF (20 wt %) upon addition of concentrated TBD solution in THF leading to an overall TBD concentration of 1.25 wt%. c) Evolution of the molar mass distribution of P(S-co-DOT_{5%}) in THF (blue) after mixing with photolent TBD (2 wt %) during 120 h at RT (black) and after 10 times of 2.5 min of irradiation and 1 h of reaction (red). Reprinted from Ref. [297] with permission.

Since some studies showed that the ring-retaining products could induce some degradation via the production of a thioacetal linkage, Kamigaito and coworkers[314] developed thioamides as a new comonomer family (Fig. 49). The direct radical addition onto the C=S bond during the copolymerization of thioamide with common vinyl monomer led to the incorporation of a thioaminal linkage onto the polymer backbone. Thioformamide (AcMeThiFA) was shown to be compatible with many comonomers even if the amount of inserted thioester functionality is dependant of the vinyl monomer structure (VAc > Acrylate-Acrylamides > Styrene). The addition of a RAFT agent allowed to control of the copolymerization of AcMeThiFA with vinyl monomers. Higher T_g s than the pristine vinyl polymers were measured, likely due to the presence of highly polar pendant amide groups. Degradation was then achieved by simple AgNO₃ treatment at RT (Fig. 49). This first study then showed promises for this new monomer family to impart degradability into vinyl polymer backbone.

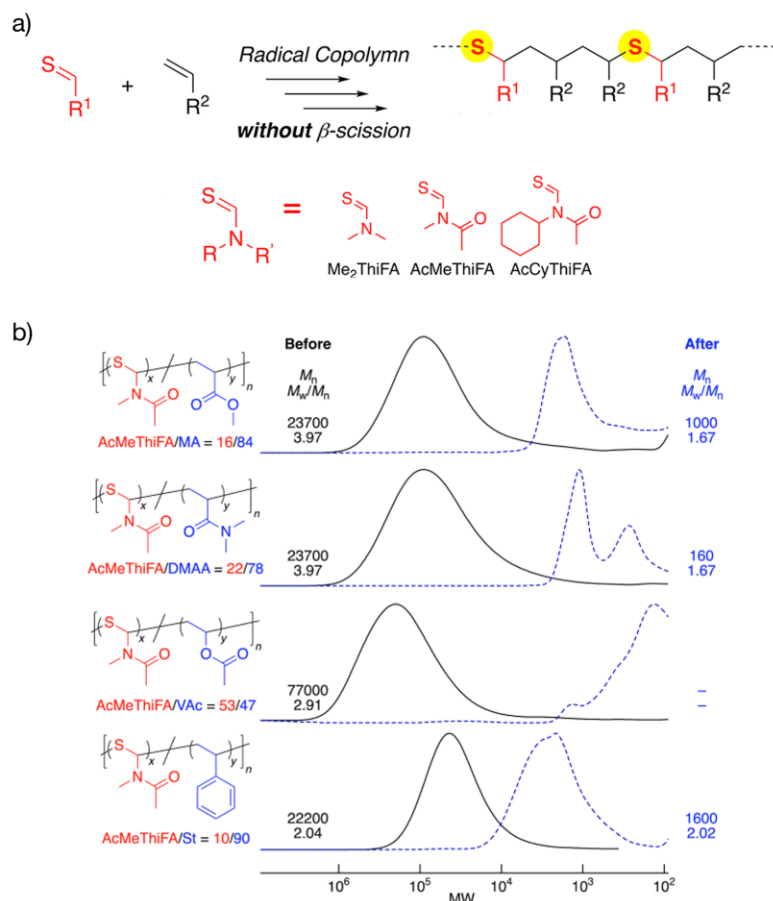


Fig. 49. a) Direct radical addition copolymerization of thioamide compounds and vinyl monomers. b) SEC curves of the copolymers and the products obtained by treatment with AgNO_3 solution: $[\text{sulfur unit}]_0/[\text{AgNO}_3]_0 = 5/50$ mM in THF/ H_2O (19/1 v/v) at room temperature for 24 h. Reprinted from Ref. [314] with permission.

3.2.4.4 Lipoate derivatives

Unlike the well-studied above-mentioned cyclic monomers, the polymerization of disulfide monomers was hardly investigated. A cyclic disulfide is an interesting monomer without a double bond but that that could be polymerized by a radical process.[315] Some disulfides are

abundantly found in nature. Among these, lipoic acid (LpOH) and their ester and amide derivatives are the most well-known and possibly the most interesting due to their accessibility and a very low toxicity. Lipoic acid (LpOH) is frequently utilized as an antioxidant and nutritional supplement. It has been demonstrated that lipoate-based monomers and in particular lipoamide may copolymerize with typical vinyl monomers including styrene, vinyl acetate, acrylonitrile, and methyl acrylate to produce polymers containing sulfur into the backbone.[316] Depending on the monomer feed ratio, the addition of two lipoate monomers led to the production of a disulfide bonds (Fig. 50) that could impart degradability of the backbone.[317]

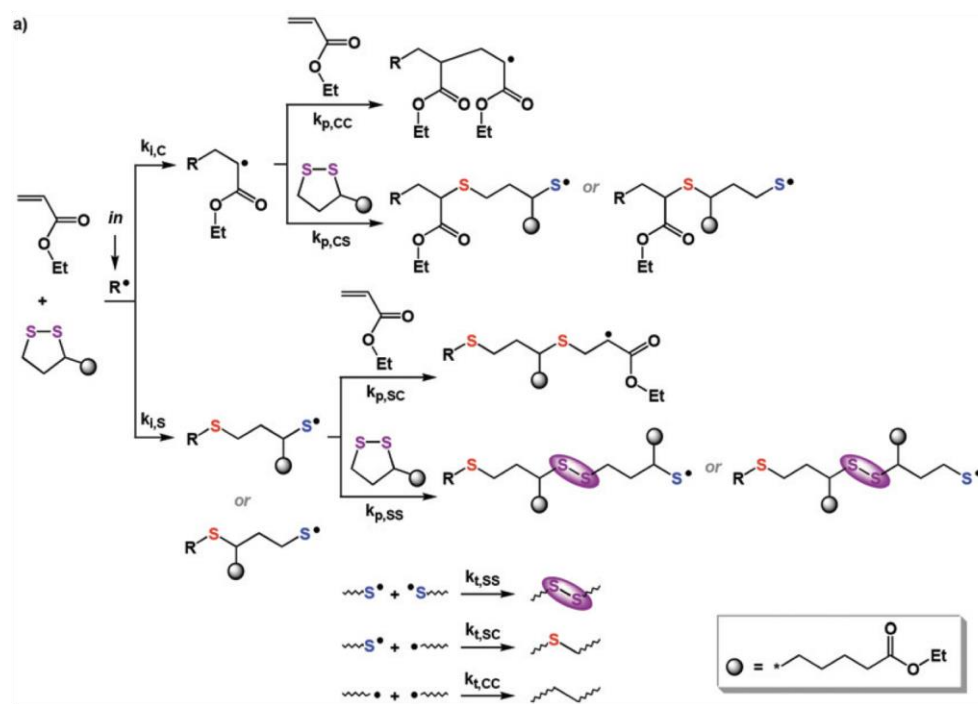


Fig. 50. Main reaction steps in the copolymerization of EA and ELp, leading to the formation of partially reductively degradable (disulfide containing) polymers. Reprinted from Ref. [317] with permission.

Tsarevsky *et al.*[318] studied in details the kinetics of the radical homopolymerization of ethyl lipoate. The limiting conversion of the polymerizations was usually lower at higher reaction temperatures and/or in diluted solutions. The lipoate polymerization is shown to be reversible and presented a ceiling temperature of 139°C. Due to the monomer-polymer equilibrium, the polymer degraded quickly at 150°C or even lower temperatures, especially when radical initiators are present. Additionally, the polymer was quickly degraded when reducing agents (such tributylphosphine) are present. Recently Bates and coworkers used the copolymerization of lipoate derivatives with acrylates to prepare degradable dynamic bottlebrush materials[319, 320] and degradable adhesives[321] (see Section 4.6 for details).

3.2.5 Simultaneous Chain- and Step-Growth Radical Polymerization

The radical polymerization is described in all textbooks as a chain growth polymerization of vinyl monomers that lead to a C-C backbone and thus to non-degradable materials. In contrary polymers prepared by step-growth polymerization consist in mainly polymers chains containing heteroatoms in their backbone. Kamigaito and coworkers[322] reported in 2010 a very elegant way to combine chain growth and step growth polymerization in a radical process by using the metal-catalyzed radical copolymerization of conjugated vinyl monomers and specific comonomers possessing unconjugated C-C and active C-Cl bonds. In their first study, they prepared random copolymers containing both polyacrylate and polyester units in the same backbone using the catalysts CuCl/1,1,4,7,10,10-hexamethyltriethylenetetramine- or RuCp*Cl(PPh₃)₂ with methyl acrylate (MA) and 3-butenyl 2-chloropropionate. The mechanism is described in Fig. 51.

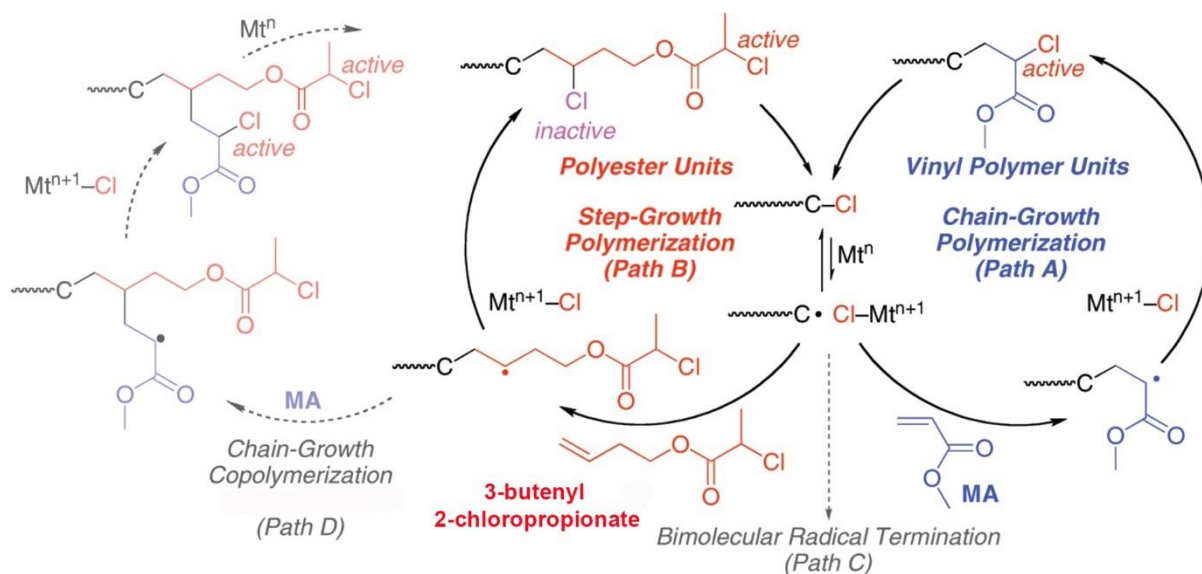


Fig. 51. Mechanism of Simultaneous Chain- and Step-Growth Radical Polymerization.

Adapted from Ref. [322] with permission.

This mechanism is based on the metal-catalyzed living radical polymerizations in which a metal catalyst can activate the C-Cl bond in α position to the stabilizing carbonyl group of the vinyl monomers (in this case methyl acrylate) to generate the growing radical that causes the chain-growth propagation. After some activation/deactivation cycles and vinyl monomer insertions (blue circle in Fig. 51), the growing radical added on the less activated double bond of the 3-butenyl 2-chloropropionate and the resulting radical is irreversibly trapped by the halogen atom since the C-Cl is not activated anymore. Nevertheless, this compound also bears a chloro-propionate group that is able to reinitiate again the polymerization. Reducing any potential side reactions, such as the bimolecular radical termination and chain-growth copolymerization of 3-butenyl 2-chloropropionate with MA (dotted circle in Fig. 51)), is one of the most crucial factors in the effective simultaneous polymerizations.[322]

To favor the synthesis of linear random copolymers without branching structures, the choice of catalysts and reaction conditions is important. A catalyst with a moderate activity is essential

to increase the selectivity of the activation and avoid side-reaction. By playing with the monomer feed ratios, the architecture of the copolymers produced could be varied from random to multiblock copolymers and the vinyl monomer segment lengths inserted between the polyester units could be also modified.[322] Since esters moieties are inserted into the polymer chains, the copolymers can be degraded by methanolysis into oligomers.

Kamigaito and coll.[323] extended this work to acrylamide and especially NIPAM. They showed that good degradability could be obtained via this technique. Moreover, due to the thermosensitivity of PNIPAM, a change in the cloud point can be observed after degradation (Fig. 52). The cloud points of the methanolized products increased with the increasing of specific comonomer contents in the copolymers, that suggests a higher hydrophilicity of the oligomers via the hydroxy groups created after the hydrolysis of the ester moieties.[323]

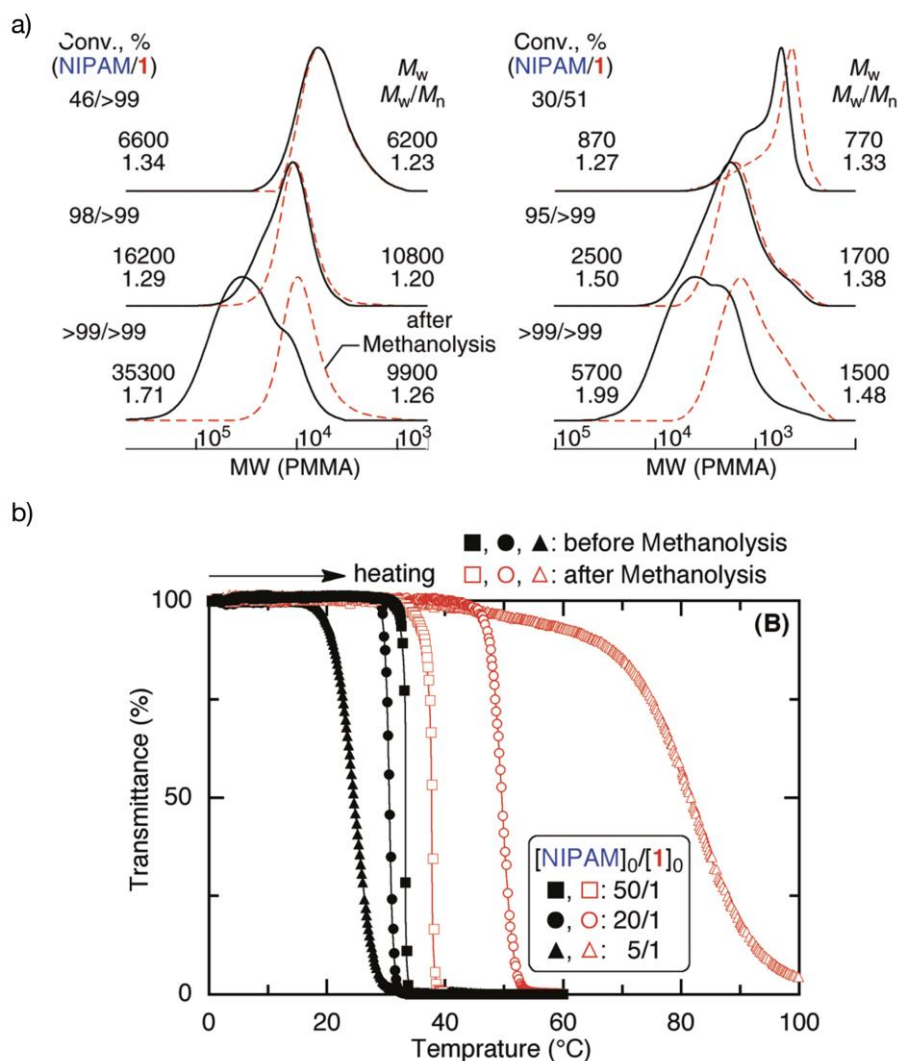


Fig. 52. a) Size-exclusion chromatograms of the obtained copolymers (solid lines) and the methanolyzed products (dashed lines) in the simultaneous chain- and step-growth radical polymerization of NIPAM and 1 with CuCl/Me₆TREN in DMF/H₂O = 1/1 at 20 °C: [NIPAM]₀ = 4.0 M; [1]₀ = 0.080 (A) or 0.80 M (B); [CuCl]₀ = 40 or 100 mM; [Me₆TREN]₀ = 40 or 100 mM b) Cloud-point curves for the aqueous solutions of the copolymers and the methanolyzed products in the simultaneous chain and step-growth radical polymerization of NIPAM and 1 with various monomer feed ratios ([NIPAM]₀/[1]₀ = 50/1, 20/1, and 5/1). Conditions: concentration = 10 mg/mL, heating rate = 1.0 °C/min, cloud point was determined by the temperature at which the transmittance ($\lambda = 500$ nm) of aqueous solution reaches 50%.

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The same authors used this methodology to prepare self-degradable antibacterial polymers[324] using the copolymerization of *t*-butyl acrylate and 3-butenyl 2-chloropropionate, followed by the transformation of *t*-butyl groups into various ammonium salts. The copolymers with pendant primary amine showed only moderate antimicrobial activity against *E. coli*. The change from primary amine to quaternary ammonium or acrylate to acrylamide decreases the antimicrobial activity. An interesting self-degradation in water was observed for copolymers having acrylate and primary amine via the amidation of the ester groups of the polymer chains by the nucleophilic addition of primary amine groups in the side chains resulting in cleavage of the polymer main chain.[324] The simultaneous chain- and step-growth radical polymerization was also tested with various vinyl monomers (styrene, 2-dimethylaminoethyl acrylate DMAEA, hydroxyethyl acrylate HEA) and various specific step-growth monomers containing different functionalities, such as oxyethylene, disulfide, or amide group.[325] Contrary to styrene, the combination of functional acrylates, such as DMAEA and HEA, and 3-butenyl 2-chloropropionate failed to produce controlled multiblock polymers, even at a high [acrylate]₀/[3-butenyl 2-chloropropionate]₀ ratio. This is in contrast to the almost satisfactory results for the multiblock copolymers of alkyl acrylates and functionalized step-growth monomers. For such functional acrylates, catalytic systems or conditions need to be optimized.[325]

3.3 Cationic Polymerization

3.3.1 Vinyl ethers

Many monomers that are either cyclic or based on a vinyl functionality could be polymerized via a cationic mechanism. In the 70s, living cationic polymerization of styrene, vinyl ethers or isobutylene were reported and led to an important development of such field.[326] In 2010, Aoshima and colleagues[327] investigated new initiation systems and discovered that benzaldehydes (BzA) could be copolymerized with vinyl ethers. The use of GaCl₃ as lewis acid in combination with ethanesulfonic acid as initiator allowed to obtain a living poly(isobutyl vinyl ether) containing benzaldehyde moieties (25-30%). An interesting feature of this system is the very specific reactivity of the different monomers that avoids any reaction leading to benzaldehyde – benzaldehyde sequence. The kinetics is thus governed by the crossover reaction between the BzA growing end and the homopropagation and crossover from the IBVE active center (Fig. 53a). By playing with monomer structures, that means a more reactive BzA derivative such as p-methoxyBzA coupled with IBVE or a less reactive VE than IBVE coupled with BzA, alternating copolymers could be obtained.[328] In that case an acetal linkage will be formed every two monomer units. The treatment with HCl in H₂O/THF solution led to complete degradation of the polymer chains in 2h at 30 °C. The alternating structure of the copolymer yields only to a single low-molecular weight product that was ascribed to cinnamaldehyde or p-methoxycinnamaldehyde (Fig. 53b).[328] The authors also degraded the previous P(IBVE_{75-co}-BzA₂₅) copolymer that was not an alternating structure and obtained a good degradation profile with oligomers between (100 and 4500 Da) confirming the random incorporation.[328]

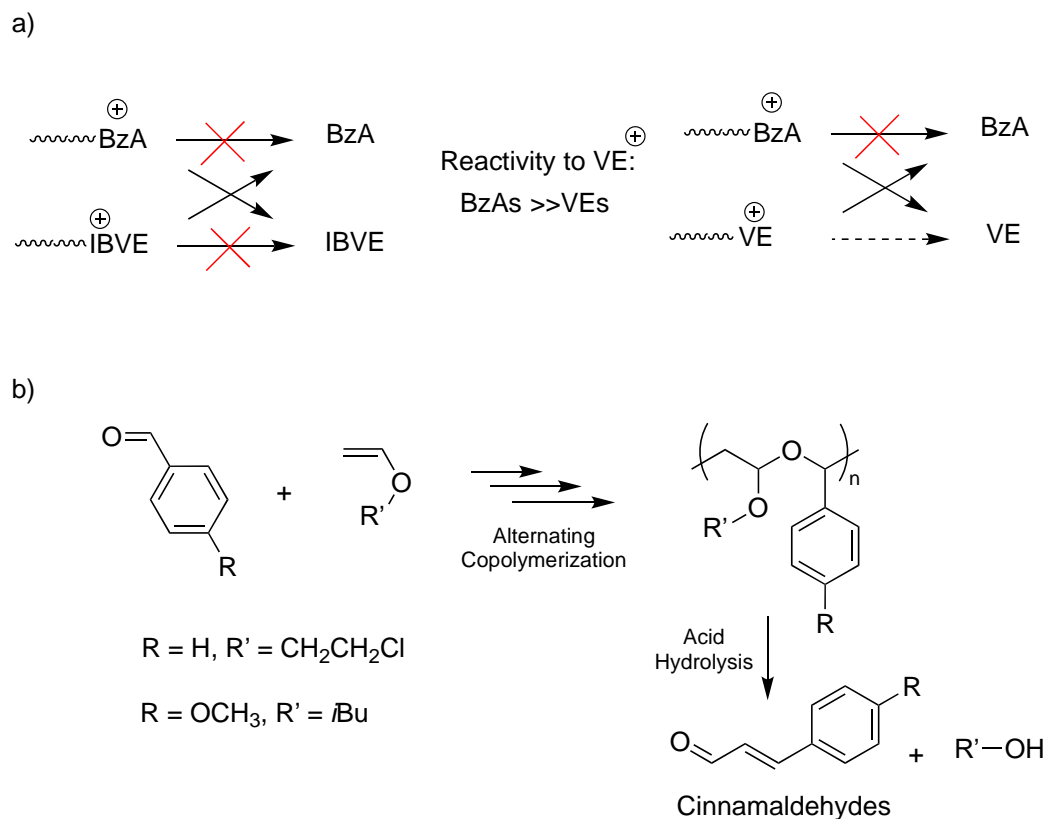


Fig. 53. Copolymerization and Alternating copolymerization of vinyl ether and benzaldehyde derivatives.

In order to expand the library of degradable VE-based copolymers, additional naturally occurring cyclic conjugated aldehydes were tested.[329] Three terpenoids was investigated namely (1R)-(-)-myrtenal (myrtenal), (S)-(-)-perillaldehyde (PA), and β -cyclocitral (CC) (Fig. 54). Myrtenal is a chiral bicyclic conjugated aldehyde and a key ingredient in the essential oils of Asteraceae plants. PA was extracted from perilla and is a chiral monocyclic conjugated aldehyde with an olefinic component. CC, a monocyclic conjugated aldehyde with three methyl substituents close to the polymerizable carbonyl group and could be obtained from citral that is found in lemongrass oil. Myrtenal and PA were copolymerized with vinyl ethers, leading to alternating copolymers with a living fashion.[329] It's interesting to note that the propagating chain reacted only via 1,2-carbonyl addition reaction. The copolymerization of CC did not achieve quantitative conversion and only formed oligomers. It was shown that conjugated

structures were essential for a good copolymerization behavior and that a bulkier side group was also desired for obtaining a well-controlled copolymerization. Conversely, slower polymerization and termination processes were the result of increased bulkiness surrounding the carbonyl groups (CC structure).[329] As previously, the degradation led to an aldehyde with an extended conjugated structure.

The same authors[330] played with the vinyl ether moieties to prepare stimuli-responsive copolymers. They used for example tri(ethylene glycol) methyl vinyl ether (TGMVE) to impart thermo-sensitivity, and ethyl 4-[2-(vinylloxy)ethoxy]benzoate (EVEB) and diethyl [2-(vinylloxy)ethyl]malonate (VOEM) as VE bearing precursors of carboxylic acid group to impart pH-sensitivity (Fig. 54b). By adapting the experimental conditions, and deprotection of the carboxylic acid via basic hydrolysis, alternating degradable stimuli-responsive copolymers were obtained. The copolymer containing TGMVE showed a very sharp transition at 13.3 °C, and the copolymer containing deprotected EVEB presented a pH-sensitive transition at pH = 6.7. In contrast, the copolymer with deprotected VOEM units is totally water soluble. The degradation in mild acidic conditions was demonstrated with the production of only aldehyde and alcohol as side-product.

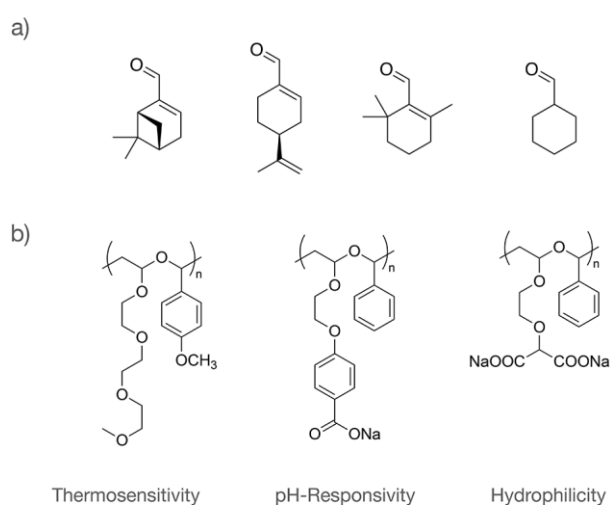


Fig. 54. a) naturally occurring cyclic conjugated aldehydes used in copolymerization with vinyl ether derivatives. b) Structure of various VE derivative copolymerized with benzaldehyde derivatives to prepare alternating degradable stimuli-sensitive copolymers.

Besides these systems, Aoshima *et al.* also prepared degradable copolymers using a vinyl ether bearing a ionic liquid[331] or with other PEG chains with different lengths[332] to tune the thermo-sensitivity of the materials. Ouchi *et al.*[333] also used this system but with a vinyl ether bearing a *o*-nitrobenzyl (oNBn) group as a photo-cleavable pendant group. They showed that upon irradiation, the polymer degraded without any other reactant via the production of the unstable hemiacetal group.

Aoshima and coworkers[334] then played with the polymerization process to prepare sequence controlled degradable copolymers using the same monomer pair. Due to the exclusive cross-over from a conjugated aldehyde to vinyl ether, single or multiple additions of a small quantity of conjugated aldehydes during the living polymerization of vinyl ethers could be an efficient method to inserted cleavable parts at predetermined positions into the polymer backbone. To illustrate this approach, living cationic homopolymerization of CEVE was carried out. A small amount of pMeBzA (five equivalents to the propagating chain) was added to the reaction mixture when the conversion of CEVE reached 32% (Fig. 55). After the addition, pMeBzA was consumed significantly more quickly than CEVE, achieving practically a quantitative conversion in a few hours, and then the polymerization of CEVE still continue until the conversion of CEVE reached 70% to obtain similar poly(CEVE) length before and after the copolymerization. Mild acid hydrolysis led to a narrow polymer with half of the M_n of the starting materials confirming the precise location of the degradable part in the copolymer.

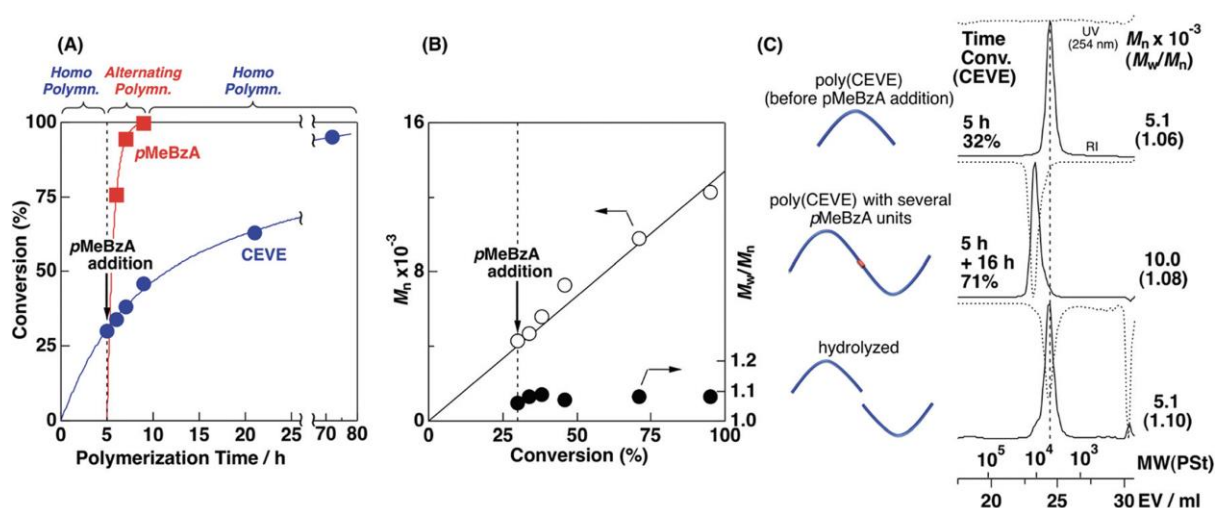


Fig. 55. (A) Time–conversion curves, (B) M_n and M_w/M_n values, and (C) MWD curves of a product obtained by the addition of a small amount of pMeBzA during the living cationic polymerization of CEVE and its acid-hydrolysis product. Polymerization conditions: $[CEVE]_0 = 1.2$ M, $[pMeBzA]_{added} = 40$ mM (five equivalents to the propagating chain), $[EtSO_3H]_0 = 8.0$ mM, $[GaCl_3]_0 = 4.0$ mM, $[1,4\text{-dioxane}] = 0.50$ M, in toluene at -78 °C; hydrolysis conditions: 0.50 M HCl in 1,2-dimethoxyethane/water (23/1 v/v) at room temperature for 2 h, 0.33 wt% polymer. Reprinted from Ref. [334] with permission.

This example was extended to multiple addition, to block copolymer in which only one block is degradable and also to the preparation of star polymers in which the core is degradable (addition of difunctional isophthalaldehyde). By testing various monomers structures the authors defined two criteria that have to be fulfilled to obtain precise location of degradable part: “(i) both homopolymerization of a VE and copolymerization of an aldehyde with a VE proceed in a controlled manner under the same conditions. (ii) Second, aldehyde monomers react quickly after being fed into the reaction solution of the living propagating VE polymer.”[334]

After the copolymerization of vinyl ether derivatives with conjugated aldehydes, the group of Aoshima[335] investigated their copolymerization behavior with cyclic acetals. Indeed, the

conditions that allow the living cationic polymerization of vinyl monomers may promote the controlled copolymerization of a vinyl monomer and a cyclic acetal because a cyclic acetal is converted into a carbocation that has a comparable structure to the carbocation obtained from a VE. Three cyclic acetals were investigated: 1,3-dioxepane (DOP), 2-methyl-1,3-dioxolane (MDOL), and 1,3-dioxolane (DOL). The reaction using a $\text{TiCl}_4/\text{SnCl}_4$ initiating system at -78°C led to the copolymerization of CEVE and DOP reaching high conversion of both monomers but only moderate control of the copolymerization ($\mathcal{D} = 2.45$). The analyses showed rather a multiblock structure than a statistical incorporation of DOP into the chain. Hydrolysis in mild acid condition nevertheless produced oligomers (Fig. 56a). In that case the cleavage occurred from the acetal functions generated either the crossover reaction between CEVE and DOP or via the homopolymerization of DOP. To decrease the reactivity of the cyclic acetal, MDOL was used. In that case, the copolymerization was successful with a better control than with DOP (Fig. 56b).[335] Detailed analyses confirmed no homopropagation of MDOL.

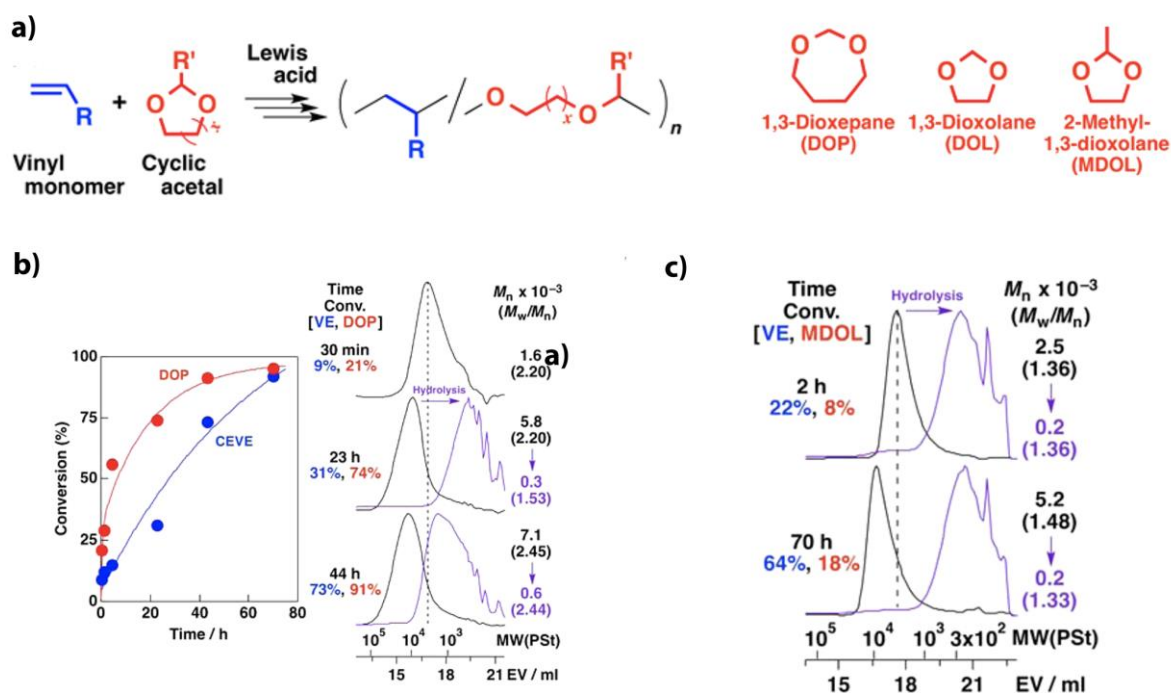


Fig. 56. a) Time–conversion curves for the copolymerization of CEVE and DOP using $\text{TiCl}_4/\text{SnCl}_4$ and b) MWD curves of the poly(CEVE-*co*-DOP)s (black) and acid hydrolysis products (purple). c) MWD curves of poly(CEVE-*co*-MDOL)s (black) and acid hydrolysis products (purple). Adapted from Ref. [335] with permission.

Trimethylsilyl vinyl ether was also copolymerized with cyclic acetal.[336] The selective deprotection of the silyl ether via the use of base or fluoride anion led to the formation of the unstable hemiacetal that spontaneously degraded. A terpolymer was also possible with the addition of common vinyl ethers.[336] This induces a possible stepwise selective cleavage with first production of oligomers via the degradation of the hemiacetal group coming from the copolymerization of trimethylsilyl VE followed by a further cleavage of the acetal moieties into the oligomers via acidic conditions.[336]

In addition to ketal moieties, Aoshima and coworkers[337] investigated the copolymerization of vinyl ether derivatives with 1,3-dioxo-2-silacycloalkane to introduce in the polymer chain the silyl ether functionality that presents the advantage to be sensitive to different mode of degradation. Cationic copolymerizations of 1,3-dioxo-2-silacycloalkanes with VEs were first investigated. The analyses showed negligible cross-over between the two end-groups, leading to a diblock-type macrostructure instead of a homogeneous incorporation of the two monomer units. The degradation is thus very low. The formation of a diblock copolymer rather than a multiblock copolymer is most likely due to the inertness of the oxonium ion derived from the silyl monomer to the VE and the negligible generation of a silyl cation by ring opening of the oxonium (Fig. 57a). Since it has been shown that carbonyl compounds react well with the oxonium ion, the authors investigated the terpolymerization of silyl monomers, vinyl ethers and conjugated aldehydes.

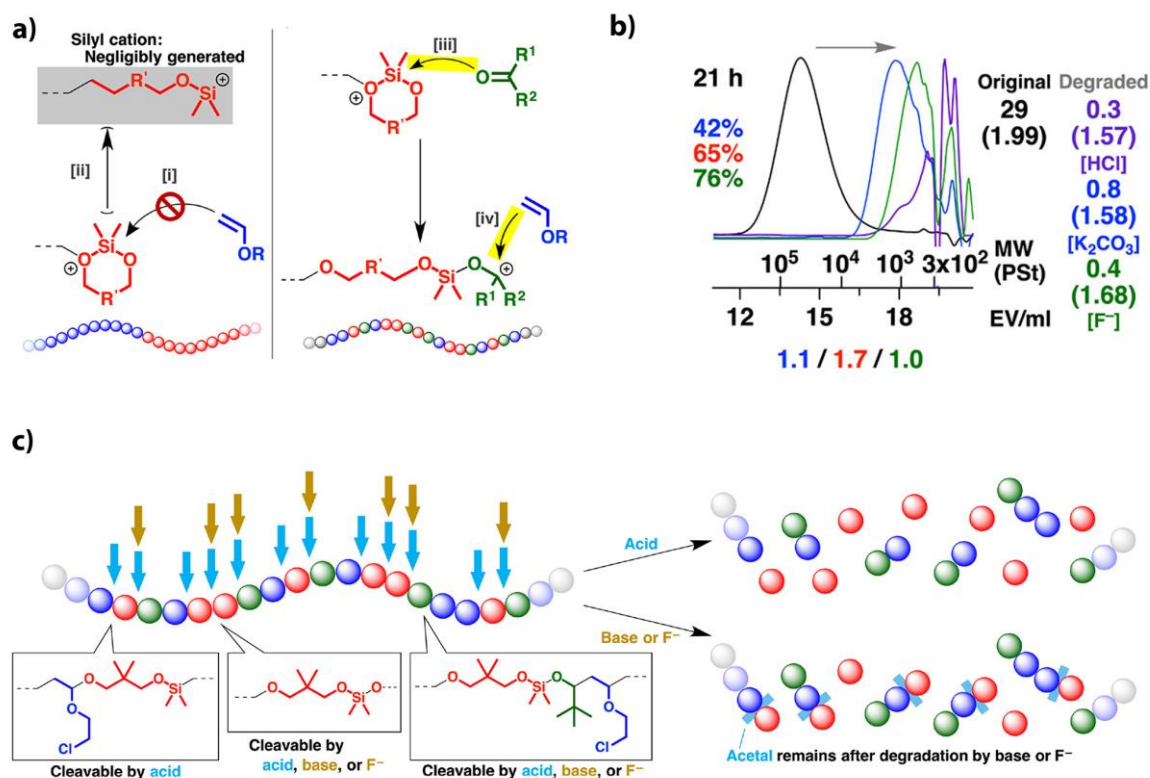


Fig. 57. a) Reactions at the 1,3-Dioxa-2-silacycloalkane-derived end in the absence and the presence of a carbonyl compound. b) MWD curves of the CEVE–Si6M–Pivalaldehyde terpolymers. c) Cleavages of acetal and silyl ether moieties in the main chain by acids, bases, or fluoride ions. Adapted from Ref. [337] with permission.

Using B(C₆F₅)₃ as a catalyst in dichloromethane at -78 °C, the terpolymerization of CEVE, Si6M and conjugated aldehyde was successful with frequent crossover reactions. It was shown that aldehydes with a bulky substituent is necessary to obtain high-MW polymers. Since both acetal and silyl ethers are present in the backbone, different modes of degradation are possible, with mild acidic conditions degrading all the weak bonds whereas basic or fluoride anions impacting only silyl ether moieties (Fig. 57b-c).[337]

Kamigaito and coworkers[338] investigated the use of seven-membered thioacetals to introduce cleavable thioacetal moieties into poly(vinyl ether). They chose to use such functional group since they previously showed that thioacetals or thioethers could be efficient and reversible chain-transfer agents for the cationic polymerization of vinyl ethers and are quite stable compound that could be handled in air. During the copolymerization of ethyl vinyl ether and the seven-membered cyclic thioacetals, the cyclic monomer was first consumed very rapidly followed by a complete consumption of the vinyl ether. The concurrent degenerative chain transfer mechanism induced by the thioacetal moieties led to rather broad molecular weight distribution but at the end of the polymerization, the analyses confirmed that all the chains contained similar thioacetal moieties, similar number of polyvinyl ether segment of controlled length. The characteristics of the polymer chains are governed by the ratio between vinyl ether and cyclic thioacetal concentration and also by the amount between total monomer to the initiator.[338] Poly(ethyl vinyl ether) with M_n close to 100,000 g.mol⁻¹ could be obtained. The presence of the thioacetal moieties into the polymer backbone also allowed to prepare degradable multiblock copolymer by the sequential addition of a second vinyl ether that insert into the multiple dormant bond (Fig. 58).

The degradation of the copolymers was shown either by hydrolysis using metal salts such as AgNO₃ in THF/H₂O or via organic acids. Assuming that the length of the vinyl ether oligomers was governed by the feed ratio of EVE and the cyclic thioacetal, the M_n values of the degraded products were in good agreement with the calculated values and this whatever the original M_n (Fig. 58b) of the polymers (5,000 to 100,000 g.mol⁻¹ leading to oligomers of M_n close to 2,000 g.mol⁻¹). Similarly, polymers with similar M_n but with various ratios of EVE and the cyclic thioacetal were prepared and the M_n followed the expected trend (Fig. 58c).

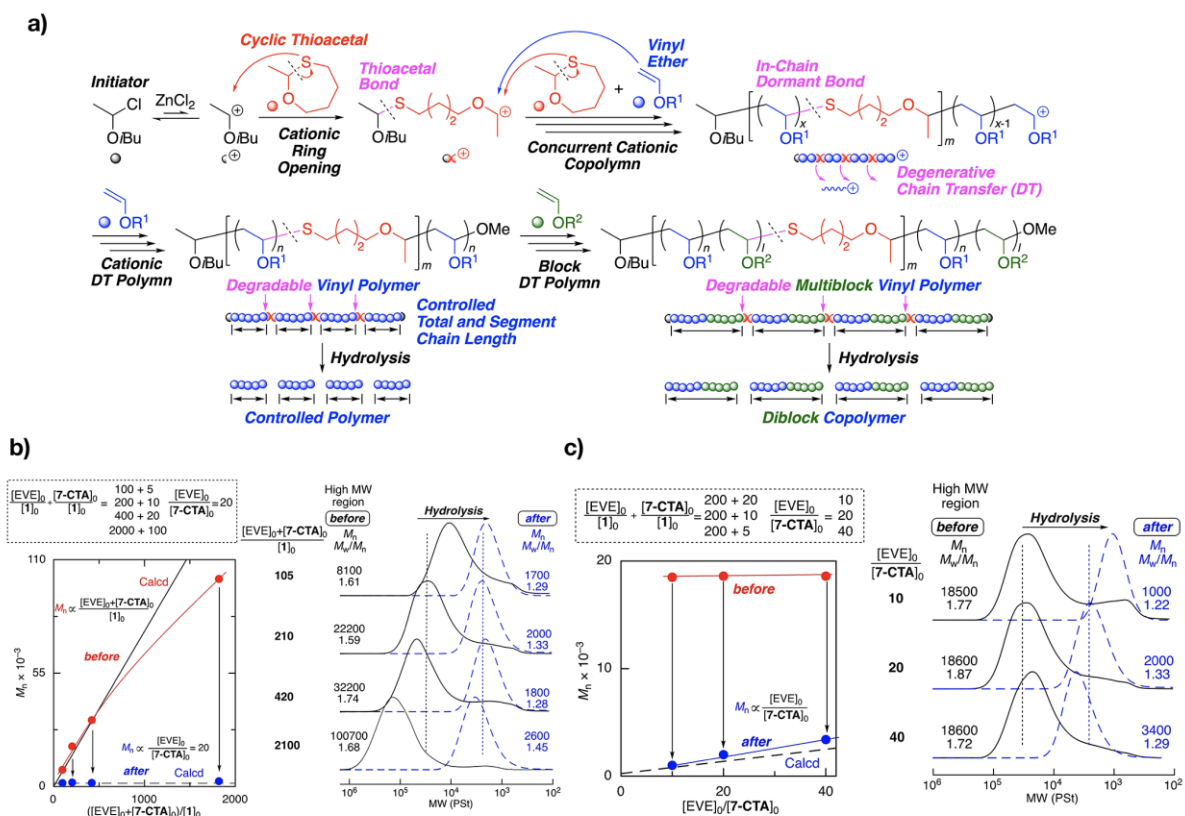


Fig. 58. a) Precision synthesis and degradation of poly(vinyl ether)s and multiblock copolymers with periodically distributed thioacetal bonds in main chains by cationic degenerative chain-transfer copolymerization of vinyl ethers and cyclic thioacetals. b) Effect of varying $([EVE]_0 + [7-CTA]_0) / [1]_0$ with constant $[EVE]_0 / [7-CTA]_0$ on the polymers obtained in controlled cationic copolymerizations of EVE and 7-CTA before and after hydrolysis. c) Effect of varying $[EVE]_0 / [7-CTA]_0$ with constant $[EVE]_0 / [1]_0$ on the polymers obtained in controlled cationic copolymerizations of EVE and 7-CTA before and after hydrolysis. Reprinted from Ref. [338] with permission.

A side-product that is commonly found during the copolymerization of vinyl ether and conjugated aldehyde is the cyclic trimer consisting of one VE and two aldehyde units (Fig. 59a). By a right choice of the catalytic system, the copolymerization of vinyl ether and

conjugated aldehyde only led to alternating copolymer but with other catalysts and at higher temperature, this trimer could be the sole product.[339] If a dialdehyde is used, the trimer is difunctionalized with residual aldehyde groups and thus could be used in polyaddition reaction to prepare linear polymers with cyclic acetal structures, imparting degradation properties of the material.[339] The same authors then extended this polyaddition to a tandem reaction by combining the bis-aldehyde cyclic adducts with a vinyl ether via a Tischchenko reaction to yield cyclic acetal structure and ester in the same chain (Fig. 59b).[340]

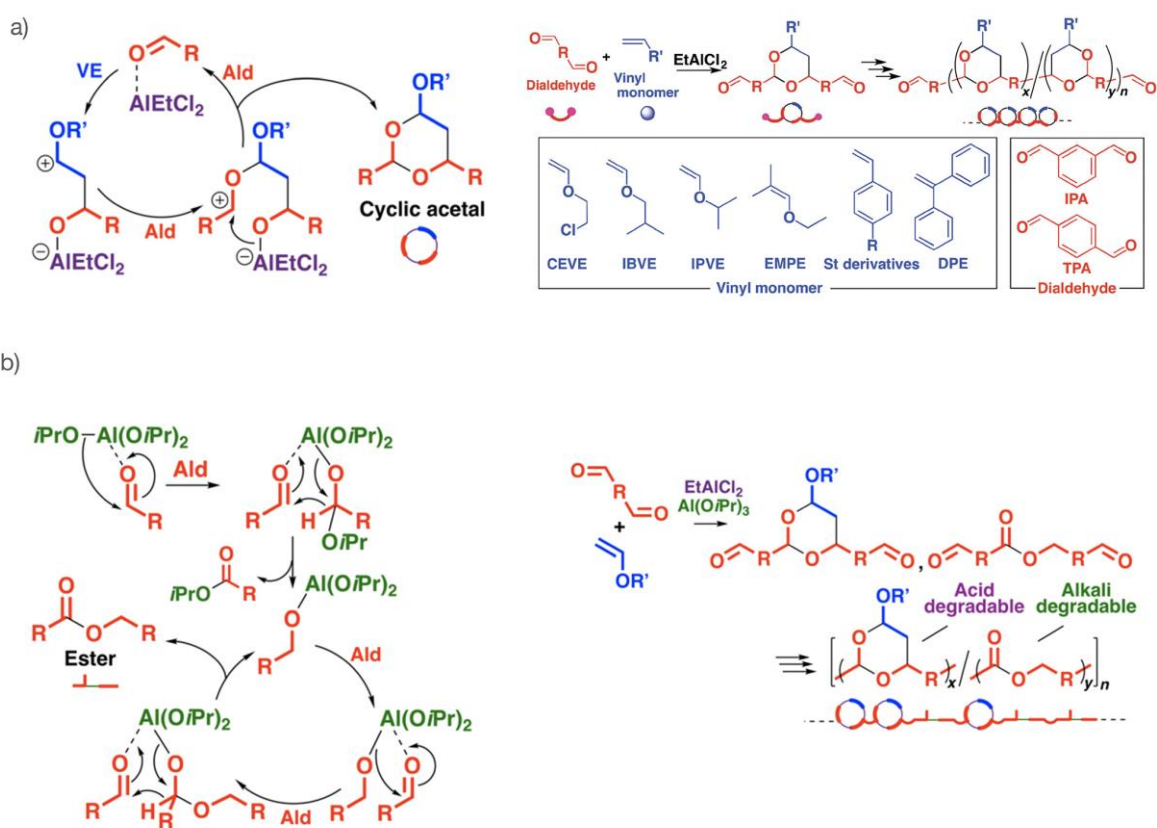


Fig. 59. a) Mechanism of the cyclotrimerization reaction and preparation of the linear polycyclic acetal. b) mechanism of the Tischchenko reaction and the tandem polymerization of vinyl ether and conjugated aldehyde to prepare linear poly(cyclic acetal)/polyesters. Adapted from Refs. [339]- [340] with permission.

Lastly, Aoshima et coll.[341] also reported the copolymerization of vinyl ethers and isobutylene oxide (IBO) using $B(C_6F_5)_3$ as a catalyst. Crossover between the two chain-ends occurred multiple times leading to multiblock copolymers. When cross-over from VE to IBO occurred, an acetal group is produced that make the copolymer degradable under acidic conditions. The degradation fragments were in this case deblock copolymers with hydroxyl and aldehyde end-groups (Fig. 60).

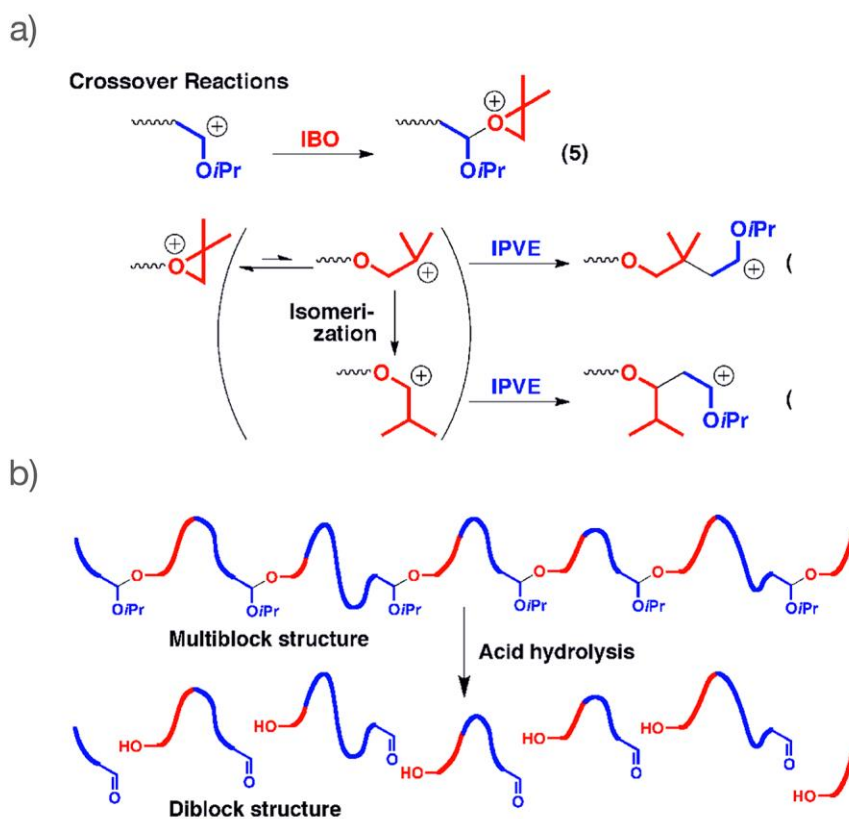


Fig 60. a) Cross-over reactions during the propagation of VE and IBO. b) Acid hydrolysis of Poly(IPVE-co-IBO). Adapted from Ref. [341]with permission.

3.3.2 Other vinyl monomers

Among the other monomers that could be polymerized by a cationic mechanism, styrene and its derivatives bearing an electron-donating group are well studied.[326] Aoshima and coworkers[342] thus extended their work on the copolymerization of vinyl ethers and conjugated aldehydes to styrenic monomers to prepare degradable polystyrene. The use of GaCl_3 at $-78\text{ }^\circ\text{C}$ and with the addition of a small amount of tetrahydropyran (THP) was necessary to obtain a good control of the copolymerization between p-methylstyrene (pMeSt) and benzaldehyde (Fig. 61a). The experimental conditions have to be tuned for each comonomer pair to ensure a good control of the polymerization. Unlike with VE, that produced an acetal group, the crossover reaction from styrene derivatives to conjugated aldehyde led to a sec-benzylic ether structure (Fig. 61b). Such structures are anticipated to exhibit acid degradability as well as characteristics similar to polystyrene derivatives. The degradation in strong acidic conditions (0.5 M TFA in dichloromethane) was then investigated and showed a strong decrease of the M_n with the appearance of hydrolysis products as chain-ends. The insertion of the ether functionality in the backbone impacts the T_g with a decrease to $86\text{ }^\circ\text{C}$ instead of $109\text{ }^\circ\text{C}$ for the reference poly(pMeSt).[342] Such copolymerization was not effective with other α - or β -substituted St derivatives (indene, α -methyl styrene, etc.).

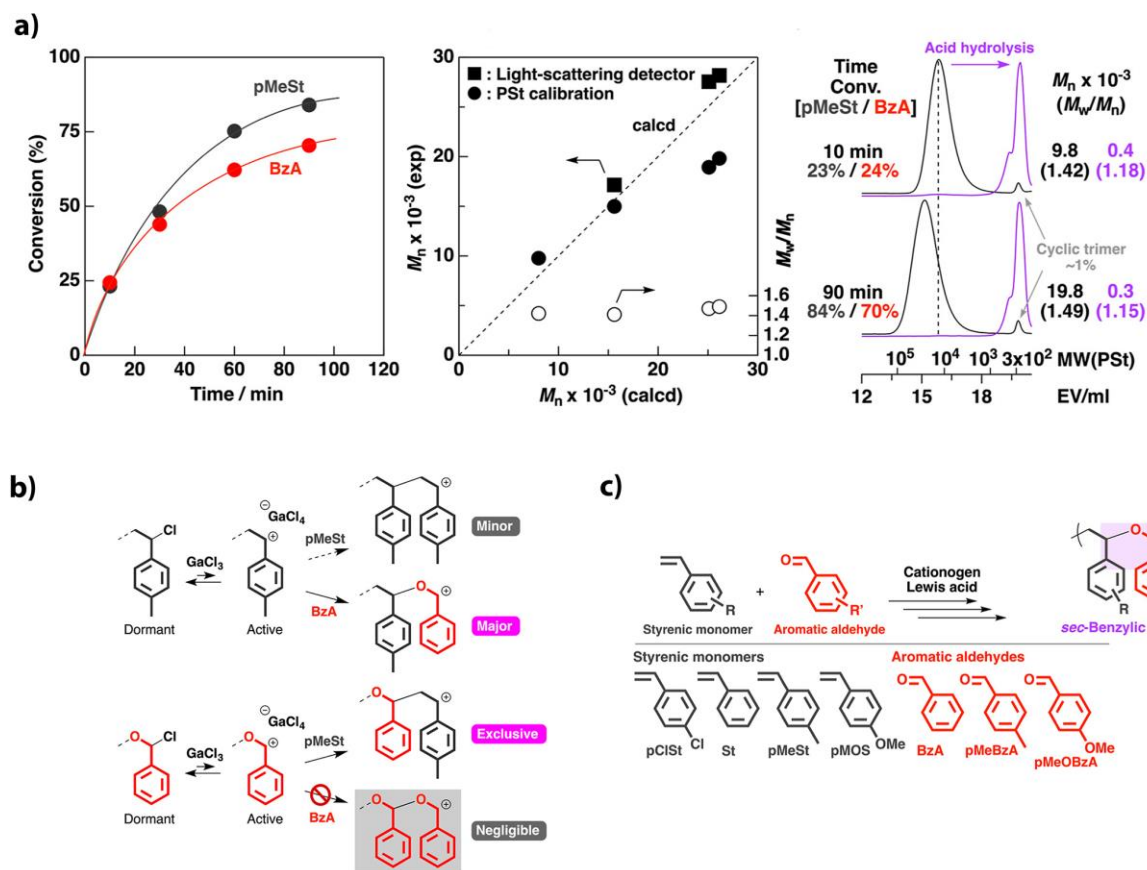


Fig. 61. a) Time-conversion curves of the copolymerization of pMeSt and BzA, M_n and M_w/M_n values, and MWD ga curves of the obtained polymers. b) Possible Mechanisms of Controlled Cationic Alternating Copolymerization of pMeSt and BzA. c) Cationic Copolymerization of Various Styrenic Monomers and Aromatic Aldehydes with the production of the cleavable sec-benzylic ether bond. Adapted from Ref. [342] with permission.

Besides the copolymerization with conjugated aldehydes, Aoshima *et al.*[335] also extended the copolymerization with cyclic acetal to styrenic derivatives. A slow rate of polymerization was observed that resulted in polymers with relatively low molecular weight and relatively wide MWDs. Nevertheless, when the monomer conversion increased, the peak of the MWD curves of the products move towards higher-molecular-weight, suggesting the formation of long-lived species. Moreover, compounds produced by acid hydrolysis have lower molecular weights than the initial polymers. The degradation was linked to the cleavage of acetal

structures in the homosequences of DOL since the crossover reaction from styrene to DOL does not produce an acetal structure, unlike copolymerizations utilizing VEs.[335] Analyses of the tailing in the SEC trace revealed the presence of non-negligible amount of inactive cyclic oligomers that is produced during the polymerization. The oligomers were found to come from frequent backbiting reactions. By lowering the concentration of cyclic acetal, such side-reaction is lowered but avoid reaching high molecular weight polystyrene.[335]

Vinyl ethers, styrene derivatives, and isobutene are examples of representative monomers for cationic polymerizations. In the case of vinyl ether, electron donation to the vinyl group due to the resonance effect of the oxygen atom increase its reactivity toward cationic species. Because vinyl acetate (VAc) is structurally related to vinyl ethers and possesses an oxygen atom next to the vinyl group, it may have resonance properties that are comparable to those of vinyl ethers. Nevertheless, the experimental inertness of VAc in cationic polymerization may be caused by insufficient reactivity of the VAc monomer and ineffective production of the VAc-derived carbocation in VAc homopropagation processes. A way to make possible the cationic polymerization of VAc is to use a comonomer that could lead to crossover of reactive species. Aoshima and coll.[343] thus investigated the copolymerization of VAc with either 1,3-dioxolan-4-ones (DOLO) or cyclic acetals to impart both controlled cationic polymerization and also degradability of the obtained material. A cationic copolymerization with VAc using GaCl_3 as the catalyst in dichloromethane at $-40\text{ }^\circ\text{C}$ was performed in the presence of DOLO-1 (Fig. 62a). Both monomers were consumed after a long reaction time, leading only to low conversion. The analyses of the copolymer confirmed the alternating sequences of VAc and DOLO-1. The change from DOLO-1 to DOLO-2 yield an alternating copolymer with higher molecular weight than the one with DOLO-1, certainly due to the better balance between reactivity and stability (methyl at the 2-position). Vinyl pivalate or vinyl benzoate could be

used as vinyl ester derivatives. The same authors investigated the use of cyclic acetals and showed that (1,3-dioxane) DOX was the best cyclic acetal to obtain the alternating structure. The copolymerizations of VAc and DOX were very slow and led to highly disperse copolymers. SEC analyses revealed that the copolymers comprised fractions with molecular weight greater than 10^5 g.mol⁻¹ (Fig. 62b) and the NMR confirmed that the copolymerization proceeded via crossover reactions and branching reactions triggered by the abstraction of an acetoxy moiety derived from VAc.

Due to its extremely low homopropagation, the DOX-derived carbocation reacted with VAc more favorably and it is the same for the VAc-derived carbocation that only minimally reacted with the VAc monomer, and thus allowed the crossover by the reaction with DOX. The main VAc-DOX sequence undergoes abstraction of an acetoxy moiety through reaction with the DOX-derived carbocation or the VAc-derived, resulting in the formation of hemiformal ester ([iv]) or diacetoxymethine (Fig. 62c). Because of the formation of a carbocation that is stabilized by electron donation from the oxygen atom's lone-pair electrons and has a structure resembling the carbocation obtained from a vinyl ether, acetoxy abstraction takes place. This carbocation could thus react with DOX or VAc to produce branching structures. In acidic or basic conditions, the copolymerization product was decomposed into low-MW molecules. Butanol or propanol were used for the acid-degradation process. In that case, the diacetoxymethine and hemiacetal ester moieties were converted into acetal structures generated from the corresponding alcohol. In basic conditions (K_2CO_3), the hemiacetal ester moieties were converted into the unstable hemiacetal moieties, which were then spontaneously degraded into aldehydes.

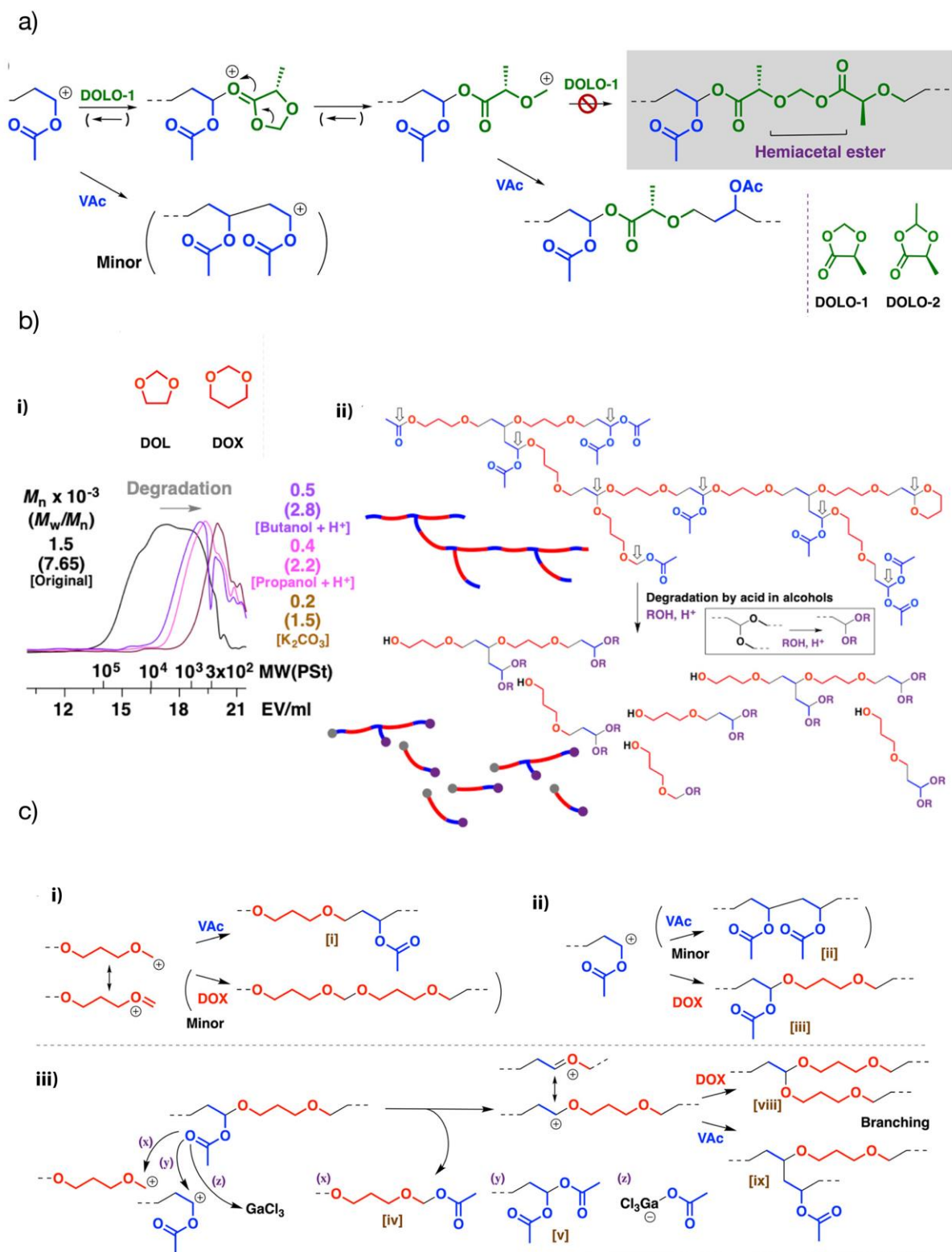


Fig. 62. a) Propagation Mechanism of the Cationic Copolymerization of VAc and DOLO-1. b) i) MWD curves of the products obtained by the copolymerization of VAc and DOX (black) and the acid (red and purple) or base (blue) degradation products. ii) Representative structure

of a copolymer chain obtained by the cationic copolymerization of VAc and DOX (upper) and the structures resulting from degradation by acid in an alcohol (lower). c) Mechanism of the Cationic Copolymerization of VAc and DOX. i) and ii) Propagation of DOX and VAc end-group respectively. iii) Side reactions that could occur. Adapted from Ref [343] with permission.

3.3.3 cyclic monomers

Besides vinyl monomers, cyclic monomers and especially epoxide compounds were mainly polymerized by a cationic process. In both existing and emerging applications, polyethers and their derivatives form an important class of polymeric materials. These polymers have ether backbones that are comparatively stable and inert. It is possible to tailor polyether properties for a variety of purposes by adding various functional groups. The main comonomer to prepare degradable polyethers is the copolymerization of epoxides with lactones or anhydrides that has been extensively reviewed[344] and is not detailed in this article. Among the various polyethers, poly(ethylene oxide) (PEO) is one of the most used synthetic materials in biomaterial and therapeutic applications. Lynd and coworkers[345] developed a very interesting strategy based on the copolymerization of ethylene oxide and epichlorohydrin (ECH) to prepare a controlled linear copolymer. The further post-modification of the chloromethyl group to a methylene ethylene oxide (MEO) moiety via an efficient elimination reaction generated the cleavable bond that will degrade the copolymer. The interest of this approach is the similar reactivity of the two epoxides that allow the random copolymerization of the two units. The elimination reaction was then performed in toluene using potassium tert-butoxide. The degradability of P(EO-*co*-MEO) was assessed by acidic treatment (1% aqueous solution of trifluoroacetic acid (TFA)) for 24 h at room temperature. It was shown that the acid-

catalyzed hydrolysis of vinyl-ether groups inside the MEO repeat-units cause the hydrolysis of the P(EO-*co*-MEO), releasing nonacidic α -hydroxy- ω -keto-PEO oligomers into solution.[345] A detailed discussion about degradable POE is provided in section 4.2.

1,3-dioxolan-4-ones (DOLOs) are interesting monomers since such cyclic structures have been produced by condensation of α -hydroxy acids, such as lactic acid, glycolic acid, and mandelic acid, with aldehydes or ketones. The cationic polymerization of such monomers is not possible, but Aoshima and coworkers[346] investigated their copolymerization with oxirane to use the crossover reaction between the two active species. Copolymerization of DOLO2 with isobutylene oxide (IBO) or 4-Vinyl-1,2-epoxycyclohexane (VCHO) using $B(C_6F_5)_3$ was successful with many crossover reactions to yield polymers with both acetal and ester moieties (Fig. 63). DOLO homopropagation did not occur and homopropagation of oxiranes were more important with VCHO than IBO. As already observed DOLO2 is a good compromise between reactivity and stability compared to DOLO1 and DOLO3. In the case of DOLO2, the terpolymerization with vinyl ether is also possible with poly(vinyl ether) homo-sequence close to 6 units. DOLO-oxirane copolymers were then susceptible to acidic degradation via the cleavage of the acetal group.[346]

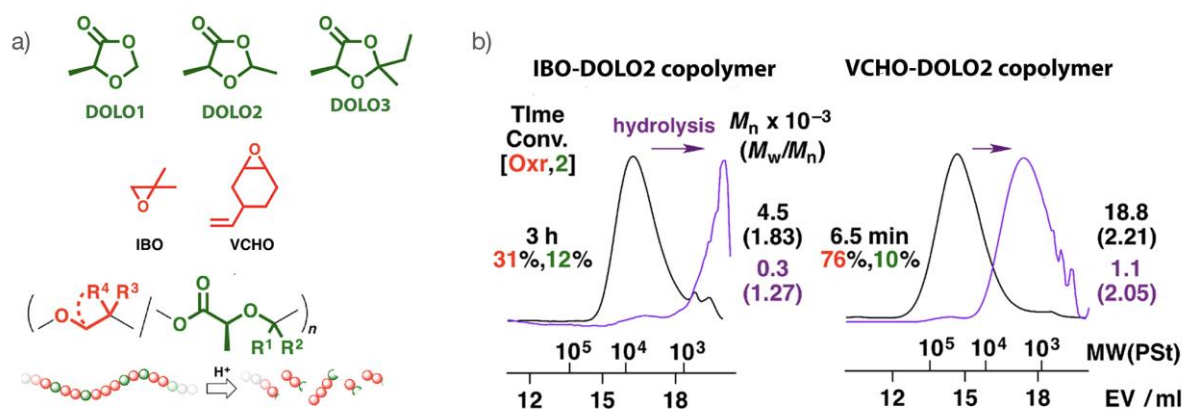


Fig. 63. a) Preparation of degradable DOLO-oxirane copolymers. b) MWD curves of IBO-DOLO2 and VCHO-DOLO2 copolymers (black) and their hydrolysis products (purple). Adapted from Ref. [346] with permission.

Aoshima *et al.*[347] also developed the copolymerization using EtSO₃H as a catalyst of ϵ -caprolactone and a cyclic acetal 2-methyl-1,3-dioxepane (MDOP) that was obtained by the spontaneous cyclisation of 4-hydroxybutyl vinyl ether (HBVE). Polymerization was initiated via the reaction of an MDOP monomer with a protonated MDOP, forming a compound with an oxonium ion and a hydroxy group. The propagation of MDOP and CL thus proceeded via the active chain end (ACE) and activated monomer (AM) mechanisms (Fig. 64). Intra- and inter-molecular coupling reactions between the two ends occurred, leading to copolymers with various sequences. NMR analyses showed negligible HBVE homosequences and multiple HBVE-CL or CL-HBVE heterosequences per chain. The acidic degradation and the further analyses of the oligomers confirmed the copolymer structure: disappearance of the peak of the acetal moiety and oligo(caprolactone) with a 4-hydroxybutoxy end group.

It was shown that random segmental exchange via transacetalization also called polymer scrambling was also present during the process.[347] This feature and the equilibrium that governed the homopropagation of cyclic acetal led the authors to prepare alternating copolymer via a elegant polymerization process (Fig. 64b). They first prepared a copolymer with no CL homosequences by choosing a much smaller concentration of CL than that of HBVE. In a second step, the pressure is reduced to remove the cyclic acetal (MDOP with bp=154 °C), that is produced by shifting the equilibrium and that could be seen as an unzipping reaction. This reaction removed the HBVE homosequences at the oxonium chain end. Unzipping stops when a CL unit is located close to the chain end. The scrambling of the active species thus recreated HBVE homosequences at the chain end that was again eliminated by unzipping. The repetition

of these steps eliminates all the HBVE homosequences and thus produced a pure alternating copolymer. The M_n after vacuuming was reduced due to the elimination of acetal homosequence but more interestingly the degradation products after vacuuming are much smaller than the one before vacuuming (Fig. 64c).

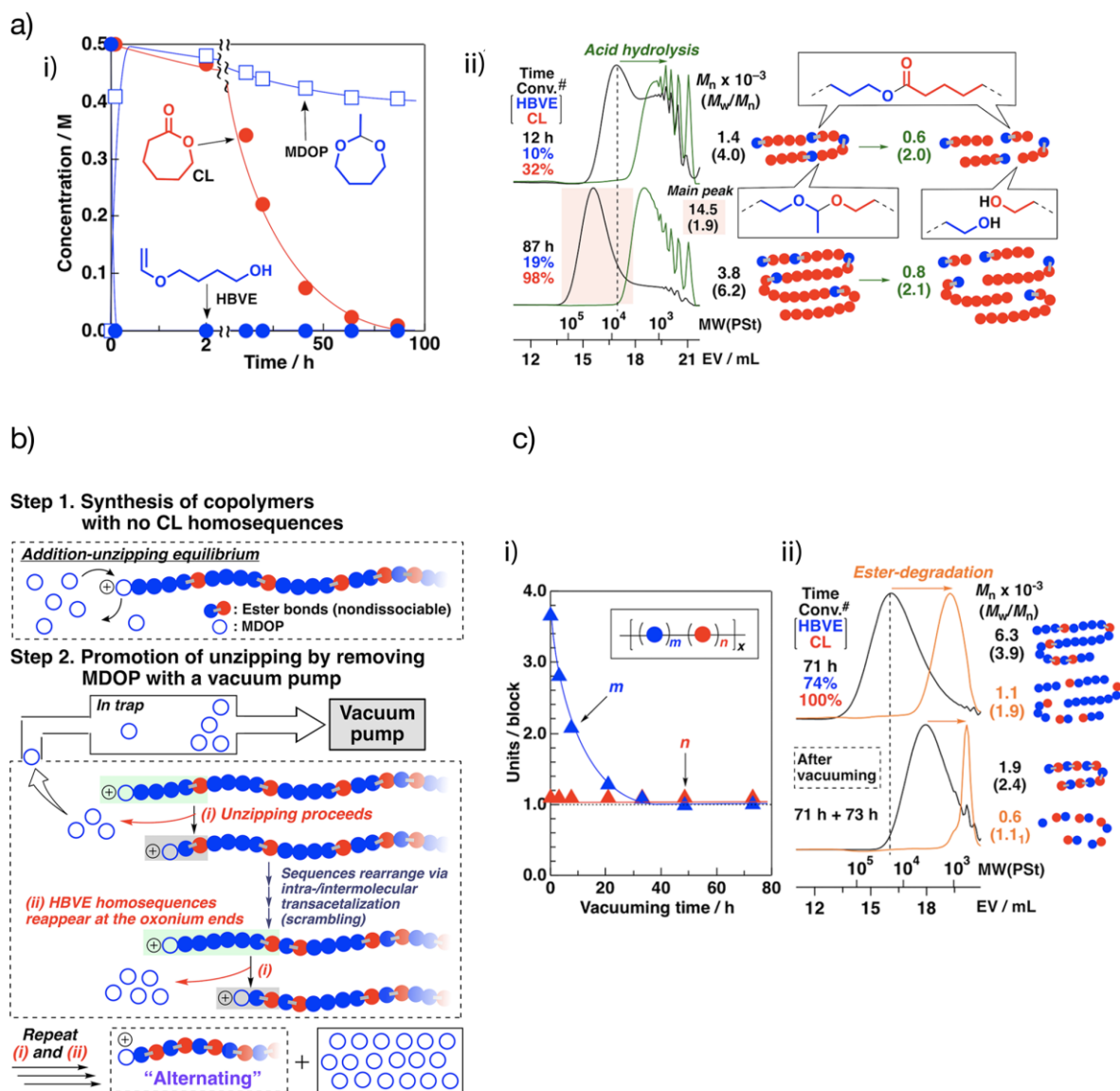


Fig. 64. a) i) Time-concentration plots for the copolymerization of HBVE and CL, ii) SEC chromatograms of poly(HBVE-co-CL)s (black,) and their acid hydrolysis products (green). b) Strategies for the Transformation of Poly(HBVE-co-CL) with No CL homosequences to Poly(HBVE-alt-CL) by Removing MDOP. c) i) Vacuuming time-units per block plots for the

copolymerization of HBVE and CL (the values were calculated from ^1H NMR integrals), and ii) SEC chromatograms of the products before (upper) and after (below) vacuuming (orange: transesterification products). Reprinted from Ref. [347] with permission.

The cationic ring-opening copolymerization of cyclic esters and cyclic acetals was extended to other structures to demonstrate the universality of the sequence control by unzipping and scrambling reactions.[348] Besides this generalization, the authors also showed that the unzipping reaction could be triggered by increasing the temperature instead of reducing the pressure.[348]

Finally, cationic ring-opening polymerization (CROP) has been envisioned since the 60s to prepare synthetically polysaccharides from anhydrosugars.[349, 350] Depending on the monomer structure, different type of glycosidic linkage could be obtained. Recently Niu and coworkers[351] reported the living cationic polymerization of anhydrosugars in the presence of boron trifluoride and a glycosyl fluoride. The obtained polysaccharides are highly stereoregular, and their mechanical and thermal properties are dependent on the pendant group. Interestingly, in the presence of boron trifluoride, a complete depolymerization could be achieved at 80 °C, allowing a close-loop recycling.[351] The combination of such block with other monomers compatibles with CROP could be of particular interest to prepare degradable/recyclable materials.

Uryu and coworkers[352] reported the copolymerization of 1,6-anhydro-2,3,4-tri- O-benzyl- α -D-glucopyranose with three- and four-membered cyclic ethers and with dioxolane. Depending on the comonomer, the structure of the copolymers were blocky (dioxolane) to alternating (epichlorohydrin). Reineke and Ellison[353] used the same approach and copolymerized levoglucosan derivatives with ϵ -caprolactone by cationic ring-opening

copolymerization. They managed to prepare copolymers from tribenzyl levoglucosan and ϵ -caprolactone, as well as from tribenzyl and triallyl levoglucosan derivatives using bismuth triflate as catalyst. The copolymer composition was controlled by the feed ratio and the reactivity ratio ($r_{\text{levoglucosan}} = 0.32$ and $r_{\text{CL}} = 2.94$). The reactivity ratio indicated a predominantly gradient microstructure for such levoglucosan-based copolymers. The degradation profile of such copolymer was not investigated.

3.4 Anionic Polymerization

3.4.1 Vinyl monomers

Anionic polymerization has been widely investigated since the pioneering work of Swarc on living anionic polymerization.[354] Now many monomers are available, even (meth)acrylate monomers which was thought to be non-compatible with such technique, and this technique is widely used for especially for rubber preparation but also for specialty materials.[354] In 2010, Zhang and coworkers[355] described the anionic copolymerization of MMA and ϵ -caprolactone mediated by the (1-tert-butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)-phosphoranylideneamino]-2 Λ 5, Λ 5-catenadi(phosphazene) (t-BuP₄) superbase. Such base was already reported to control the polymerization of cyclic ester but also to be compatible with the anionic polymerization of MMA initiated with a primary alcohol. The copolymerization of CL and MMA was carried out in THF at room temperature with MeOH as the initiator. The polymerization was very fast and led to polymers whose mole fraction of the polymer units were similar to the feed ratio in the feed. Moreover, the DSC and NMR analyses showed signals that are compatible with the statistical copolymerization of the two monomers. Indeed, signals of diads/triads were present and only one T_g was observed that

follow the Fox law (Fig. 65). The SEC analyses nevertheless presented a bimodal distribution that was ascribed to the undesired side-reaction of the propagating species with the carbonyl of MMA, a reaction that occurred frequently in anionic polymerization of such monomers. The molecular weight distribution is thus a mixture of linear and branched structure but with the same random CL – MMA microstructure. This copolymerization system was then named hybrid polymerization since there is a concomitant anionic vinyl and ring-opening polymerization.[356] The same authors thus extended this system to other monomers pairs such as ϵ -caprolactone with butyl acrylate and lactide or cyclic carbonate ester with methyl acrylate.[357, 358]

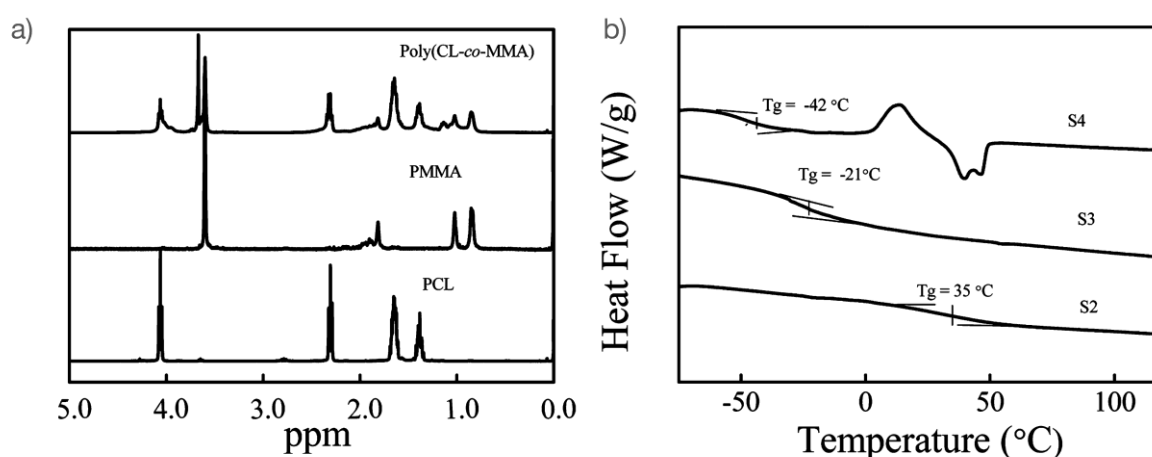


Fig. 65. a) ¹H NMR spectra for poly(CL-co-MMA) copolymer, PCL, and PMMA. b) DSC curves for the poly(CL-co-MMA) copolymers (S2: F_{MMA}=0.75, S3: F_{MMA}=0.5, S4: F_{MMA}=0.25) at a heating rate of 10 °C/min. Adapted from Ref. [355] with permission.

Zhang *et al.*[359] also extended their work on functional methacrylate to prepare materials that combined biodegradability and protein resistance. They thus combined the polymerization of L-lactide to impart degradability with 2-(2-Methoxyethoxy)ethyl methacrylate to bring protein resistance. Copolymers with a fraction of lactide in the polymer chain between 40 and 70%

was prepared. The analyses confirmed the random incorporation of the two monomer units. Due to the copolymer microstructure, the crystallinity of polylactide was decreased and thus the copolymers exhibited enhanced enzymatic degradation compared to the reference PLA. The protein resistance was assessed by quartz crystal microbalance with dissipation (QCM-D) and surface plasmon resonance (SPR). A 5-20-fold decrease in protein adsorption was observed, depending on the amount of 2-(2-Methoxyethoxy)ethyl methacrylate unit in the copolymer. Moreover, the cytotoxicity was also investigated and whatever the copolymer, the cell viability is above 85% for concentration up to 0.2 mg/mL.[359]

Matsuoka *et al.*[360] recently contested the hybrid mechanism proposed by Zhang. By a careful analysis of the hydrolyzed products, they believed that the microstructure of the copolymer is not a random incorporation of the two units but a simple graft structure with PMMA main chain and PCL graft chains. Zhang and coll.[361] responded to this article by preparing both the PMMA-g-PCL and the previous P(MMA-*co*-CL). Analyses by DSC confirmed the different behavior of the two copolymers. The degradation of the two copolymers is also different. P(MMA-g-CL) produced only PMMA oligomers whereas P(MMA-*co*-CL) led to oligomers with the presence of both monomer units but with a low amount of CL that has not been hydrolyzed yet since protected by the strong hydrophobic PMMA environment. The authors thus confirmed a simultaneous propagation leading to a random copolymerization but also a side-reaction of transfer onto the carbonyl of the MMA producing a branched structure (Fig. 66).

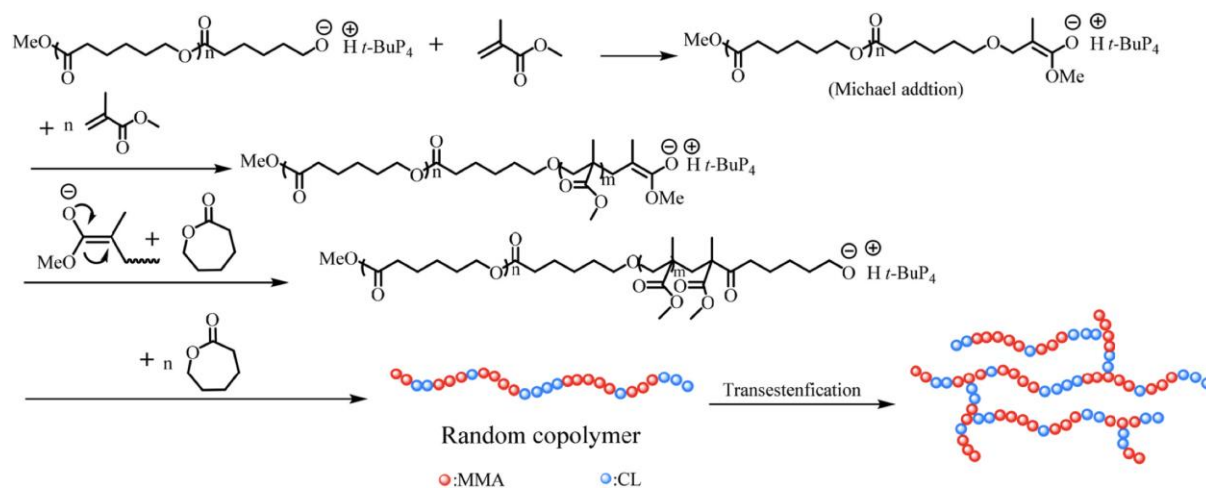


Fig. 66. Proposed mechanism for the $t\text{-BuB}_4$ -catalyzed copolymerization of CL and MMA. Reprinted from Ref. [361] with permission.

To confirm the mechanism, Zhang *et al.*[362] investigated the anionic hybrid copolymerization of N,N -dimethylacrylamide (DMA) and CL, where no transesterification could occur between DMA and CL units because the vinyl monomer does not have an ester group. The polymerization is carried out using similar conditions than previously established, that are $[\text{DMA}]/[\text{CL}]/[\text{BnOH}]/[t\text{-BuP}_4] = 50/50/1/1$ at $25\text{ }^\circ\text{C}$. The polymerization reached 95% conversion in 5 min. DSC, TGA, MALDI-TOF-MS confirmed the hybrid copolymerization and the random incorporation of the two monomer units. Moreover, the SEC chromatogram presented only one distribution that confirmed the impact of the transesterification reaction that occurred when MMA is copolymerized with CL.[362]

Jiang *et al.*[363] reported a new hybrid copolymerization system via the simultaneous oxo-Michael addition of diols onto diacrylate with the ring-opening copolymerization of ϵ -caprolactone catalyzed by a phosphazene base. The selected phosphazene base was the moderate $t\text{-BuP}_2$, since the deprotonation of the OH proton was desired to perform the oxo-Michael addition and a stronger based should have also promoted the unwanted vinyl addition mechanism. The mechanism is depicted in Fig. 67.

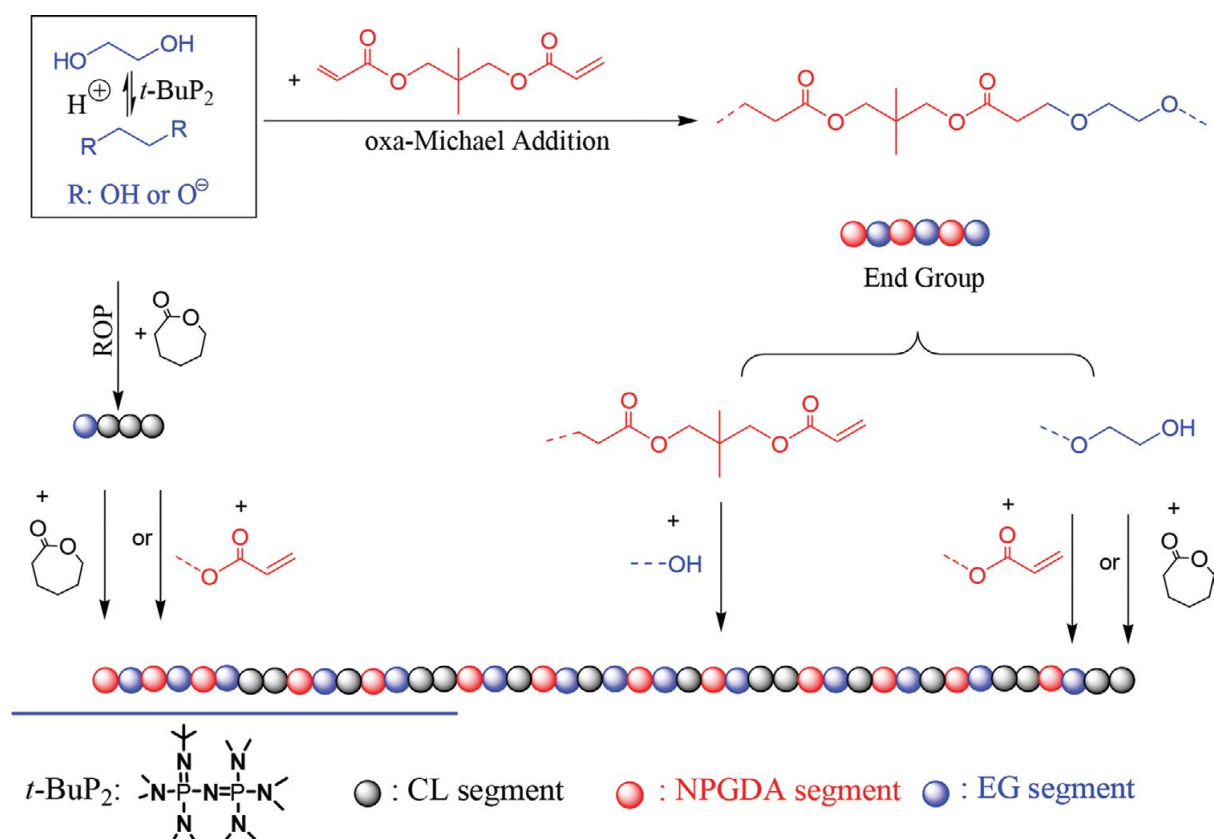


Fig. 67. Mechanism of phosphazene-catalysed hybrid copolymerizations of EG, CL, and NPGDA. Reprinted from Ref. [363] with permission

The final copolymer is thus a random poly(ester ether) with ethylene glycol, caprolactone and neopentyl glycol ester moieties. The random structure was proven by a detailed NMR analysis that suggest various diads. The preparation of the block copolymer by a sequential addition of the monomers that led to a different NMR signal confirmed the supposed microstructure. The presence of both ester units and hydrophilic ether units is supposed to lead to a copolymer with good hydrophilicity and degradability.[363]

3.4.2 Cyclic monomers

Besides vinyl monomers, anionic ring-opening polymerization is a well-established method to polymerize oxirane, epoxide, cyclic esters, etc. Among the most studied polyester, polycaprolactone is typically utilized as a long-term degradable material due to its slow breakdown rate brought on by its high crystallinity and this stability restricts its applicability in many applications. In this context, several efforts have been undertaken to change the pace at which materials based on PCL degrade. Zhang *et al.*[364] and latter Zhao and coworkers[365] tackled this problem by inserting polyether fragments onto the PCL backbone by the reaction between α,ω -dihydroxyl PCL and various epoxides such as ethylene oxide or monosubstituted epoxides catalyzed by strong phosphazene bases (Fig. 68a). The reactions were conducted at 60 °C in toluene involving using a PCL precursor and EO or monosubstituted epoxides in the presence of 0.8 equiv. of phosphazene base in comparison to the original PCL terminal hydroxyl groups.[365] A whole conversion of EO occurs in 24 hours. Both efficient transesterification reaction and nucleophilic ring-opening of EP were catalyzed by the catalyst's high basicity. The easy and effective conversion of PCL into ester-ether copolymers was demonstrated to have a strong effect on crystallinity (Fig. 68b) but minimal effect on the copolymer thermal stability. Ethylene oxide, propylene oxide and butyl oxide were inserting in a randomly manner unlike styrene oxide and ethylhexyl glycidyl ether. The P(CL-*co*-EO)s become more hydrophilic as the quantity of EO units increases, as seen by the steady reduction in static water contact angle (WCA). At ambient temperature, the copolymer with the highest amount of ethylene oxide (89%) became totally water soluble. QCM-D was then used to measure the rate of enzymatic degradation of P(CL-*co*-EO)s in phosphate buffer saline (PBS; pH=7.0). P(CL-*co*-EO)s with 38% presented the highest rate of enzymatic degradation since the crystallinity is low and the amount of ester moieties is accessible enough to have a fast rate of hydrolysis.

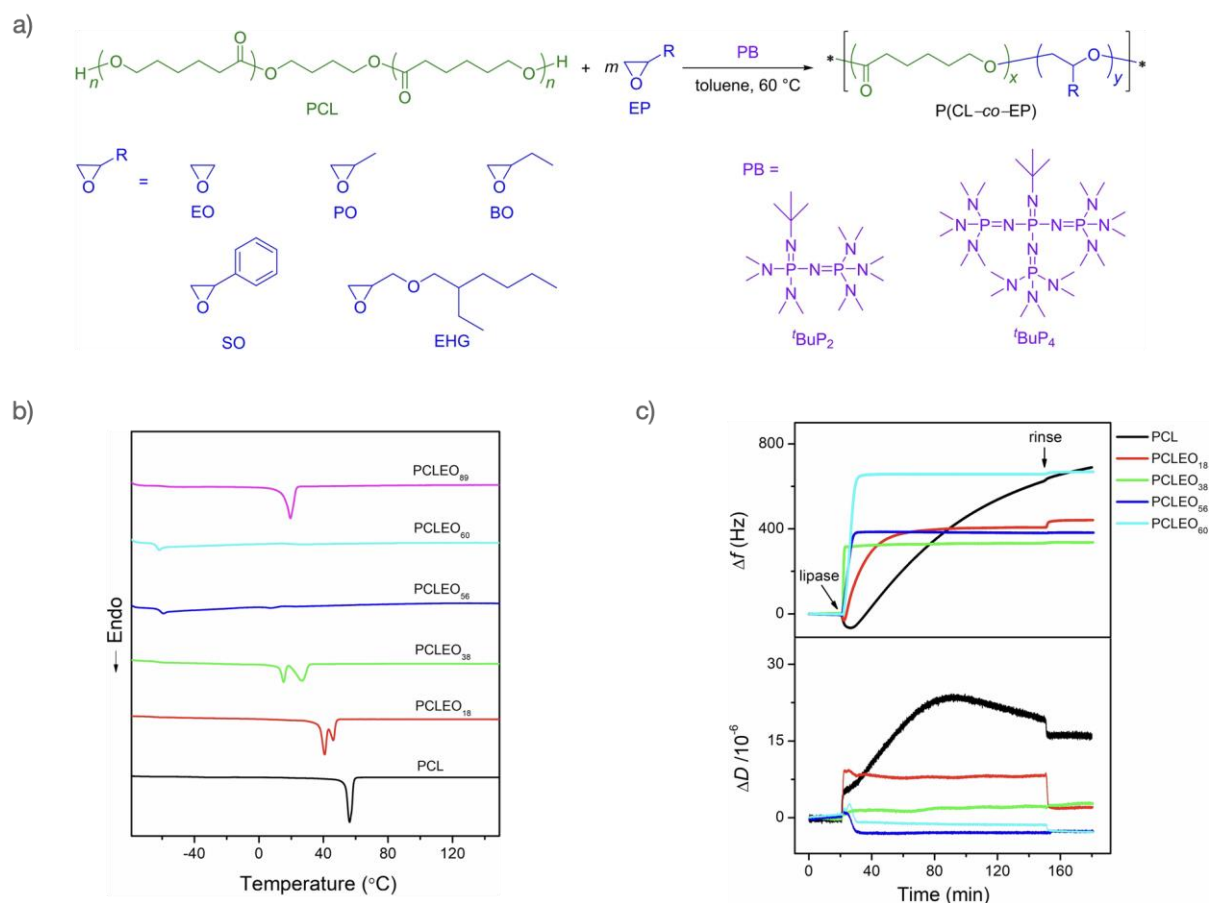


Fig. 68. a) General reaction scheme for the synthesis of P(CL-co-EP) ester-ether copolymers by reaction between a PCL diol and EPs catalyzed by phosphazene bases. b) DSC traces (second heating curves) of PCL precursor and P(CL-co-EO)s. c) Time-dependent frequency shift (Δf) and dissipation shift (ΔD) in QCM-D measurements for the enzymatic degradation of P(CL-co-EO)s in PBS at 25 °C. Reprinted from Ref. [365] with permission.

Besides cyclic esters, the anionic polymerization of epoxides has been well studied to prepare functionalized polyethers. In order to prepare degradable poly(ethylene oxide)s (see part 4.2), Frey and coworkers[366] carried out the copolymerization of ethylene oxide with 3,4-epoxy-1-butene to introduce an unstable vinyl ether functionality into the PEO backbone. With this comonomer, well-defined PEO with tunable length and amount on functionality are easily prepared by anionic ring-opening polymerization using NaH as catalyst and primary alcohol as initiator. The allyl moieties that are inserted were in a second step converted to vinyl ether

by isomerization using the Wilkinson catalyst (Fig. 69). With this approach, the hydroxy end-group is retained that is a prerequisite for bioconjugation. A mixture of E and Z isomers were obtained at the end of the isomerization reaction. The degradation of the copolymers was assessed in acidic environment by ^1H NMR (D_2O , 37°C). The Half-life times varied from 12 h to 112 h for pH between 4.4 and 5.4 respectively (Fig. 69b). After hydrolysis, as predicted, there were notable changes to lower molecular weights along with a broadening of the molecular weight distribution with moderate dispersities (1.6–1.8). The average molecular weights of the hydrolyzed copolymers were close to $1000\text{ g}\cdot\text{mol}^{-1}$ for different copolymers having a constant 4 mol% of vinyl ether functionality. This value that is close to the theoretical length between two vinyl ether moieties proved a random distribution of vinyl ether units along the backbone. This suggests that the quantity of vinyl ether inserted can alter the average molecular weight of hydrolysis products. Frey and coworkers[367] thus extended this work to degradable PEO networks by modifying the end groups of the degradable PEO with methacrylate groups and their further cross-linked by irradiation at 365 nm in the presence of DMPA as initiator.

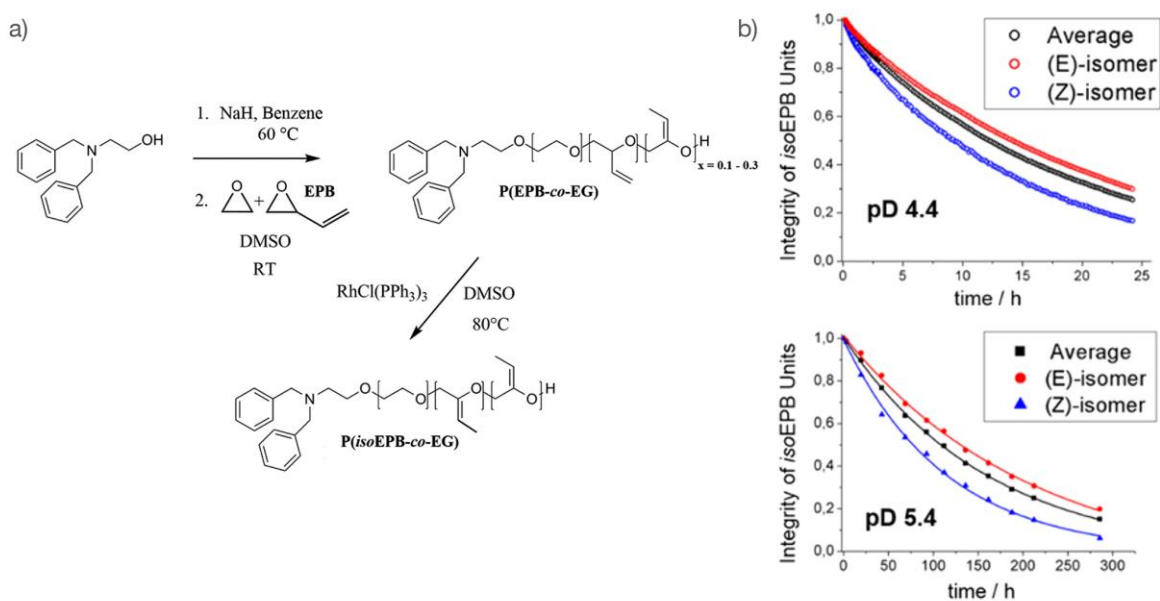


Fig. 69. a) Synthesis Procedure for P(isoEPB-*co*-EG) Copolymers b) Quantitative analysis of ^1H NMR hydrolysis studies for P(isoEPB₅-*co*-EG₁₄₃) showing the integrity (integral ratio $I(t)/I(t_0)$) of isoEPB units plotted vs time for pD 4.4, and 5.4. Adapted from Ref. [366] with permission.

Huang and coworkers[284] recently managed to prepare a chain growth polymerization based on a thiol-Michael addition and whose propagation is performed by a thiolate anion. He used similar structures than the one developed by Niu and coworkers[283] to perform radical ring-opening polymerization. Even if this very recent approach has not yet been used in a hybrid polymerization system hold great promise to introduce degradability into polymer backbone via an anionic mechanism.

3.5 Ring-Opening Polymerization

There is many kinds of ring-opening polymerization and a vast majority of them led to polymers with heteroatoms into the polymer backbone that make them inherently degradable. In this part we will mainly focus on polyesters that is the representative exemple of the polymers prepared by ROP. Traditional degradable polymers, including lactide-glycolide copolymers (PLGA), polycaprolactone (PCL), and polylactide (PLA), have not received much attention as sources of plastic wastes due to the widespread belief that they would disintegrate in any environment. Biodegradable polymers, however, actually only decompose under specific environments (temperature, humidity, light, oxygen availability, and microbes). The fact that they are referred to as "biodegradable polymers" does not, therefore, rule out the possibility that they may cause environmental pollution. To investigate this feature Agarwal and coworkers[368] studied the degradation of many polyester films ($1.2\text{ cm} \times 1.2\text{ cm} \times 320$

µm) in seawater and freshwater using controlled conditions. The only polyester that presented complete degradation is PLGA that totally decomposed in 270 days. PHB only slightly decomposed (8.5 %) in one year and other polyesters such as PCL, PLA, PBAT did not show any degradation similarly to PET as negative reference. Thus in the case of polyesters, that is biodegradable in specific conditions, there is room for innovation to speed up the degradation to extend the range of experimental condition in which biodegradation could occur such as freshwater or seawater. In the following we will focus on the modification of the polymer backbone by copolymerization to speed up the degradability.

Almost all PLGAs are random copolymers, where the only intrinsic characteristics that can be altered to tailor hydrolysis behavior are the L:G monomer ratio and molecular weight. Sequence is a potent but underutilized technique for designing PLGAs with finely tailored behavior. Mayer and coworkers[369, 370] have prepared various PLGA via either ROP of lactide/glycolide or via segment assembly polymerization (SAP) approach[371] with similar M_n and dispersity. The copolymers were then suspended as microparticles at pH 7.4 in a phosphate buffer for 8 weeks and their hydrolytic degradation behavior was monitored (Fig. 70).

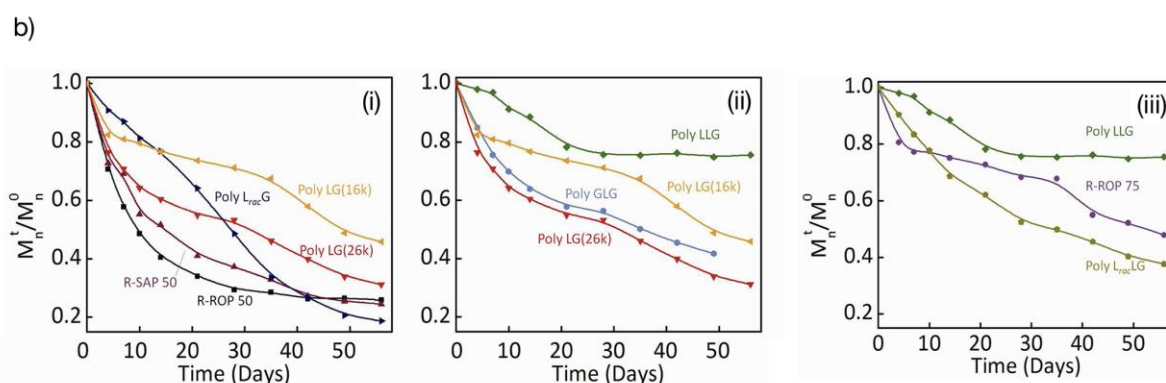
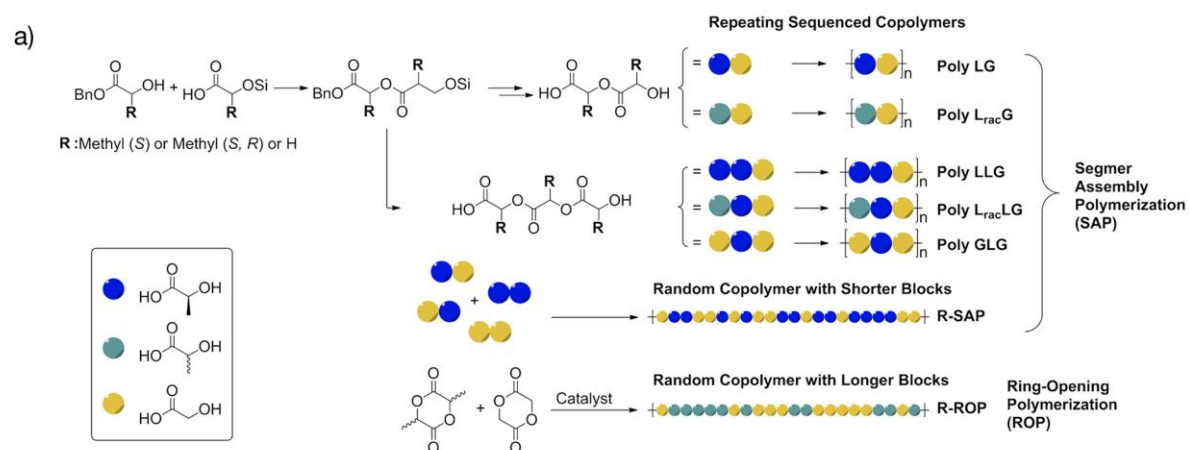


Fig. 70. a) Different method to prepare sequence copolymers and random copolymer of poly(lactic-co-glycolic acid). b) Molecular weight loss as a function of hydrolytic degradation time for the repeating sequenced and random sequenced PLGAs: (i) comparison of all polymers with a 50:50 LG ratio; (ii) comparison of polymers with varying L:G ratios; (iii) comparison of LLG polymers with varying stereochemistries. Adapted from Ref. [370] with permission.

After an initial weight loss, the rate of hydrolysis did not appear to be significantly influenced by the initial molecular weight (Poly LG 16k Vs Poly LG 26k Fig. 70b). While there are differences in the initial relative weight losses, the rate after the first loss seemed to be largely unrelated to the initial molecular weight. The sequenced copolymers deteriorate more gradually and at a more steady pace than the random copolymers with the same L:G composition, which is the most significant trend that can be seen in the hydrolysis investigations.[370] R-ROP 50

and R-SAP 50, the 1:1 L:G random copolymers, both have exponential weight loss patterns, as was previously demonstrated. It's interesting to note that the R-ROP 50 copolymer deteriorated faster than the R-SAP 50 copolymer (M_n half-life = 14 days). The authors also looked at how the L:G ratio in the polymers relates to the rate of degradation. For random copolymers, it is widely known that the L:G ratio affects the rate of degradation; a greater lactic unit concentration causes slower hydrolysis rates. It can be observed from the subset of hydrolysis profiles presented in Fig. 70b-d that this pattern persisted for the random copolymer, R-ROP 50 and RROP 75. The sequenced copolymers follow this pattern as well. The importance of the stereochemistry is also demonstrated. In comparison to their stereopure equivalents, the 1:1 and 2:1 L:G polymers' racemic analogues, poly LracG and poly LracLG, hydrolyzed substantially more quickly.[370]

Another way to increase the degradability of PLA is to enhance the hydrophilicity of the polymer. In that way, many approaches have been used. Coudane and coworkers[372] for example used a lactide functionalized with a protected gluconic acid derivative to insert hydroxy group along the polymer chains. The interest of inserted hydroxy group is to enhance the T_g via the formation of hydrogen bonds. Six-membered cyclic carbonate are interesting comonomers for lactide since they could be readily degraded by the reaction of nucleophilic reagents on the carbonate groups. Zhuo and coworkers[373] thus prepared the cyclic carbonate 9-phenyl-2,4,8,10-tetraoxaspiro-[5,5]undecane-3-one and copolymerized them with D,L lactide. After deprotection of the ketal group, a poly(carbonate-ester) containing pendant hydroxyl groups was obtained. The copolymers were then degraded *in vitro* using proteinase K and either phosphate buffer solution (pH 7.4) or Tris-HCl buffer solution (pH 8.6). By changing the ratio of two monomers, the rate of degradation may be controlled. The pendant hydroxyl groups on the copolymer significantly accelerated the rate of breakdown in PBS.[373]

This copolymerization system was also studied by Jing and coworkers[374] that confirmed the enhanced degradation due to the hydroxyl groups. Carboxylic acid was also inserted into via a six-membered cyclic carbonate monomer.[375] Its homopolymer, the poly(glyceric acid carbonate) presented a very fast degradation profile in both deionized water and buffer solution.[376] Copolymers of lactide (either L-lactide or D,L-lactide) and the cyclic 2-methyl-2-benzyloxycarbonyl-1,3-trimethylene carbonate were obtained via an immortal polymerization process and the debenzoylation was performed by Pd/C hydrogenation.[375] Different structures such as block, tapered and random copolymers were tested in in basic buffer aqueous solution (pH = 9.97). If the carboxylic acid is protected no degradation was observed within a week. The degradation profile was presented in Fig. 71 that followed the appearance of the degradation products of either the lactide group (2-hydroxypropanoic acid HPA) or the cyclic carbonate (2,2-bis(hydroxymethyl) propionic acid DMPA).

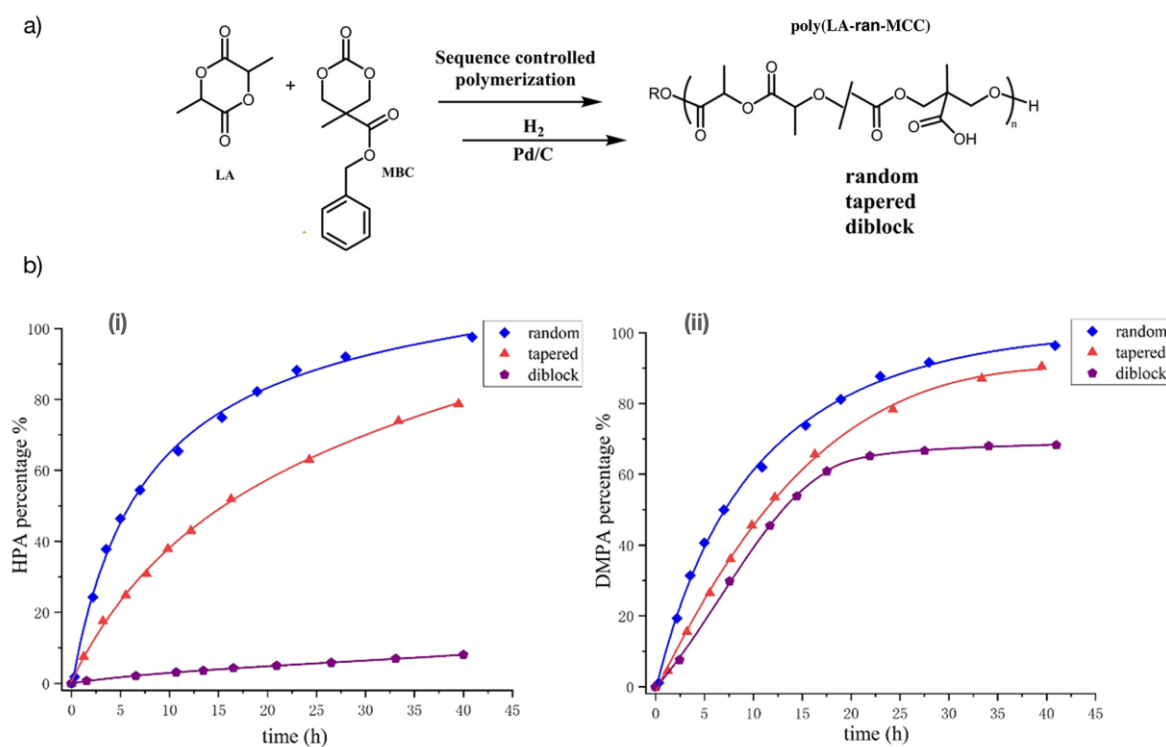


Fig. 71. a) Preparation of carboxylic acid containing PLA via the copolymerization of LA with 2-methyl-2-benzyloxycarbonyl-1,3-trimethylene carbonate (MBC) and subsequent

debenzylation to produce poly(LA-ran-MCC). b) Plots of the percentage of degradation products (i) 2-hydroxypropanoic acid (HPA) and (ii) 2,2-bis(hydroxymethyl) propionic acid (DMPA) versus degradation time for random poly(LA-ran-MCC), tapered poly(rac-LA-tap-MCC), and diblock PLLA-*b*-PMCC. Reprinted from Ref. [375] with permission.

Only the random copolymer presented a complete degradation on this time scale. Regarding the diblock polymer, DMPA is produced significantly more quickly than HPA, demonstrating that the hydrophilic polycarbonate chain segment is more readily broken down than the hydrophobic PLLA segment. Nevertheless, no complete degradation occurred since long hydrophobic PLA chains may shield some of the carbonate moieties in block and tapered copolymers. By a careful NMR analysis, the authors demonstrated that the Lactide–Carbonate (L-C)/Carbonate–Lactide links in copolymers are the more fragile bonds, followed by Carbonate/Carbonate (C link) and the strongest being the Lactide/Lactide one. This finding confirmed that the quantity of L-C and C-links in polymer main chains is the key parameter to determine how quickly the copolymer would degrade.[375] Another possibility to introduce hydrophilicity into PLA chain is by the copolymerization of lactide with a cyclic monomer derived from aspartic acid.[377] The copolymers with 10 and 20 mol% of benzyl ester of the aspartic acid presented a two-fold increase of the rate of degradation in PBS compared to the pure PLA as reference.[377]

Hillmyer and Ellison[378] focused on the insertion of salicylate ester units (Fig. 72) into the polyester chains to enhance the degradability of poly(lactides). This strategy expands upon their finding that salicylic acid, a hydrolysis byproduct of synthetic salicylate-based polymers, can cause autocatalytic acceleration of water degradation due to its high acidity (pKa 2.3).[379]

Different methods of incorporation of such additive was tested. First the copolymerization of lactide and salicylic methyl glycolide (SMG) (Route A) but also the *in-situ* polymerization – transesterification of salicylic methyl glycolide in the presence of an already prepared PLA (Route B) and finally the transesterification between PLA and Poly(salicylic methyl glycolide) (Route C). ^1H NMR analyses showed that the two last routes led to random copolymers poly(lactide-*co*-SMG) (PLS) whereas the direct copolymerization produced multi-block like microstructures. The characteristics of the pristine PLA are only slightly affected due to the transesterification reaction, the small decrease of M_n that could be seen originated from trace impurities that caused chain fragmentation. With amount of SMG up to 25 mol%, degradation temperature, elastic modulus, elongation at break, and oxygen barrier properties were not impacted. The T_g of the copolymers even slightly increased from 57 to 67 °C.

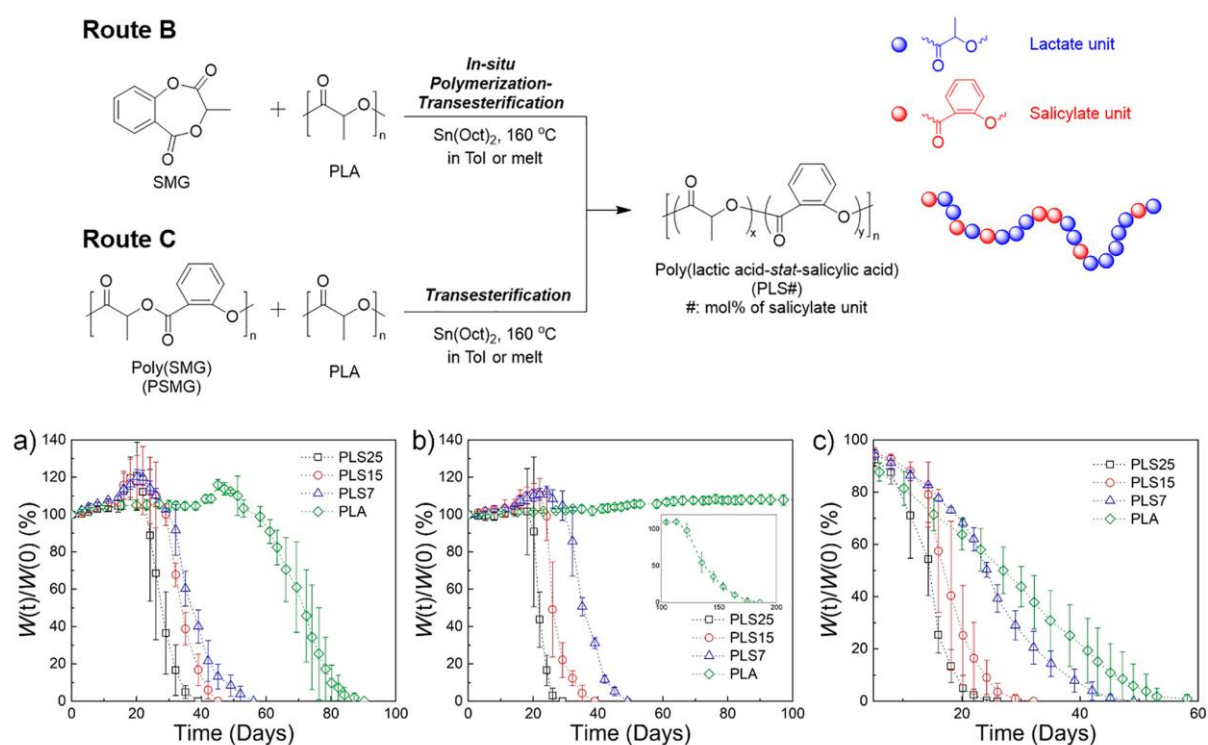


Fig. 72. Preparation of random copolymers poly(lactide-*co*-SMG) (PLS). Mass loss profiles of polymers under the hydrolytic degradation conditions at 50 °C in (a) 1 M PBS (pH 7.4), (b) seawater (pH 8.1), and (c) 0.1 M NaOH (aq.). Possible facilitated degradation mechanisms of

PLS by salicylate sequences under (d) basic and (e) acidic (autocatalysis) conditions. Reprint from Ref. [378] with permission.

The copolymers were then placed at 50 °C in aqueous phosphate buffer solution (PBS, 1 M, pH 7.4), artificial seawater (pH 8.1), and NaOH solution (0.1 M) to conduct degradation studies (Fig. 72). After a brief induction time, PLS samples exposed to PBS revealed total mass loss. PLA also demonstrated total mass loss following water absorption, but with a double reaction time. In simulated saltwater, PLS showed even quicker bulk erosion, losing all of its mass in just 29 days (Fig. 72) whereas PLA do not present a significant degradation. Additionally, PLS demonstrated faster mass loss profiles than PLA in an alkaline solution (0.1 M NaOH). The authors also successfully extended this approach to poly(caprolactone) (PCL) and poly(ethylene glycol-co-cyclohexanedimethanol terephthalate) (PETg).[378]

Another additive that could enhance the degradation of PLA is the insertion of an acetal bond as an abiotic hydrolysable group.[45] The copolymerization of D,L-lactide with 1,3-dioxolan-4-one (DOX) that is produced from potentially biosourced glycolic acid and formaldehyde produced the poly(ester acetal) copolymer with various L:DOX ratios (Fig. 73). The structure was confirmed by ¹H NMR and demonstrated the persistence of the acetal group into the polymer backbone. The insertion of DOX into the polymer chains acted as defects and thus decreased the melting temperature but the T_g was only slightly impacted due to the rigidity given by anomeric interaction. The polyesteracetal copolymer, with 4% DOX incorporation, was degraded in various environments with a commercial polylactide as reference. Thin films (0.25 mm thick) were prepared and immersed in various aqueous solution (Fig. 73). The films mass and molecular weight were used to track their changes over time. Analysis showed that

unlike the reference PLA, the polyesteracetal copolymer significantly degraded over the course of 45 days, losing more than 1% mass and 35% of the M_n .

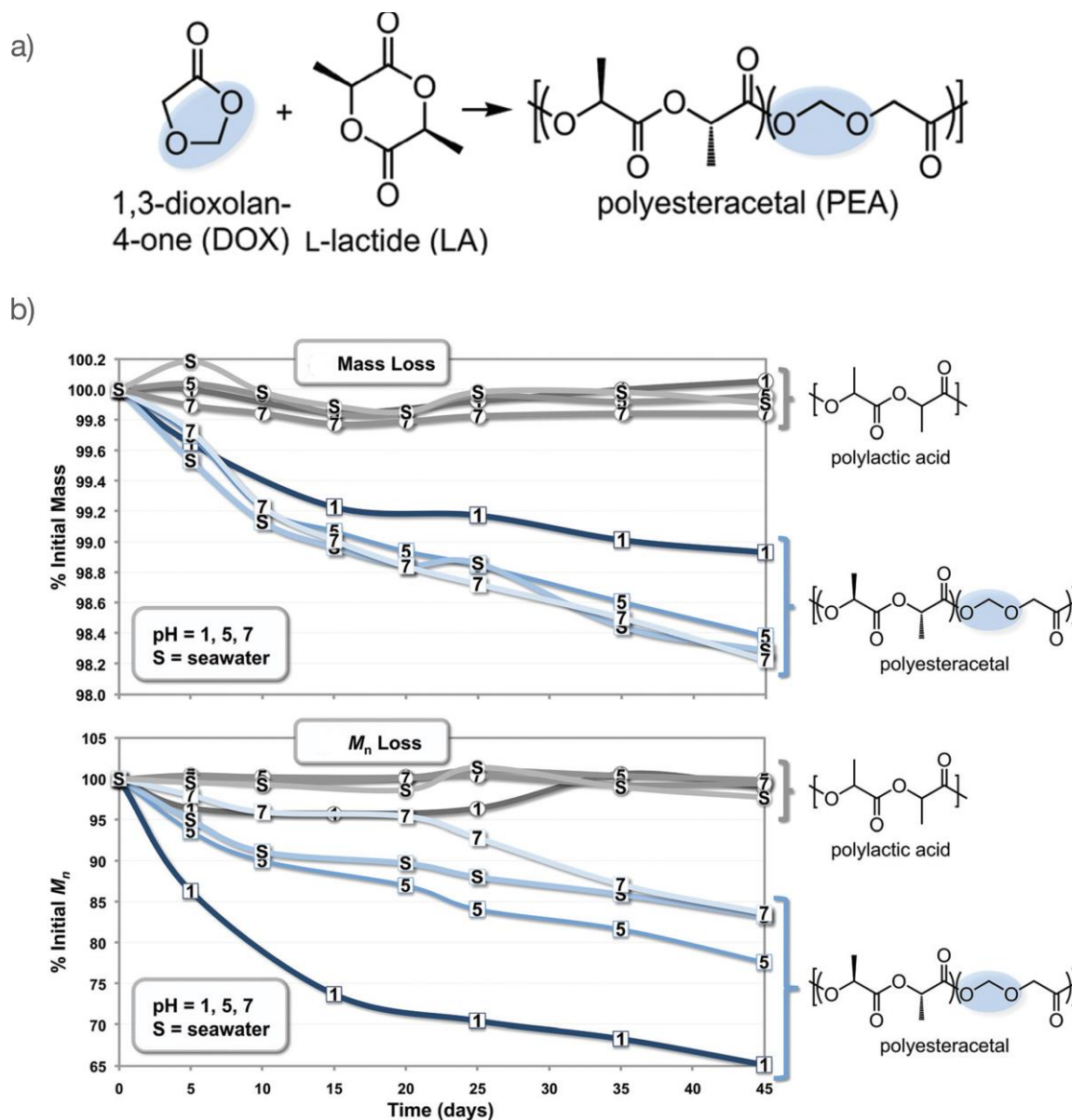


Fig. 73. a) Copolymerization strategy for synthesizing the polyesteracetal copoly(lactide/1,3-dioxolan-4-one). b) molecular weight loss and mass loss upon exposure to aqueous environments of pH 1, pH 5, pH 7 (distilled water), and seawater, over 45 days. Reprint from Ref. [45] with permission.

The polyesteracetal copolymer degraded also in mildly acidic (pH=5), neutral, and mildly basic conditions and seawater (Atlantic Ocean, pH = 7.5). It's interesting to note that under neutral conditions, the polyesteracetal copolymer had the fastest mass loss,[45] indicating that the key parameter for degradation is in that case unclear and maybe the cleavage do not occur preferentially at the acetal site but the change of hydrophilicity of the could be also another important parameter.

Buchard and coworkers prepared sugar based cyclic monomers in order to develop renewable polymers. Among the various prepared structures, they identified sugar-derived xanthates[380] as interesting monomers to induce fast et efficient UV degradation of the obtained polymer.[381] Such monomers were then tested in copolymerization with L-lactide to prepare UV-sensitive PLA.[382] Copolymers were obtained with 1-29 mol% of thioester/thionocarbonate moieties with a slightly lower incorporation of thiocarbonyl functionality than in the feed. The mechanism consists in the attack of the xanthate monomer by PLLA and the cleavage of the C-S bond leading to a thionocarbonate bond. The released thiol thus attacks some lactide monomers to produce the thioester functionality. The copolymers presented similar thermal and stability behaviors than reference PLLA. The degradation was thus performed in THF via irradiation at 365 nm and a gradual decrease of M_n was monitored during the irradiation process (Fig. 74). Up to 60% decrease of M_n could be obtained in 6 hrs at room temperature with the presence of only 3 mol% of additive in the polymer backbone.

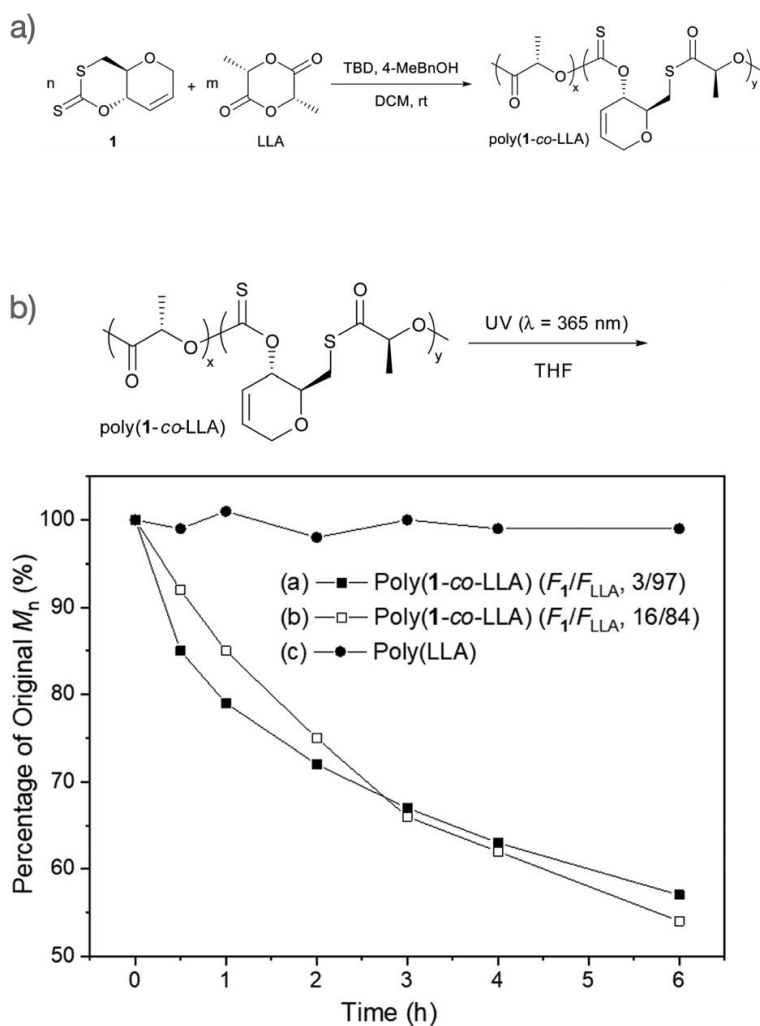


Fig. 74. a) Ring-opening copolymerization of cyclic xanthate with L-LA catalyzed by TBD b) Percentage of original M_n vs. time, following the exposition of poly(1-co-LLA) copolymers to UV irradiation ($\lambda = 365$ nm). Reprinted from Ref [382] with permission.

Besides xanthates, phosphorous containing groups could be interesting functionalities to insert into PLA chain to enhance the degradability. Buchard *et al.* studied first the copolymerization between lactide and cyclic phosphonate monomers.[383] They showed that this copolymerization system led to tapered block copolymers due to the difference of reactivity of the two monomers. By changing the catalyst, inverse reactivity could be reached, and the compositional drift could be lowered by a temperature sequence protocol, allowing to tune the

properties of the resulting poly(phosphonate-*co*-esters). The degradation of the copolymers and the impact on the phosphonate insertion was not studied in detail.

One interesting approach to enhance degradation of PLA in mild conditions such as seawater is to introduce an intramolecular transesterification reaction. This approach is inspired by the RNA mechanism of degradation whose 2'OH in the ribose unit is in β -position of the polyphosphoester backbone, favoring the cyclic intermediate and thus the rate of hydrolysis. Wurm *et al.* [384] translated this mechanism for the preparation of seawater-degradable PLA (Fig. 75). They thus performed the copolymerization of lactides with a cyclic phosphate bearing a protected hydroxy-functionality, the 2-ethylene glycol vinyl ether-1,3,2-dioxaphospholane 2-oxide (EVEP).

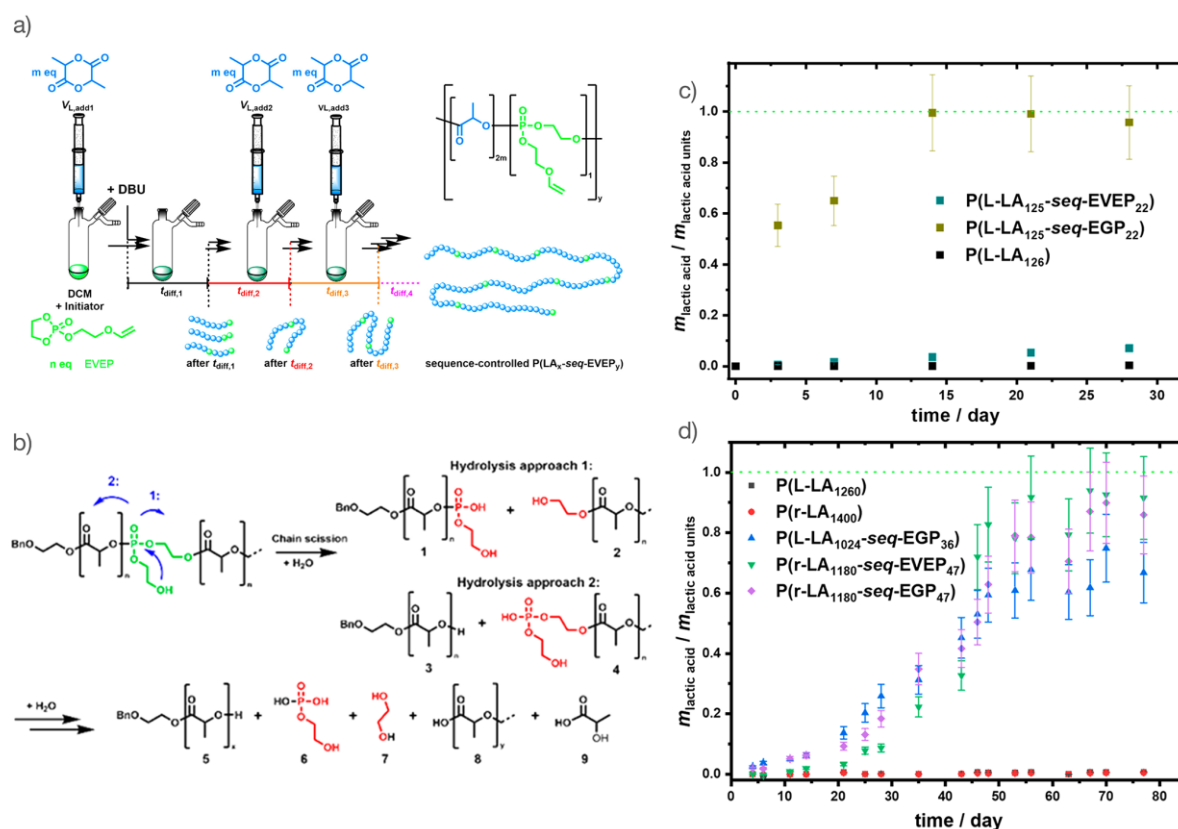


Fig. 75. a) Sequence-controlled copolymerization of EVEP and LA with multiple sequential additions. b) Two possible ways of hydrolysis in the first step leading to different intermediates.

Subsequent hydrolysis forms ethylene glycol, 2-hydroxyethylphosphate, and the corresponding lactic acid oligomers. c-d) Degradation of PLA, P(LA-seq-EVEP), and P(LA-seq-EGP) copolymer films in artificial seawater (lactic acid was quantified using an enzymatic assay). Reprint from Ref. [384] with permission.

The copolymerization of LA and EVEP was performed in the presence of DBU as catalyst and a strong gradient copolymerization was obtained. To counterbalance this reactivity difference, sequential multi-additions of monomers were performed to insert homogeneously the phosphoester moieties into the PLA backbone. When less than 3mol% of phosphoester units were inserted, the mechanical and thermal properties of PLA were unaffected. Without deprotection, the copolymers were perfectly stable for several months. After mild acidic vinyl ether deprotection, films of the copolymers were prepared and their degradation in buffered artificial seawater was monitored. When the chain length of the copolymer was close to 150, the degradation of PLA with 15 mol% was complete in 15 days, whereas the reference PLA and the vinyl ether protected PLA was not affected. For longer chains, degradation is obtained between 50 to 80 days depending on the amount of phosphoester units. After hydrolysis of the phosphoester breaking point, PLAs with free OH-end groups are produced, which will be further hydrolyzed by backbiting. The fast degradation process results from the combination of an increase in chain ends and an increase in hydrophilicity.

Finally, the insertion of weak bonds could also be compatible with other ring-opening systems. For example, polysarcosine (PSar), that is, poly(*N*-methyl glycine), is become very popular in biomaterials as biocompatible, noncytotoxic, and stealth-like polymer.[385] This polymer is prepared via the ring-opening polymerization (ROP) of α -amino acid *N*-thiocarboxyanhydrides (NTAs). Ling et al.[386] propose to copolymerize sarcosine with alanine that is prone to

enzymatic degradation to prepare a degradable polysarcosine (Fig. 76). The *N*-thiocarboxyanhydrides ring-opening polymerization of the two comonomers initiated by Acetic Acid in DMAc led to a controlled and living polymerization with 0-43 mol% of alanine moieties. The copolymers were then incubated with porcine pancreatic elastase in PBS for 50 days. Whereas the reference PSar do not show any degradation, the copolymer containing alanine residue presented a degradation that increased with the amount of weak bond inserted. Complete degradation in 50 days was even observed with the presence of 43 mol% of alanine. The biodegradability and the non-cytotoxicity of this copolymer make it as a promise alternative to PEG for drug delivery application.[386]

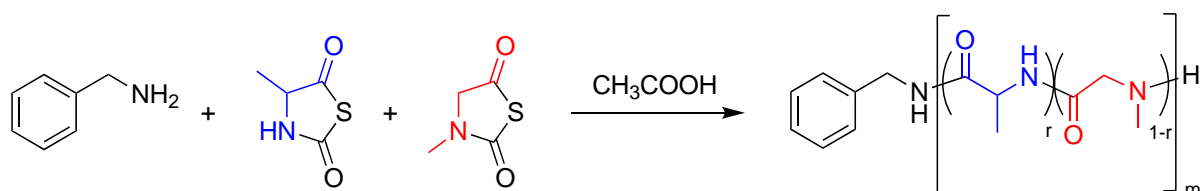


Fig. 76. Preparation of degradable polysarcosine via the insertion of alanine residue.

3.6 Step-Growth polymerization

Many different systems could undergo step growth polymerization. In this part we will illustrate the use of this technique to prepare precisely designed degradable materials. The polycondensation reaction of diols/diacids or hydroxy-acids will be discussed in the PE-mimic section (4.1). The preparation of telechelic polymers could be performed using various techniques. Post-modification of polymer chain ends prepared by ATRP or RAFT by nucleophilic substitution or aminolysis can install azide or thiol functionalization to perform step growth polymerization via click chemistry.

Lee and coworkers[387] prepared pH-degradable polystyrene via the ATRP of polystyrene whose bromine end-group was modified to an azide functionality and whose initiating group was modified to insert a propargyl functionality via a carbamate function (Fig. 77a). In the presence of CuBr/2,2'-bipyridyl (bpy) in DMF, the PS with an alkyne group on one end and an azide group on the other end was then self-coupled to produce the desired multisegmented PS. Its molecular weight and molecular weight distribution grew over time, as expected for such step-growth-type polymerization processes. Finally, the multisegmented PS's ester and carbamate linkages were hydrolyzed in the presence of HCl to give back the individual PS chains.[387]

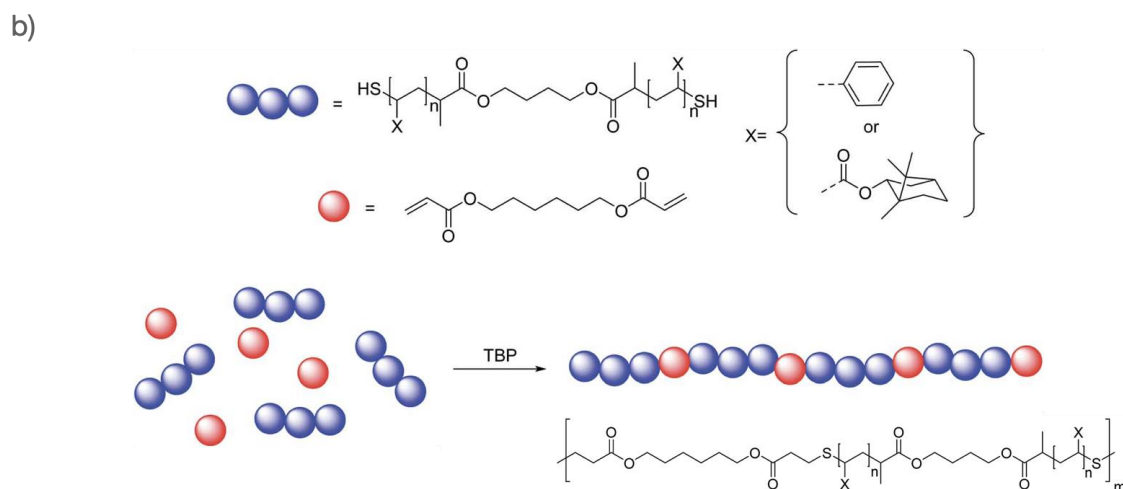
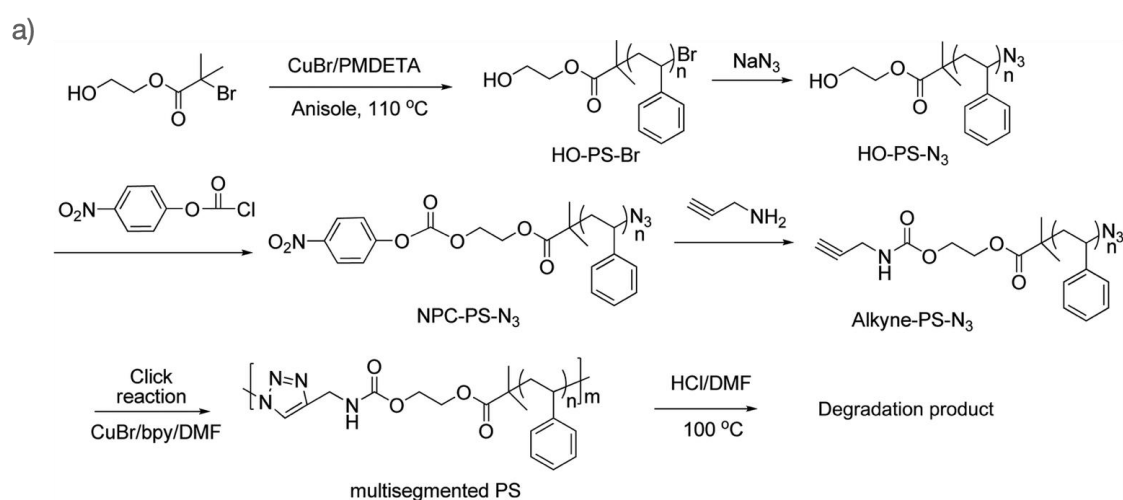


Fig. 77. a) Preparation of pH degradable multi-segmented polystyrene. b) Preparation of (bio)degradable polystyrene or poly(isobornyl acrylate) via thioether linkage.

α,ω -dithiol-telechelic polystyrene (PS) and poly(iso-bornylacrylate) (PiBoA) polymers were prepared by RAFT polymerization followed by aminolysis with hexylamine to produce thiols. The produced dithiol polymers were then used as Michael donors in a thiol-ene step-growth polymerization catalyzed by phosphine, either with hexanediol diacrylate to produce linear polymers with evenly spaced diacrylate units, or with multifunctional acrylates to produce multi-segmented poly(β -thioester) (PBT) linear polymers and networks (Fig. 77b).[388] Aminolysis and thiol-ene Michael addition processes may be carried out in a single pot, although purifying the polymeric thiols first yields better results. The materials have T_g s between polystyrene and pure poly(β -thioester)s and are extremely thermally stable. Furthermore, basic or enzymatic hydrolysis of the labile ester bonds in the polymer backbone demonstrates the materials' (bio)degradability leading to the original low molecular weight PS precursors.

More sophisticated trigger could be inserted into the polymer chains. For example, α,ω -telechelic PHPMA chains prepared by RAFT polymerization were linked together by means of a difunctional peptide GFLG sequence via copper(i)-catalyzed azide-alkyne Huisgen cycloaddition (Fig. 78).[389] This versatile method allows for additional GFLG sequences to be inserted in the polymer structure, either in the middle of each PHPMA chain by using a GFLG-containing difunctional RAFT agent, or on the side chain between each drug and the polymer scaffold to promote the drug release. This system was proven to be biodegradable and bioresorbable by means of pharmacokinetics and biodistribution studies and has been applied to various anticancer agents (for example, Dox, gemcitabine, paclitaxel, platinum drugs) and prostaglandin E1 as an anabolic agent in bone.

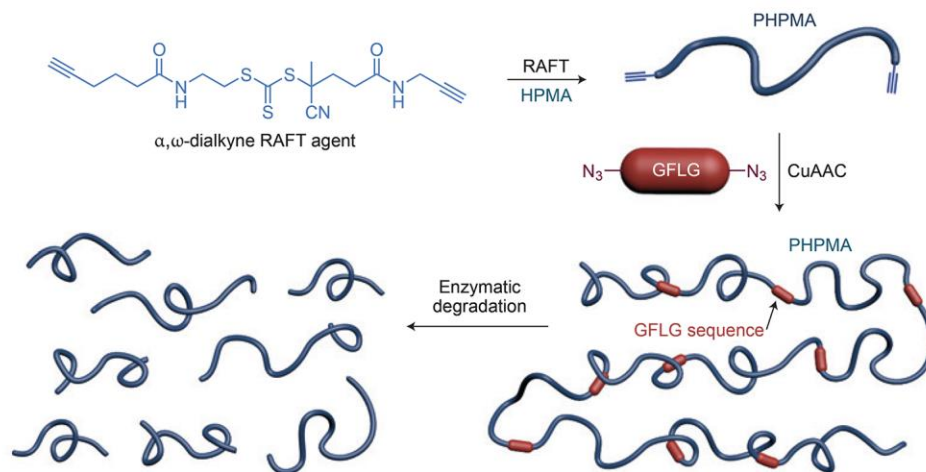


Fig. 78. Multisegmented polymer comprising biodegradable sequences in the main chain. Reprinted from Refs. [389] and [129] with permission.

Telechelic polyesters could also be prepared by ROP. Fuoco[390] developed a strategy that combines ring-opening polymerization (ROP) and step-growth polymerization (SGP), that could be performed sequentially by a simple catalyst switch. The main goal was to extend esters' degradability functions to reactive groups that facilitate surface erosion, including acetal linkages. Indeed, the cleavage of acetal bonds occurs under hydrolytic or acidic conditions, is quicker than water penetration in the polymer bulk, and forms lower molar mass, neutral molecules that are more likely to diffuse off the polymeric surface, promoting surface erosion. These properties all differ from the bulk degradation of polyesters, and novel degradability results can be obtained by combining both types of linkages in the same chain.

The simplest initiator that could be used is ethylene glycol vinyl ether. The methodology was first done using caprolactone as lactone. 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) was used as organocatalyst for promoting the ROP of CL at rt and in THF to produce vinyl ether oligoCL with regulated length and complementary chain-ends (Fig. 79).

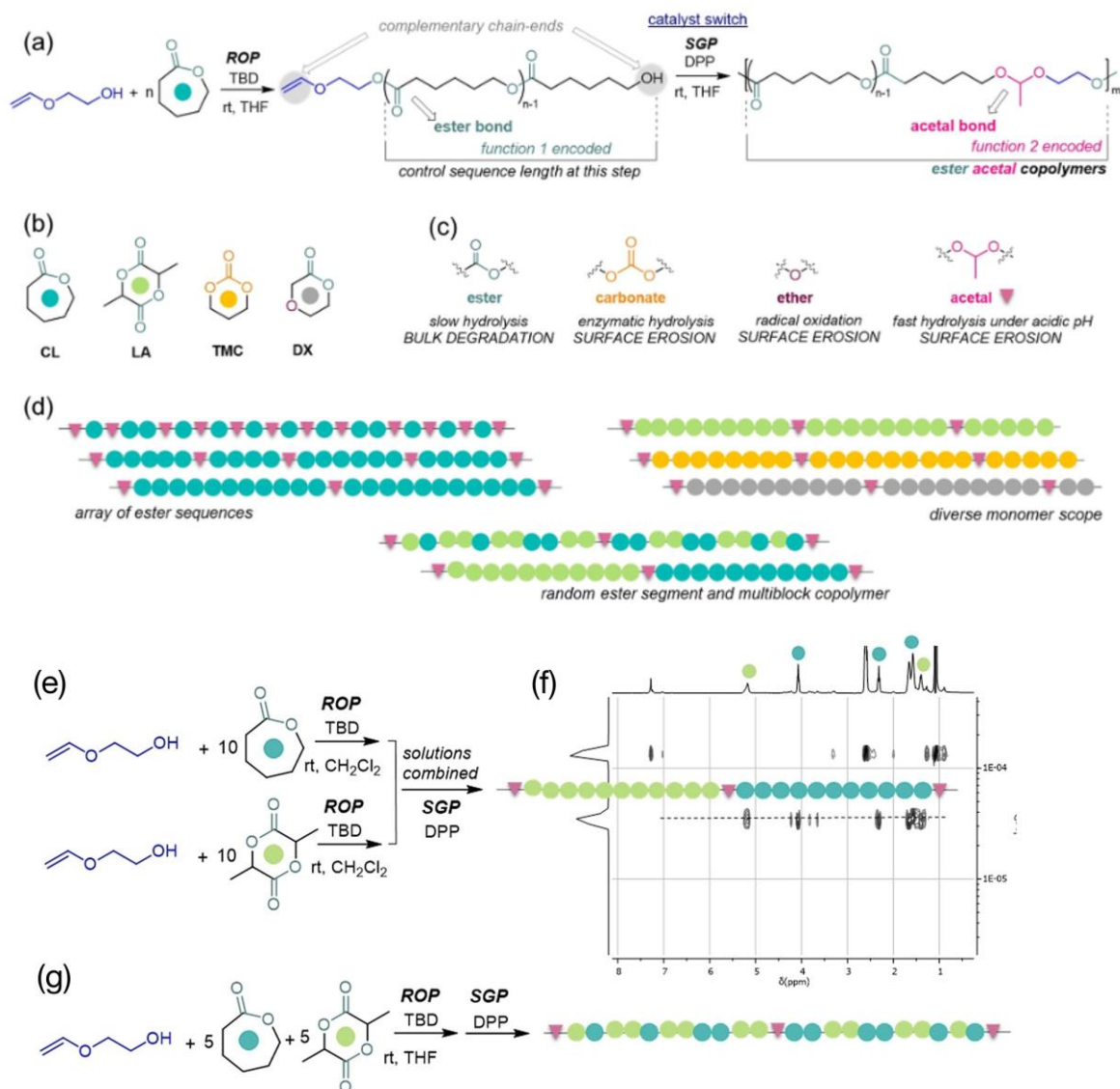


Fig. 79. a) Reaction scheme of the polymerization approach combining two macromolecular concepts, i.e., ring-opening polymerization (ROP) followed by step-growth polymerization (SGP) with CL as model monomer. b) monomer scope; degradability functions incorporated along the macromolecules; designed microstructures. Reaction scheme for the synthesis of c) multiblock and d) random ester acetal copolymers of CL and LA. DOSY NMR spectra (400 MHz, CDCl₃) of the multiblock LA/CL copolymer with spatially regulated acetal bonds. Reprinted from Ref. [390] with permission.

Switching from ROP to SGP was achieved easily by adding an excess amount (3 equiv. to TBD) of Bronsted acid diphenyl phosphate (DPP) to the polymerization mixture, which changed the reaction conditions from basic to acidic. Therefore, the heterotelechelic macromonomers undergoing acid-catalyzed SGP between the complementary chain ends via the addition of the -OH directly to the CH₂=CHO-producing acetal bonds in a Markovnikov reaction. Following the SGP, the molar mass significantly increased, reaching the sample's highest M_n value for the oligoPCL prepared with a CL:initiator ratio = 10:1. The materials degradation is affected by the placement and quantity of acetal bonds, which are controlled by choosing the monomer to initiator ratio. Under hydrolytic circumstances over an 8-day period, the mass loss of all films containing ester acetal copolymers of CL was assessed and contrasted with a commercial PCL. Each copolymer sample, in contrast to the PCL, demonstrated mass loss from the earliest stages of degradation, and the erosion grew through time as well as by adjusting the ratio of acetal to ester functionalities. This methodology was also extended to L-lactide, trimethylene carbonate (TMC) and dioxanone (DX). Moreover, multisegmented copolymers could be prepared using two telechelic oligomers prepared separately targeted the same characteristics (caprolactone and lactide oligomers for example). The two reaction solutions were then merged, and the reaction conditions were changed to SGP (Fig. 79). This resulted in a multiblock copolymer, where each block was made up of either CL or LA segments separated by acetal moieties that was supported by DOSY NMR. Statistical copolymerizations of lactide and caprolactone were also performed and the oligomers were subjected to the SGP mechanism, producing a multisegmented random copolymer. All these results illustrate the various polymer microstructures that could be prepared.[390]

Step-growth polymerization was also performed with telechelic polymers prepared from other polymerization technique. Brocchini *et al.*[391] for example prepared poly(ethylene oxide) containing acetal moieties with the reaction of α - ω -diol PEO and triethyleneglycol divinyl ether

with reaction conditions close to the one described previously. The properties of such polymer will be discussed in section 4.2.

Among the polyesters that have been presented as interesting biodegradable materials, poly(butylene succinate-adipate) (PBSA) and poly(butylene adipate-co-terephthalate) (PBAT), could be degraded quickly in soil or compost but hardly degraded in seawater. To enhance the degradation in seawater, Zhu *et al.*[392] inserted diglycolic acid to promote the hydrophilicity, which will also be helpful to improve the affinity with degrading enzymes. Diglycolic acid moiety could also lower the crystal area, improved chain flexibility, and might provide room for the reaction with water or enzymes. The PBDT copolymers was then prepared by the reaction of butanediol, dimethyl terephthalate and diglycolic acid via a two-step procedure consisting of a first transesterification followed by the polycondensation. Unlike the PBT reference that do not show any degradation, the insertion of diglycolic acid led to degradation in PBS, in the presence of enzyme and in artificial seawater at 15°C and that is more and more important with the increased amount of the hydrophilic comonomer. The degradation is also well correlated with the contact angle measurement confirming the importance of the hydrophilicity for the degradation of the material.[392] In a similar approach Heller and coworkers[393] also prepared a α,ω -diol glycolic dimers and then reacted them with ketene acetals to prepare poly(diglycolide-*co*-ortho esters).

Recently, Zhang and coworkers[394] used a cascade step-growth polymerization to prepare polymers from sustainable reactants that are carbonyl sulfide (COS), water and diacrylate compounds. The mechanism is based on the O/S exchange of COS/H₂O that will release CO₂ and a highly reactive H₂S, that is then coupled *in situ* to diacrylates via the highly efficient thiol Michael addition (Fig. 80).

This cascade mechanism could be catalyzed by a lot of different bases and is compatible with various diacrylates, from triethylene glycol diacrylates to prepare alternative to PEO, to long aliphatic chains that could mimic high-density polyethylene. The properties of such materials will be discussed in section 4.1. Fast polymerization kinetics were obtained, and the molecular weight could reach 150 kDa. If diacrylates are used in excess, end-functional polymers were obtained with double bonds as end-groups that is promising as reactive polymer precursors. Moreover the authors did some recycling (Fig. 80) without purification (Cycle 2) or after purification (Cycle 1), confirming the interest of this methodology.

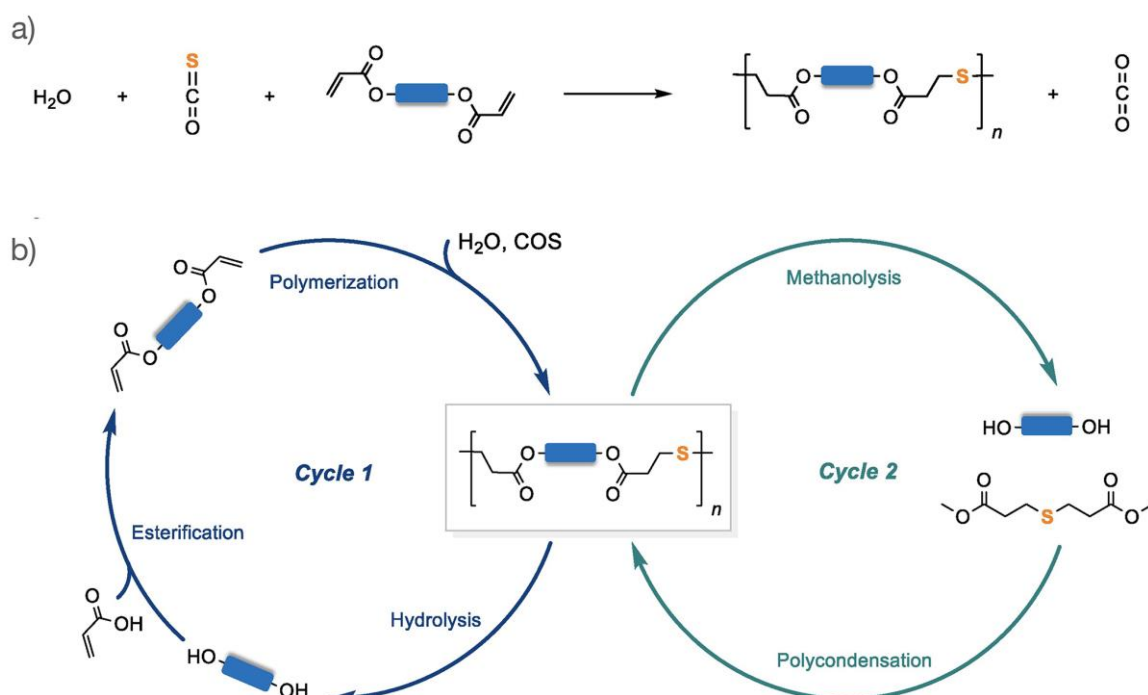


Fig. 80. a) Synthesis of polymers with in-chain ester and thioether groups from polymerization of COS, H₂O, and diacrylates. b) Recycling of the polymers completed through two cycles: Cycle 1 via hydrolysis, esterification, and polymerization; Cycle 2 via methanolysis and polycondensation. Reprinted from Ref. [394] with permission.

Polymers able to degrade under specific stimuli are now desirable since such materials have a good thermal, chemical and mechanical stability before the action of the stimulus and thus could be degraded on demand after their use. Niu and coworkers[395] reported a novel class of enyne that could undergo depolymerization in the specific presence of Grubbs catalyst that initiated a cascade metathesis reaction (Fig. 81). Such very specific degradation trigger could be very interesting for polymers that should have very severe service conditions but that still could be degraded. The polymers were prepared by polycondensation between bromo and sulfonamide functionalities via a basic catalysis following either a reaction between A-B type monomers or AA and BB. The polymers presented excellent stability in strong acid, base, nucleophiles, and at elevated temperatures. The rate and efficiency of the degradation was linked to the presence of absence of terminal alkene group but in all cases the degradation occurred readily in the presence of the Ru catalyst.

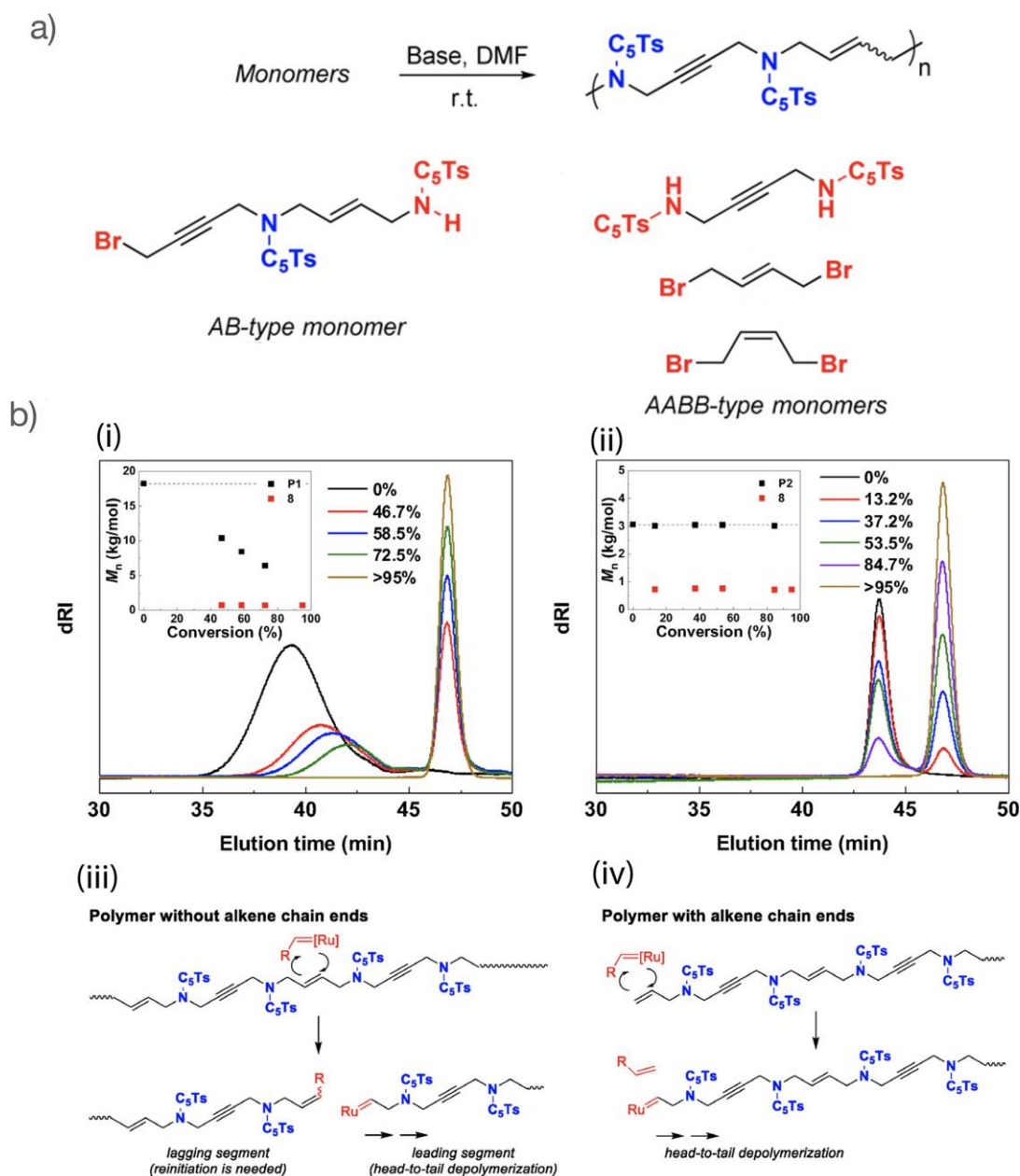


Fig. 81. a) Preparation of degradable enyne polymers. C₅Ts = 4-pentylbenzenesulfonyl group.
 b) Degradation of polymers without (i) and with (ii) terminal alkene moieties implying degradation followed by depolymerization (iii) or complete depolymerization (iv). Reprinted from Ref. [395] with permission.

3.7 Conjugated polymers

The majority of today's consumer electronics are built using nondegradable inorganic semiconductors, which are frequently hazardous and necessitate high-vacuum and high-temperature production procedures. The enormous demand for electronics has resulted in enormous amounts of waste and the quick consumption of rare materials like gallium and indium due to the fast growth of technology and the short turnover times for electronic products. Moreover, a growing number of electronics are or soon will be used in devices that form the so-called "Internet of Things" (IoT) and will require the production of stretchable or skin-inspired semiconductors that need to have (bio)degradability to be accepted for a large audience.

Transient electronics, or "green" electronics,[396, 397] offer up a new field of use, such as (i) implanted medical devices that can be removed without surgery since they can be reabsorbed by the body. application such as contrast agent for photoacoustic imaging, sensors, batteries, transistor memories, etc. In this review we will thus discuss how imparting degradability to conjugated polymers via the modification of the microstructure and thus the introduction of comonomers.

To impart degradability and still keeping high conjugation of the polymers to maintain the electronic properties, Kuhene *et al.*[398] inspired from nature and chose imidazole units that are combined with thiophene. Indeed, an imidazole ring is a common component of biological light emitting units (Coelenterazine, green fluorescent protein GFP). By fusing aminoacids to form the imidazole unit, the light emitting unit is created. Through further oxidation and scission of the imidazole ring, the emitting units are biodegradable and give back aminoacids and amides, which may then be further metabolized. Reactive oxygen species (ROS), which are produced by activated macrophages for example, can cause this degradative oxidation.

A conjugated polymers prepared from the reaction of diiodo-N- methyl-imidazole with an acetylene functionalized thiophene co-monomer via Sonogashira dispersion polymerization was obtained and gave directly interesting conjugated nanoparticles (Fig. 82). Methoxy- or oligoethyleneoxy- sidegroups where introduced into the thiophene monomer unit to control the particle shape, offer stability for the particles in water, and enhance the solubility of the subsequent degradation products.[398]

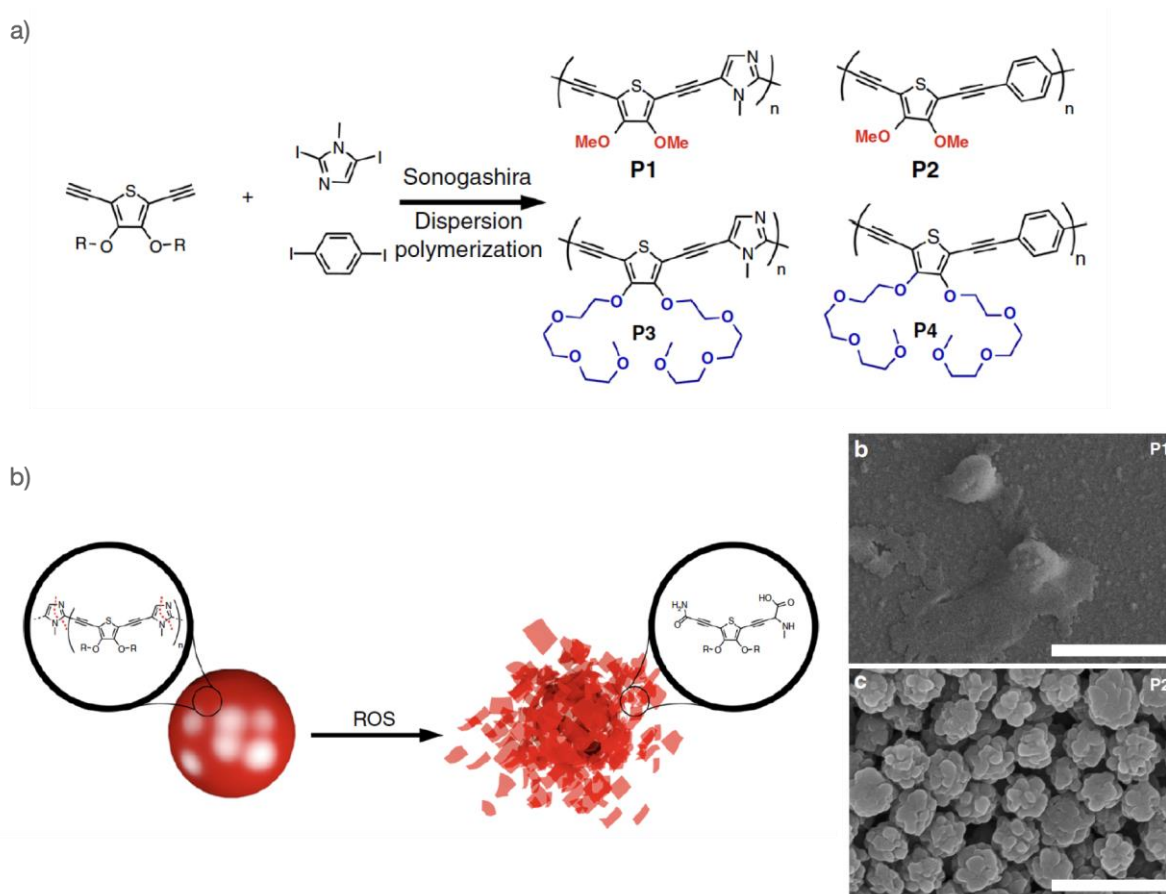


Fig. 82. a) Conjugated polymer nanoparticle synthesis via the Sonogashira dispersion polymerization of thiophene monomers with imidazole monomers. b) Degradative imidazole oxidation of particle by reactive oxygen species to decompose into methyl amino acid and amide terminated 2,5-diethynylene-3,4-methoxythiophene. Adapted from Ref. [398] with permission.

Nanoparticles containing imidazole groups were exposed to hydrogen peroxide (H_2O_2) at a concentration of 20 μM in water for 48 hours. Both visual and MEB analyses confirmed the degradation of the nanoparticles and ^1H NMR confirmed the degradation mechanism based on the opening of the imidazole group and thus the production of 2,5-diethynylene-3,4-methoxythiophene with amide and methyl aminoacidyl end groups (Fig. 82b).[398] The authors also extended these experiments to biodegradation by incubating the nanoparticles with J774A.1 macrophages in cell culture. Lipopolysaccharides (LPS), a well-known stimulant to activate the macrophages to create ROS, such as H_2O_2 , were also added. By confocal microscopy of macrophages (stained in blue) incubated with degradable and non-degradable particles, it was shown that if imidazole are inserted into the conjugated polymers, the signal disappear in 11 hours whereas the signal keep constant with the benzyl analogue, thus confirming the degradation via the activated macrophages.

Pu and coworkers[399] inserted a vinylene bond into the conjugated polymer structure. The vinylene linkages tend to undergo $\pi^2\text{-}\pi^2$ cycloaddition with oxidants, followed by hydrolysis, that allowed conjugated nanoparticle to progressively break down in a biological medium rich in oxidative species. Additionally, the presence of vinylene bonds could also promote chain packing and raises the mass absorption coefficients, which improves photothermal conversion that boost photoacoustic and photothermal therapy efficiencies. The copolymer was prepared by palladium-catalyzed Stille polymerization between 3,6-bis(5-bromothiophene-2-yl)-2,5-bis(2-hexyldecyl)pyrrolo[3,4-c]pyrrole-1,4(2H,5H)-dione and trans-1,2-bis(tributylstannyl)ethene (Fig. 83a).[399] Reference conjugated nanoparticles without vinylene units were also prepared. The nanoparticles were obtained by coprecipitation with poly-(ethylene glycol) methyl ether-block-poly(lactide-co-glycolide) (PLGA-PEG), to obtain nanoparticles with good water solubility and without impacting their biodegradability.

Nanoparticle's biodegradability was examined in a medium that mimics an *in vivo* environment. In presence of myeloperoxidase (MPO), a peroxidase enzyme that is highly expressed in immune cells, hydrogen peroxide (H_2O_2) reacted to produce hypochlorous acid (HClO), a potent oxidant. The absorption of the nanoparticle containing the vinylene bond steadily reduced during incubation with MPO and H_2O_2 but remained unchanged in the absence of MPO. The biodegradability was then confirmed using activated macrophages.[399]

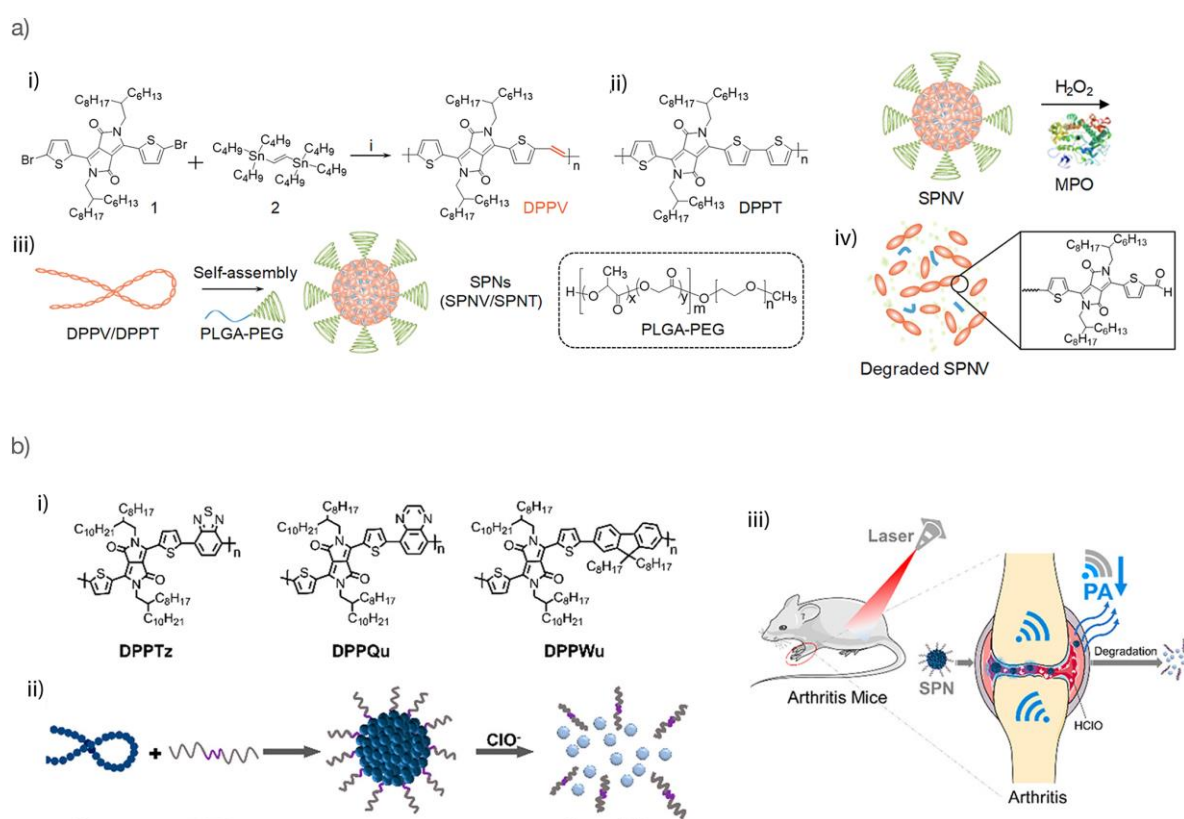


Fig. 83. a) i) Preparation of degradable conjugated polymers (DPPV) via the insertion of a vinylene bond and ii) the non-degradable conjugated polymer DPPT as a reference. iii) Preparation of the nanoparticles (SPNV) by co-precipitation with an amphiphilic copolymer. iv) Biodegradability test in the presence of myeloperoxidase. b) i) Chemical structures of the degradable conjugated polymers via the insertion of a thiophene unit. ii) Preparation of the nanoparticles (SPNV) by co-precipitation with an amphiphilic copolymer. iii) Schematic

illustration of a mouse model of λ -carrageenan-induced arthritis in the right hind foot joint in which the nanoparticles were inserted. Adapted from Refs. [399, 400] with permission.

Pu and coworkers[401] extended the range of degradable comonomers with the thiophene bridge. The conjugated copolymers could be nano-precipitated as performed in the previous study and a similar biodegradability was observed. Similar copolymers were then prepared with the highly efficient diketopyrrolopyrrole (DPP) moiety.[400] Since thiophene is not a strong electron-donating group and could only produce a little red shift, conjugated polymers with D-A1-D-A2 structure were prepared (Fig. 83b). As a result, DPP was chosen as one of the electron-withdrawing groups while the thiophene group was chosen as an electron-donating group. Benzo[c][1,2,5]thiadiazole (Tz) and 4a,8a-dihydroquinoxaline (Qu) and fluorene (Wu) were chosen as the other electron-withdrawing groups. As previously the copolymers were shown to degrade in vitro in the presence of ClO⁻ anion and in the presence of activated macrophage RAW264.7 cells. In vivo experiments were also performed in mice using an arthritis disease model that is known to overexpress hypochlorous acid in the joint. After photoacoustic analysis the signal in the arthritis mice decreased quicker than the one in normal mice confirming the degradation of the nanoparticles via oxidation with ClO⁻.

Bao and coworkers[402] chose imine as another weak bond to be inserted into conjugated polymers. Such bond is a stable conjugated linker at neutral pH but could be totally degraded using mild acidic conditions. The preparation of the decomposable polymer is shown in Fig. 84. To increase the solubility, the authors combined succinic ester with 2-thiophenecarbonitrile in tert-amyl alcohol, and then added branched alkyl chains. Octyldodecanol was used to create the branched alkyl chain. Succinic ester and tert-amyl alcohol, two of these substances, may be derived from natural sources, while octyldodecanol is a harmless substance that is frequently

used in a range of cosmetics. When two aldehyde groups were added to the DPP monomer, DPP-CHO was produced with a 77% yield. Through the condensation of DPP-CHO and p-phenylenediamine in the presence of p-toluenesulfonic acid as a catalyst, the degradable conjugated copolymer was obtained. The presence of CaCl_2 is needed to reach high molecular weight.

Following the addition of 1%(vol/vol) acetic acid in water, the absorption spectra and color changes of the degradable copolymer was noticeable after three hours, and the absorbance spectra and color of the solution were comparable to those of the pure monomer DPP-CHO after 10-days. The purple color of the DPP core was shown to fully vanish and turn into a clear solution after a 40-day test, suggesting that the polymer had completely broken down under acidic circumstances via the hydrolysis of the lactam rings. The polymer degradation can take place in good solvents but also in thin film and was totally stable in neutral or basic conditions. The authors thus used cellulose as green materials as substrate to prepare pseudo-complementary metal–oxide–semiconductor (CMOS) logic circuits. Such circuits exhibit performance equivalent to complementary-type logic circuits while using only one kind of semiconductor, which greatly simplifies the complexity of production. Direct device manufacturing may be done on top thanks to the cellulose substrate's excellent chemical and thermal resilience. The gate, source, drain, and interconnects were made of iron, while the dielectric layer was made of 25-nm Al_2O_3 via Atom Layer Deposition. Using a fluoropolymer-protected oxygen plasma etching approach, the degradable conjugated polymer could be directly spin-coated and patterned on the substrate. The device was finished by depositing iron electrodes to create a top-contact arrangement. The device is then flexible and could be transfer in various substrate (Fig. 84). The choice of iron was made to prepare fully degradable electronics since gold that is usually used for electronics implants is only biocompatible. In deionized water, the device is highly stable for several days, but when pH is decreased to 4.6

in the presence of cellulase (1mg/mL), the degradation occurred readily, and the complete dissolution is obtained after 30 days (Fig. 84).

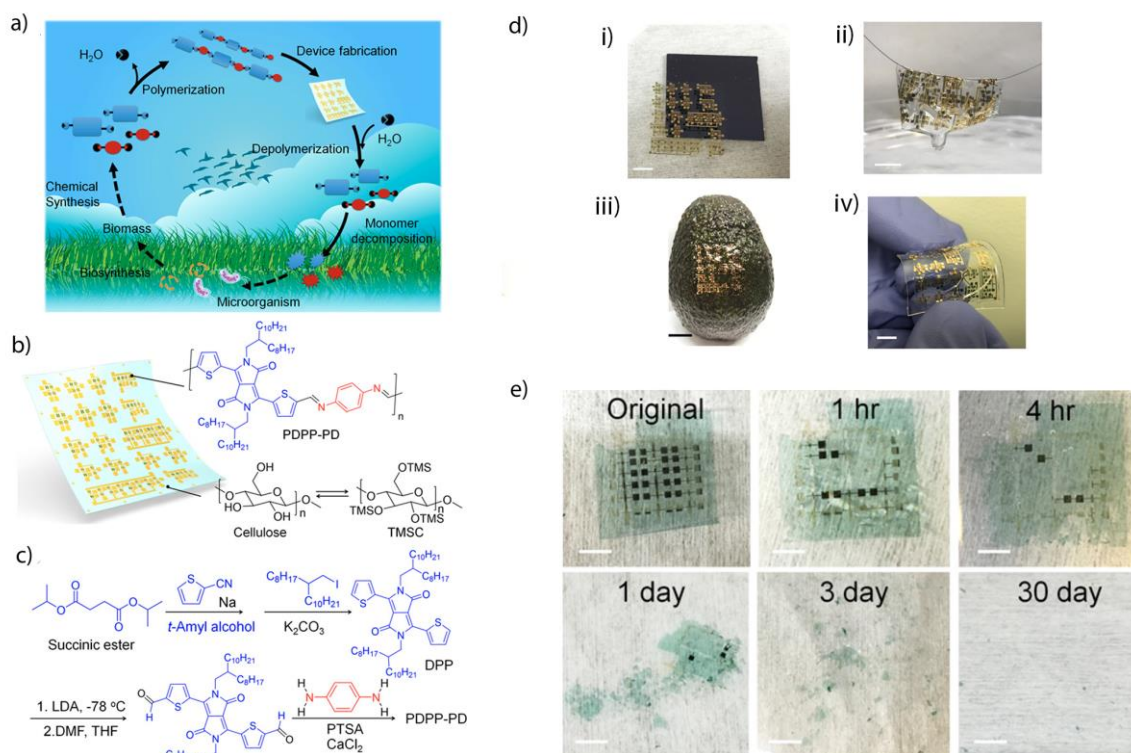


Fig. 84. a) Flexible device using disintegrable polymers as the active material or substrate. b) Preparation of the device on a degradable substrate. c) Synthesis of the disintegrable PDPP-PD using imine chemistry d) i) After dissolving the dextran layer, the device floated on water. (Scale bar: 5 mm.). ii) Device was picked up by a human hair. (Scale bar: 5 mm.). iii) Device was transferred onto the rough surface of an avocado. (Scale bar: 10 mm.). iv) Device transferred onto a PDMS substrate for electrical measurement e). Totally disintegrable electronics using iron as electrodes. Photographs of a device at various stages of disintegration. (Scale bars: 5 mm.). Adapted from Ref. [402] with permission.

The Bao group[403] thus investigated the various parameters that impact the rate of degradation and in particular the influence of the side-chains (length, branching structure, hydrophobicity, etc.). Using UV spectroscopy to follow degradation kinetics, they showed that the polymer degradation in solution is affected by the aggregation depending on the branching point and M_n , with faster degradation rates made possible by lower aggregation. Increasing the polymers' hydrophilicity also increase water diffusion, which in turn encourages acid hydrolysis of the imine linkages along the polymer backbone (Fig. 85). These polymers' aggregation characteristics and degradation durations are very solvent-dependent, with chlorobenzene taking six times longer to disintegrate than chloroform. The degradation of imine-based polymer semiconductors in thin film is impacted by the same variables and considerations (such as interchain order, crystallite size, and hydrophilicity). The presence of both hydrophilic and hydrophobic sidechains was shown to be an interesting approach to tune the rate of degradation.

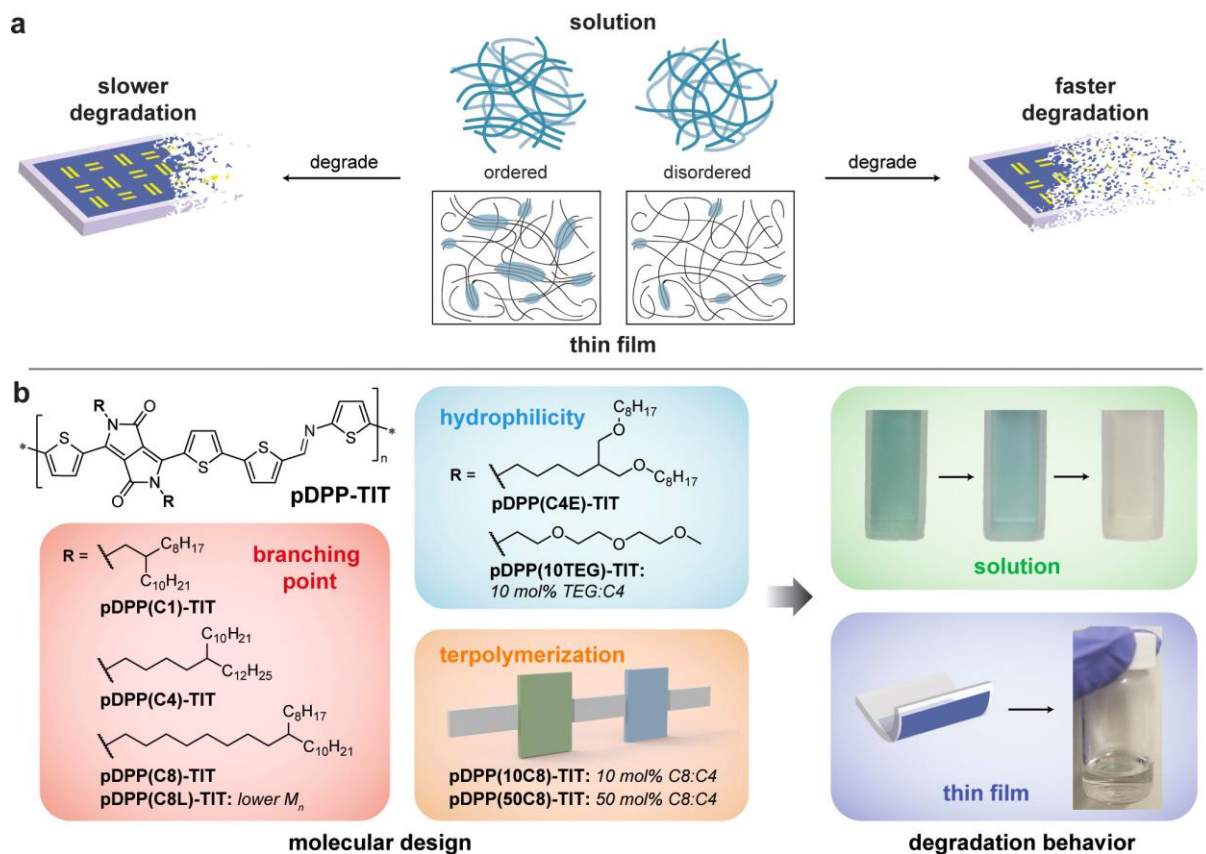


Fig. 85. a) Structure–property relationships of degradable polymer semiconductors to obtain transient electronics with controlled degradation lifetimes. (b) Molecular design parameters and polymers explored for investigation of solution and thin film degradation behavior. Reprint from Ref. [403] with permission.

The same team[404] then extended the use of the degradable conjugated polymer bearing imine groups to stretchable substrates via the use of a biodegradable elastomer. The phase segregation induced by the modification of the side chains of the conductive polymer allowed to obtain semiconductive nanofibers giving very interesting properties of stretchability and degradability.

To develop even greener conjugated polymers, Tran et coll.[405] developed biobased degradable conjugated poly(azomethine) from carotenoids compounds. Due to their reported

high conductance, photoinduced charge transfer, and known degradation routes, carotenoids that mimic polyacetylene are of particular interest. They focused more particularly on C10 dialdehyde that is commercially available and is obtained from the oxidative degradation of β -carotene. The reaction with p-phenylene diamine will lead to conjugated polymers through a degradable imine bond. When incorporated into the polymer chains, carotenoid units are vulnerable to UV radiation, enzymatic, or chemical oxidation damage, providing different triggers for on-demand degradation. The polymers were then prepared by the polycondensation of C10 dialdehyde, p-phenylenediamine derivatives in *N*-Methyl-2-pyrrolidone (NMP) with PTSA as catalyst and excess calcium chloride (CaCl_2) as drying agent (Fig. 86). Hexyl side chains were mandatory to obtain a good solubility in many organic solvents.[405]

Since both light and acid could trigger the degradation of the imine bond, the authors investigated the different experimental conditions to determine the main parameters and also see if synergistic effects could occur. One polymer solution was kept in the dark, another was continuously exposed to artificial light, a third was kept in the dark with acid, and a fourth was continuously exposed to artificial light with acid. Over a 45-day period, the degradation was followed by monitoring the relative reduction in absorbance at 470 nm (Fig. 86). According to this degradation investigation, the polymer solution held in the dark maintained a high degree of stability. Although the sample exposed to artificial sunshine shown some resistance, it nonetheless lost absorbance over the course of 45 days. The samples exposed to acid decomposed quickly even if the sample stored in the dark showed a slower rate of disintegration than the one exposed with artificial sunlight. The mass spectrometry analyses showed different side-products depending on the degradation mode: under acid conditions alone, the polymers revert to the C10 dialdehyde and diamine whereas under light irradiation, C10 dialdehyde was also degraded to other colorless small molecules. This confirmed the complex degradation

pathway that occur when both degradation trigger were used and that some synergy occurred that enhance the rate of acidic hydrolysis of the imine bond.

Other degradable poly(azomethine)s were prepared using biomass isosorbide-derived diamine and photoactive 9,9-di-*n*-octylfluorene-2,7-dicarboxaldehyde (FLDA) and biomass-based 2,5-furandicarboxaldehyde (FCA).[406] These polymers were used as organic field effect transistor (OFET) memories. The memory properties persisted even after 1000 bending cycles but after one week in acidic medium, the polymer chains were degraded in small molecules.[406] This finding indicated that the produced photoresponsive polyazomethines would be suitable for application in eco-friendly electronics.

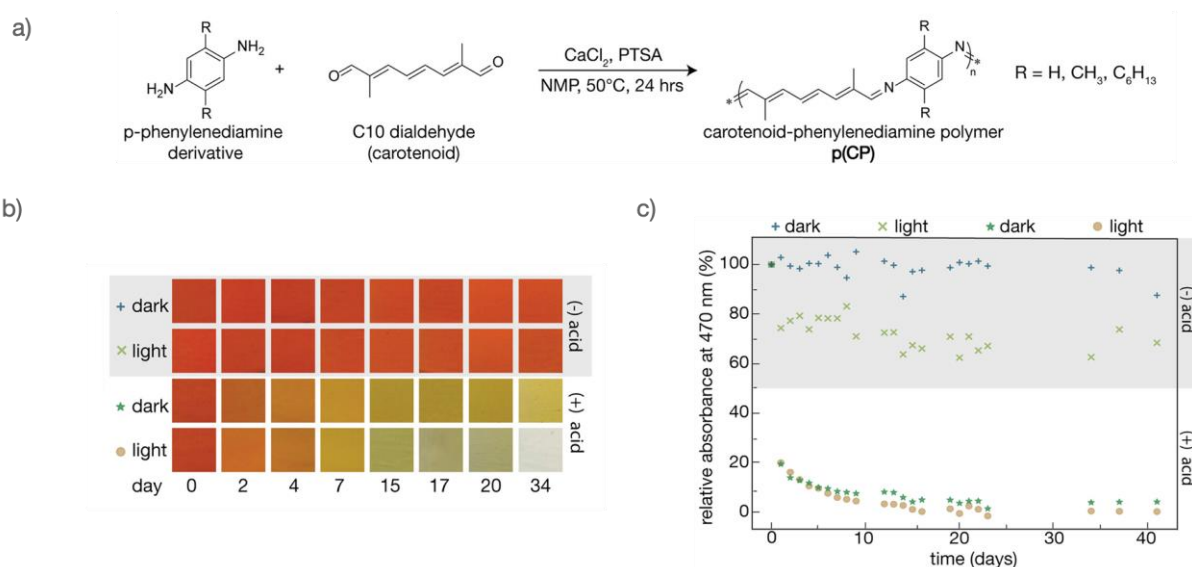


Fig. 86. a) Synthesis of biobased degradable poly(azomethine). b) Color change observed upon degradation of each polymer solution over time. c) Long-term degradation study monitored by UV-vis of poly(azomethine) under the presence of artificial sunlight (polymer solution 0.015 mg/mL) and acid (polymer solution 0.05 mg/mL, 1.2×10^{-7} mM HCl added), with their respective negative controls (solutions kept in the dark). Adapted from Ref. [405] with permission.

4 Alternatives to Common Polymers and Applications

4.1 Polyolefin alternatives

In terms of volume produced, polyethylene (PE) is the biggest class of polymers. PE production annually totals more than 100 million tons globally.[407] There are several grades of PE that may be used to meet various requirements. The most well-known grades are HDPE (high-density polyethylenes), LDPE (low-density polyethylene), and LLDPE (linear low-density polyethylene). The crystalline arrangement that results from non-covalent contacts (van der Waals interactions) between adjacent stretched lengths of hydrocarbon chains is a characteristic shared by all of these PEs. The difference between the PEs deals with the amount of crystalline parts that is present in the whole material. Such amount is impacted by the branching that broke the crystallinity and thus lead to ductile materials (LDPE).[407]

PEs are also hydrophobic and apolar due to their hydrocarbon composition. In other words, they won't readily bind to polar materials like metals or wood or absorb water. In addition, PEs are resistant to degrading processes because the hydrocarbon chains are chemically inert. When discharged into the environment, this high stability makes such materials persistent.[407] The preparation of PEs that maintain the desirable properties of polyethylene but that could be (bio)degradable should be worthwhile and will require a good balance in introducing the degradable functionality.

PEs are mainly created by ethylene chain-growth polymerizations, primarily through catalytic processes. This makes it difficult to add functional groups to PE chains, even in modest doses. To enhance the degradation of such polyolefins, the introduction of pro-oxidant compounds was first tested and led to the so-called oxo-degradable materials that is described in Part 1.2.

Another strategy is to introduce weak bonds on the main chains. These polymers are called long-chain aliphatic polymers or polyethylene mimics and their syntheses and properties have been reviewed by Mecking[408] in 2016. Many polymerization techniques could lead to such results. ADMET and ROMP was widely used, and these syntheses are described in Part 3.1.1 and 3.1.2 respectively. In that case, many functional groups were regularly inserted into an unsaturated polyalkeneamer (Fig. 87). The further hydrogenation allowed to obtain the PE-mimics.

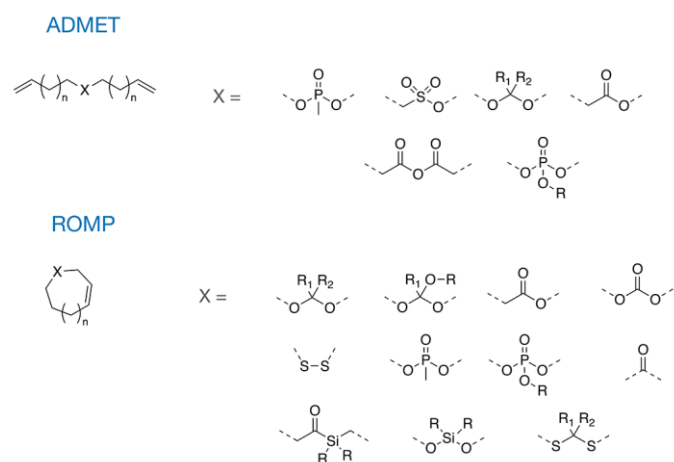


Fig. 87. Preparation of polyethylene mimics via ADMET or ROMP polymerization.

ADMET polymerization, due to the polycondensation process, is subject to the standard restrictions of step-growth reactions. However, the produced ethylene may be more easily eliminated from the chemical equilibrium, resulting in molecular weights higher than 10^4 g mol⁻¹. However, the function group in this ADMET-generated polymer are arbitrarily orientated throughout the polymer chain (ex for ester -O(C=O)- versus -(C=O)O-) and the lengths between the groups could varies. The melting point of random group orientation is then lower than that of its regularly orientated congener. symmetrical weak bonds such as acetal group or the combination of two ester into the ADMET monomers avoids this phenomenon.

The presence of double bonds in the hydrocarbon polymer backbone has a significant impact on polymer chain crystallization, resulting in lower crystallinity and melting temperatures. The use of ROMP instead of ADMET allowed to switch from a step growth polymerization to a chain-growth process and thus led polymer chains with improved controlled of the molar mass distribution even if sometimes the low ring strain of cyclic molecules could be a hurdle to obtain high molecular weight polymers.

Among the various groups, orthoester is very interesting since it was possible to prepare semicrystalline polyethylene like materials, which were only soluble in hot organic solvents.[90] The crystallization was similar to HDPE with bulky orthoester groups evicted from the crystal lattice. The orthoester substituents impacted the polymer hydrolysis rate in solution. Additionally, the authors demonstrated that non-hydrogenated copolymers with a high orthoester content were biodegraded by microorganisms from a nearby sewage plant's activated sludge. In general, all copolymers dissolved over many months under ambient conditions.[90] Wurm and coll.[81] also prepared a degradable polyethylene (PE)-like polyphosphoesters, which exhibit increased degradation rates due to an intra-molecular transesterification similar to RNA. Polymer films submerged in aqueous solutions at various pH levels degraded faster than structurally equivalent polyphosphoesters without pendant ethoxy hydroxyl groups. Polymer breakdown occurred in artificial seawater (pH 14 8), however the polymer remained stable at physiological pH of 7.4.[81]

Besides these techniques, polycondensation was also performed from long alkyl mainly biobased difunctional molecules. Direct esterification of dicarboxylic acids and diols in an A2 + B2 polycondensation with removal of water is the most frequent method for producing polyesters.[408] Transesterification (alcoholysis) of diols and diesters can also be used. The

polycondensation of activated monomers such acid chlorides, acid anhydrides, or other carboxylic acid derivatives is also reported. Transesterification, in contrast to direct esterification, is very slow, even at high reaction temperatures. As a result, the presence of a catalyst is often necessary for the synthesis of high-molecular-weight polyesters. A wide variety of catalysts have been reported but the more active seem to be the titanium alkoxides.[408] To generate polycondensates with sufficiently large molecular weights (usually above several 10^4 g mol⁻¹), extremely high conversions are required.

As an example of polycondensation, Guégan and coworkers[409] reported the polycondensation based on one building block the 1,18-(Z)-octadec-9-enedioic acid, allowing the synthesis of four polyesters after either hydrogenation and or reduction and that differ by the number of double bonds along the polymer backbone (0,1 or 2). The polymer with no unsaturation presented a T_m equal to 100 °C, with a M_n close to 50,000 g.mol⁻¹. A biodegradation was observed using urban sludge in an oxic system.[409] In order to develop a material that could move more easily towards industrialization, Dubois *et al.*[410] proposed to prepare “short-long” type long-chain polyesters. “Short -long” means that between two ester moieties there is an alternating short (2 to 4 carbons) and long (10+) aliphatic chains. Short-chain diols, particularly ethylene glycol (EG) and 1,4-butane diol (BDO), are readily accessible and inexpensive chemicals. Long-chain diacids containing 10-16 carbon atoms are also accessible commercially. They are not as inexpensive as short-chain diols, but their manufacturing costs and technological barriers are clearly lower than those of long-chain hydroxyl acids. Secondly since the polycondensation is a diffusion-controlled process, the melt viscosity, and the molecular weight (MW) increase is dependent on the diffusivity of the diol employed. The polyester made from the shortest diol and the longest diacid, PE₂₋₁₆, has the highest T_m of 94.1 °C. All of the samples showed gradual hydrolytic degradation at 30.0 °C and pH 7.0. At the 60th week, the weight loss was less than 1%, and at the 90th week, it was

less than 2%. When the temperature was raised to 60 °C, the hydrolytic decomposition was obviously accelerated, resulting in greater weight loss. Some early soil degradation experiments were also conducted to further study the possibilities of biodegradation of these polyesters. For 2 and 17 months, the film samples were buried in moistened horticulture soil at room temperature, and the appearance and weight loss were monitored. All the sample showed low weight loss after 2 months that increased with a prolonged buried time showing promises for biodegradation, the longer diacid containing polyesters having the lower rate of biodegradation.[410]

Mecking and coworkers[411] revisited the preparation of PE-mimics by preparing polyesters or polycarbonates containing long alkyl chains via the modification of fatty acids (1,18-octadecanedioic acid, produced from large-scale biorefining of plant oils by olefin metathesis technology)[412] and polycondensation. The interesting feature is the very high molecular weights of such materials (PC18 weight-average molecular weight $M_w = 300,000 \text{ g mol}^{-1}$) that give both ductility and mechanical strength. Complete analytical characterization (Fig. 88) confirmed the HDPE-like properties (mechanical properties and crystallinity).

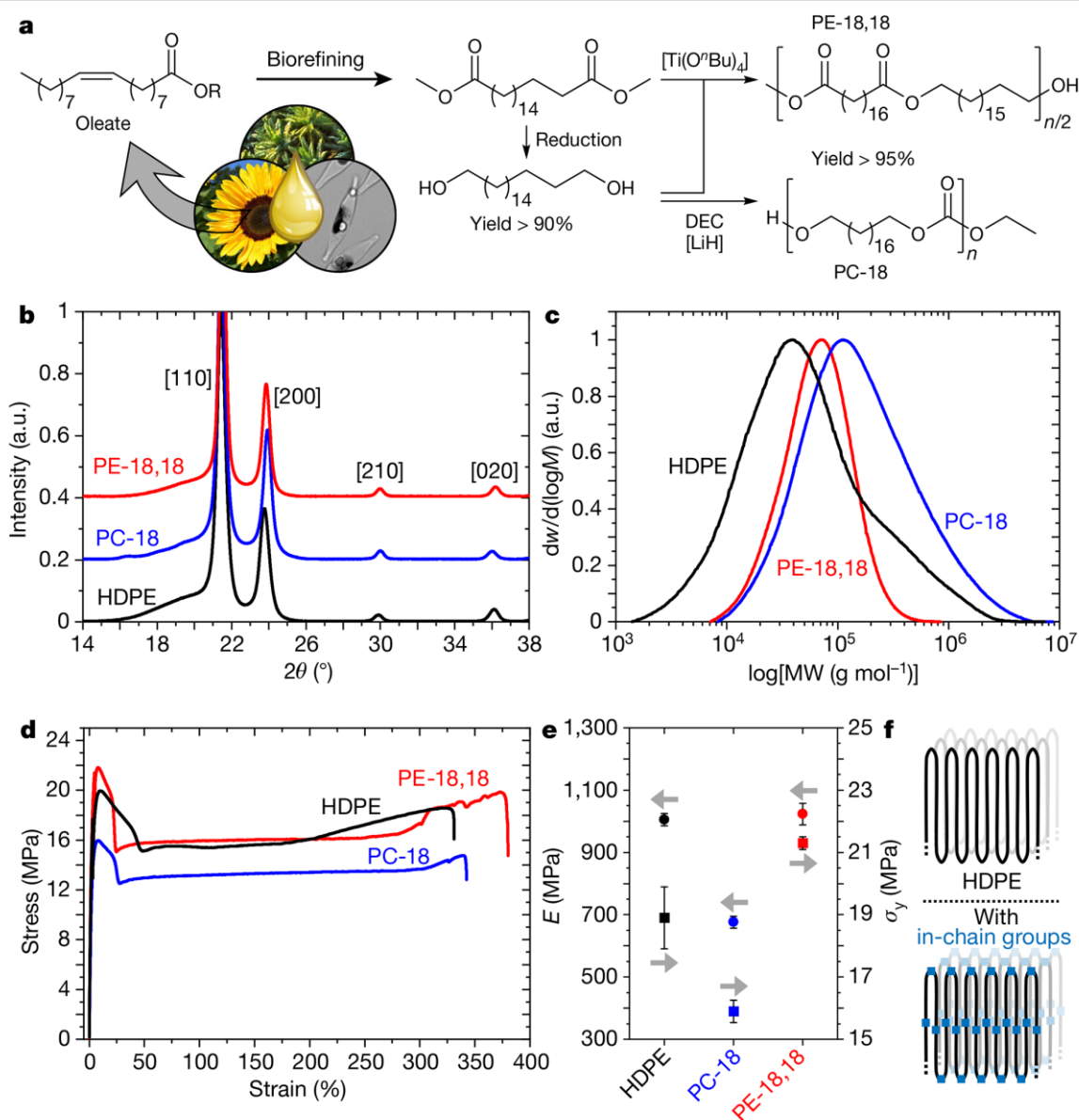


Fig. 88. Preparation and characterization of polyethylene-like polymers. a, Monomer synthesis starting from biorefining of plant or microalgae oils. b), WAXS of PC-18, PE-18,18 and commercial HDPE. Diffraction peaks correspond to the orthorhombic unit cell of polyethylene in all cases, and the traces are shifted vertically for clarity. a.u., arbitrary units. c), GPC traces of PC-18 and PE-18,18 in comparison to that of commercial HDPE. d), Representative stress–strain curves of injection-moulded PC-18, PE-18,18 and commercial HDPE. e) Young’s modulus and stress at yield values for PC-18, PE-18,18 and HDPE. f) Schematic representation

of the solid-state structure of HDPE (top) and polyethylene-like polymers with in-chain functional groups (bottom). Reprinted from Ref. [411] with permission.

The authors concentrated first on the processing and recycling feature of the materials. The use of fused-filament fabrication for additive manufacturing was in particular investigated. Closed-loop recycling with full retention of the materials properties is especially important for 3D-printing technologies. Melt extrusion of PC-18 and PE-18,18 materials produced filaments with dimensional precision, even when colorants or performance-enhancing fillers such as carbon fibers are used. Due to the incorporation of polar fragments, PC-18 and PE-18,18 were able to print effectively on conventional printing surfaces such as polyetherimide or glass (in contrast to HDPE, which needs specific surfaces). A standard benchmark for stability at extreme temperatures is stability at the boiling point of water. Although the softening points of PC-18 and PE-18,18 are too low for such applications, such approach was extended to produce a high molecular weight (M_w 90,000 g mol⁻¹) ductile PC-48 with a narrow melt transition at $T_m = 113^\circ\text{C}$ from 1,48-octatetracontane diol synthesized by catalytic chain-doubling of erucic acid. After repeated filling with hot water, a thin-walled cup 3D-printed from colored PC-48 retained its dimensions and form (Fig. 89). The authors also performed extensive close-loop recycling that will be discussed in the recycling part.[411]

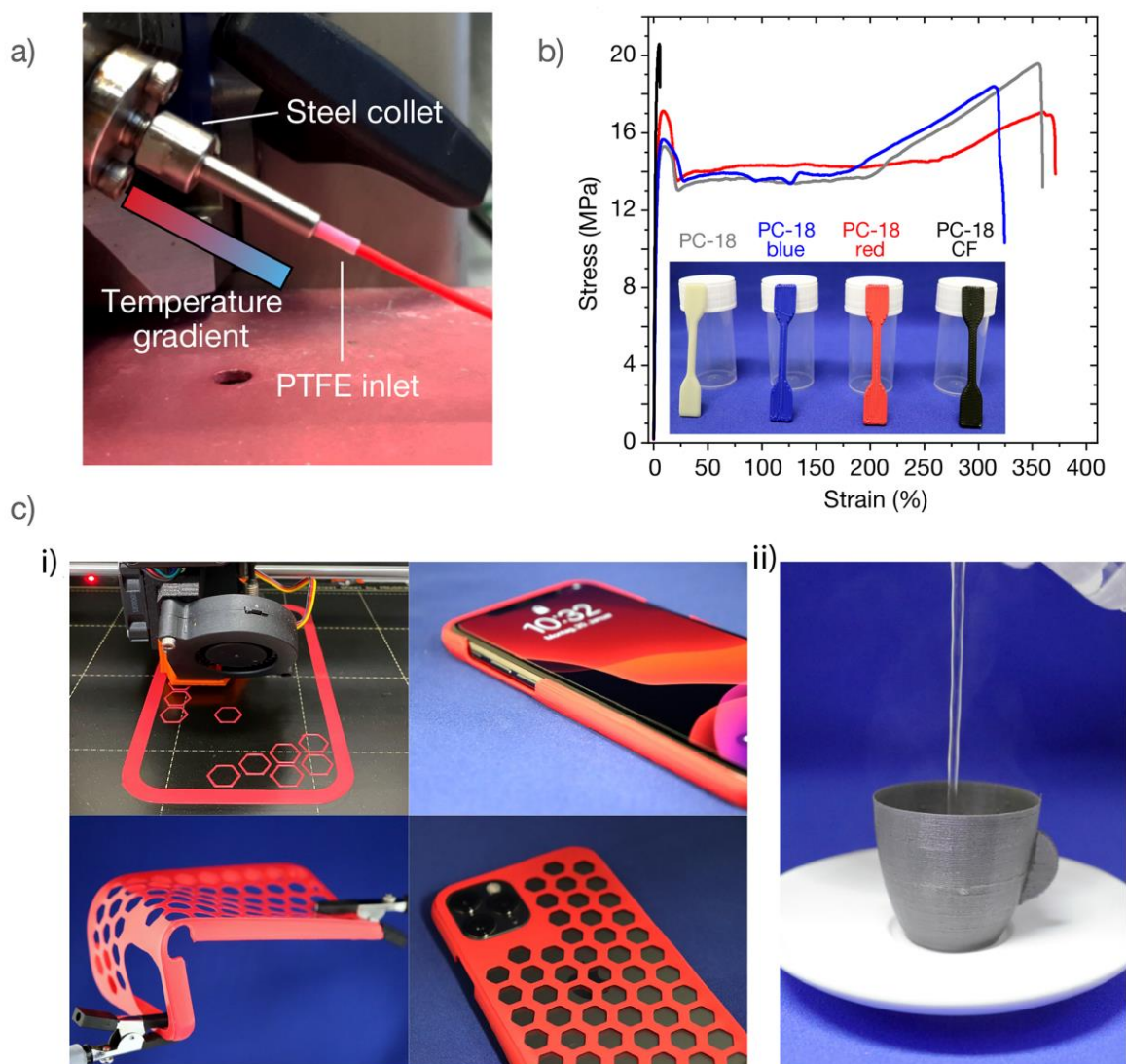


Fig. 89. Filament fabrication and 3D printing of PC-18 and PE-18,18. a) Filament extrusion from a micro-compounder. b) Stress–strain curves of 3D-printed tensile testing bars of PC-18 compounds. c) Examples of 3D objects. a, Snap-on smartphone protective cover printed with red-colored PE-18,18. Anticlockwise from top left: printing of cover, demonstration of flexibility, back view and front view. b, Boiling water (>95 °C) being poured into a 3D-printed cup of grey-colored PC-48 as a probe of dimensional stability at elevated temperature. Reprinted from Ref. [411] with permission.

Besides close-loop recycling, Mecking also investigated the biodegradation of such materials and it was shown that even using industrial composting conditions, poor biodegradation profile were obtained.[413] In a similar manner as the work of Dubois, Mecking and coworkers[413] prepared then short-long type long-chain polyesters (polyester 2,18) and showed very interesting biodegradation profile. These results are discussed in the biodegradation part (5.2). Mecking *et al.*[414] also proposed another strategy to enhance the biodegradation of PE18,18. The blend (0.5 to 20 wt%) of PE18,18 with another long-chain polycondensate that is very sensitive to hydrolysis totally modified the biodegradation profile without impacting the properties of the composite materials that remains similar to HDPE. As polycondensate that is very sensitive to hydrolysis, Mecking[415] prepared a ultralong chain poly(H-phosphonate). The polymer is produced by the polycondensation of dimethyl H-phosphonate in the presence of long diols (Fig. 90).

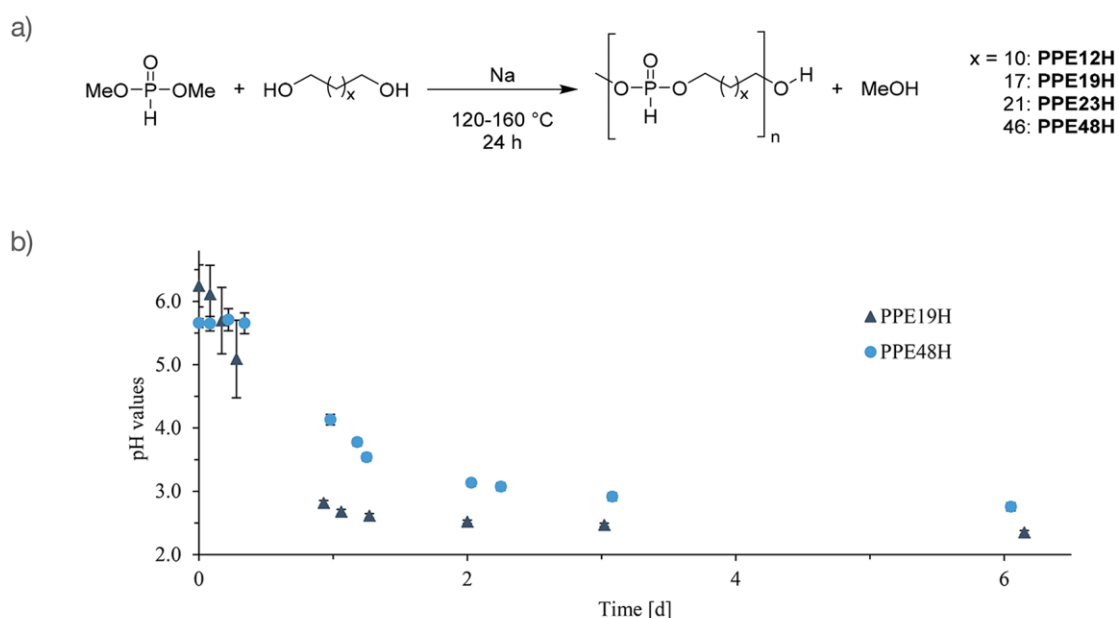


Fig. 90. Preparation of poly(H-phosphonate. b) Kinetics of degradation for 2 different poly(H-phosphonate) in water ((size of specimen: $\approx 0.1 \text{ cm} \times 0.4 \text{ cm} \times 1.0 \text{ cm}$; stirred in 25 mL of H_2O at $35 \text{ }^\circ\text{C}$ with 80 rpm)). Reprinted from Ref. [415] with permission.

Poly(H-phosphonate)s degrade fast under humid condition due to the hydrolytically unstable P-O-C bond. For instance, the poly(H-phosphonate) with 19C between the phosphonate groups degraded immediately when the polymer powder is exposed to air. Pellets of the same sample mainly totally decomposed after 22 hours in water (Fig. 90b). For longer aliphatic chain (48C), the degradation slowed down and few days are necessary to have the complete dissociation in water.[415]

The last approach to induce (bio)degradability to polyethylene is related to the insertion of ketone group to make them light-sensitive. This approach is different from the oxo-degradable materials in the sense of all polymer chains will have randomly inserted keto group that should make the degradable more homogeneous. Such materials should be prepared by the copolymerization of ethylene and a low amount of carbon monoxide. This approach was investigated since the 50s[416] but faced many challenges. Indeed, CO can first react with catalyst, displacing the efficient ligands and thus destroying the active sites. Secondly, the reactivity of CO is higher than the one of ethylene. As a result, instead of a random incorporation of ketone into the polyethylene chain, alternating polyketones are generated that have not the same properties and cannot act as polyethylene mimic materials.[417] To tackle this challenge, Mecking *et al.*[418] developed some neutral late transition metal catalysts and found the conditions to obtain mainly isolated ketone functionality into the PE chains (Fig. 91a). Efficient copolymerization (restricted to 1 mol% of keto group inserted) thus required high temperature to ensure a random incorporation of CO. However, the copolymer lowered the yield and average activities compared to homopolymerization of ethylene. The photodegradation of the polyethylene containing keto group was not studied in detail but compared to pure HDPE, the materials underwent a moderate weight loss when films floating

on a water bath were exposed to a light intensity corresponding to 5 months of natural sunlight in southern Europe.[418]

Nozaki and coworkers[419] proposed another strategy to prepare keto-containing HDPE. They used common palladium phosphine-sulfonate (P/S) catalyst but decide to investigate whether metal carbonyls, could be used as alternative CO sources. Such reactants are typically solids or liquids, as opposed to colorless and odorless CO gas, making them safer and easier to handle in ethylene copolymerization. They showed that $\text{Fe}_2(\text{CO})_9$ was very efficient to prepare HDPE containing isolated ketone groups (~1% of ketone and 95-99% of isolated ketone group) in contrary to classic CO gas. Different parameters were then tested and as expected the lower the amount of $\text{Fe}_2(\text{CO})_9$, the lower the amount of ketone functionality in the polymer but the higher the molecular weight and the better the selectivity of isolated ketone. The photosensitivity of the polymer was tested by irradiating it at 30 °C for 50h at 275 nm. The molecular weight of the copolymer (containing 0.41 mol% of keto groups) decreased significantly from 58 to 22 $\text{kg}\cdot\text{mol}^{-1}$ (Figure 91b).

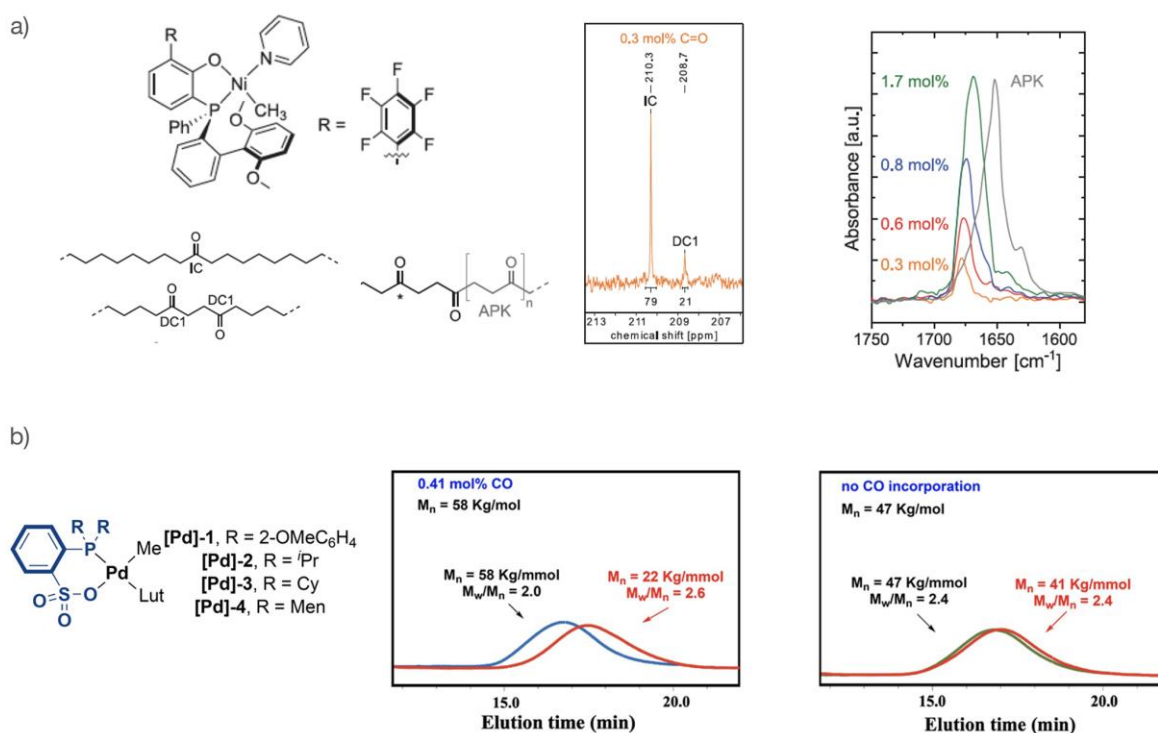


Fig. 91. a) Preparation of HDPE containing ketone group using a specific Ni catalyst and characterization of the copolymer via ^1H NMR or FTIR. b) Preparation of HDPE containing ketone group with Pd catalysts and using metal carbonyls. Characterization of the photodegradation. Adapted from Refs. [418, 419] with permission.

The main use of plastics being packaging, it seems essential to develop degradable equivalents to improve eco-responsible waste management. Among the polymers used for packaging and in particular those for single use, low density polyethylene (LDPE) is certainly the most important.[407] LDPE is prepared by radical polymerization at typically 200 °C and 2000 atm. Monteil *et al.*[420] have shown that it is possible to perform radical polymerization of ethylene using milder conditions in the presence of very specific solvents such as dimethyl carbonate avoiding the problem of chain transfer. You *et al.*[254] have thus used these conditions and showed that degradable LDPE containing ester bonds of M_n around 12,000 g/mol can be synthesized by cobalt-controlled radical polymerization (CRRP) of the cyclic ketene acetal 2-methylene-dioxepane (MDO) with ethylene. By varying the ethylene pressure as well as the volume of MDO, various poly(E-*co*-MDO) copolymers could be synthesized. The degradation of the copolymer containing 68% ethylene and M_n 11,200 g/mol was studied by SEC (1,2,4-trichlorobenzene, 150 °C). After 24h at 70 °C in a solution of triethylamine in chloroform (1/4 v/v), a clear decrease in the molar mass of the chains (M_n of 670 g/mol after degradation) was found attesting to the degradability of the initial LDPE chains (Fig. 92). The same authors[255] then showed that the polymerization of CKA and ethylene controlled by a dithiocarbamate (RAFT) also made it possible to obtain degradable PE in particular in the presence of lipases. Indeed, a poly(MDO-*co*-E) of about 12,000 g/mol and containing 13% MDO showed by SEC a fragmentation of the chains after 20 days of incubation in PBS at 37 °C by lipases.

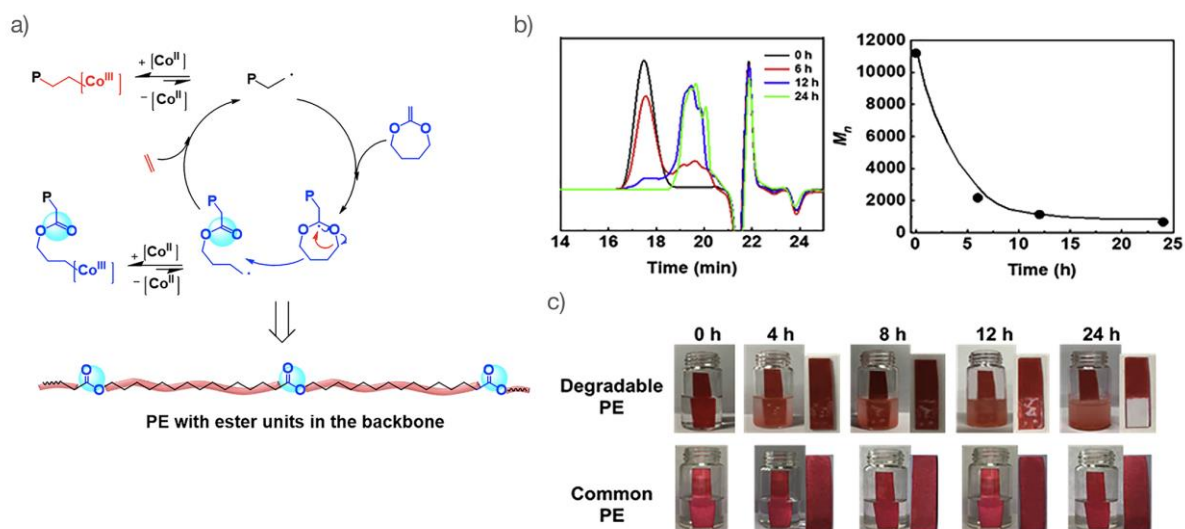


Fig. 92. a) Preparation of LDPE containing ester units via the copolymerization of ethylene and MDO via CMRP. b) degradation of the Poly(E-co-MDO). c) Pictures of film of PE-based copolymer with ester structures in the backbone and common PE film both containing a red dye treated with Et_3N at different times. Adapted from Ref. [254] with permission.

Imparting photosensitivity into LDPE was also envisioned via the incorporation of CO by radical copolymerization. Nevertheless, the low reactivity of the acyl radical that is generated after the CO addition inhibits the chain growth and thus led to oligomers. Mecking and coworkers[421] showed that using dimethyl carbonate and working at 300 bar, 100–160 °C and using low partial pressures of CO it is possible to obtain PEs with ketone contents of 1.5–13%. The ketone concentration corresponds with the CO partial pressure, as predicted, and is lower at higher polymerization temperatures. The keto units are mostly isolated, with only a few in close proximity to one another (Fig. 93). Besides linear ketones, the resulting polymers presented a large amount of ketones with one or multiple branches in α -position to the carbonyl. These can be accounted for by several abstractions, each followed by chain propagation, of the distinct α -hydrogens of a particular ketone group. The good ketone insertion homogeneity was proven by SEC with IR detection. Preliminary degradation experiments were performed. After

a light exposure corresponding to 16 months of natural sunlight in Southern Europe, a slight but significant weight loss was observed that is combined with surface degradation and embrittlement. The authors thus extended this copolymerization process to aqueous dispersion polymerization. Copolymerizations of ethylene and CO in water resulted in nanoparticles of 20 nm diameter of keto-modified polyethylene. Colloidally stable dispersions were achieved in both surfactant-free polymerizations using either the anionic initiator potassium persulfate (KPS) as a stabilizer or the water-soluble azo-initiator VA-086 as a stabilizer. Polymers prepared in solution of dispersions showed similar characteristics except the branching density that is fivefold higher due to the compartmentalization effect.

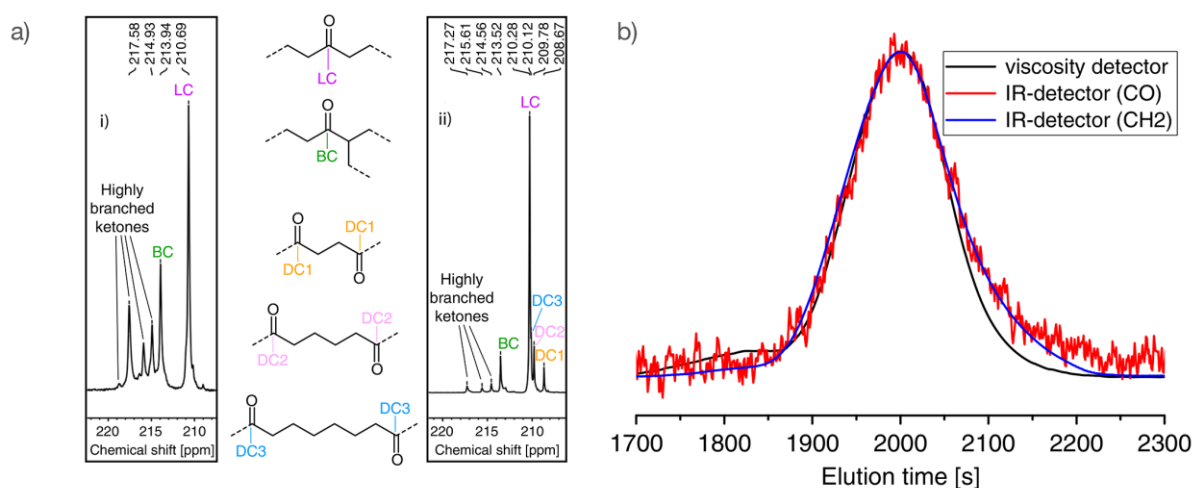


Fig. 93. a) ^{13}C NMR spectra of polyethylene containing ketone group. Resonances of different keto groups in 1,1,2,2-tetrachloroethane- d_2 of a polyethylene containing ketone group synthesized in (i) water (entry 10 in Table 2) and in (ii) DMC. LC: linear carbonyl, BC: α -branched carbonyl, DC: double carbonyls. b) Multiple detection SEC analysis of polyethylene containing ketone group. Adapted from Ref. [421] with permission.

Lastly, Coates and coworkers[422] aimed at preparing degradable polypropylene. The need for stereocontrol and the extra methyl group impede the used of ADMET and ROMP approaches

and thus the only way to prepare such materials is to perform the polycondensation of telechelic isotactic polypropylene oligomers. To obtain such building block, they established 3 steps synthesis consisting first in the preparation of a first copolymer of propylene and a small amount of butadiene in which the 1,4 insertion of butadiene is favored towards the 1,2 insertions. The polypropylene containing few unsaturation in the polymer backbone is then cleaved by cross-metathesis to obtain telechelic dihydroxy-functionalized isotactic polypropylene. To avoid any side-reaction the remaining double bonds were hydrogenated using Crabtree's catalyst (Fig. 94). Via this approach they managed to obtain a building block of 10 kDa that was reacted in the presence of $\text{Ti}(\text{O}i\text{Bu})_4$ to obtain the ester-linked polypropylene with a molecular weight of 32.6 kDa that is close to the molecular weight of the first propylene-butadiene copolymer. The obtained copolymer has characteristics of linear low-density polyethylene (LLDPE) with a $T_m = 95^\circ\text{C}$, yield point at 7 MPa and strain at break of 1200%. The copolymer could be degraded using TBD in ethylene glycol to the original building block and further repolymerized using the previous procedure.

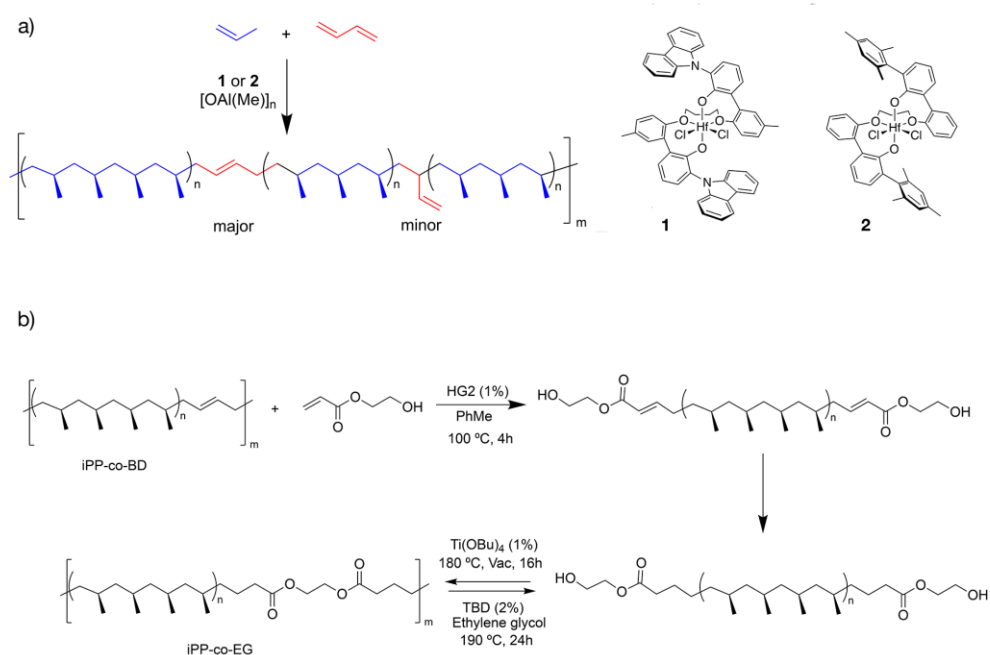


Fig. 94. Preparation of ester-linked polypropylene.

4.2 PEO alternatives

The vast majority of poly(ethylene glycol) (PEG) also called poly(ethylene oxide) (PEO) are employed in the production of nonionic surfactants, a crucial class of industrial goods with uses ranging from food emulsifiers, agrochemicals, and household detergents to various industrial preparations. PEOs are extensively used in the pharmaceutical sector to prepare ointments, suppositories, tablets, and injection solvents. They are also applied in cosmetics, such as creams, lotions, powders, and lipsticks, due to their low toxicity and absence of skin irritation.

Since PEOs will ultimately play a big role in both residential and commercial wastewater systems, their biodegradability has received a lot of study during the past 40 years.[423] It was shown that PEG up to 4,000 was assimilated by various bacteria, identified or unidentified, and by activated sludges. PEG with a molecular weight of more than 4,000 was assimilated by a limited number of species such as *Pseudomonas aeruginosa*. the degradation mechanisms involved—whether aerobic or anaerobic—require that at least one terminal hydroxyl group must be free. When the molecular size is increased, the ratio of terminal hydroxyl groups per molecule is decreased, and this leads to difficulties in the enzyme attacking the hydroxy end-group.[424]

Because of its nontoxicity, protein resistance, and non-immunogenicity, PEOs or PEGs is also one of the most extensively utilized biopolymers in the biomedical industry.[425-427] PEG is a "stealth" polymer that could bypasses cell phagocytosis, thus lowering the immunogenicity of PEGylated conjugates (covalent linking between proteins, peptides, and other pharmacological molecules). Such approach is called PEGylation that can extend the chemical stability and biocirculation time of these drugs. It has been discovered that the efficiency of

PEGylated compounds is dependent on PEG molecular weight.[425-427] PEG, on the other hand, is a nondegradable polymer, and its elimination from the body is determined by the molecular weight. PEG molecules with less than 10 kDa may be eliminated by renal filtration, but longer PEG chains must be removed by the kidneys, causing a possible PEG buildup in these organs and increasing the risk of toxicity.[425-427]

To circumvent these drawback, biodegradable PEGs can be synthesized by including physiologically degradable functional groups into PEG structures. Since telechelic dihydroxy-functionalized PEO or PEG could be easily obtained, the first degradable PEGs were produced by step growth polycondensation and in particular from polyesterification of commercialized PEG diols and dicarboxylic acid.[428] Unfortunately, the challenges with polyesterification make it difficult to create high molecular weight degradable PEG using this method. Zhu *et al.*[429] overcome these difficulties by combining carboxyl-terminated prepolymers of PEG diol and carboxyl-ester transesterification. This two-step process consists in a first melt polycondensation of PEG diols and excess dicarboxylic acids under argon flow at 120 °C. in the second polymerization stage under elevated temperature and high vacuum (130–200 °C, <100 Pa), terminal carboxyl groups and terminal ester bonds in the prepolymers may be exchanged in the presence of SnCl₂ to regenerate the dicarboxylic acids. The molecular weight of products could then be increased by means of the sublimation of dicarboxylic acids to reach pure stoichiometry and thus high molecular weight. M_n up to 60,000 g.mol⁻¹ could be obtained via the reaction of PEG600 with succinic acid. Biodegradability via enzymatic hydrolysis in a simulated body fluid was confirmed.[429] The HMW biodegradable PEGs were also evaluated for immunogenicity, cytocompatibility, immunogenicity, pharmacokinetics, and biodistribution investigations, which indicate a possible use for drug administration.

Since ester bonds require enzyme to be cleaved, the introduction of more labile bonds was investigated. Brocchini et coll.[391] for example prepare PEG containing acetal groups via the polyaddition of telechelic dihydroxy-functionalized PEO or PEG with divinyl ethers and especially tri(ethylene glycol) divinyl ether. The resulting polyacetals made with PEG₄₀₀ had a weight-average molecular weight (M_w) in the range of 7000–9000 g/mol ($D= 2.0$ – 2.9), whereas those prepared with PEG₃₄₀₀ had a M_w of 36 000–43 000 g/mol ($D= 1.6$ – 1.8). The authors also inserted pendant chain functionality by incorporating a low amount of functionalized diol that was a more efficient route than using functionalized divinyl ether. The hydrolytic degradation was then studied, and it was shown that complete decomposition of the polyacetal was obtained in less than 15 min when stirred at RT at pH=1. At pH more relevant for in vivo degradation (7.5 for bloodstream, 6.5 for endosome and 5.5 for lysosome), the decomposition kinetics is slower and is presented in Fig. 95. The total decomposition of the polyacetal at pH=5.5 is obtained after 10-12 days.

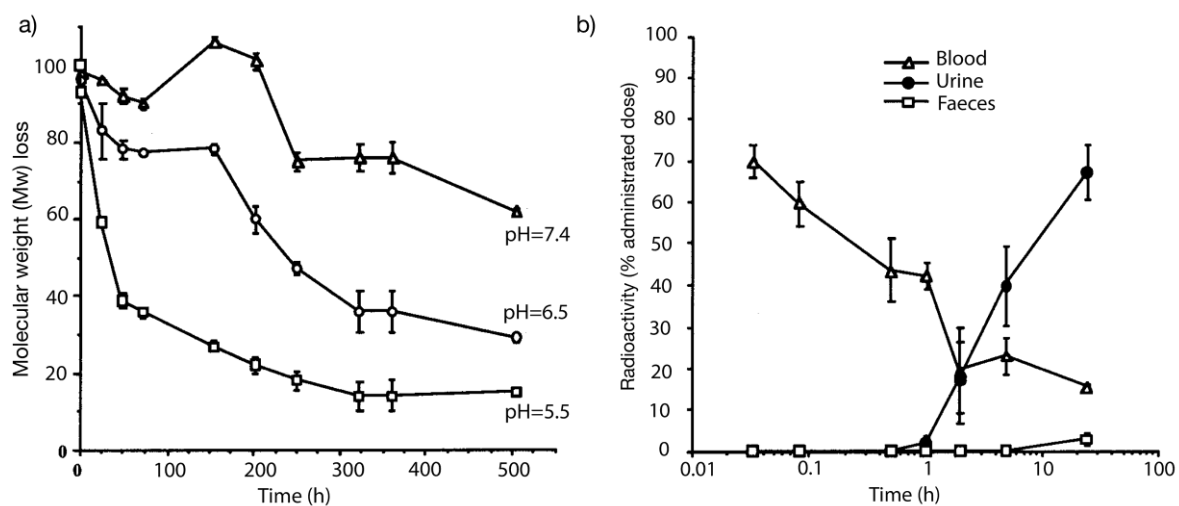


Fig. 95. a) pH-dependent degradation profile of polyacetal obtained at the physiologically relevant pH values of 7.4 (blood), 6.5 (endosome), and 5.5 (lysosome). b) Distribution of radioactivity in the blood, urine, and feces following iv injection. Reprinted from Ref. [391] with permission.

The biocompatibility of the polyacetal was confirmed and the *in vivo* body distribution was also monitored via the covalent linking of an isotope via the pendant functionality (Fig. 95b). No specific organ presented bioaccumulation and radio-labelling was observed in the bloodstream for more than 50 hours showing the interest of such polymer for *in vivo* applications. Frey and coworkers[430] used the same approach but introduced a single cleavable acetal bond at tunable position of the PEG.

To speed-up the degradation of acetal containing PEO, Zimmerman et coll.[431] developed an acetal that will auto-catalyze the degradation. The key point is to generate after the hydrolysis of the acetal linkage a compound that will produce an acidic moiety that enhance the degradation. The authors thus prepared an ADMET monomer bearing a 3-iodo-1,1-dialkoxy core (Fig. 96). Indeed, after the acetal decomposition, 3-iodopropanal is generated that spontaneously undergo β -elimination to produce acrolein and hydroiodic acid HI (pKa close to -10).

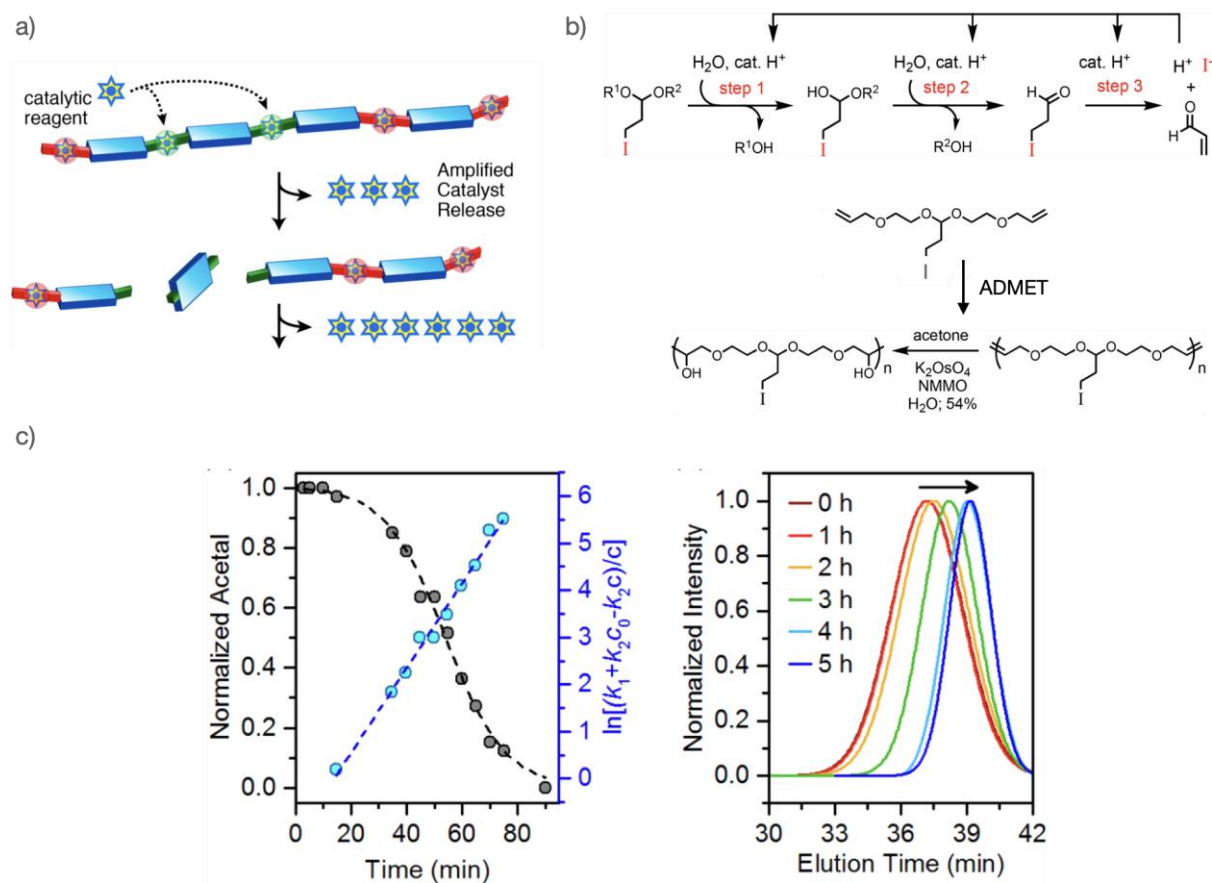


Fig. 96. a) Schematic representation of the self-amplified polymer degradation mechanisms b) Mechanism of acid generation and synthesis of the PEO-bearing acetal group. c) Monitoring the disappearance of acetal functionality of the polymer by ^1H NMR as a 3 mM solution in $\text{D}_2\text{O}/\text{CD}_3\text{CN}$ at 70°C . GPC traces of the degradation of the polymer in a 0.3 M solution in $\text{H}_2\text{O}/\text{CH}_3\text{CN}$ over time at 70°C . Adapted from Ref. [431] with permission.

The polymerization of this monomer was then performed using the Grubbs I catalyst and led to a polymer with a M_n close to $10,000 \text{ g}\cdot\text{mol}^{-1}$. The double bonds were then oxidized using a Upjohn dihydroxylation reaction to increase its water solubility. The degradation profile was then monitored at $\text{pH}=5.5$. A sigmoidal signal was obtained that is consistent with the self-amplified degradation that was induced by the *in situ* HI production.

The production of acetal group was also possible by oxidation of a preformed polymer. Indeed, using the Fenton reaction, Elisseff and coll.[432] managed to produce hemiacetals within the

backbone via the H-abstraction of hydroxy radicals and the further trapping of the macroradical by recombination with a second hydroxy radical. Nevertheless, targeting higher amount of hemiacetal or using high molecular weight PEO led to unwanted degradation of the polymer. Oxidation of PEG was also reported using Ruthenium oxide-based catalysts.[433]

Besides acetal functions, disulfide bonds are interesting since their cleavage occurred in reductive conditions. Such conditions could be reached in the cells and not in the cell exterior that is interesting for in vivo applications. Oligo(ethylene glycols) were then functionalized with thiols end-groups via a multi-step synthesis consisting in tosylation, then thioacetylated and deacetylated in the presence of NH_3 . The thiol functionalities were finally polymerized in DMSO/Water at 25°C to obtain degradable poly(ethylene glycol)s containing disulfide weak bonds.[434] Stability of the copolymers was demonstrated in a medium that mimics cell exterior (PBS + $40\ \mu\text{M}$ cystine, $2.8\ \mu\text{M}$ reduced glutathione, and $9.7\ \mu\text{M}$ cysteine). The addition of $5\ \text{mM}$ reduced glutathione to the sample to mimic the interior of the cell led to an important decrease of the molecular weight.[435]

Using the step-growth polymerization, other kinds of linkage were also tested such as carbonate,[436] imine oxime and the combination of both[437] and also poly(β -amino ester)[435] by the reaction of PEG-diacrylate and linear poly(ethylene imine) via the Michael addition. A similar work was also performed by replacing the amines with thiols to prepare poly(β -thio ester).[438, 439] The polycondensation of PEG bis(succinimidyl carbonate) with oligopeptide diamine consisting of glutamic acid and lysine residues that was designed as a substrate for cathepsin B, a lysosomal enzyme was also reported.[440] Kopecek *et al.*[441] reported a similar approach but in that case using a sequence that is specific to the chymotrypsin enzyme.

Maleamic acid was also investigated as interesting cleavable bond to impart (bio)degradability to PEG. Initial works were performed by Brocchini[442] but non optimal degradation profile was obtained due to side-reaction that occurred during the synthesis. Li and coworkers[443] thus revisited this approach and prepared well-defined acid-degradable PEG from the reaction between PEG diamines and bis(maleic anhydride)s. Three different linkers were tested (Figure 103). The degradation in phosphate buffer was then carried out (Fig. 97). It was shown a good sensitivity of the pH for these copolymers with the copolymers using the M2 linker being the most selective with a ratio between the half-life time at pH=7.4 to the half-life time at pH=5.5 equals to 766. M2 is also the more selective for the degradation since no undesired maleimide formation was observed in contrary to the M1 linker. The more hydrophobic linker M3 do not show an interesting profile whatever the pH.

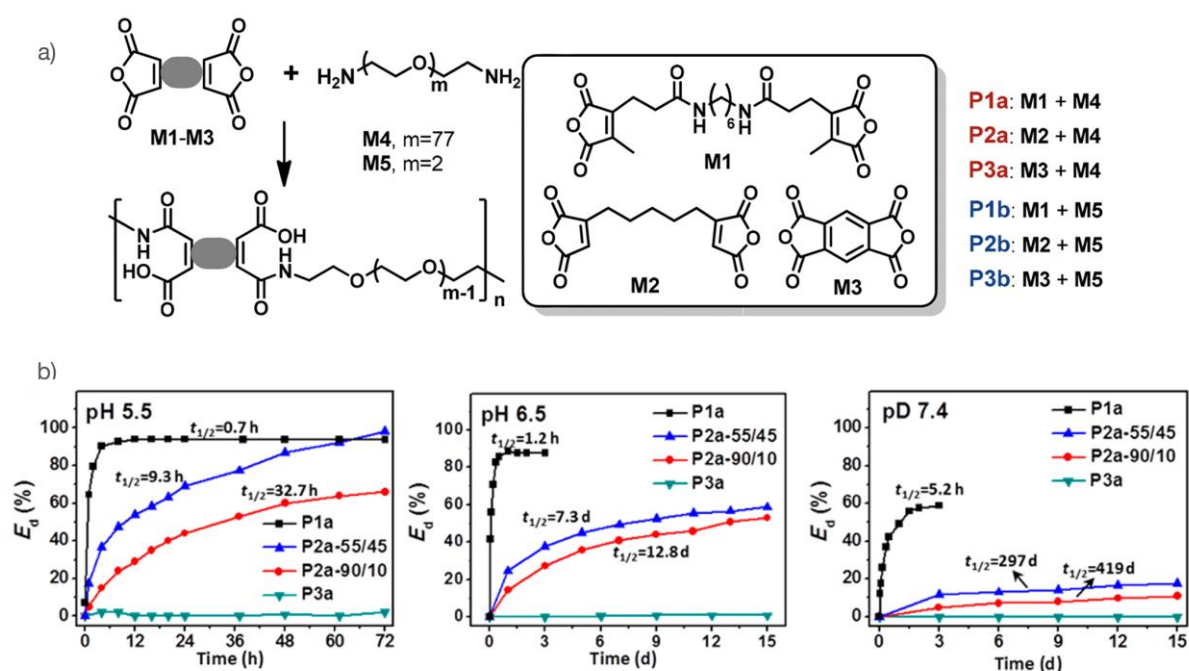


Fig. 97. a) Syntheses of Acid-Cleavable PEGs from Bis(maleic anhydride)s and Diamines b) Hydrolysis kinetic curves of P1a, P2a-55/45, P2a-90/10, and P3a at various pHs (pH 5.5, 6.5, and 7.4). Reprinted from Ref. [443] with permission.

The use of step growth polymerization allowed to prepare promising degradable PEG but the chain-ends are ill-defined and the dispersity is quite high, that could be a problem for drug conjugation and use for biomaterial applications. Chain growth polymerization is a good way to tackle these issues. Lynd and coworkers[345] reported the cationic copolymerization of ethylene oxide and epichlorohydrin (ECH) to insert randomly a chloromethyl pendant group onto the PEO backbone. Deshydrochloration of the functionality using tBuOK produced degradable methylene ethylene oxide (MEO) repeat units within the PEO chain (Fig. 98). The polymerization stoichiometry may be used to define molecular weight, and the comonomer feed-ratio can be used to change the amount of degradable sites, which determines the average molecular weight after degradation. Acid-catalyzed vinyl-ether group hydrolysis inside the MEO repeat-units was found to cause the hydrolytic decomposition of P(EO-co-MEO), which releases nonacidic -hydroxy--keto-PEO oligomers into solution. Samples were kept as dry powders at 20 °C and in a pH 7.4 buffer solution at 6 °C to evaluate storage conditions. Significantly, when kept as a dry powder, no significant deterioration was observed for three months. Additionally, when placed in a pH 7.4 buffer at 6 °C for 72 hours, no discernible degradation was observed. The rate of hydrolysis in two buffer solutions at pH 5.0 and 7.4 at 37 °C to simulate in vivo conditions was determined. The copolymer containing 9 mol% of MEO was shown to hydrolyze completely at pH 5.0 within 6–24 hours, but at pH 7.4, hydrolysis was not complete in 72 hours.

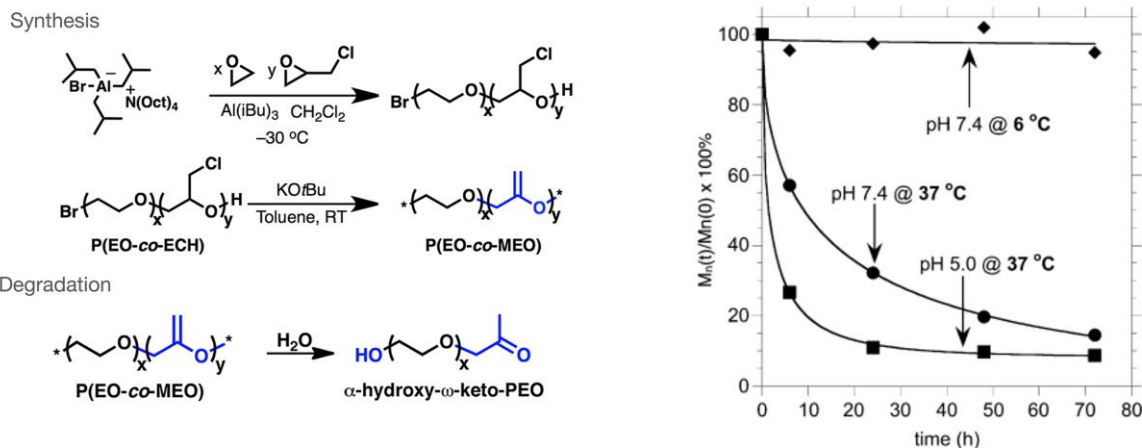


Fig. 98. Preparation of poly[(ethylene oxide)-*co*-(methylene ethylene oxide)]s and their degradation in different buffer solutions. Adapted from Ref. [345] with permission.

Anionic polymerization was also used. Frey and coworkers[366] proposed 3,4-epoxy-1-butene as a comonomer to be used in the anionic copolymerization with ethylene oxide. The interest of such approach is to obtain very well-defined polymer in term of end-group and dispersity. The copolymer is then easily isomerized using the Wilkinson's catalyst to get the vinyl ether moiety (Fig. 69). By the *in situ* NMR analyses, the aster degradation of (Z)-isoEPB units were demonstrated. The degradation was shown to produce homogeneous PEO oligomers whose size depend on the vinyl ether/PEG ratio.[366]

Recently, Ring-opening polymerization was also envisioned as a way to prepare (bio)degradable PEG. Chen and coworkers[444] studied the ROP of 2-oxo-15-crown-5 macrolactone (Fig. 99a). By the combination of a sodium salt that increases selectively the electrophilicity of the carbonyl group of O-15C5 compared to the polymer and an organobase catalyst, they manage to prepare well controlled PEG-like polyesters, poly(O-15C5) that consists in the alternating structure of tetra(ethylene glycol) linked to one glycolic ester. The low Gibbs free energy of the ROP of O-15C5 allowed to have a very efficient depolymerization

procedure to bring back the monomer. Moreover, the hydrolysis experiments were conducted in water and PBS buffer solutions to simulate the physiological environment. This polymer was totally hydrolyzed in 7 day in this medium whereas the degradation is faster at higher pH or at pH <3 following the classic trends of ester hydrolysis.[444] PEG containing carbonate was prepared by ROP of cyclic ethylene carbonate using a dual catalyst set-up (Fig. 99b).[445] Instead of having only a classic poly(ether carbonate) via the use of Lewis base (phosphazenes and nitrogen bases), the additional use of Lewis acid such as LiCl provides polymer with high ether content (90–99%, $M_n = 800\text{--}10\,000\text{ g/mol}$).[445]

Instead of using the ROP of these specific monomers, the metal-free copolymerization of ethylene oxide with L-Lactide (LLA) was performed by Gnanou and coworkers[446] to introduce very low content of lactide into the PEO backbone. They used triethylborane as catalyst to selectively enhance the reactivity of ethylene oxide and suppress transesterification reactions (Fig. 99c). Well-defined PEO containing 1-5 mol% of LLA were obtained. Accelerated degradation conditions (0.5M KOH) were performed and showed a drastic decrease of the M_n (from 50 to 2-3 $\text{kg}\cdot\text{mol}^{-1}$) confirming the random incorporation of LLA into the PEO chains.[446]

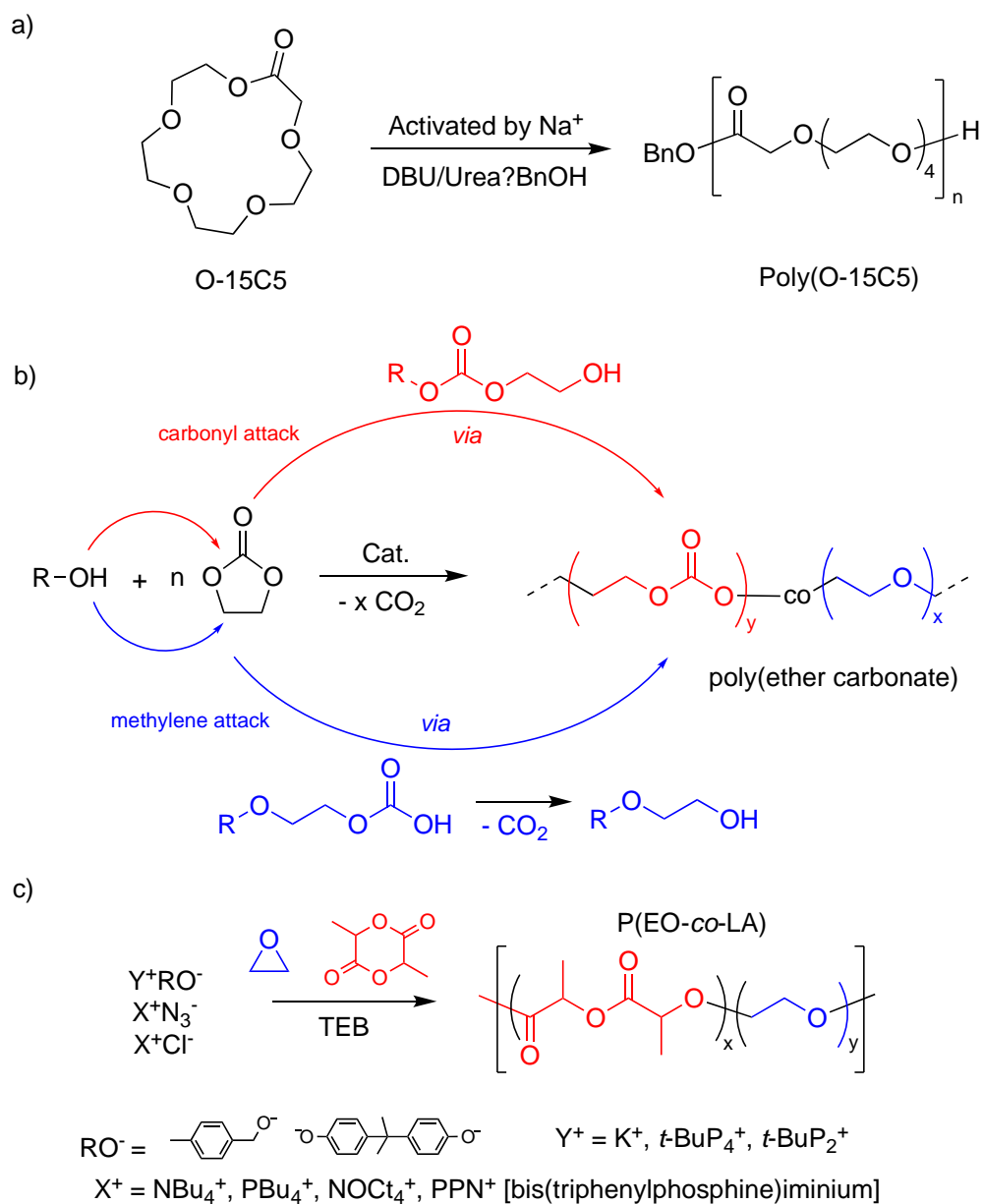


Fig. 99. Preparation of degradable POE via Ring-opening polymerization of a) O-15C5 macrolactone, b) Cyclic ethylene carbonate via a dual catalytic system, c) of Ethylene oxide and L-Lactide in the presence of triethylborane as cocatalyst.

4.3 Water-soluble polymers

There are many water-soluble polymers, ranging from uncharged linear homopolymers (e.g., polyethylene oxides) to branched and charged copolymers (e.g., polyacrylates, modified polysaccharides, and polyamino acids). Due to their chemical diversity, water-soluble polymers cover a wide range of properties and functionalities (e.g., thickening, stabilization, and emulsification) that are essential for their use in many applications. Their use in some applications results in their release into artificial and natural environments. For example, water-soluble polymers contained in cleaning and cosmetic products enter wastewater and sewage treatment plants without being recycled. Despite the known pathways and their wide use, little attention is currently paid to the environmental fate of these polymers, but in the near future regulations will become stricter. In this context, the replacement of non-biodegradable water-soluble polymers by biodegradable analogues becomes a major issue. The case of poly(ethylene oxide) or poly(ethylene glycol) is already addressed below.

The main water-soluble polymers belong to anionic homo- and copolymers of acrylic acid, and cationic polyquaterniums. They could be used as thickeners, emulsifiers, lubricants, conditioners, and film formers. Acrylamide-acrylic acid copolymers are used at high tonnages as flocculants, e.g., in wastewater treatment plants. Such copolymers either charged or neutral are mainly prepared by radical polymerization of vinyl monomers.

An example of the interest in synthesizing degradable water-soluble polymers by rROP was described by Thoniyot *et al.*[213] in the case of poly(acrylic acid) (PAA). Indeed, despite its water-soluble character (in particular in basic medium), this polymer is not biodegradable. PAA is also widely used on an industrial scale in cosmetics and hygiene products as a thickener or super-absorbent due to its ability to absorb water. In order to limit the release of polymers into the environment (and its accumulation in the biosphere), the authors sought to introduce ester functions into the PAA backbone in order to be able to break the long chains into

oligomers considered as biodegradable (*i.e.* bioassimilable) when the number average molar mass does not exceed 1000 g/mol. This feature has been experimentally confirmed by Carter and coll,[447] who prepared discrete oligomers of PAA and subjected them to OECD 301F testing. For this purpose, MDO was copolymerized by rROP with *tert*-butyl acrylate (Fig. 100). By using a feed ratio of tBuA/MDO = 1:1, 10-30 mol% of ester units were introduced into the backbone and M_n in the range 35,000-160,000 g.mol⁻¹ were obtained. Hydrolysis in an acid medium to remove the *tert*-butyl group then led to the desired copolymer, namely poly(AA-*co*-MDO). The step of protecting the carboxylic acid function is essential here to ensure the stability of the MDO monomer. The polymers were then degraded chemically and under biodegradation conditions. Using KOH degradation, oligomers displayed a M_n of 350 g.mol⁻¹, that is in good agreement with the amount of ester units into the backbone.

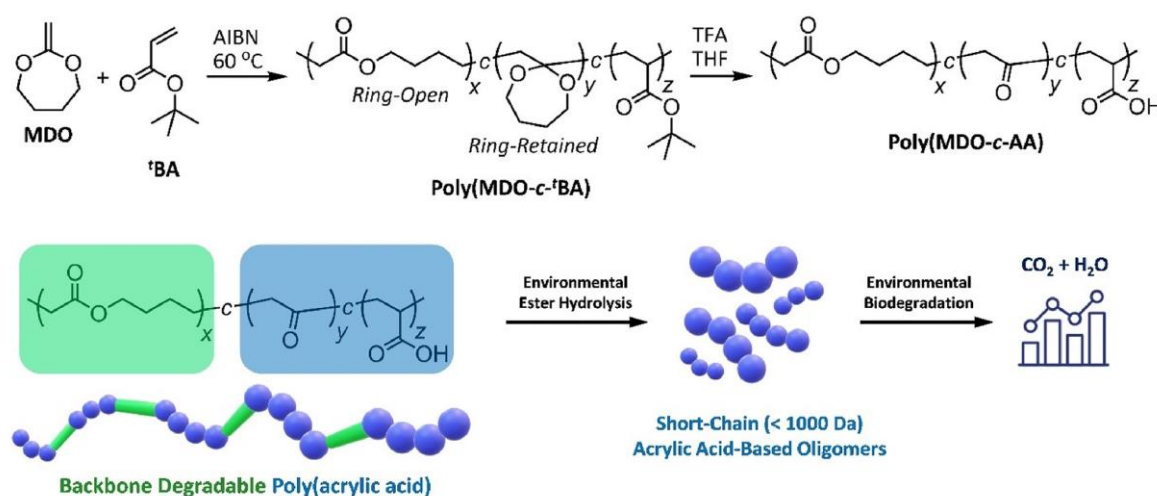


Fig. 100. rROP of MDO and tBA furnishing poly(MDO-*co*-tBA), followed by *tert*-butyl deprotection under acidic conditions affording backbone degradable poly(MDO-*co*-AA). Reprinted from Ref. [213]with permission.

Polyacrylamide is another major non-degradable water-soluble polymer.[448] One of the main uses of this polymer is the flocculation of solids in a liquid. This process is applied to water

treatment and processes such as papermaking and screen printing. Polyacrylamide can be used in powder or liquid form. In order to make it (bio)degradable, Nicolas *et al.*[449] copolymerized acrylamide with CKA and in particular with MDO and BMDO. The aim of this work was to find copolymers containing CKAs with rapid hydrolysis kinetics under physiological conditions to consider their use *in vivo* as biomaterials. With MDO pure water-soluble polymers were obtained whereas the use of BMDO led to very promising tunable UCST materials. Both copolymers and in particular water-soluble copolymers comprising between 2 and 7 mol% of BMDO showed an extremely fast degradation under physiological conditions (PBS, pH 7.4, 37 °C) with a decrease in M_n between 21 and 58% in 24h depending on the BMDO content (Fig. 101). It should be noted that this degradation rate is higher than that observed under the same conditions with reference polyesters such as PLGA and PLA. Moreover, the copolymers containing between 9 and 13 mol% of BMDO showed degradation kinetics in the presence of lipases (from *Candida antarctica*) similar to those observed in physiological conditions. These results therefore pave the way for the use of CKA rROP to develop degradable biomaterials for use *in vivo*. [449]

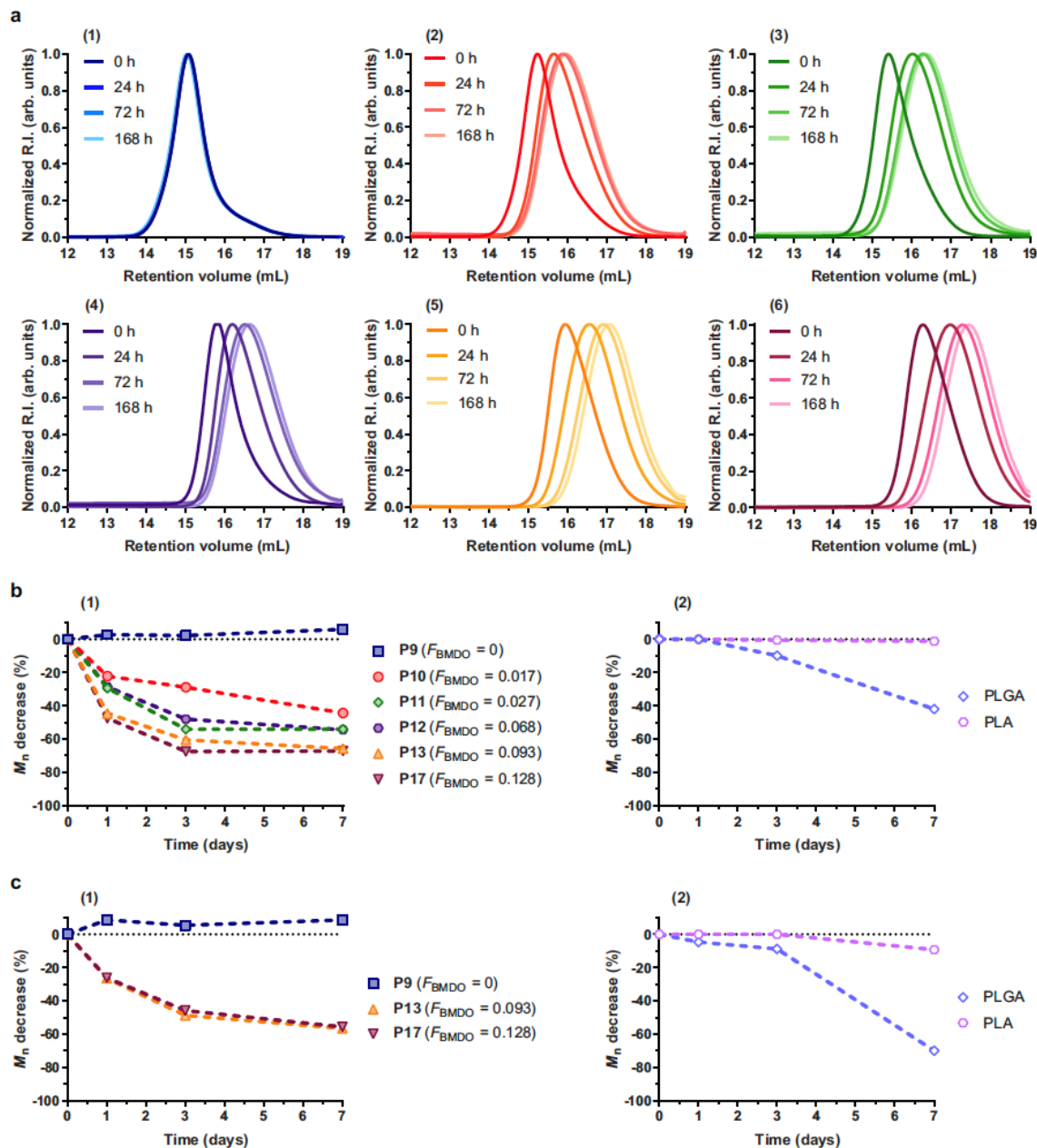


Fig. 101. Hydrolytic degradation in physiological conditions of P(AAm-co-BMDO) copolymer s, PLA, and PLGA. a) Evolution of the SEC chromatograms at different time during hydrolytic degradation in PBS (pH 7.4, 37 °C) of P(AAm-co-BMDO) copolymers as a function F_{BMDO} : (1) P9 ($F_{\text{BMDO}}=0$); (2) P10 ($F_{\text{BMDO}} = 0.017$); (3) P11 ($F_{\text{BMDO}} = 0.027$); (4) P12 ($F_{\text{BMDO}}=0.068$); (5) P13 ($F_{\text{BMDO}}= 0.093$) and (6) P17 ($F_{\text{BMDO}} = 0.128$). b) Evolution of the number-average molar mass, M_n , with time during hydrolytic degradation in physiological conditions (PBS, pH 7.4, T =37 °C) of: (1) PAAm (P9), P(AAm-co-BMDO) copolymers P10–P13 and

P17 and (2) PLA and PLGA; c) evolution of the M_n with time during enzymatic degradation with lipases (*Candida antarctica*, PBS, pH 7.4, T = 37 °C) of: (1) PAAm (P9), P(AAm-co-BMDO) copolymers P13 and P17 and (2) PLA and PLGA. Reprinted from Ref. [449] with permission.

Roth *et al.*[305] used the better reactivity of thionolactones and in particular DOT to prepare degradable polyacrylamides. Different monomers (primary, secondary and tertiary neutral and zwitterionic acrylamides) were successfully copolymerized using a small amount of DOT. The intact copolymers exhibited thermally responsive behavior (LCST or UCST-like), tunable by molar composition and comonomer sequence (exploiting non-azeotropic copolymerization behavior). Various conditions led to selective and complete degradation of the backbone thioesters by hydrolysis, aminolysis, transthioesterification (including under physiological conditions), and oxidative hydrolysis, which significantly increased the aqueous solubility of the degraded fragments.[305]

4.4 The case of thermosets

4.4.1 3D printing

3D printing has revolutionized the industrial world by allowing the rapid fabrication of objects of various sizes with high resolution, directly via a computer-aided design. The most recent 3D printing techniques use a photopolymerization process (VAT photopolymerization).[450] With this technique, objects are obtained by cross-linking (via photopolymerization) of liquid resins.[450] Up to now, the resins that are commercially available are composed of multi-(meth)acrylate monomers. The object obtained is thus a network, *i.e.* a cross-linked material

with a C-C type skeleton. If this architecture allows to obtain very good thermal and mechanical properties, it also has the disadvantage of providing non-degradable objects.

Second, this stability is incompatible with subtractive manufacturing, a process that allows printed objects to be erased or excavated after being created. This method is highly promising because it makes it simple to remove templates or sacrificed sections from 3D objects.[451] Many authors have prepared specific resin whose core of the multi-functional monomer contained degradable moieties. Recently, very sophisticated methods for creating new monomers and resins for two-photon lithography were proposed by Barner-Kowollik and colleagues that allow stimuli-induced or controlled degradation and are based for example on silane-based[452] monomers, o-nitrobenzyl ester[453] monomers, and chymotrypsin-cleavable[454] monomers. Di or multi-(meth)acrylate monomers with a core consisting of a poly(beta amino ester)[455] or an acetal[456, 457] that is basic- or acid-degradable respectively were also synthesized and shown good degradability. In all cases, the resins are specifically designed to be degradable, but do not take into account the mechanical and thermal properties of the resin.

Since radical polymerization is used to print these resins, Carlotti *et al.*[458] used the copolymerization of MDO with multiacrylate compounds such as pentaerythritol tetraacrylate (PETA) (ratio 90 :10) to prepare cross-linked polyesters by DLW (for direct laser writing) at 2 photons. They were able to obtain very high-resolution microstructures (Fig. 102a) that could be rapidly degraded on demand (under acid or basic conditions). Moreover, the authors confirmed the interest of this approach to elaborate degradable scaffolds or masks as well as protective coatings (Fig. 102b).

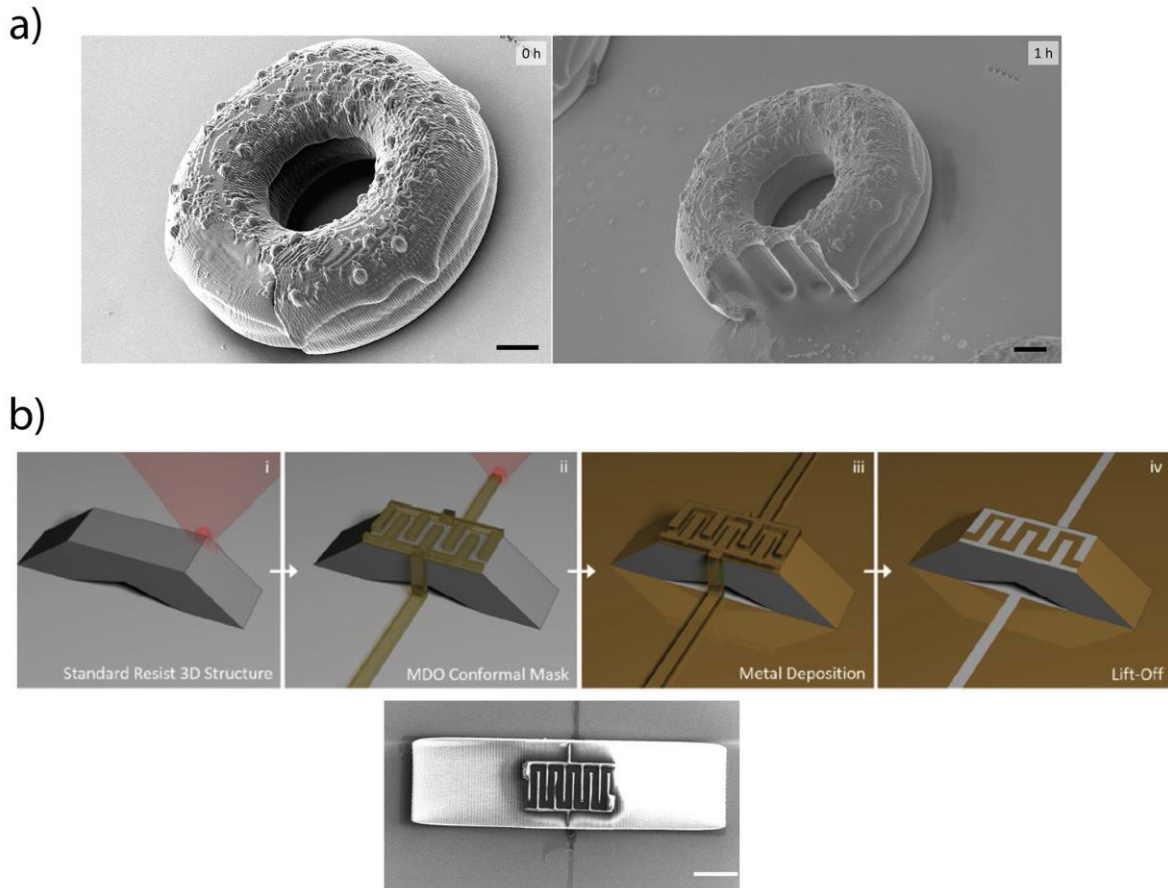


Fig. 102. A) Partial degradation (SEM) of micro-donut structures made with MDO:PETA 90:10 (scale bar 20 μm). Only the last part degrades leaving the bite mark. B) Illustration of a 3D masking methodology for fabricating an isolated coil on a DLW printed 3D structure: i) the main structure is printed by DLW; ii) an MDO formulation is used to prepare a 3D sacrificial mask; iii) the metal is evaporated on top; and iv) the mask is finally removed leaving a negative imprint on the structure (scale bar 50 μm). Reproduced from Ref. [458] with permission.

This approach, although very interesting, allows to print a low cross-linked polyester. In addition, the 2-photon stereolithography technique requires little material since only microstructures of a few microns are produced. 3D printing of larger objects is based on 1-photon lithography and the technology of choice today is the DLP (for digital light processing)

method, which has many advantages such as fast printing (several centimeters/hour), a resolution that can go down below 100 μm , compatibility with different inks and low cost.

An effective method for imparting degradability properties to DLP-developed objects while maintaining their thermo-mechanical properties was developed by Guillaneuf *et al.*[459] They used the cyclic monomer DOT as a 2 w% polymerization additive in commercial multi-acrylate resins such as pentaerythritol triacrylate (PETIA). Since the reactivity ratios of DOT and acrylates are closer than those of MDO and acrylates, it is possible to use DOT only as an additive. It was shown that the introduction of DOT has only a slight impact on the kinetics of the photopolymerization and on the mechanical properties of the obtained materials.[459]

Besides, the introduction of rROP-cleavable thioester functions into the main chains allowed the development of structures degradable under basic conditions (KOH (5%) in a methanol/THF mixture). Moreover, this approach has shown its interest by being able to be used for any technology based on UV irradiation, UV microfabrication, 2-photon stereolithography or even with commercial 3D printers (Figure 109). Copolymerization of multiacrylate resins with a cyclic monomer by rROP also makes it possible to consider using this technique to fabricate z-axis objects with degradable sacrificial supports (Fig. 103).

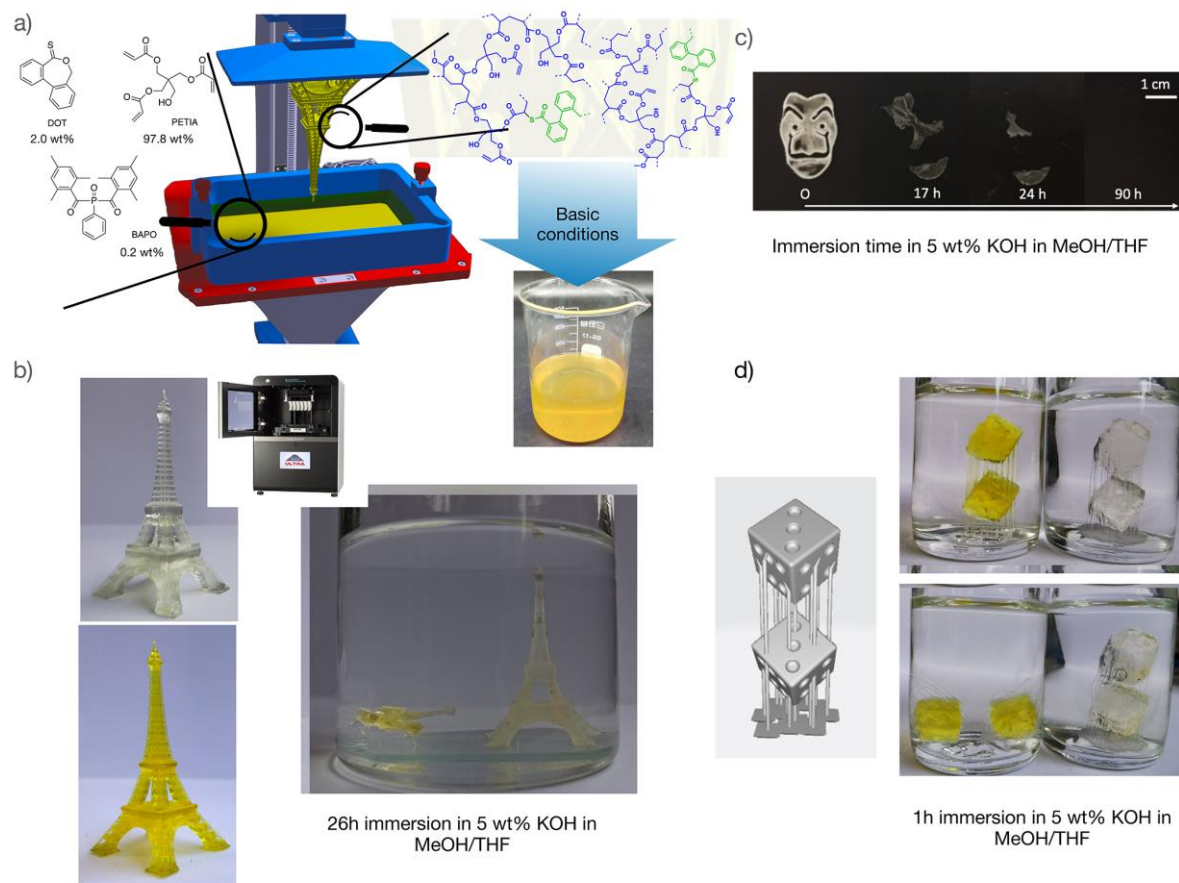


Fig. 103. a) Preparation of degradable 3D objects using thionolactone as resin additive. b) Eiffel tower printed with and without additive using a commercially available 3D printer and the degradation of the objects in basic conditions. c) Dissolution of a macroscopic object (resin PETIA+2 wt % DOT printed with a DLP-UV setup) using KOH (5 wt %) in MeOH/THF d) Preparation of a stack of dice using the Miicraft 3D printer and its degradation using 5 wt % of KOH in MeOH/THF at room temperature and without agitation. Adapted from Ref. [459] with permission.

Recently it has been shown that Ru-based metathesis catalysts can be activated by light, either directly or using photosensitizers, leading to the use of ROMP in additive manufacturing.[460] The main resin component in these studies has been dicyclopentadiene (DCPD). The resulting cross-linked polymer possesses high notch-impact strength and very important properties such

as high temperature, corrosion, and chemicals stability. The DCPD market is estimated to 500 million Euro in 2019 and is expected to grow by 5% annually.[461] 5-ethylidene-2-norbornene (ENB) has to be added to prepare a low viscosity resin that produce a thermoset material with a high T_g , good thermal stability, and outstanding mechanical performance.[462] As already discussed below, DHF is one of the more interesting degradable comonomer for ROMP since it is commercially available, can be prepared from sustainable feedstocks, possesses low viscosity and is compatible with various norbornene and diynes derivatives. Foster and coworkers[463] thus tried to combine ROMP, additive manufacturing and DHF. The authors demonstrated first that they managed to print the resin despite the volatility of DHF and its propensity to decrease the rate of polymerization, impacting negatively the time required for gelation. Moreover, the object presented nearly total degradation of DHF-containing thermosets in 1 M HCl for both UV-cured and thermally post-cured materials with DHF loadings above a critical level (ca. 20 mol%).[463] To illustrate their work, they prepared a "hidden message" in which a degradable 2D object made using digital light processing (DLP) was embedded inside of a nondegradable material. The "message" would be exposed if the degradation produced a negative of the original printed piece (Fig. 104). Using a DCPD/ DHF resin, a biodegradable thunderbird item was created, and it was then enclosed in a brand-new DCPD resin without DHF. A control that do not contain DHF for both the two steps of the DLP printing process was also prepared as reference. As seen in Fig. 104, when the compound objects were incubated in acidic THF, the thunderbird component made with DHF completely degraded whereas the control thunderbird showed no signs of deterioration. Despite the swelling pressures encountered during deterioration, the 2D thunderbird geometry was well preserved, indicating that only a small amount of unreacted DHF diffused into the surrounding resin.[463] This proof of concept showed the premises of degradable 3D objects prepared by ROMP but optimization in monomer structure is still necessary to counterbalance the low

reactivity of DHF that led to long exposure times and resulted in a loss of resolution as compared with resin without additive.

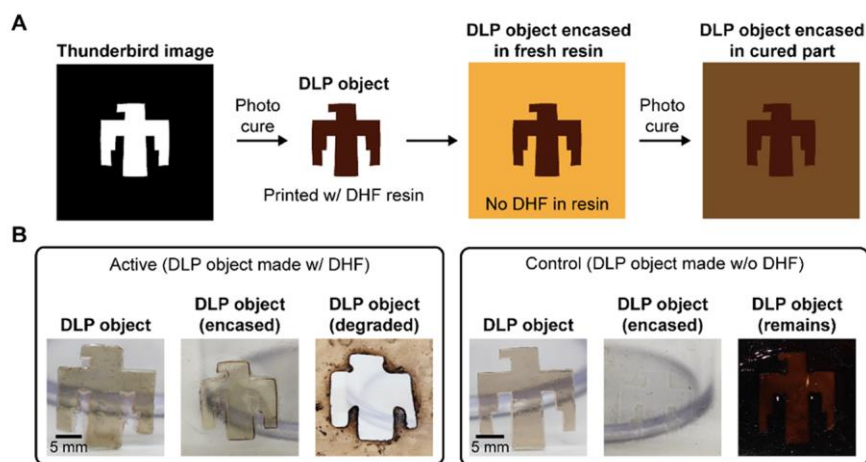


Fig. 104. (A) Schematic representation of the two-step curing process used to create a compound object with an embedded, degradable shape. (B) Photographs of objects obtained from the various steps in (A). Shown are an embedded object containing degradable DHF linkages and a nondegradable control. Reprinted from Ref. [463] with permission.

Using the same combination of monomers (DCPD with 5mol%ENB and DHF), Moore and coworkers[112] investigated the frontal ROMP polymerization to prepare degradable thermosets. They obtained similar results than previously, that are range of concentration of DHF between 1 and 15 mol%, with a decreased reactivity with increase amount of DHF. Nevertheless, the authors used the inhibition behavior of DHF to prepare a resin that is compatible with freeform 3D printing. Indeed, a viscoelastic gel with shear thinning rheological behavior is easily formed by this formulation, a property that may make them acceptable for freeform printing.

Each formulation successfully frontally polymerizes after reaching their gel point, enabling simultaneous freeform printing (3D helix, Fig. 105) and curing. The capacity of the gelled resins to degrade was confirmed by acidic treatment. After 18 hours, the helix fully disassembled, leaving behind a very low amount of insoluble material (about 1 wt%) that was attributed to the strongly crosslinked oxidized layer at the surface of the object.[112]

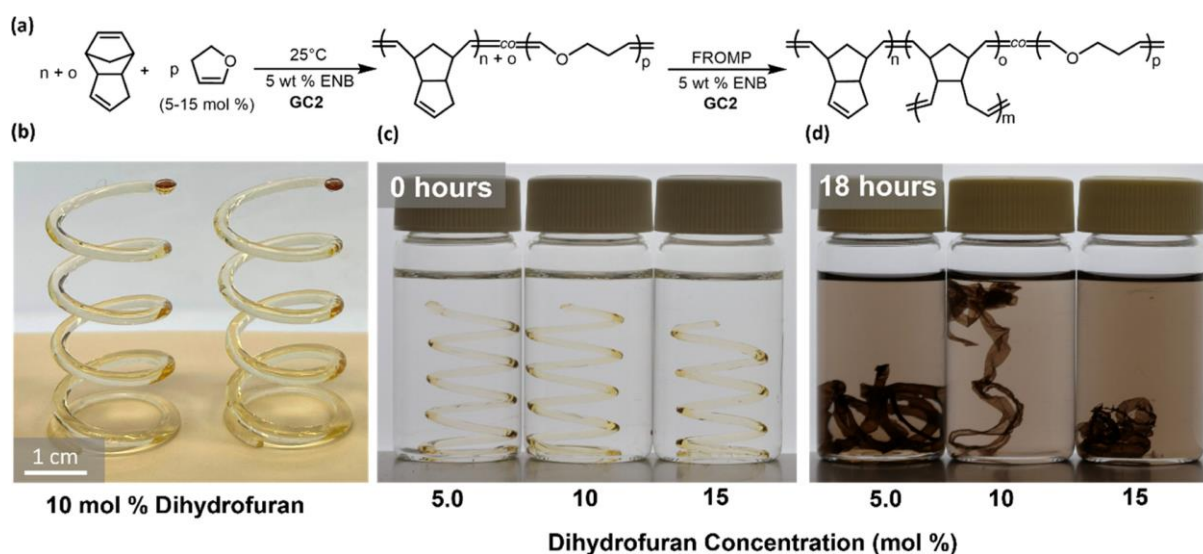


Fig. 105. Fabrication and deconstruction of 3D-printed helical architectures of p(DCPD-*co*-DHF). (a) Schematic of p(DCPD-*co*-DHF) fabrication process beginning with incubation at 25 °C until each resin reaches its gel point, followed by extrusion onto a heated substrate, thereby initiating FROMP. (b) Representative image of 3D-printed helix containing 10 mol % DHF. (c) Initial image of p(DCPD-*co*-DHF) samples containing 5–15 mol % DHF immersed in 1 M HCl in CPME. (d) Image of p(DCPD-*co*-DHF) samples containing 5–15 mol % DHF immersed in 1 M HCl in CPME after 18 h. All samples deconstructed into soluble fragments while leaving behind a residual insoluble film (about 1 wt %). Reprinted from Ref. [112] with permission.

4.4.2 Poly(dicyclopentadiene) thermosets

A thermoset is a chemically cross-linked polymer that is infusible, insoluble, and is generated by an irreversible curing process between formulations that could be in a liquid, soft solid, or viscous state. Thermosets are often utilized in applications including coatings, adhesives, composites, electronic packaging, and more because they display excellent thermal and mechanical capabilities as well as outstanding dimensional stability. Thermosets are essential in several applications, including high-performance coatings, adhesives, rubbers, light-emitting diode lenses, and solar cell encapsulants. Over 18% of all created polymers are thermosets, with more than 65 million tons produced year globally between 2010 and 2015. Conventional thermoset materials cannot be heated or chemically processed or molded because of the covalently cross-linked networks and thus are non-degradable.

By breaking labile bonds in a thermoset, it may be possible to degrade the original material into smaller molecules and dissolve in solvents, or, alternatively, reduce the cross-linking density to make it easier for the cross-links to be removed from the materials' high-value components under relatively benign conditions. The preparation of degradable thermosets based on labile linkage was reviewed by Ma and Webster.[50] With the concept of dynamic covalent networks,[464] also called vitrimers,[49] thermosets could thus be recycled and are seen as self-healing or reworkable. In this review we will focus on the insertion of cleavable comonomers that make common thermoset degradable.

As presented above, Johnson and coworkers[51] presented a theoretical approach to rationalize the optimization of the location of cleavable bonds within thermosets that could allow a mild chemical degradation at low cleavable bond loadings using commercially available resins, The authors thus employed previously reported silyl ether monomers **ROMP22**[96] that copolymerize efficiently with norbornene derivatives by ROMP to form degradable statistical

copolymers to test the validity of its model. DCPD and **ROMP22** was mixed and cured for 30 min at 120 °C in the presence of G2 catalyst at a monomer/catalyst ratio 2500:1. A similar experiment was performed in the presence of a bicyclooctene containing a silyl ether linkage (SiXL Fig. 106). The performance of the degradable thermoset (up to 20 mol% of **ROMP22**) was similar to the reference poly(DCPD) materials in term of Young modulus, elongation at break and laser-induced projectile impact test, showing the interest of such approach. Only the T_g of the materials decreased with increase amount of **ROMP22**, reaching 138 °C for 10 mol% of **ROMP22**.

Tetrabutylammonium fluoride (TBAF) was employed in excess to degrade samples of **ROMP22**-doped, SiXL-doped, and reference poly(DCPD) at ambient temperature. The reference was completely intact after 12 hours, while samples that included 7.5 to 15 vol% **ROMP22** was solubilized (Fig. 106). Even at 80% SiXL loading, materials that were doped with SiXL did not break down into soluble compounds. Fluoride was shown to cleave SiXL at a rate comparable to that of **ROMP22** in this system, indicating that the variation in the amount of degradation is attributable to the location of the labile bond. Composites containing carbon fibers were also prepared and it was shown that the carbon fibers could be fully recovered without any damage as proven by Raman analyses.

Johnson and coworkers also characterized the degradation products whose size is dependent on the amount of **ROMP22** (2-8 kDa and particle size of 4 nm). Recycling of the oligomers was performed by mixing them up to 25 wt% with pure DCPD led to a material with identical properties as the reference one.

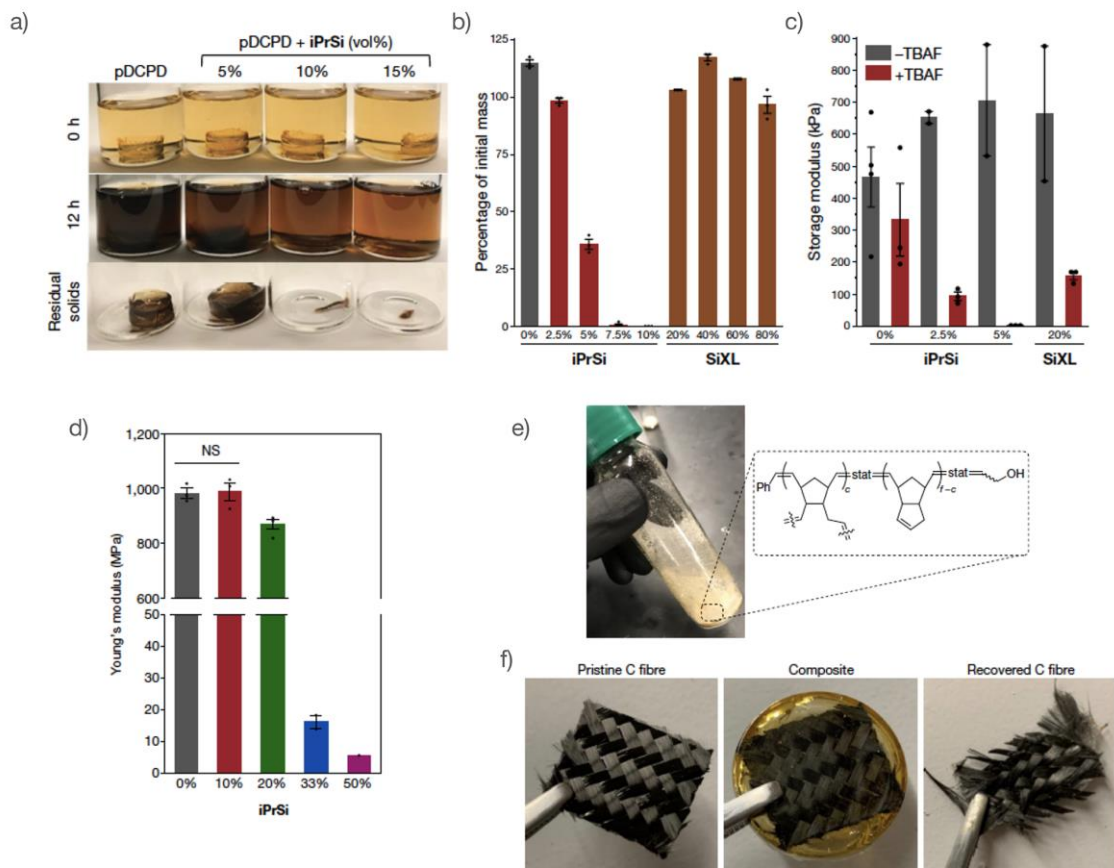


Fig. 106. a) **ROMP22**-doped poly(DCPD) samples show **ROMP22** volume-fraction-dependent dissolution in a THF solution of TBAF. Samples containing 10% or 15% **ROMP22** are almost entirely dissolved. b,) Quantification of residual mass of poly(DCPD) samples after TBAF treatment at room temperature for 12 h or 17 d for **ROMP22** - or SiXL-doped samples, respectively. c), Shear rheology on THF-swollen samples. Samples were exposed to TBAF for 12 h at room temperature. d) **ROMP22** -doped poly(DCPD) Young's modulus (measured at room temperature); e) Dried poly(DCPD) fragments from 10% **ROMP22** -doped material. f) Carbon fibre recovery from 10% **ROMP22** -doped poly(DCPD) composites. Adapted from Ref. [51] with permission.

Since the T_g of the thermoset is impacted by the introduction of 10 vol% of cleavable silyl-ether comonomer additive, Johnson et coll.[98] developed new cleavable comonomer additive

to counterbalance the conformational flexibility imparted by **ROMP22** and thus kept the thermomechanical properties unaffected.

The thermomechanical characteristics of thermosets can be improved by increasing crosslink density. Nevertheless, the chemical breakdown of thermosets containing permanent, non-cleavable crosslinks into soluble products cannot be facilitated by the addition of cleavable crosslinks. Johnson *et al.* overcome this issue by introducing "strand-cleaving crosslinkers" (SCCs) (Fig. 107). The advantage of SCCs is adding cleavable branch points to thermoset networks, which increases crosslink density while allowing for chemical breakdown into soluble fragments at loadings comparable to cleavable comonomers.

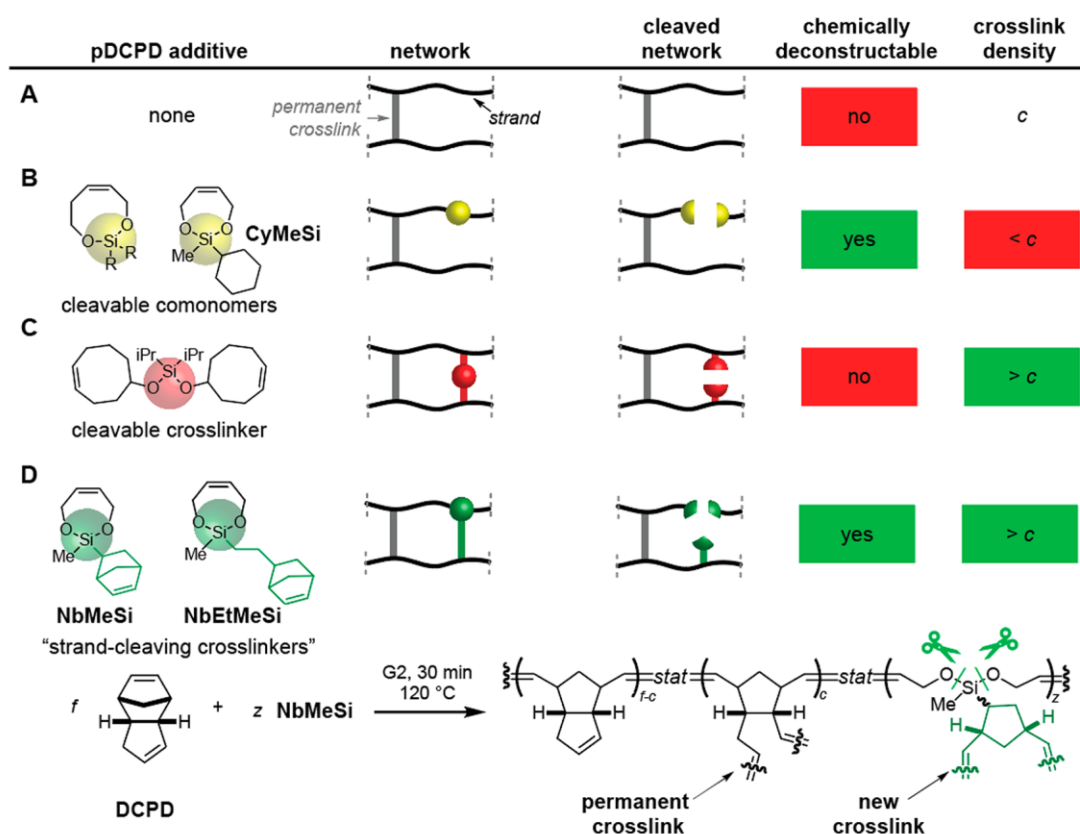


Fig. 107. (A) Thermosets such as poly(DCPD) are composed of linear strands and, assuming no intramolecular reactions, c permanent crosslinks. These materials cannot easily be

chemically deconstructed to yield soluble products. (B) Cleavable comonomers that introduce labile bonds into thermoset strands enable deconstruction at the expense of a lowered crosslink density. (C) Cleavable crosslinkers can increase crosslink density but do not enable material deconstruction. (D) Strand-cleaving crosslinkers (SCCs) combine the advantages of these two traditional approaches, enabling mild chemical deconstruction of thermosets while simultaneously increasing crosslink density. For example, the SCC NbMeSi can add up to z new crosslinks (assuming complete conversion and no intramolecular reactions) into poly(DCPD), thus increasing total crosslink density while providing cleavable network junctions. G2 = Grubbs second-generation catalyst. Reprinted from Ref. [98] with permission.

The thermosets containing NbMeSi (Fig. 107) could nearly entirely break down into soluble products at 10% v/v in 24 hours at 50 °C. Due to their higher cross-link density, the SCC-containing thermosets dissolve more slowly than the reference degradable thermoset. For virgin poly(DCPD) and NbMeSi-based materials, tensile-mode dynamic mechanical analysis (DMA) experiments were performed to determine the storage moduli E' and T_g . The T_g value remains constant at 172.2 °C and 173.1 °C for virgin poly(DCPD) and 10% v/v NbMeSi containing samples, respectively. The value could even rise to 178.2 °C for 20% v/v NbMeSi. Contrarily, using monomer similar to NbMeSi but with a cyclohexane ring instead of the pendant norbornene (Fig. 107) resulted in notable reductions in T_g : 125.2 °C at 10% v/v, 85.9 °C at 20% v/v and 16.7 °C at 50% v/v. The SCC strategy is thus a convenient way to combine degradation behavior without impacting the thermomechanical properties of the thermoset.[98]

It takes a huge amount of energy to produce thermoset polymers and composites for high-performance structural applications (10^6 to 10^8 J per kilogram of polymer produced), since massive ovens or autoclaves are necessary for curing.[465] Frontal polymerization is a process

that uses the resin's chemical energy to power material synthesis, and then produces thermosets and fiber-reinforced polymer composites that are similar to those obtained by conventional techniques while using >10 orders of magnitude less energy to produce. In addition to energy savings, FP do not need the use of massive ovens, significantly lowering the production costs. poly(DCPD) has been shown to be a monomer of choice for FR producing fiber-reinforced polymer composites. Moore and Johnson[108] thus investigated if this system could be compatible with cleavable comonomers and in particular with **ROMP4-ROMP33** and **ROMP22-ROMP23** bearing either acetal or silyl-ether linkage. With these two structures a statistical incorporation into the thermoset is obtained.

For the two comonomers in the range of 0 - 25 mol%, frontal copolymerization of DCPD with cleavable cyclic monomers produces products of excellent quality without voids. The thermal properties of the thermosets are impacted as previously by the presence of cleavable comonomers (Fig. 108), introducing flexible aliphatic chains into the backbone decreasing the T_g . Nevertheless, the mechanical properties such as the Young's modulus and yield strength are maintained at least up to 15 mol%. The degradation was performed using either tetrabutylammonium fluoride (TBAF) in THF for silyl ether-based thermosets and 1.0 M HCl in CPME for acetal-based thermosets. Complete thermoset dissolution was observed for thermosets containing at least 7.5 mol% of cleavable comonomer. This threshold value required to cause full degradation is similar to the ones of thermosets produced previously, indicating that the frontal polymerization mechanism do not induce any change compared to classic ROMP mechanism. By dropwise precipitation into methanol, degradation fragments are recovered as white powders from the soluble fraction. The degradation fragments are then upcycled to produce a new thermoset with higher T_g (see the recycling part).

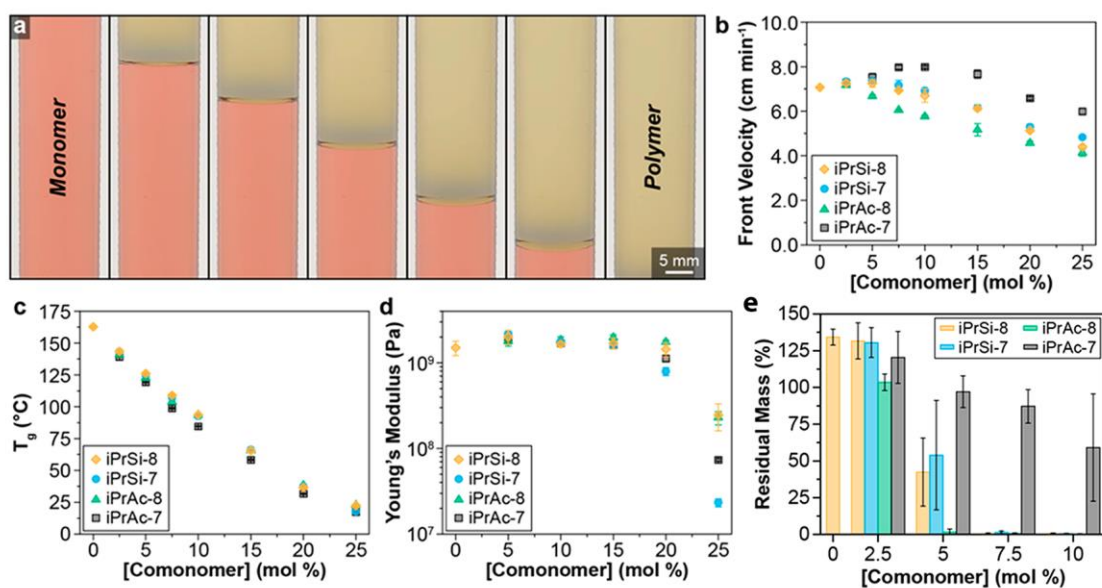


Fig. 108. Frontal ring-opening metathesis copolymerization of dicyclopentadiene and cleavable comonomers. (a) Optical images taken during FROMP of DCPD containing 10 mol % **ROMP23** and 150 ppm Grubbs second-generation catalyst (GC2) inhibited with 1 molar equivalent (with respect to GC2) of tributyl phosphite (TBP). Images were taken at 5 s intervals. (b) Front velocity measured at various cleavable comonomer loadings. All measurements were conducted at 25 °C with 150 ppm GC2 and 1 molar equivalent of TBP. (c) Glass transition temperatures (T_g) obtained during dynamic DSC traces (5 °C min⁻¹). (d) Young Modulus of copolymers with various cleavable comonomer loadings determined via quasi-static tensile loading. (e) Residual masses retrieved after removing the soluble fraction at various deconstructable comonomer loadings. A residual mass of >100% is a consequence of residual solvent trapped in the matrix. iPrSi8 = **ROMP22**; iPrSi7 = **ROMP23**; iPrAC7 = **ROMP4**; iPrAC8 = **ROMP33**. Reprinted from Ref. [108] with permission.

The incorporation of cleavable comonomers into poly(DCPD) was thus a convenient way to prepare degradable thermoset with interesting mechanical and thermal properties. The structure and amount of cleavable comonomers is nevertheless a key parameter to tune the macroscopic

properties of the materials. In an effort to still improve the system, Johnson and coworkers[111] used machine learning model ensemble that was able to predict with a good accuracy the T_g of a thermoset containing cleavable monomers. With this tool, they designed new cleavable comonomers that were able to be used with DCPD to prepare thermoset with tunable T_g with an accuracy of 15 °C.

4.4.3 Other thermosets

Although being one of the oldest reported polymers, polyurethanes (PUs) and also cross-linked polyurethane continue to play an essential role in a variety of industries such as automobiles, sporting goods, medical equipment, construction, electronics, etc.[466] The success of this material and thus the important consumption of PU products contributes significantly to plastic pollution. As an example, close to 1.3 million tons of PU waste per year is produced in the US.[467] It appears to be very challenging to obtain a controlled degradation of cross-linked PU thermosetting materials because of the remarkable stability of carbamate bonds combined with the crosslinking network. The chemical degradation of the carbamate bonds in the backbone of PU wastes required harsh conditions such as high temperature and reactions such as alcoholysis, acidolysis, aminolysis, or pyrolysis.

Wang and coworkers[468] then inserted a silyl-ether group in the middle of the POE prepolymer (with either a methyl, ethyl or isopropyl alkyl pendant group) and used it to prepare the cross-linked PU via the reaction with hexamethylene diisocyanate trimer (Fig. 109). The mechanical properties of these thermosets were measured by DMA. The T_g was -27 °C and the melting point of the POE segment was measured at 30 °C. The authors thus investigated the degradability rate in both neutral and acidic conditions. The PU thermoset with the pendant iPr group do not show degradation in neutral PBS at 60 °C for 150 min whereas the same thermoset

with methyl and ethyl group degraded within 45 and 90 min respectively. In the presence of vinegar, all the PU thermostets were degraded very rapidly (Fig. 109).[468]

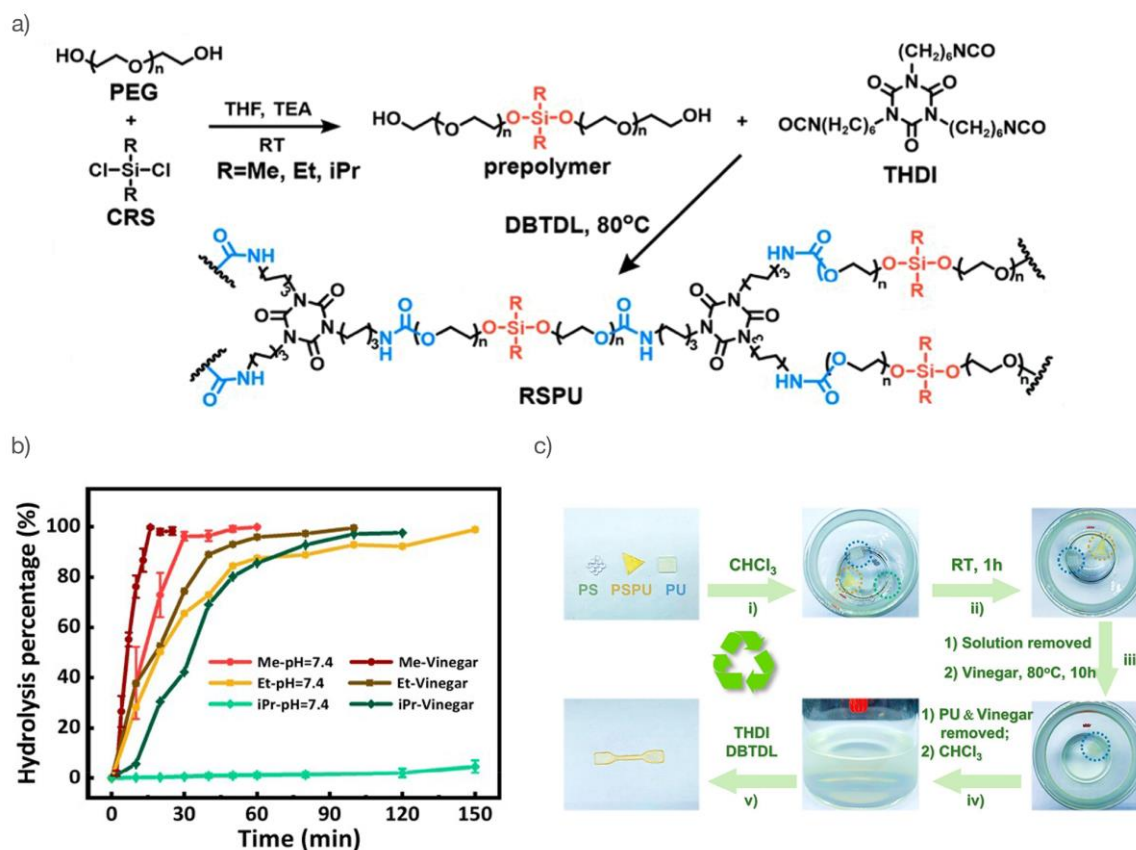


Fig. 109. a) Preparation of the PU thermostet containing the silyl-ether moiety. b) Rate of hydrolysis of the various PU thermostet containing the silyl-ether moiety in function of the degradation conditions. c) Waste separation of PS, traditional PU thermostet and PU thermostet containing silyl-ether moieties. Adapted from Ref. [468] with permission.

In order to show wastes separation, polystyrene (PS), PU thermostet containing silyl-ether moieties, and traditional PU thermostet were mixed. PS could be readily separated from the two PU thermostets by soaking for one hour in CHCl₃ solution since traditional linear thermoplastic polymers are soluble and thermosetting polymers can only swell in excellent solvents. The combination of two thermosetting polymers was then immersed in vinegar at 80 °C for 10

hours, until the PU sample containing silyl-ether moieties vanished as a result of polymer breakdown while the shape of the traditional PU thermoset sample stayed the same. A recycled dogbone sample was even produced by extracting the degraded hydroxy functionalized oligomers products from vinegar, mixing it with THDI and DBTDL, and casting the resulting mixture.

Following a similar concept, Camerino *et al.*[469] inserted a silyl moiety into a PU thermoset. The Si-C bond is less prone to hydrolysis but is specifically attacked by fluoride anions. The authors developed various tri-functional hydroxy cores with different arm lengths and pendant alkyl group (Fig. 110) they crosslinked with 1,6-hexamethylene-diisocyanate. To evaluate the rate and duration of degradation, the thermosets were submerged in solutions of 1.0 M tetrabutylammonium fluoride (TBAF) in THF, 1.0 M TBAF in acetone, and 0.5 M cesium fluoride (CsF) in THF under static circumstances at room temperature. After being submerged in both fluoride salt solutions for 24 hours, the nonsilyl PU control similarly exhibited no discernible change, proving it was unresponsive to fluoride ion stimulation. After 6 hours of immersion in 1.0 M TBAF (THF), all silyl-PU's with extended aliphatic chains totally degrade, however the one with the pendant phenyl group took up to 24 hours to visually degrade in the same solution. With shorter arms, the thermosets degraded after 30–36 h. Reduced network swelling in comparison to THF and lower fluoride ion nucleophilicity as a result of acetone's higher water content are two possible explanations for the better efficiency of THF over acetone for network degradation.

The degradation reaction started with the fluoride ion and the silyl trigger, which was followed by the breakage of the SiC bond and additional cascade bond cleavages to produce ethylene, carbon dioxide, a fluoride bound adduct, and a primary amide ion, was the mechanism of degradation for these networks.

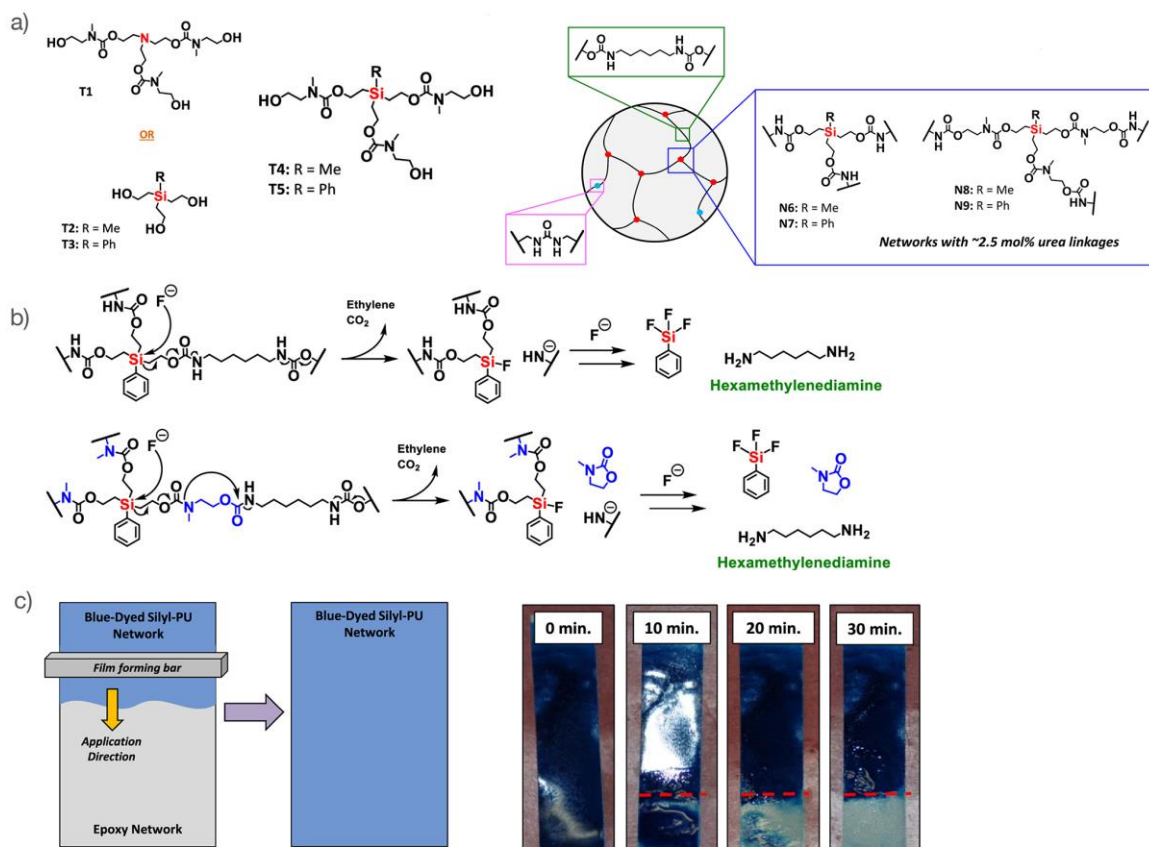


Fig. 110. a) Triol structures used to prepare degradable PU thermoset and synthesis of the polyurethane thermoset in the case of excess diisocyanate. b) mechanism of degradation of the silyl-PU thermoset according to the arm length. c) Selective degradation of the Silyl-PU thermoset coated on an epoxy layer. Adapted from Ref. [469] with permission.

The networks needed three fluoride ion additions at each trigger to be completely disassembled, and as a result, byproducts such as 3-methyl-2-oxazolidinone and hexamethylenediamine (HMDA) were produced as well as trifluorophenylsilane and HMDA (Fig. 110). One of the limitations of degradable networks is that the selective removal of a strongly adhered polymeric network from an underlying network of similar or different chemical composition, without changing the chemical structure of the latter. To test this issue, a cross-linked epoxy-amine network was prepared and then a coating of degradable PU networks containing a blue-dyed was added. After dipping in a solution of TBAF in THF, silyl-PU networks were completely removed

from the underlying epoxy network without any modification of the epoxy layer, showing the promise of such approach. Besides these interesting results, the authors also showed recycling issues since they managed to isolate 1,6-hexamethylene diamine and convert it back to 1,6-hexamethylene diisocyanate that was used to reprepare the PU thermoset.[469]

Apart these soft PU thermosets, another kind of interesting networks are the one derived from acrylate derivatives. For example, networks made from poly(ethylene glycol) diacrylate are interesting for ion-separating membranes since they are both soft and hydrophilic.[470] Even sometimes when cleavable crosslinkers with labile bonds are used, networks created by radical polymerization of acrylate derivatives could be non-totally degradable.[471] This is a result of the fast propagation rate constant of these monomers that led to very high molecular weight polymers that causes microgelation and a highly clustered, heterogeneous internal structure of the network. To counterbalance such non-degradability, Guillaneuf *et al.*[297] showed that DOT could be used to impart degradability to thermoset. This result was first exemplified on polystyrene thermoset. The result was confirmed by Johnson *et al.*[301] After this first result, Guillaneuf and coll.[459] extend this feature to 3D printing of multiacrylate derivatives. Then Roth *et al.*[52] did a detailed study of the degradation of polyacrylate networks made by conventional free radical polymerization. They demonstrated that the gelation time is strongly dependent on the DOT concentration but lead to networks with the same thermomechanical properties than the reference polyacrylate network. Secondly the compositional drift that is occurring during this copolymerization process led to a non-uniform distribution of the cleavable site into the network and thus if high conversion is reached, a higher amount of DOT than cross-linkers is necessary to obtain full degradation.[52]

4.5 Biomedical applications

The biomedical sector is a field where the need for degradable materials is very great. Indeed, biodegradation without polymer accumulation in the organism or production of toxic compounds is essential for use as resorbable materials or active ingredient/drug cargo, for example. A great deal of work already exists on the use of polyesters, polypeptides, natural polymers, etc. for this type of application. Nevertheless, the versatility and ease of use of both ROMP and radical polymerization make it the technique of choice for the production of (bio)materials. In both cases, the C-C carbon impedes the (bio)degradation of the polymers.

The main application of polymer in nanomedicine is related to the development of efficient drug carrier. Johnson *et al.*[472, 473] developed a very interesting platform based on the ROMP of norbornene derivatives to prepare brush-arm star polymers (BASPs) using a “brush-first” approach. By the copolymerization of various norbornene derivatives and the possibility to insert any functionality, BASPs have shown to be interesting scaffolds for drug delivery[474, 475] and magnetic resonance imaging.[476, 477] With the development of silyl ether-based ROMP monomers such as **ROMP22**, such materials could then be combined (bio)degradability.[96] BASP with a acetal-based core and also containing a POE shell and **ROMP22** were then prepared.

The biological performance of these bottlebrush copolymers labelled with the Cy5.5 chromophore was also assessed, both *in vitro* and *in vivo* (Fig. 111). At a dosage of 0.75 mg/ml in the cell experiments, all copolymers shown minimal cytotoxicity. An *in vivo* study with female BALB/c mice were performed and the authors administered 5 mg/ml of polymer in 5% aqueous glucose through tail vein injection. At various time points, the Cy5.5 fluorescence in the blood and organs was assessed to ascertain the pharmacokinetics of the injected polymers. The addition of the degradable silyl ether facilitated the long-term clearance (6 to 10 weeks) of

the copolymer in the blood, liver, and spleen as opposed to the non-degradable control, even though no discernible difference was seen for the short-term pharmacokinetics. The silyl ether system has thus the potential to be employed as a safer drug delivery strategy since bioaccumulation/deposition can result in immune response and toxicity.

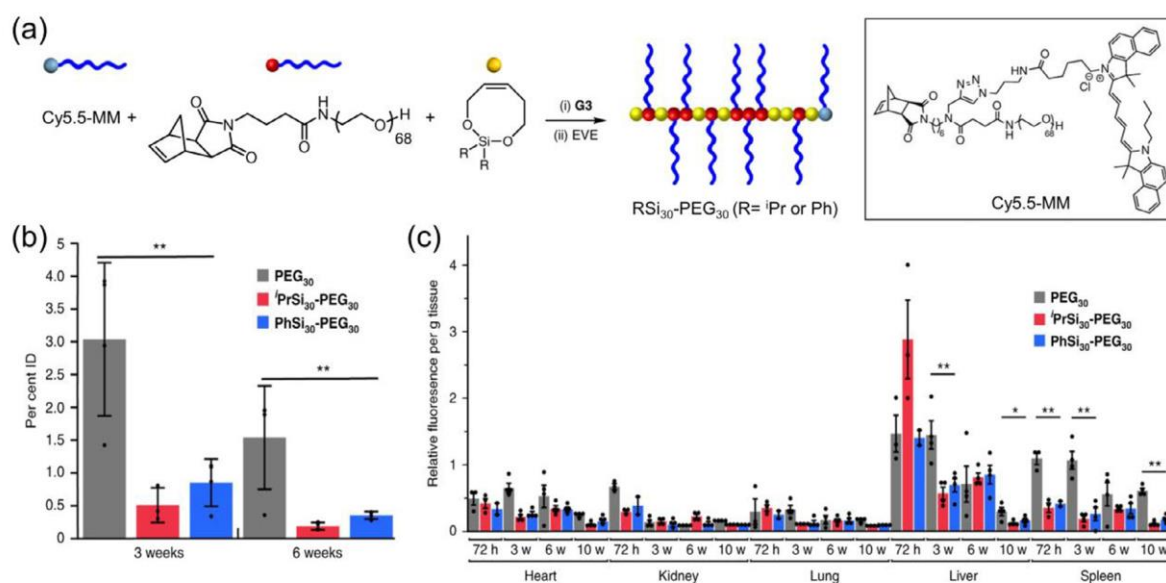


Fig. 111. Animal studies on fluorescently labelled bottlebrush (co)polymer. (a) Synthesis of fluorescently labeled block (co)polymers. (b) Pharmacokinetics of the polymers in blood samples after three and six weeks determined by fluorescence analysis. (c) Biodistribution of polymers in the organ.[96] Reprinted from Ref. [69] with permission.

Besides ROMP, radical polymerization due to its versatility, ease of synthesis and functionalization possibilities is now widely used to prepare drug-delivery systems but their non-degradability impede their translation use in humans. The use of rROP therefore makes it possible to combine the advantages of radical polymerization with the (bio)degradation of these materials. For example, Paulusse *et al.*[478] have demonstrated the value of rROP for preparing degradable NPs that can be used as cargo for gene transfection (Fig. 112). In their work, NPs are obtained by intramolecular cyclization of polymer chains (single-chain technology, SCT).

The degradability of the NP polymeric backbone is enabled by RAFT copolymerization of vinyl monomers with a cyclic sulfide cyclic methacrylate monomer (3-methylidene-1,9-dioxo-5,12,13-trithiacyclopentadecane-2,8-dione (MDTD)). The interest of this approach is to introduce disulfide functions into the backbone that degrade under conditions identical to those encountered in the cellular environment, namely a strong reducing medium. More precisely, the authors showed a marked decrease in the number-average molar mass in 30 min (M_n going from 9.9 to 2.8 kDa), when poly(DMAEMA-*co*-MDTD-*co*-TEGDA)-type polymers with 5% of the MDTD monomer were placed in the presence of a hydrazine hydrate reducing solution.[478] NPs formed from this polymer also exhibited good efficacy as a gene transfection agent, as well as a lack of toxicity towards 3T3 and HeLa cells.

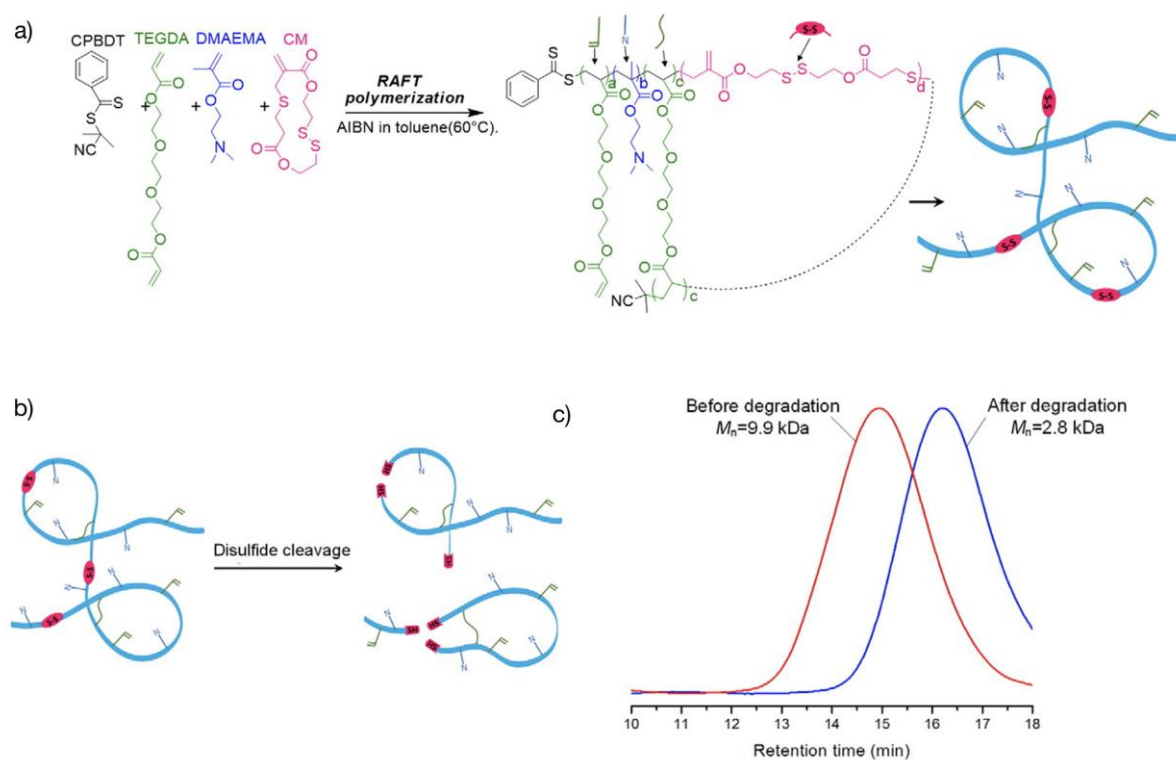


Fig. 112. a) Synthesis of single-chain cyclized polymers via RAFT copolymerization. b) degradation of backbone-reducible poly(DMAEMA-*co*-MDTD-*co*-TEGDA). c) Comparison

of the SEC chromatogram before and after disulfide degradation. Adapted from Ref. [478] with permission.

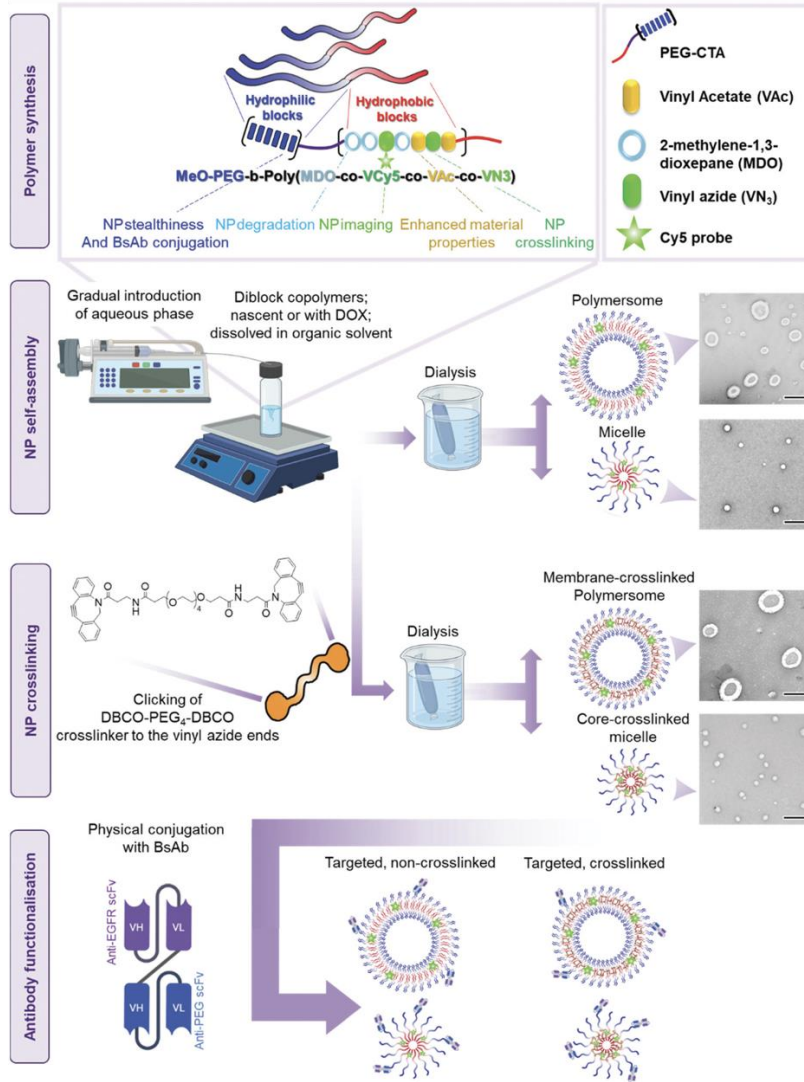
Nanoparticles with PEO or PEG shell are very interesting platform for drug-delivery applications. Nicolas *et al.*[271, 273] prepared copolymers from oligo(ethyleneglycol) methacrylate (OEGMA) and CKA using Nitroxide mediated polymerization. The degradability of the controlled/living copolymers was evaluated under accelerated conditions. Due to their water-solubility, P(OEGMA-*co*-MPDL) copolymers were for example tested for their cytocompatibility, and the results showed that both the original copolymers and their degradation products had high cell viability up to 1 mg/mL on NIH/3T3 cells and J774.A1 cells, which is a promising step toward their biocompatibility. The hydrolytic degradation of P(OEGMA-*co*-MPDL) copolymers was then benchmarked[234] against conventional aliphatic polyesters, which are considered as the gold standards in terms of biodegradable materials for biomedical applications, such as poly(lactide-*co*-glycolide) (PLGA), polylactide (PLA), and polycaprolactone (PCL). As a function of FMPDL, P(OEGMA-*co*-MPDL) displayed a tunable degradation kinetics that fell between those of PCL (for FMPDL = 0.09) and PLA (for FMPDL = 0.27). It's interesting to note that while PLA's pH dropped to 5.5 throughout degradation, P(OEGMA-*co*-MPDL) solution's pH remained above 6.8.[234] The enzymatic degradation of such copolymer was only moderate in the presence of lipases (*Candida antarctica*). Such result was ascribed to the high steric hindrance of MPDL, and potential steric repulsion of PEG chains. To enhance the enzymatic degradation, PEGylated nanoparticles were prepared by the copolymerization of MDO and vinyl ether.[264] These nanoparticles demonstrated excellent cytocompatibility on three representative cell lines as well as great colloidal stability for up to 6 months. Copolymers rapidly degraded in the presence of lipases (*Candida antarctica*) and

displayed hydrolytic degradation under physiological conditions comparable to those of conventional PCL.[264]

Some PEG nanoparticles were also prepared by RAFT co or terpolymerization that showed good degradability behavior under accelerated conditions.[275-277] but their practical application in drug delivery or cytotoxicity was not carried out. In a similar approach, Thurecht *et al.*[479] prepared targeted micelles and polymersomes from the ter-polymerization 2-methylene-1,3-dioxepane (MDO), vinyl acetate (VAc) and vinyl bromobutanoate (VBr) initiated by a PEG-based macroRAFT agent. Degradable crosslinked or not micelles (25 nm) and polymersomes (100 nm) encapsulated doxorubicin (DOX) were prepared after azidation of the bromine groups and self-assembly (Fig. 113a). Each system demonstrated effective DOX release at physiological pH, but once the nanomaterial became unstable under acidic conditions, increased DOX release rates were observed. When exposed to MDA-MB-468 breast cancer cells, *in vitro* cytotoxicity studies employing NPs demonstrated the good biocompatibility of the systems, whilst DOX-loaded NPs shown enhanced cytotoxicities, with IC50 values larger than those of free DOX because of the controlled release from the carriers. Bispecific antibodies (BsAbs), which bind to the nanoparticle surface through an anti-PEG arm, were then conjugated to the NPs to create targeted systems with a high affinity for the epidermal growth factor receptor (EGFR) upregulated on cancer cells.

When targeted systems were applied, higher binding and increased DOX accumulation within cellular nuclei were confirmed by *in vitro* imaging and cellular association analyses (Fig. 113b). Polymersomes showed an improved capacity for avoiding non-specific binding and increased stability over extended times. In contrast, micelles showed significantly greater drug encapsulation efficiency in comparison to polymersomes, as well as quicker payload release rates after being swiftly endocytosed by cancer cells.

a)



b)

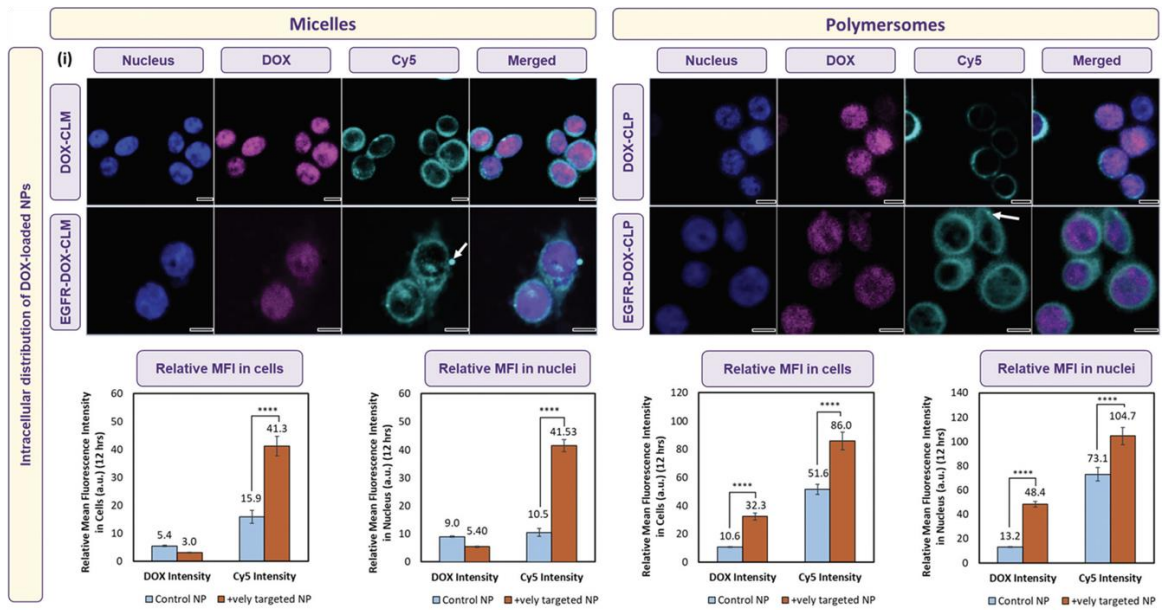


Fig. 113. a) Preparation of targeted cross-linked or not DOX-loaded degradable micelles or polymersomes. b) Intracellular distribution of DOX-loaded NPs, and cellular association of nascent and DOX-loaded NP with MDA-MB-468 cancer cells. (i) shows Representative CLSM micrographs of fixed cells treated with DOX-loaded NPs. Treatment groups (DOX concentration in each is $10 \mu\text{g mL}^{-1}$) were either EGFR-targeted or non-targeted (control) micelles or polymersomes. Cells were imaged 12 hours post exposure to treatment, before using Hoechst 33342 staining method to mark the nuclei and detect apoptosis. For each panel, the images show stained nuclei (blue), DOX fluorescence (magenta), NP (Cy5) fluorescence (cyan), and overlaid representation of the three channels (from left to right). Apoptotic blebbing (arrowed) can be clearly seen in the example cells treated with the targeted NPs. Scalebars denote $10 \mu\text{m}$ in all the images. Comparisons of relative fluorescence intensity of DOX and Cy5 within the cells and nuclei are shown, with relative MFI calculated as the ratio of fluorescence signal within the cell or nucleus to extracellular (background) signal. Reprinted from Ref. [479] with permission.

To circumvent the drawbacks of drug physical encapsulation (such as insufficient drug loading, burst release, etc.), polymer prodrug nanocarriers are of tremendous interest in drug delivery. Nicolas et al. have also evaluated the potential of the MPDL monomer for the preparation of degradable prodrug-like polymers for anticancer application. In this approach, degradable polymer chains based on MPDL and MMA or (OEGMA) are initiated using a nitroxide-controlled rROP-type process from an active molecule (gemcitabine) functionalized with the nitroxide SG1.[480] Anti-cancer activity was studied *in vitro* for copolymers of different compositions. A decrease in cytotoxicity was observed with increasing MPDL ratio, and better anticancer activity was noted with the OEGMA monomer (more hydrophilic than MMA) (Fig. 114).

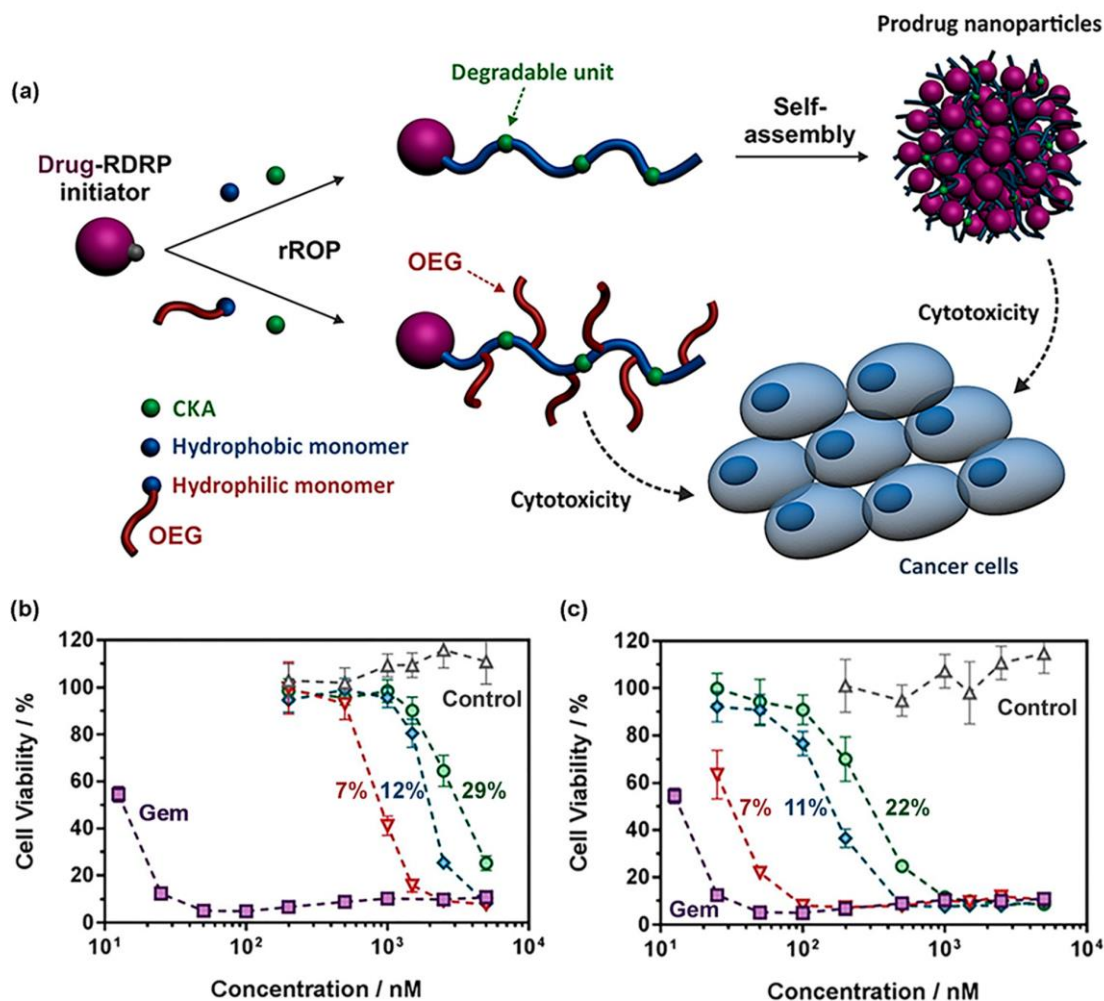


Fig. 114. a) Synthetic strategy for the design of degradable Gemcitabine-based polymer prodrugs by "drug-initiated" nitroxide-mediated radical ring-opening copolymerization. Cell viability (MTT assay) on MiaPaCa-2 cells with (b) Gem, Gem-P(MMA-*co*-MPDL) of variable FMPDL and P(MMA-*co*-MPDL) as a control and (c) Gem, Gem-P(OEGMA-*co*-MPDL) of variable FMPDL and P(OEGMA-*co*-MPDL) as a control.[480] Reprinted from Ref. [190] with permission.

It was further demonstrated that other polymer prodrugs could be prepared by rROP using a "grafting through" method via the RAFT-mediated copolymerization of MDO and a methacrylate monomer containing gemcitabine (Gem) active species.[481] When made into nanoparticles, the copolymer demonstrated hydrolytic degradation under accelerated

conditions (pH 11, 40 °C) and shown sustained Gem release in the presence of cathepsin at pH 5.2 in addition to some cytotoxicity on pancreatic cancer cells.

Among the different polymer-prodrugs that have been prepared, the ones based on the polyisoprene backbone were particularly interesting due to the similarity between the isoprene moiety and natural terpenoid structures that make the polymer biocompatible.[482] To confer degradability to such structure, the copolymerization of isoprene (I) with the thionolactone DOT was carried out.[308] P(I-co-DOT) nanoparticles were prepared and demonstrated comparable cytocompatibility to their PI counterparts on J774.A1 and HUVEC cells. Additionally, Gem-P(I-co-DOT) prodrug nanoparticles were synthesized using the "drug initiated" approach using a Gem-functionalized alkoxyamine and the nanoparticles showed considerable cytotoxicity on A549 cancer cells. P(I-co-DOT) and Gem-P(I-co-DOT) nanoparticles were degraded slowly in the presence of cysteine or glutathione mimicking physiological conditions.[308]

Due to the specific recognition and/or binding between carbohydrates and proteins, glycopolymers have been of great interest for the synthesis of biocompatible materials for targeted drug delivery. Such copolymers were then combined with the synthesis of degradable backbone via the insertion of weak/labile bonds. In the case of ROMP, Kiessling and coworkers[102] prepared water-soluble poly(oxazinone) bearing a protected mannose via post-modification modification. Through oxime conjugation, they were able to attach a variety of functional moieties, including fluorophores, reporter groups, and bioactive epitopes, to the polymer backbone. A number of copolymers containing varying amounts of ligand were created by adjusting the feed ratio of the applied alkoxyamines. They demonstrated that the polyoxazinone backbone itself cannot interact with biological systems, but may be used as an antigen to stimulate immunological signaling when the immunogenic epitope 2,4-

dinitrophenol (DNP) is added by treating A20HL B cells with these copolymers that expressed a DNP-binding receptor. Copolymers containing the oligoguanidinium artificial transduction domain, on the other hand, were capable of being internalized by two kinds of B lymphocytes (A20 and A20HL) via active cell penetration.[102]

CKA monomers have also been studied for the preparation of glycopolymers. For example, Maynard *et al.*[247] showed that poly(BMDO-*co*-BMA-trehalose) copolymers synthesized by a RAFT process were effective in stabilizing proteins (such as G-CSF for granulocyte colony-stimulating factor) when heated to 40°C (66% stabilization rate). However, the degradation by-products of this glycopolymer proved toxic to murine fibroblasts and myeloblasts. Nicolas and coworkers[266] focused on the copolymerization of CKA (MDO) and vinyl ether functionalized by a Pd-catalyzed thioglycoconjugation to prepare glycopolymers (Galactose Gal, Glucose Glc). With these monomers whose reactivities are similar, a statistical incorporation of glyco units into the polymer backbone could be obtained and it is also possible to prepare a polyester rich polymer containing the glyco unit. The resultant thioglyco-polymers (Fig. 115a) were nano-precipitated into self-stabilized thioglyco-nanoparticles that were stable in water for up to 4 months but enzymatically degraded in one day via Lipase B from *C. antarctica* (Fig. 115b). Nanoparticles and their degradation products were shown to be non-cytotoxic with two healthy cell lines. The presence of specific carbohydrate/lectin interactions as well as nonspecific hydrophobic interactions were demonstrated.[266] Fluorescent thioglyconanoparticles were employed to demonstrate cell internalization of thioglyconanoparticles by lung adenocarcinoma (A549) cells, highlighting the high potential of such glycopolymer (Fig. 115c).

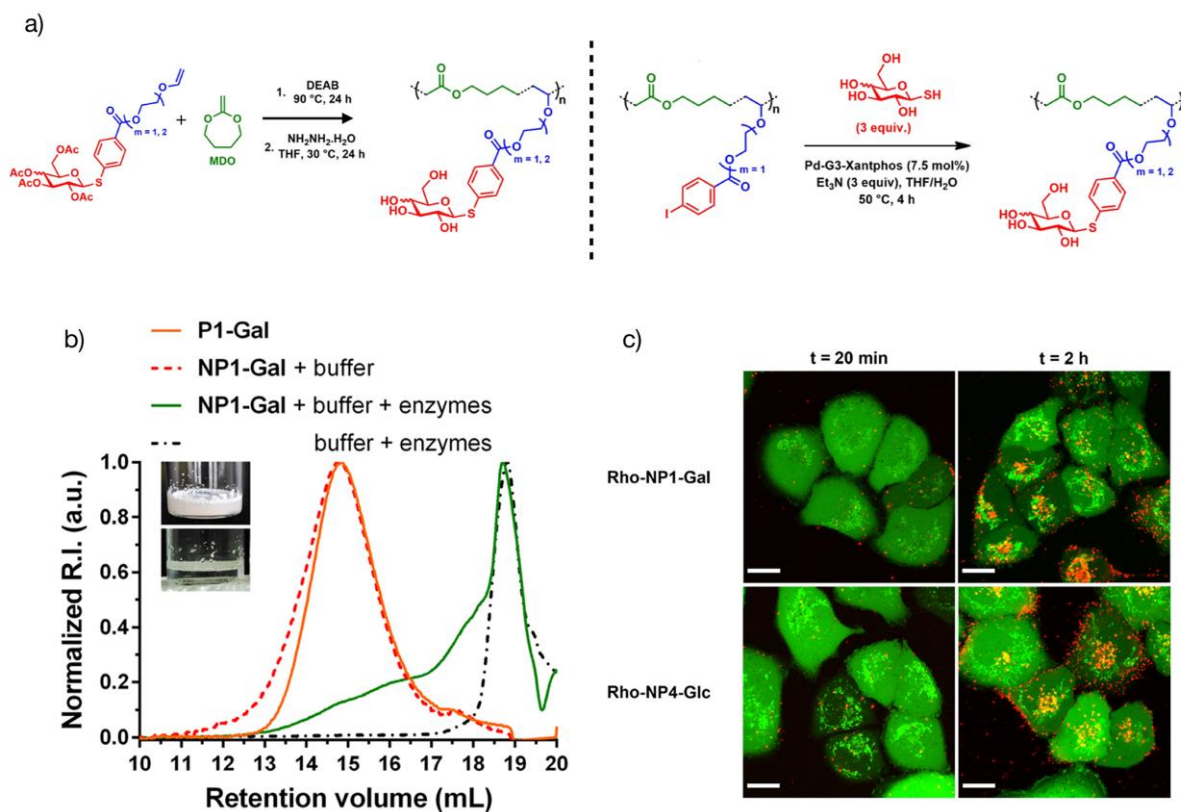


Fig. 115. a) Synthesis of degradable vinyl thioglycopolymers by (left) free-radical copolymerization of MDO and sugar-functionalized VE (“grafting through” approach) and by (right) free-radical copolymerization of MDO and iodoaryl vinyl ether IArVE, followed by grafting of 1-thiosugars catalyzed by Pd-G3-Xantphos (“grafting to” approach). b) SEC chromatograms (CHCl_3/TFA 0.1 vol %) of P1-Gal copolymer (dashed red), NP1-Gal nanoparticles after incubation with (solid green) or without (solid orange) enzymes, and incubation of enzymes without nanoparticles (dashed–pointed black). Inset: Pictures of NP1-Gal nanoparticles at $t = 0$ (top) and $t = 1$ day (bottom) during enzymatic degradation with *C. antarctica*. c). Merged fluorescence signals from the green (calcein) and red (rhodamine B) channels by confocal microscopy taken from the median plane of A549 cells after incubation with Rho-NP1-Gal (top row) or Rho-NP4-Glc (bottom row) for 20 min (left column) and 2 h (right column). Pictures were taken from median plane of cells. Scale bar = 10 μm . Adapted from Ref. [266] with permission.

Since PMDO is hydrophobic, the degradation of copolymers containing MDO units is rather slow under physiological conditions (phosphate-buffered saline, pH 7.4, 37 °C). To enhance the degradation of the glycopolymer, the same authors replaced MDO by the more hydrophilic MTC that produce an ester – ether unit in the main chain.[46] Due to MTC's hydrophilicity, the resulting copolymers degraded quicker under both accelerated and physiological circumstances. Surfactant-free nanoparticles were prepared from the corresponding MTC-based glycopolymers. The colloidal stability, cytocompatibility and enzymatic degradation were similar but importantly, MTC-based glyconanoparticles demonstrated higher lectin affinity than MDO-based glyconanoparticles. These findings suggest that using a more hydrophilic copolymer backbone, such as MTC instead of MDO, resulted in a significant increase in the specific interaction between LecA and the corresponding glyconanoparticles by decreasing nonspecific hydrophobic interactions that have been hypothesized to mask the binding sites and/or Gal residues.[46]

Another interesting application of biomaterials is related to cryopreservation of cells to develop cell-based therapies. The current method to obtain cryopreservation is based on the addition of 5-20 wt% of DMSO before freezing to inhibit ice recrystallization.[483] Nevertheless DMSO is slightly toxic and leads to cell loss. Synthetic polymers such as poly(vinyl alcohol) (PVA) could be very interesting ice recrystallization inhibitors (IRI) but has the drawback that the polymer backbone is non-degradable in the conditions used. Indeed, PVA is reported to be biodegradable,[484] but the rate of biodegradation is slow and requires specific enzymes. To make more efficient, the insertion of weak bonds will enhance the degradation. Dove and Gibson[485] thus developed a PVA-based copolymer that contained ester units in the polymer backbone via the copolymerization of MDO and vinyl chloroacetate (Fig. 116). The use of the

chloroacetate monomer allowed for selective deacetylation without impacting the esters coming from the MDO into the polymer backbone.

Quantitative IRI experiments demonstrated that the MDO content has to be tightly regulated in order to preserve IRI activity, with greater loadings (24 mol %) resulting in complete loss of IRI activity. These biodegradable polymers will aid in the translation of PVA, a benign and biocompatible substance, into a variety of biomedical applications.

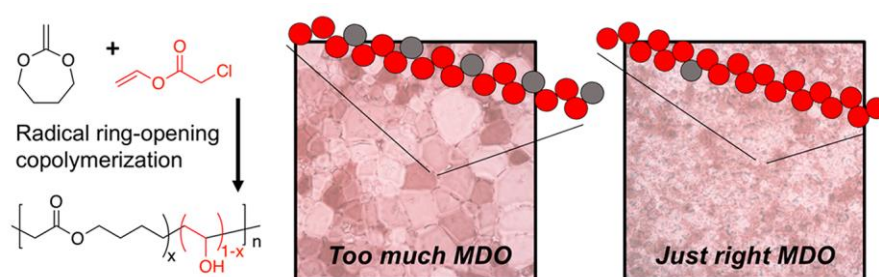


Fig. 116. Preparation of degradable PVOH and its use in ice recrystallization inhibitor. Reprinted from Ref. [485] with permission.

Macromolecular cryoprotectants based on polyampholytes appear promising as additional cryoprotectants to DMSO-based freezing. Gibson *et al.*[245] subsequently used radical ring-opening (ter)polymerization to create ester-containing cryoprotective polyampholytes (poly(DMAEMA-*co*-MAA-*co*-BMDO)) that are degradable. When degradable polyampholytes were added to DMSO in a difficult cell monolayer cryopreservation system, they were shown to improve post-thaw recovery (Fig. 117).

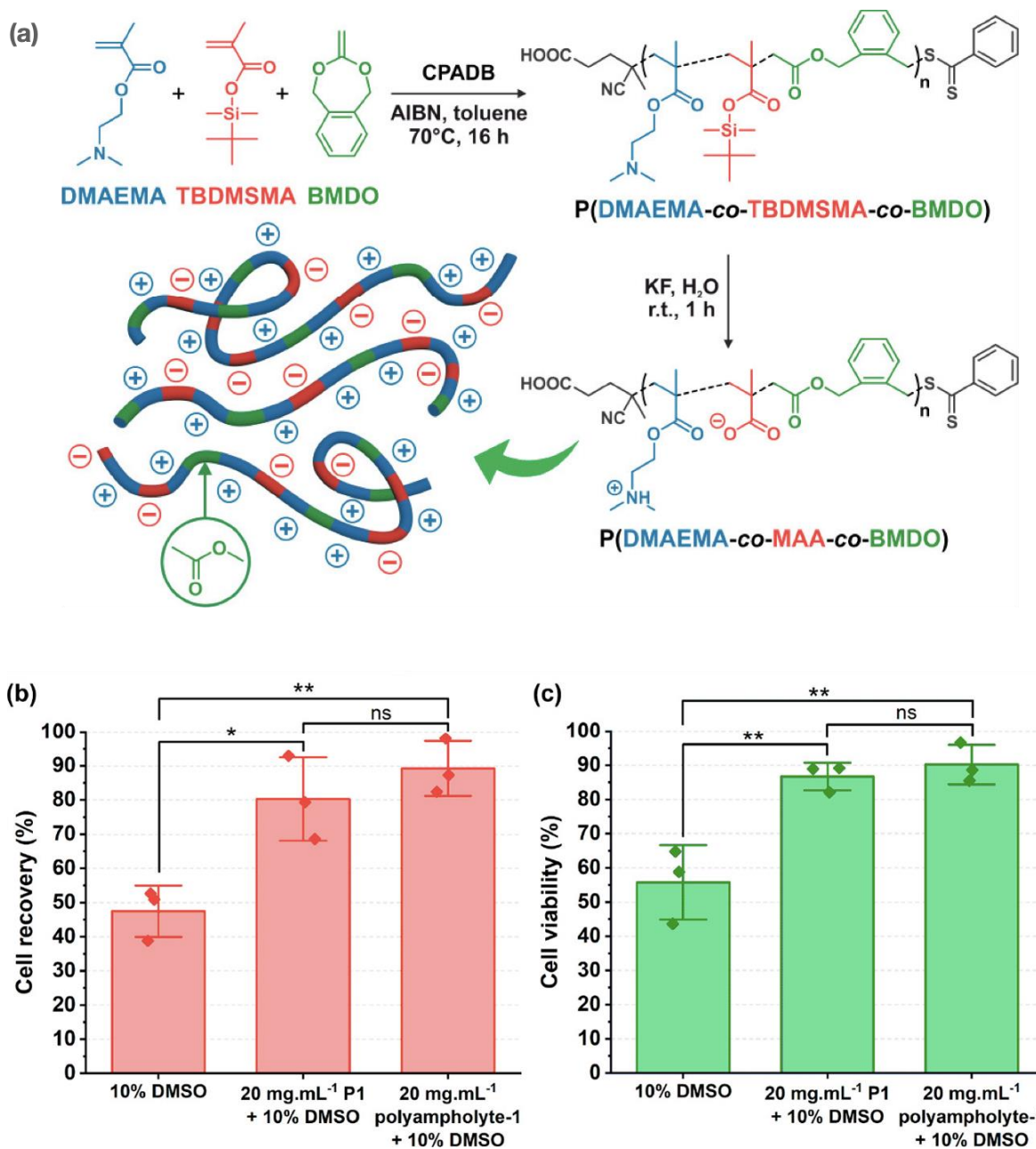


Fig. 117. a) Preparation of the degradable polyampholyte. b) Cell recovery 24 h post-thaw, relative to pre-freezing, determined using trypan blue exclusion test. c) Cell viability 24 h post thaw determined using trypan blue exclusion test. Reprinted from Ref. [245] with permission.

Finally, bulk materials were also envisioned. First, CKA was used to confer degradability to phosphorylcholine-based polymer coatings that cover biodegradable drug-eluting stents. A terpolymer of MDO, n-butyl methacrylate (nBMA), and 2-

methacryloyloxyethylphosphorylcholine (MPC) was prepared (34% MDO, 19% MPC, and 47% BMA) and was applied by ultrasonic spraying. This process generate a durable coating with high blood compatibility, anti-adhesion characteristics, biodegradability, and rapamycin eluting capability.[486] Finally, P(MDO-*co*-MMA) copolymers containing 5mol% of ester units and loaded with N-acetyl cysteine have also been explored as bone filling material to replace traditional PMMA bone cement.[487] Superior mechanical properties, good biocompatibility, some degradability and mineralization properties were obtained.[487] compared with the reference PMMA, the copolymer loaded with N-acetyl cysteine showed better osteoconductive level, confirming the interest of this biomaterials.

4.6 Miscellaneous

4.6.1 Degradable latexes

Latexes are dispersed systems composed of polymer nanoparticles suspended in (most often) water. They are obtained by polymerization processes in dispersed media, the most widespread being radical polymerization in water emulsion. Latexes are used in many industrial applications such as paints, coatings, drug delivery, cosmetics and adhesives.

It is very difficult to prepare (bio)degradable latexes because of the strong intolerance of CKAs to aqueous media as they are rapidly hydrolyzed. In order to overcome this problem, Nicolas *et al.*[488] developed a technique called organic rROPISA to elaborate in one step nanoparticles (NPs) with a degradable core. This technique is based on polymerization-induced self-assembly (PISA) in a solvent and then consists of the chain extension of a solvophilic macro-initiator (or macro-transfer agent) with monomers that are miscible in this solvent but that form from a certain degree of polymerization a solvophobic and immiscible polymer,

leading to the self-assembly of the chains and the formation of NPs. The advantage of PISA is that high solid contents and different morphologies (spheres, vesicles etc.) can be easily achieved.[489]

As a first step, Nicolas *et al.*[488] prepared degradable NPs by rROPISA in heptane. To do this, they used a RAFT macro Chain Transfer Agent (macroCTA) (based on poly(lauryl methacrylate)) to control the copolymerization of a vinyl monomer (benzyl methacrylate) with a cyclic CKA monomer (MPDL). During the copolymerization, the RAFT macroagent that was soluble in the solvent (solvophilic block) is extended by a second solvophobic block (containing CKA). By varying the amount of CKA in the copolymer chains (4 - 40 mol%), the authors showed that the NPs were stable and that those composed of at least 15 mol% MPDL degraded completely in a mixture (THF/methanol, 2.5 % KOH).[488] In a following study, the same authors[490] used the same lauryl methacrylate/benzyl methacrylate system but inserted CKA in either the shell or the core of the nanoparticle but also in both part to prepare fully degradable nanoparticles (Fig. 118).

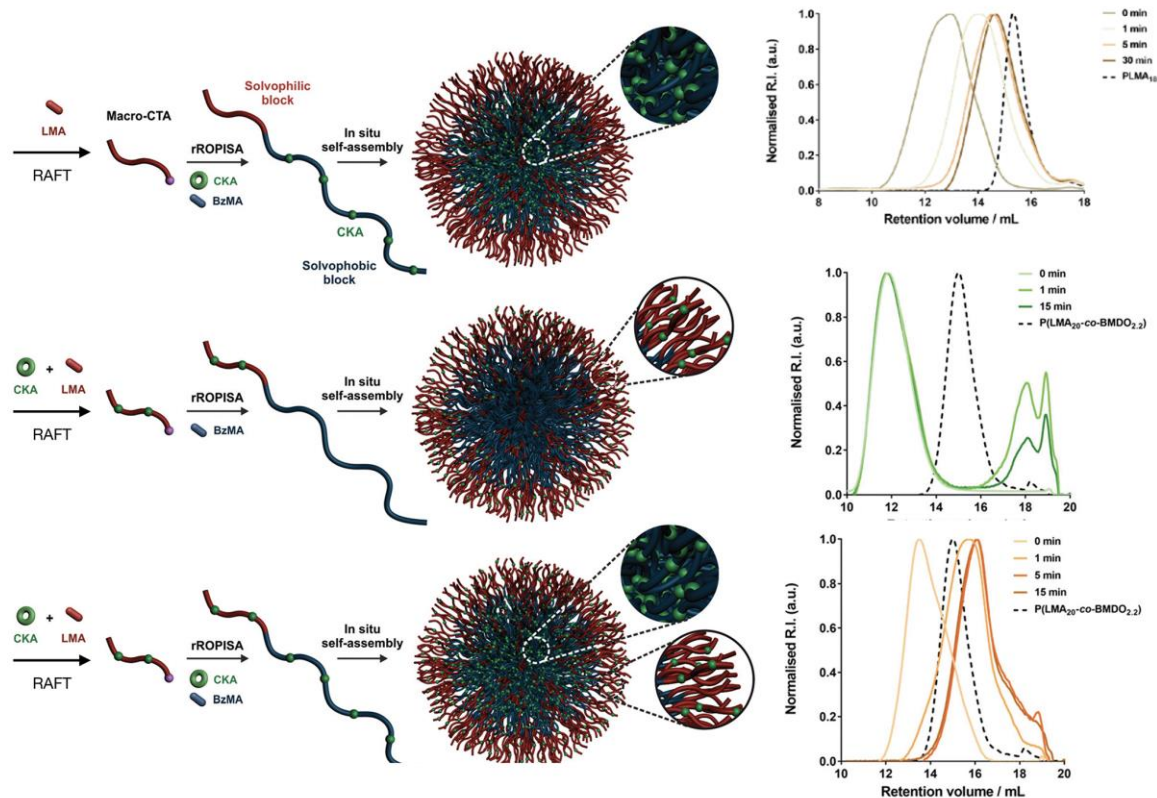


Fig. 118. Preparation of degradable nanoparticles with ester bonds inserted in either a) the core of the nanoparticle, or b) the shell of the nanoparticle or c) both in the shell and in the core of the nanoparticles. Adapted from Ref. [490] with permission.

These NPs are nevertheless dispersed in organic solvents. In order to extend this approach to the preparation of NPs in water, the same team developed a two-step process (Fig. 119).[491] The first one consists in the preparation of NPs with a PEG crown in DMF. The obtained nanoparticles were then transferred into water by simple dialysis, during which their colloidal properties were maintained. These NPs were thus successfully degraded in water under accelerated conditions and the NPs showed no greater cytotoxicity than the reference NPs on three healthy cell lines.[491]

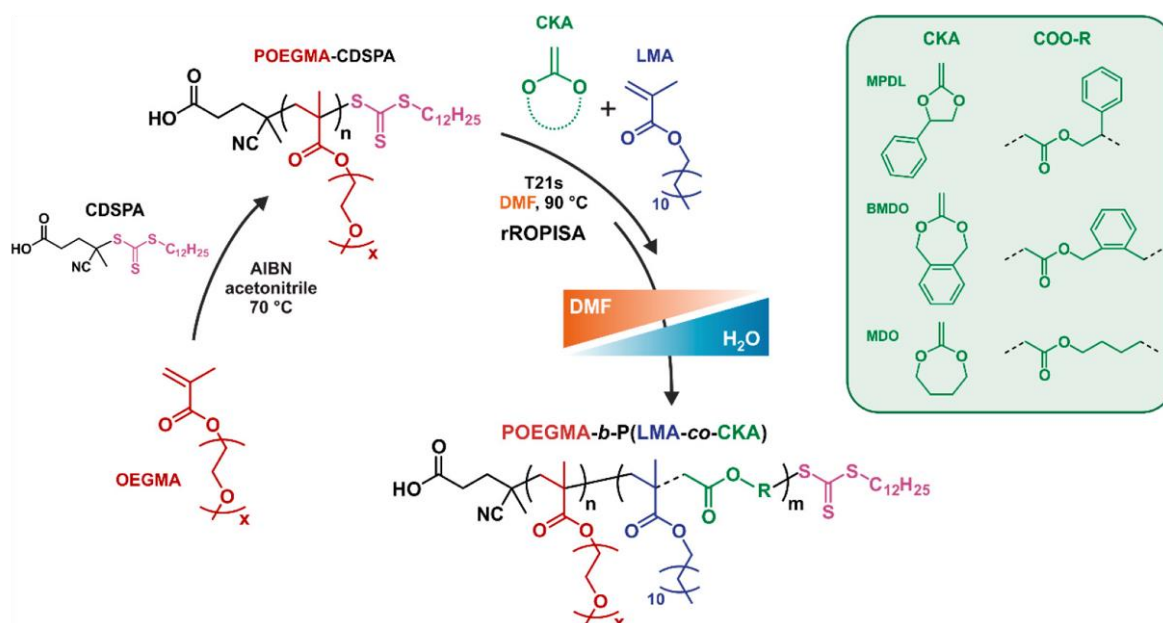
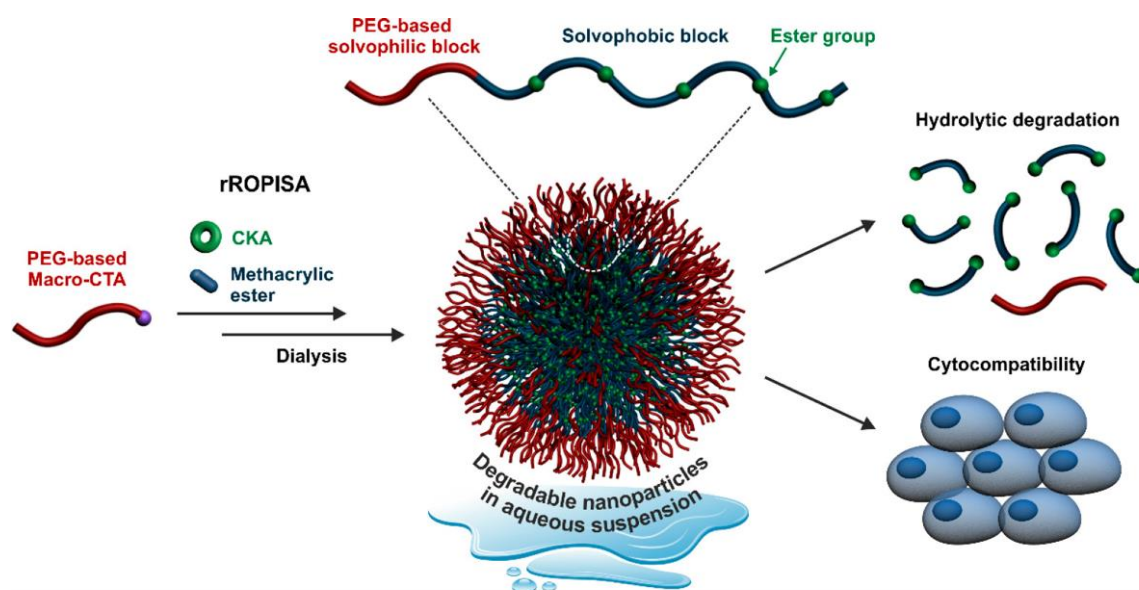


Fig. 119. Synthesis of aqueous suspensions of core-degradable diblock copolymer nanoparticles by consecutive radical ring-opening copolymerization-induced self-assembly (rROPISA) from cyclic ketene acetals (CKAs), followed by transfer to water. Reprinted from Ref. [491] with permission.

Although this approach is promising in the biomedical field, this process is too complicated for other applications. A one-step process is needed. In recent work, Carter *et al.*[492] have shown

that it is possible to synthesize degradable vinyl acetate (VA) and MDO latexes by emulsion polymerization in water under specific experimental conditions (at pH 8 and not exceeding 40 °C). These conditions allow to preserve the CKA from hydrolysis. The intended use is for food packaging (containers, boxes or cups) for take-away sales. The use of plastic for this type of packaging as well as for disposable tableware has led manufacturers to make these objects from paper and/or cardboard. However, in order to improve the mechanical and barrier properties (especially to oils) of these materials, a synthetic coating is necessary. One of the problems encountered with these materials is that once contaminated by food, their recovery and recycling becomes impossible. A coating with a biodegradable polymer would therefore be a major asset to improve the biodegradation and composting of these objects.

Carter *et al.*[492] showed that degradable latexes based on vinyl acetate (VAc) and MDO were stable for 50 days at pH 7.4 but degraded up to 50% by mass in 50 days at pH 10. Moreover, these latexes, once coated on paper, showed very good barrier properties to oils. These results are very encouraging to consider using the rROP technique to make recyclable take-away tableware. Recently Agarwal and coworkers[195] investigated the kinetics of MDO degradation in water and stated that “neither the adjustment of a specific pH range nor maintenance of a special temperature can slow down the hydrolysis effectively enough to achieve substantial incorporation of MDO into the polymer chain under emulsion polymerization conditions.” Lansalot and coworkers,[493] inspired by a pioneering study of Landfester *et al.*[494] on a miniemulsion process, managed to prepare degradable PMMA latexes via the incorporation of BMDO using a classic *ab initio* emulsion recipe. By adjusting the pH to basic conditions, 2 to 6.4 mol% of BMDO units were inserted into the polymer backbone leading to an interesting decrease of the M_n from 100-30,000 g.mol⁻¹ to 5-8,000 g.mol⁻¹ for the degraded products.

The introduction of thionolactones by Roth[294] and Gutekunst[295] eliminated the hydrolysis susceptibility of these monomers and thus allows the use of rROP in aqueous dispersed media. D'Agosto and Lansalot[302] showed that standard aqueous emulsion copolymerization of DOT with styrene, butyl acrylate, or a combination of both was possible using a conventional formulation with KPS as initiator and SDS as stabilizer. Stable latexes, obtained in less than 2 h and containing between 1 and 5% DOT were shown to be degradable in the presence of a strong base or by aminolysis.[302]

The absence of hydrolysis of thionolactones was also used by Nicolas[303] to extend their rROPISA technology to a totally aqueous process. In this case, the nitroxide (NMP) controlled copolymerization of DOT and styrene/butyl acrylate monomers was carried out using a SG1 nitroxide AAP macroinitiator (Fig. 120). Stable NPs of 80 -120 nm were obtained. By varying the DOT content in the chains from 1 to 3 mol%, different degradation rates of the dry extracts as well as of the NPs (evaluated as the percentage decrease of the number-average molar mass) were obtained under different hydrolysis conditions, namely by aminolysis (in the presence of *N*-isopropylamine) or by basic hydrolysis (with TBD).[303]

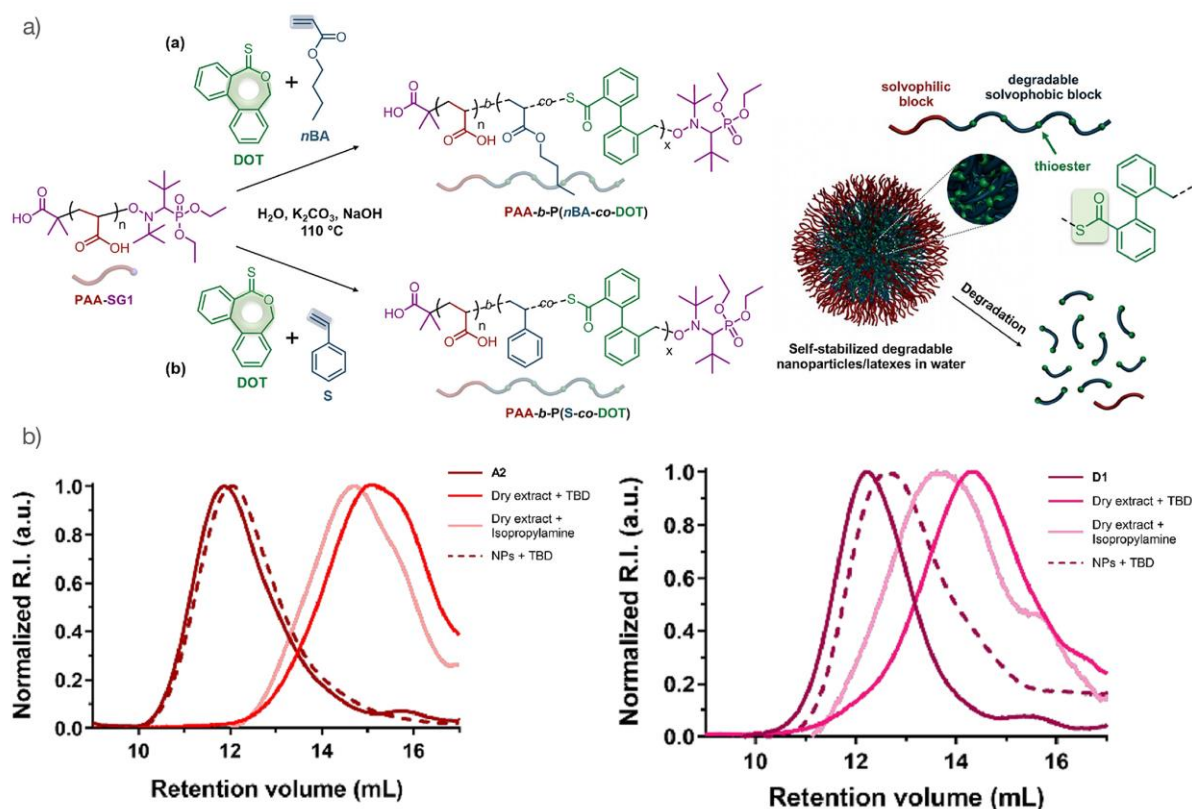


Fig. 120. a) Synthesis of poly(acrylic acid)-*b*-poly(*n*-butyl acrylate-*co*-dibenzo[*c,e*]oxepane-5-thione) (PAA-*b*-P(*n*BA-*co*-DOT)) and poly(acrylic acid)-*b*-poly(styrene-*co*-dibenzo[*c,e*]oxepane-5-thione) (PAA-*b*-P(S-*co*-DOT)) diblock copolymer nanoparticles via aqueous nitroxide mediated radical ring-opening copolymerization-induced self-assembly (rROPISA) of DOT and *n*-BA (or S) from a SG1-terminated poly(acrylic acid) macroalkoxyamine (PAA-SG1). b) Degradation of PAA-*b*-P(*n*BA-*co*-DOT) copolymers (A2: $F_{\text{DOT}} = 3 \text{ mol\%}$, $M_n = 56,700 \text{ g}\cdot\text{mol}^{-1}$; D1: $F_{\text{DOT}} = 1 \text{ mol\%}$, $M_n = 57,600 \text{ g}\cdot\text{mol}^{-1}$) after treatment of dry extracts or nanoparticles (NPs) with *N*-isopropylamine or TBD. Adapted from Ref. [303] with permission.

In parallel, Lansalot and D'Agosto[304] developed a RAFT mediated PISA process combining a PEG or Poly(*N*-acryloylmorpholine) macroRAFT agent and the copolymerization of DOT with *n*-butyl acrylate or styrene to prepare degradable nanoparticles.

4.6.2 Degradable surfaces

Functional or functionalizable surface coatings are of great interest in the industrial field. However, a biodegradable character of these coatings is also often required. To meet these needs, different methods of surface modification using rROP copolymerization of cyclic monomer with other monomers have been described in the literature.

Klok *et al.*[495] for example prepared a coating of poly(PEGMA) polymers on the surface of silica substrates. The introduction of a CKA, BMDO in this polymer allowed the preparation of coatings that were stable at pH 9 but could degrade rapidly at pH 3 in contrast to the reference coatings. Moreover, depending on the PEGMA/BMDO ratio, the thickness of the coating decreases at different rates under acidic conditions, as shown by AFM and ellipsometry measurements (study between 5 and 30 days of exposure).

Lahann *et al.*[496] used rROP to confer a degradable character to polymer films prepared by CVD (chemical vapor deposition polymerization). The CVD technique is indeed a well-established technique for depositing on different substrates very thin films of polymers but until now only non-degradable. Films based on BMDO and [2,2]para-cyclophanes (or 4-hydroxymethyl-[2,2]para-cyclophanes) could be realized proving the possibility to couple CVD and rROP. These films showed by XPS, FTIR and IRRAS (Infrared Reflection absorption spectroscopy) studies a hydrolysis under basic conditions of the films by a surface erosion mechanism and this without inducing toxicity (XTT tests).[496]

Biofouling is a very important issue for surface in contact with water. Since the banning of tributyltin self-polishing copolymer (SPC) coatings in 2008, many studies were conducted to find an effective and ecologically acceptable marine anti-biofouling coatings. Besides the toxic tin compound, SPC is made up of a vinyl polymer that can react in a regulated way with

saltwater and has hydrolyzable side groups like silyl, copper, and zinc ester. Under the influence of saltwater, their unstable side groups hydrolyze, causing the polymers to turn more hydrophilic and be polished away by vigorous water flow. Since the SPC main chain does not degrade, the fragments enter the ocean, as marine microplastics. The preparation of degradable antifouling coatings was thus widely studied. [497] Radical ring-opening polymerization also offers the possibility of preparing films with anti-biofouling and degradable properties (Fig. 121).

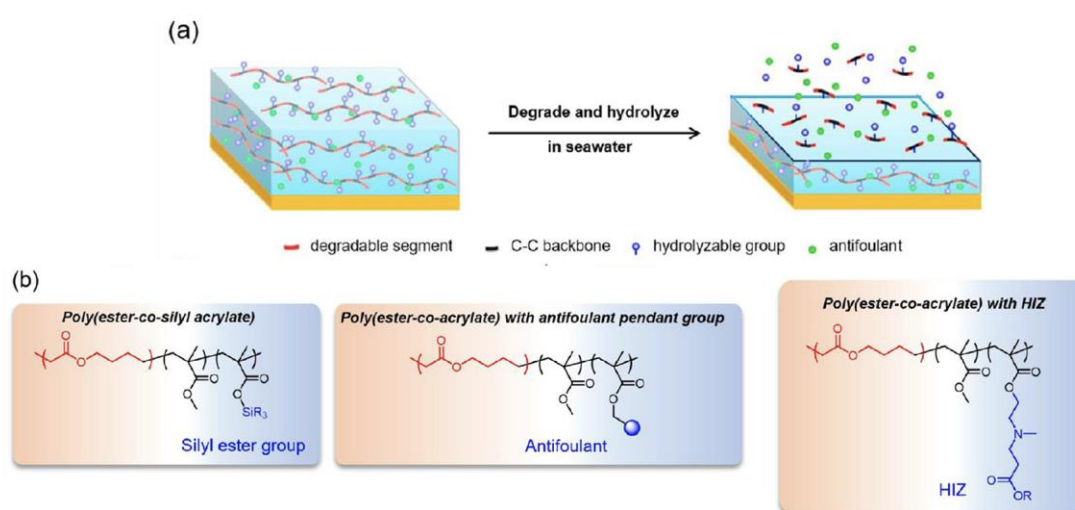


Fig. 121. Different approaches to prepare degradable antifouling materials by radical ring-opening polymerization. Adapted from Ref. [497] with permission.

This type of coating is particularly sought after for applications in the marine environment. Zhang *et al.*[498] were first interested in the copolymerization of MDO and MMA to prepare antifouling coatings. The latter exhibits good adhesion to the substrate due to the incorporation of MMA moieties. The ester bonds in the main chain of MDO allow the copolymer to degrade enzymatically and hydrolytically, and the degradation rate increases with the ester content. In order to improve the antifouling properties, the authors incorporated the organic antifouling agent 4,5-dichloro-2-octylisothiazolone (DCOIT) into the polymer, whose release rate

increases with the ester content.[498] Sea trials show that the system composed of the copolymer and DCOIT has an excellent antifouling performance for more than 3 months. For example, to accelerate the hydrolysis kinetics, Zhang *et al.*[499] showed that degradable and hydrolyzable poly(ester-*co*-silyl acrylate) copolymers based on MMA, MDO, and tributyl silyl methacrylate (TBSM) could be used to prevent biofilm. The rapid hydrolysis of the silyl ester groups forms hydrophilic carboxyl groups that allow for better water absorption from the surface and thus accelerated degradation of the MDO-containing backbone.[499]

Another possible improvement is to covalently bond an organic antifouling substance to the polymer coating to better control the release rate. In particular, copolymers based on MMA, MDO and N-methacryloyloxymethyl benzisothiazolinone (BIT) with 47 wt% MDO showed a mass loss of 7.3 wt% in 90 days in a seawater model (Fig. 122).[500] In addition, marine tests showed that copolymers with 23 wt% ester units and 28 wt% BIT monomer exhibited excellent anti-biofouling properties according to ASTM D69990-05 (2011) test (less than 5% of the surface area colonized). [500]

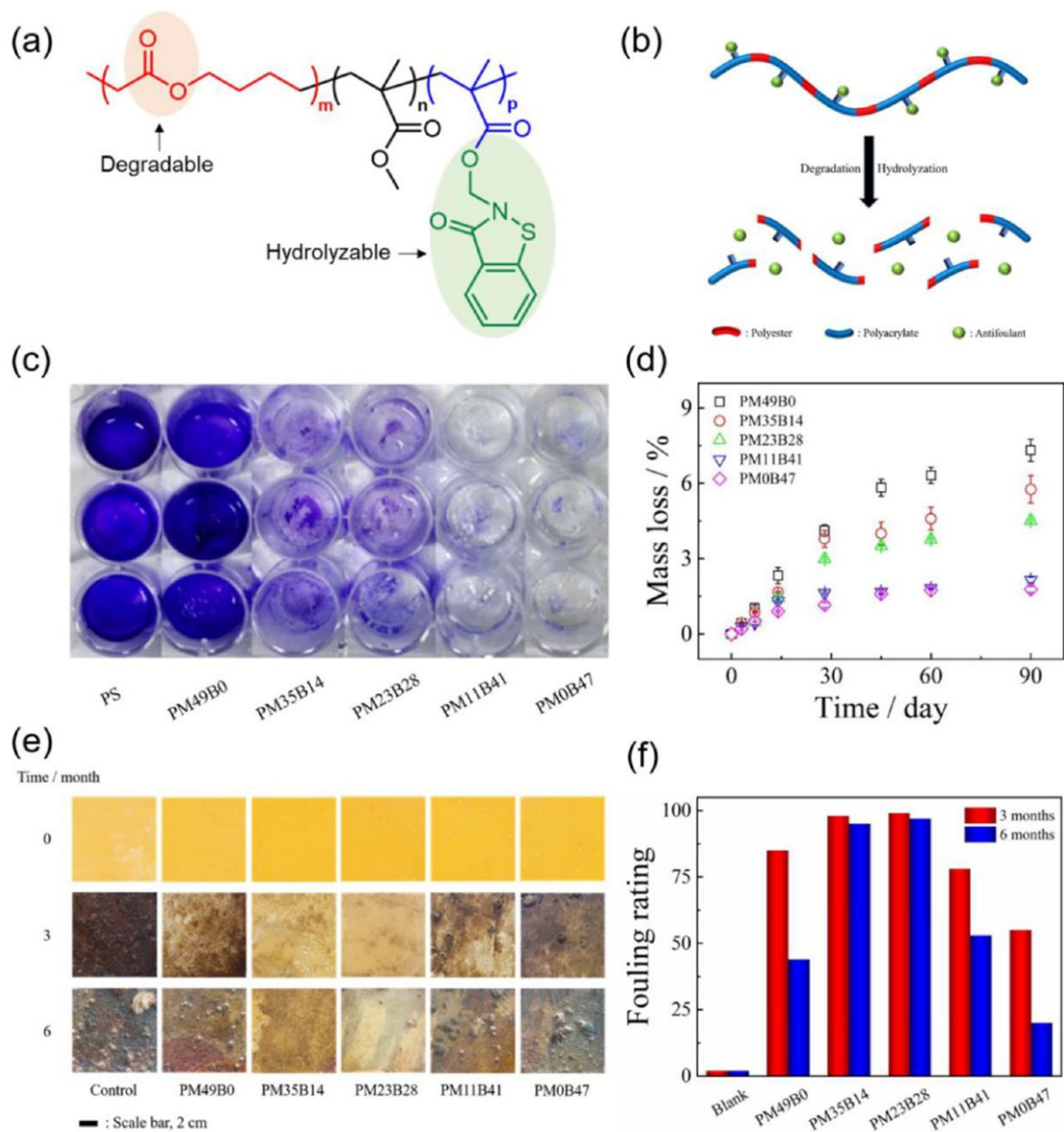


Fig. 122. (a) Structure of poly(ester-co-acrylate) with BIT pendant groups. (b) Degradation and hydrolyzation mechanism of the polymers. (c) Biofilm of *Pseudomonas* sp. grown on the coating surfaces stained with crystal violet. (d) Variation of mass loss of the polymers in ASW at 25 °C. (e) Images and (f) fouling rating of the coatings after immersion in Xiamen Bay for 6 months. Adapted with permission from refs [497, 500]

Finally, Zhang and coworkers[501] also combined the polymerization of MDO and MMA with another acrylate monomer (the ethyl acrylate of the tertiary carboxybetainetriisopropylsilyl ester HIZ), precursors of hydrophilic zwitterions after hydrolysis (Fig. 121). The coating is thus hydrophobic upon application and then this polymer can undergo cleavage of the ester bonds under the attack of seawater to form a constantly renewed surface, and its side groups hydrolyze to generate zwitterions, which allows the surface to have antiprotein, antibacterial and anti-diatom properties.

4.6.3 Adhesive materials

Adhesives are a type of polymer that is utilized in a wide range of applications, from building materials and packaging to advanced technology such as automobiles, airplanes, electronics and medical equipment. among adhesives, pressure-sensitive adhesives (PSA) are of particular interest in modern life (duct tape, post-it notes, etc.). Most PSAs are difficult or impossible to remove from a substrate, resulting in adhesive residue contaminating recycling equipment and preventing even recyclable plastics, paper, and cardboard from being reused. PSAs are mainly polyacrylate copolymers with one monomer bringing low T_g (*n*-butyl acrylate) and a second bringing a polar substituent (acrylic acid) to provide adhesion and improve cohesive strength after cross-linking. Bates and coworkers[321] proposed to replace acrylic acid by lipoic acid and a part of *n*-butyl acrylate by ethyl lipoate to prepare degradable PSA (Fig. 123).

The diad sequence and degradability of these copolymers are substantially dependent on the reaction conditions employed during polymerization. The average sequence of monomers throughout a polymer chain is controlled by the concentration of ethyl lipoate and T, with higher concentration and lower T favoring the creation of degradable disulfide bonds. The

copolymers were then formulated with $\text{Al}(\text{acac})_3$ at low loadings to increase cohesive strength by mild cross-linking, as is usual in commercial poly(acrylate) PSAs. Frequency-dependent rheological properties and cohesive strength studies demonstrate the same performance of degradable and nondegradable materials due to chemistry and cross-link density similarities (Fig. 123). The biodegradable material has significantly better adhesive performance which is most likely owing to interactions between sulfur and the glass substrate.

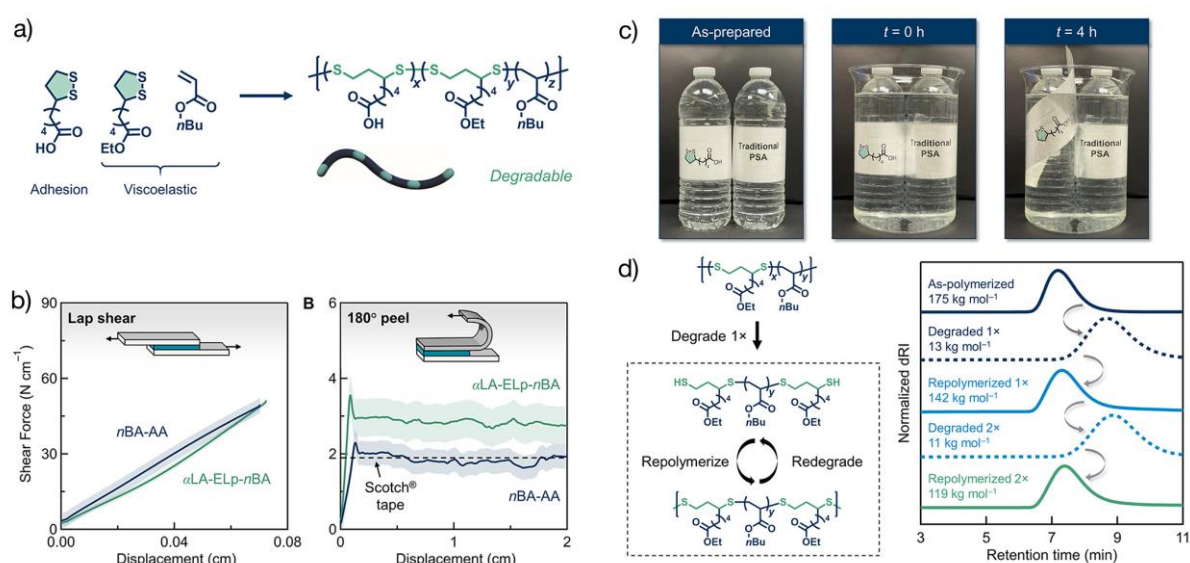


Fig. 123. a) Preparation of degradable PSAs. b) Lap shear with a uniaxial extension rate of 0.5 mm min^{-1} . 180° peel test with a uniaxial extension rate of 100 mm min^{-1} . Error envelopes represent two standard deviations from replicate runs. Commercial values for Scotch tape were obtained from literature c) Removal of label adhesive ($\alpha\text{LA-ELp-nBA}$ and nBA-AA) attached to recyclable plastic bottles. d) Model adhesive with functional chain-ends produced after degradation can undergo repeated oxidative repolymerization and reductive degradation for closed-loop recycling, as evidenced by SEC. Adapted from Ref. [321] with permission.

In a similar study, Bates and coworkers[319] prepared dynamic bottlebrush elastomers via the light-mediated polymerization of mono and bis-lipoate bearing poly(dimethyl siloxane) (PDMS) chains. Bottlebrush elastomers with high gel fractions (83-98%) and adjustable,

supersoft shear moduli in the 20-200 kPa range resulted from formulations using a bis-LA functionalized cross-linker. Due to the disulfide bonds, liquification occurs when samples are heated to 180 °C, which could be explained by the relatively low ceiling temperature of polymer chains based on LA repeat units. The depolymerized slurry may be recured under UV light, yielding a solid material with a lower modulus than the initial sample. At lower temperatures, the reactive character of disulfides can be used to degrade the backbone of LA-derived bottlebrush elastomers under basic or reducing conditions.

Besides PSA, medical adhesives are also of particular interest. One of the highly studied biomimetic adhesive systems is based on 3,4-dihydroxyphenylalanine (DOPA) and/or DOPA-mimetic catechol. The C-C backbone in many of DOPA/catechol-containing polymeric adhesives in the literature hampers biodegradability and so restricts their application. Aggarwal *et al.*[502] thus prepared a polar polyester-based adhesive via the copolymerization of 2-methylene-1,3-dioxepane (MDO), glycidyl methacrylate (GMA), and OEGMA, followed by the immobilization of the catechol group on the epoxy rings of GMA. Two cross-linking agents were utilized for adhesive applications, medical grade hydrogen peroxide (30% in water) or $\text{Fe}(\text{acac})_3$ (10 wt% in water). Fresh pig skin was employed as a sample soft tissue and the test for adhesion properties were performed using the lap shear strength test. The results showed better lap adhesion strength value than the existing medical adhesives.[502] The cross-linked adhesive demonstrated high adhesion stability against pH 7 PBS solution in at least 7 days at body temperature (37°C). MDO was designed to be used in terpolymers to produce enzymatically degradable ester linkages in the polymer backbone. Enzymatic degradation were performed in vitro using $\text{Fe}(\text{acac})_3$ cross-linked sample in PBS buffer (pH 7) with lipase from *Pseudomonas cepacia*. After 30 days, half of the mass was lost confirming the interest of the material.

Degradable hydrogel adhesives show promise as hemostatic agents, surgical sutures, and wound dressings. Xiao and coworkers[503] prepared hydrogel adhesives made from natural resource catechol-conjugated gelatin, iron ions (Fe^{3+}), and a synthetic copolymer of BMDO and *N*-(2-ethyl *p*-toluenesulfonate) maleimide (Fig. 124). Such copolymer good degradability and antibacterial properties due to the insertion of ester bonds in the backbone and the coupling with quaternary ammonium salt pendants in the polymer. Surprisingly, doping the synthetic polymer into the 3,4-dihydroxyphenylacetic acid-modified gelatin network results in the formation of a semi-interpenetrating polymer network that may significantly increase the stiffness, tissue adhesion, and antibacterial properties of manufactured hydrogel adhesives.

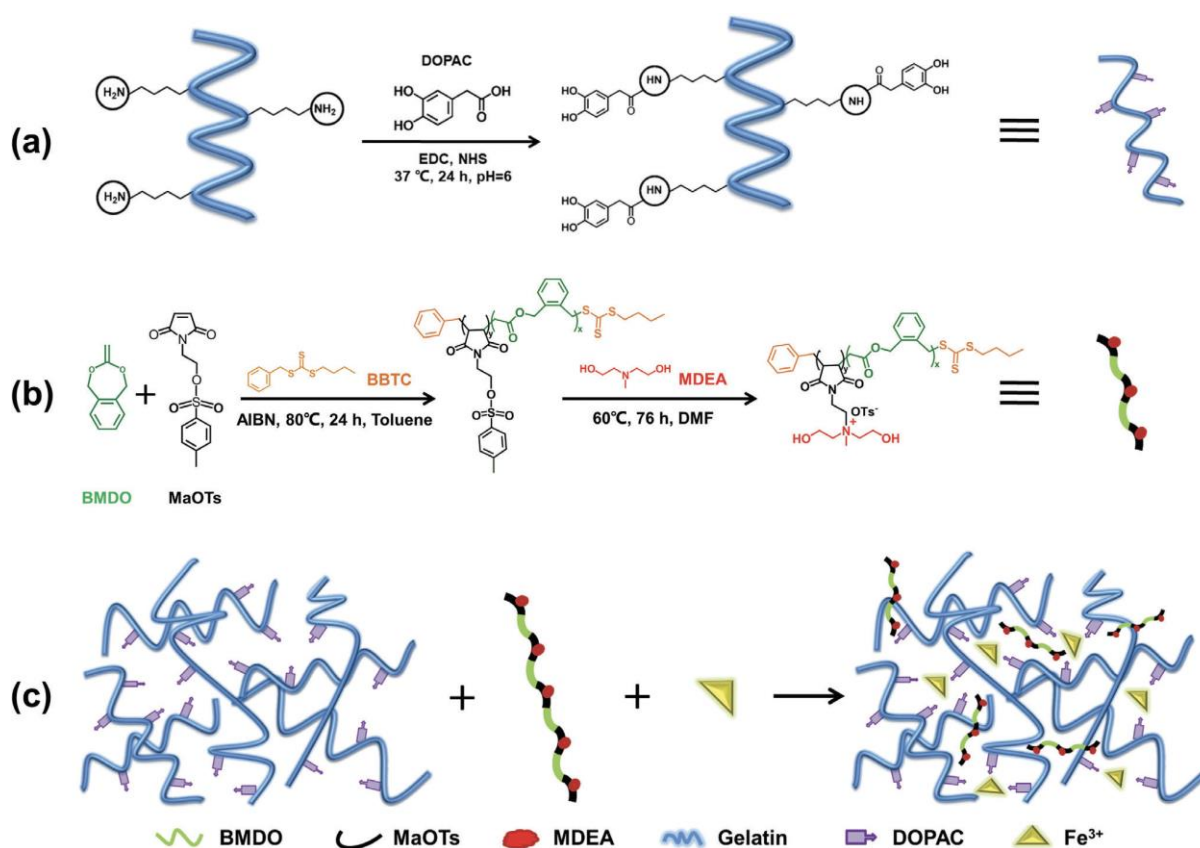


Fig. 124. Synthesis of the hydrogel adhesive. a) DOPAC-modified gelatin (G), b) quaternary ammonium cations-functionalized degradable copolymer (P), and c) hydrogel adhesives (GxFyPz) Reprinted from Ref. [503] with permission.

These hydrogel adhesives, which have several advantages such as degradability, increased tissue adhesion, better self-healing, strong cytocompatibility, and antibacterial properties, have a high potential for usage as tissue adhesives in biomedical sectors.

5. Biodegradation / Recycling properties

5.1 Biodegradation

The degradation of commodity thermoplastics is not possible due to the stability of their backbone. The introduction of labile/weak/cleavable bond into the backbone is now well established for preparing materials that can be degraded by a chemical degradation process under accelerated conditions (most often in a concentrated basic medium). These proofs of concept are considered by many authors to be very promising. However, the end-of-life analysis of these materials needs to be further developed. Agarwal *et al.*[504] state in their review article: "The concept seems promising and requires further extension to specific applications with relevant biodegradation tests under controlled laboratory and field conditions."

The term "biodegradable" can refer to a wide range of outcomes, including primary biodegradable polymers, compostable polymers, and polymers that can be fully mineralized.[505] Numerous studies measured evolved CO₂ to assess the degree of biodegradation.[506] Others evaluated the level of biodegradation by monitoring oxygen use.[506] Some authors utilized radiolabeled materials or chemically specific analyses, respectively. The design of several of these studies relied exclusively on primary deterioration

end points. Sometimes the sole parameter used to assess deterioration was mass loss. Due to the lack of readily visible residue, these materials can be considered biodegradable; nevertheless, it is unclear whether they were totally mineralized or merely broken up into tiny, unrecoverable fragments. Comparing various biodegradation studies is thus challenging due to the lack of uniformity in polymer biodegradation testing.[505]

The most advanced materials that already undergo biodegradation tests are the polyethylene mimics since these materials are the most relevant to replace HDPE or LDPE that are the most produced polymers and that represent the higher amount of waste. Guégan and coworkers[409] for example showed that PE mimic containing ester moieties in the presence of an urban sludge led to O₂ consumption and CO₂ release (OxiTop measurement) that confirmed a partial mineralization of the polymer (Fig. 125).

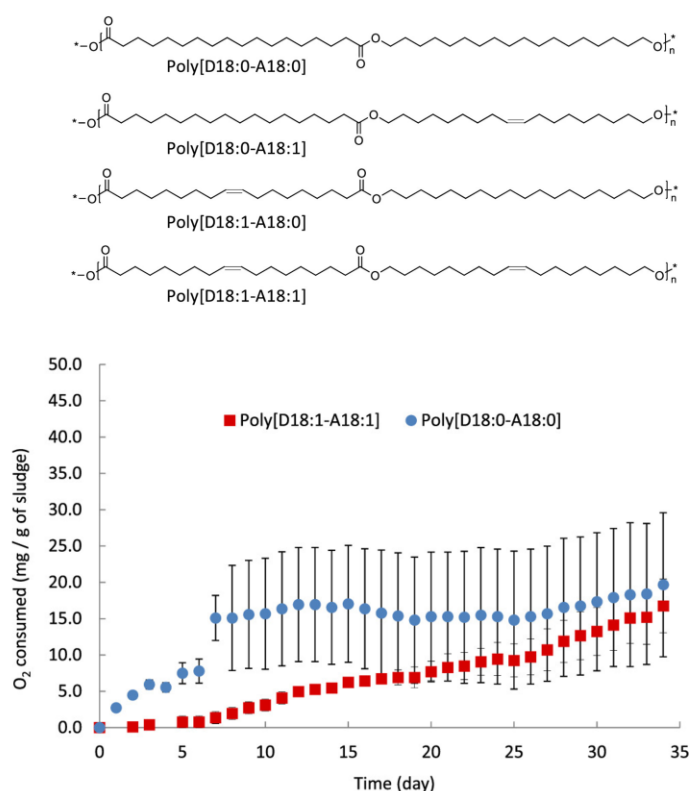


Fig. 125. Consumption of O₂ by a biomass from sludge mixed with poly[D18:1-A18:1] or poly[D18:0-A18:0], endogen respiration deduced. Error bars represent the standard deviation of mean of three replicates. Adapted from Ref. [409] with permission.

It is interesting to notice that while the oxidation of the polyester containing unsaturated bonds doesn't start for 5 days, the absence of a latency phase with the saturated polyester suggests that the necessary enzymes to degrade this polymer are generated by the microorganisms without an adaptation time. It is challenging to predict how long it will take for microbes to completely consume these polyesters since the measurement set-up was not optimal to follow such biodegradation.

Wurm and coworkers[90] studied the biodegradation of PE mimics containing orthoester fragments prepared via ROMP. Both unsaturated and saturated copolymers were obtained. Only the saturated compounds have properties that mimic HDPE. They chose the OECD 301F test using activated sludge from a sewage plant as inoculum and increasing the surface of the sample by grinding. None of the saturated polymers showed biodegradability in contrast with the unsaturated analogue that presented up to 25% of biodegradability in 10 days.[90] The difference lies in crystallinity and enhanced hydrophobicity that make this test not very relevant for such materials. The authors nevertheless noticed that saturated polymers underwent hydrolysis upon 6-month storage at RT under air that suggest a possible biodegradation at this timeframe.

Instead of studying ready biodegradability tests (OECD 301 type tests), PE mimics were also tested in composting conditions. Mecking and coworkers[413] studied their recyclable and renewable PE mimics and they showed that the combination of long diacid compound with ethylene glycol to prepare PE-2,18 allowed to obtain HDPE-like crystalline materials but at the same time this polymer is sensitive to degradation by natural enzymes such as *Humicola*

insolens cutinase (HiC), *Thermomyces lanuginosus* lipase (TIL), and *Aspergillus oryzae* cutinase (Fig. 126).

A controlled laboratory composting test in accordance with ISO standard 14855-1 was used to evaluate the degradability of PE-2,18 by microorganisms by following the formation of carbon dioxide generated by the mineralization of the polyester. Despite being crystalline, PE-2,18 mineralization reached $96 \pm 2\%$ (n=3) after two months at 58°C (Fig. 126).[413] This mineralization profile meets the criteria for biodegradation under industrial composting settings and compares favorably to the behavior of commercial, less crystalline, biodegradable polyesters. Comparatively, pure PE-18,18 only partially degraded in industrial composting, reaching a plateau at roughly 30% mineralization after two months.

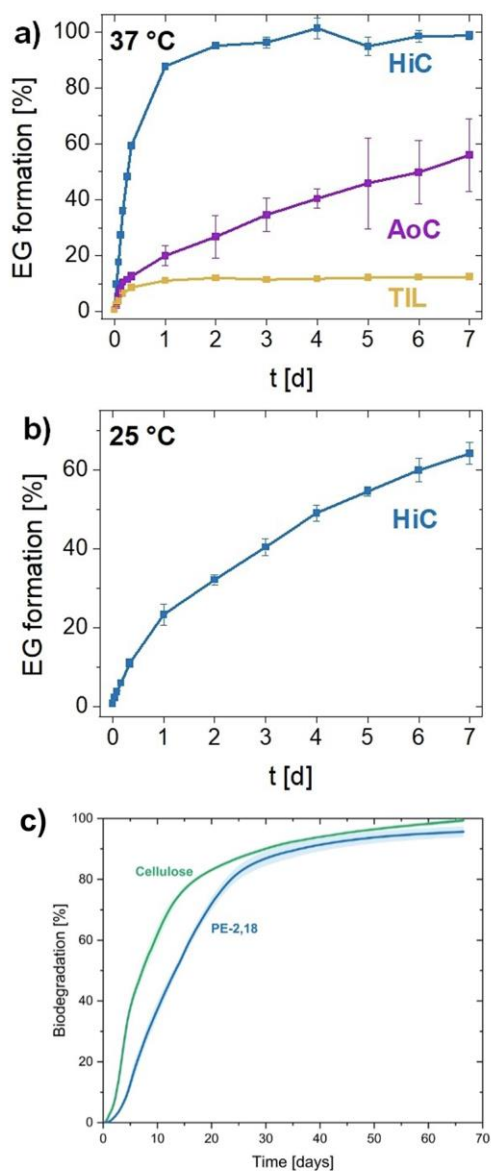
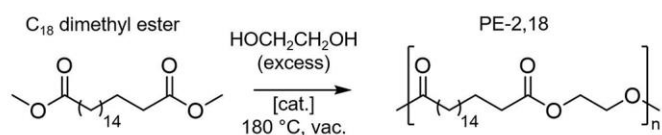


Fig. 126. a) Hydrolysis of PE-2,18 by *Humicola insolens* cutinase (HiC), *Thermomyces lanuginosus* lipase (TIL), and *Aspergillus oryzae* cutinase (AoC) at 37 °C and pH 7.2, monitored via HPLC-RI quantification of formed ethylene glycol (EG). b) Hydrolysis of PE-2,18 by HiC at ambient temperature (25 °C, pH 7.2). c) Mineralization curves based on CO₂ evolution measured under industrial composting conditions following the standard ISO 14855-

1 for PE-2,18 and for cellulose as a reference material. Shadows in light color correspond to the standard deviations. Reprinted from Ref. [413] with permission.

The preparation of short-long polyesters that mimic HDPE was also reported by Dubois and coworkers.[410] These materials were then tested in soil degradation. The appearance and weight loss of the film samples after 2 and 17 months of burial in moistened horticulture soil at room temperature were monitored (Fig. 127). In particular, PEs210 lost 2.2 wt% of its weight and developed a rough surface, indicating biodegradation in the soil. The PEs210 film was plainly fractured and brittle after 17 months. The reduction in weight was at least 35.6 wt%. At 17 months, other samples likewise became brittle and developed minor surface fissures but were not fractured.

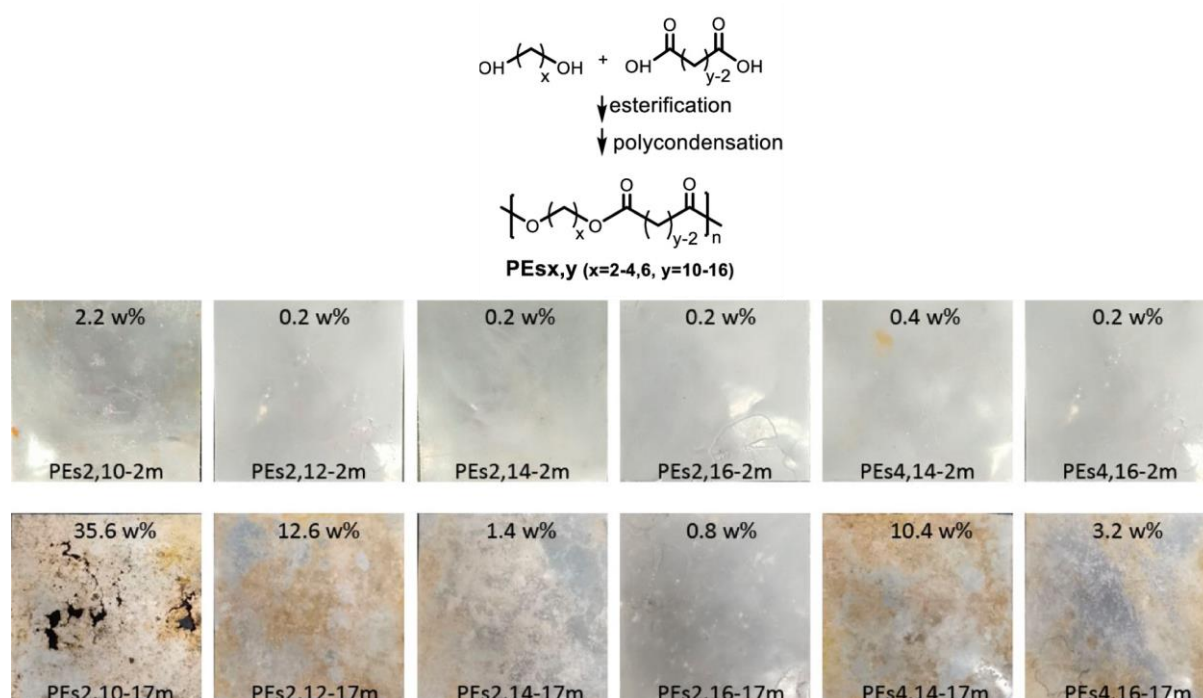


Fig. 127. Weight loss and appearance of some long-chain polyesters films after biodegraded in soil for 2 and 17 months (2 m, 17 m). Reprinted from Ref. [410] with permission.

To enhance the biodegradation of PE mimics, Mecking and coworkers[414] blended long-chain aliphatic polyester PE18,18 with a long-chain aliphatic poly(H-phosphate). Such poly(H-phosphate) was shown to be very instable even stored in powder at RT under air.[415] The blend with 5-20 mol% of poly(H-phosphate) presented similar melting point, crystallinity and mechanical properties than the pure PE18,18 with a good stability under air.[414] Samples prepared by injection molding (film of 10×7×1 mm) were then tested for stability in water (pure or in phosphate buffered media). After 4 months, NMR analysis of the complete specimens showed that the hydrolytically labile poly(H-phosphonate) hydrolyzed to the underlying long-chain aliphatic diol. The number-average molar masses of the virgin blends ranged from 50 to 70 kg.mol⁻¹, and the values decreased to 7 - 11 kg.mol⁻¹ after being hydrolyzed. Since there were no remaining high molar mass fractions in the SEC chromatograms, the abiotic hydrolysis had taken place throughout the bulk of the materials. This is in contrast to the hydrolysis of PE18,18 that showed stability under acidic and basic conditions.

Besides polyolefins, polymers prepared by radical polymerization due to their very persistent C-C backbone were another very interesting targets to impart biodegradability. Many studies focused on accelerated degradation conditions and do not investigate the biodegradability. Before moving on to a precise biodegradation study, several studies focused on the enzymatic degradation of copolymers containing ester-like functions in the chain originating from the ring opening of CKA monomers. For example, some studies focused on nanoparticles where the ester bonds were located either in the crown,[507] or in the core of the nanoparticle[264] and degradation was studied by tracking the decrease in nanoparticle size in the presence of lipases from bacteria of the type *Pseudomonas sp.* and *Candida antarctica*. For these objects, enzymatic degradation was observed after several days of reaction. Agarwal *et al.*[240] used lipase from

Pseudomonas cepacia bacteria to study the enzymatic degradation of an amphiphilic copolymer of MDO, PEGMA and a methacrylate bearing a pendant coumarin. Further studies were carried out on cross-linked materials immersed in PBS containing lipases from *Pseudomonas cepacia* bacteria. Under these conditions, enzymatic degradation occurs but due to cross-linked materials the kinetics are rather slow (followed over 30 days).[502, 508] An interesting procedure has been reported by Liu and colleagues.[224] They studied the enzymatic degradation of linear MDO/methyl acrylate copolymer films prepared by solvent evaporation. These films were immersed in enzyme-containing PBS for 10 to 25 days, and both mass loss and decrease in molar mass distribution were monitored by SEC. As expected, the higher the MDO level, the greater the degradation.

There is very little work reporting biodegradation studies following standard procedures (OECD 301 test). In 1985, Gapud and Bailey[509] prepared copolymers of ethylene and MDO with MDO contents ranging from 2 to 10 mol%. Preliminary biodegradation tests show that these copolymers are biodegradable in a soil model containing microbiota. Recently, Thonyiot *et al.*[213] prepared a poly(acrylic acid) containing ester functions proven to be biodegradable. In addition to chemical degradation, these authors studied the biodegradation of this water-soluble polymer under near-environmental conditions (standard OECD 301 D test). The results were encouraging, since a biodegradation rate of 27.5% in 28 days was measured in the case of a poly(AA-*co*-MDO) of 7700 g/mol and 19% open MDO units, whereas a PAA of the same molar mass showed no degradation (Fig. 128). These results are encouraging, although it should be noted that according to the standard used, a compound will be considered biodegradable if the biodegradation rate reaches 60% in 14 days.

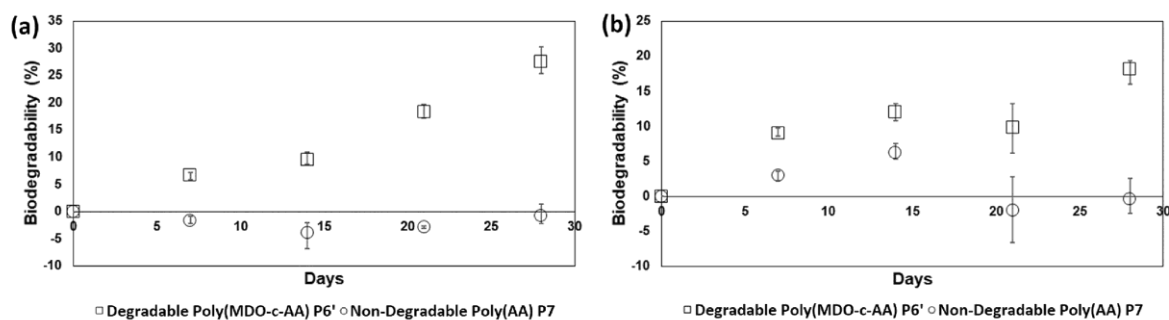


Fig. 128. OECD 301 D Closed Bottle Test biodegradability (%) results of degradable poly(MDO-c-AA) (P6') and non-degradable poly(AA) (P7) using secondary effluent from domestic wastewater treatment plant, as inoculum. Results shown are the average of the triplicates, from (a) Biodegradability test service provider I and (b) Biodegradability test service provider II. Following the OECD Guideline for Ready Biodegradability, the test results were valid since reference compound achieves more than 60% biodegradability on Day 14. Reprinted from Ref. [213] with permission.

This result is the first that confirmed the interest of inserting weak bonds into polymers made by radical polymerization to impart biodegradability. This result is in line with a recent study from Carter *et al.*[447] that confirmed the biodegradability of poly(acrylic acid) oligomers up to DP=17 with a decrease of biodegradability with increasing chain length. More data on others polymer structures are mandatory to establish structure – biodegradability relationships.

5.2 Recycling

Development of a circular material economy is a logical and optimal approach to address the end-of-life problem of waste plastics, reduce environmental harm, and lessen our dependency on finite fossil raw materials. Chemical recycling (sometimes referred to as tertiary recycling)

is a dynamic, adaptable strategy for addressing the worldwide plastic problem. Expanding the sorts of plastics that can be recycled and converting post-consumer polymers back into their original monomers, oligomers, or new chemical feedstocks are both possible using chemical techniques like glycolysis and pyrolysis. Additionally, certain chemical recycling processes (such the high-temperature, oxygen-free pyrolysis process) are still energy-intensive and nonselective, producing complicated mixes of oils, waxes, hydrocarbon gas, and char that need to be further treated. Recently, a contentious idea known as "chemical upcycling" that is based on chemical recycling has been developed. The development of plastic waste upcycling technology, albeit still in its infancy, is generating a lot of attention around the globe due to its potential to create chemicals, fuels, or items with greater values through chemical processes. Pure depolymerization process will not be treated in this review since we focus on the introduction of labile/weak bonds to induce degradation of the polymers.

Similarly to biodegradation, only a small part of the studies deals with recycling and the main examples are also conducted on PE mimics due to the importance of polyolefins in plastic production. Polyethylene with ester or carbonate moieties located precisely onto the backbone (1 ester or carbonate every 18 to 48 carbons) were prepared by polycondensation of biobased derivatives and was showed to behave similarly as HDPE in both melting temperature, crystallinity and mechanical properties.[411] This material was processed by classic methods such as injection molding and filament for fused-filament fabrication was also demonstrated. Tensile bars made of PE containing 1 carbonate group every 18 carbons was used as model sample to perform depolymerization in presence of KOH (20 g of polymer for 250 ml of basic 10 wt% KOH against polymer ethanol solution.) Complete depolymerization took place in 24h at a depolymerization temperature of 120 °C without the need for additional steps such as vigorous stirring or earlier grinding. After cooling, the long-chain diol crystallized and was separated by filtration (Fig. 129).

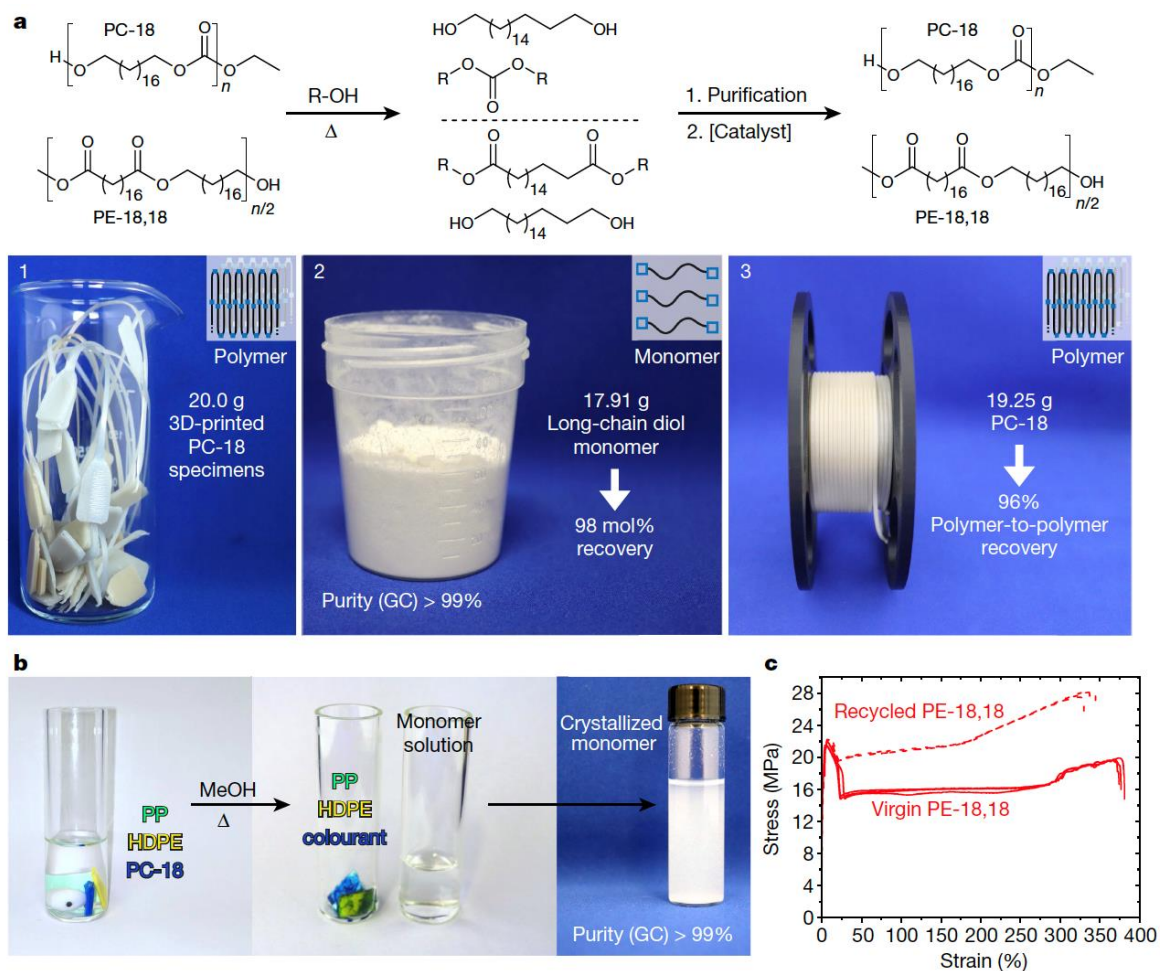


Fig. 129. a) Chemical recycling of PC-18 and PE-18,18 via solvolysis and repolymerization. b) Use of a mixture of PP (polypropylene), HDPE and blue-coloured PC-18 as an example of a potential polyolefin waste stream. Left, mixture in MeOH. Middle, after heating, showing the separated mixture and the monomer solution produced by depolymerization. The warm methanolic solution of 1,18-octadecane diol was allowed to crystallize at room temperature for purification (right). c) Stress–strain curves of a virgin PE-18,18 batch and its recycled analogue. Reprinted from Ref. [411] with permission.

Recrystallization produced almost quantitative amounts (98%) of extremely pure 1,18-octadecane diol. It was then possible to produce a recycled polymer of high molecular weight (M_w 240,000 g mol⁻¹, M_n 70,000 g mol⁻¹) PC-18 by reacting this recovered monomer with

diethyl carbonate once again, yielding a 96% chemical polymer-to-polymer recycling yield. As expected, this recycled PC-18 have similar material properties than the pristine PC-18. Depolymerization of PE-18,18 containing an ester bond resulted in a combination of two non-volatile long-chain monomers, diester and diol, as opposed to depolymerization of long-chain polycarbonates PC-18, which only produces the diol as a long-chain molecule. Without the need for a catalyst, depolymerization of PE-18,18 in MeOH was performed, and full depolymerization was accomplished in 12 hours (or 2 hours with a catalyst) at 150 °C. An exact 1:1 combination of C18 diester and C18 diol was then produced when MeOH was removed in vacuo from the depolymerization solution. This combination could be repolymerized using $[\text{Ti}(\text{O}n\text{Bu})_4]$ catalyst without further processing, reforming high-molecular-weight PE-18,18. Tensile tests of both injection-molded and 3D-printed specimens showed also materials properties than the pristine materials.

To highlight the interest of this technology, the authors also investigated if such materials could be degraded and recovered selectively in a mixed plastic trash stream without mechanical sorting or sink-flow density separation. They mixed PE18,18 or PC-18 with polypropylene (PP) (reusable hot beverage cup) and common polyethylene (solvent bottle cap) as well as poly(ethylene terephthalate, or PET), which is a common material found in waste streams and is recyclable. Using the basic treatment, both PE18,18 and PC-18 was totally depolymerized and disintegrated, while the PP and HDPE fragments were recovered in their unmodified original form (Figure 129b). Notably, PET having a high melting temperature ($T_m = 268$ °C) is also preserved. In the case of PC18, pure 1,18-octadecane diol was again quantitatively recovered from work-up of the filtrate by crystallization (98% yield).

Zhang and coworkers[394] developed an interesting route to prepare PE mimics that consists in a cascade reaction based on the highly efficient thiol Michael additions from cheap and

renewable reactants, i.e. H₂O, carbonyl sulfide (COS), and diacrylates. In particular the use of 1,9-nonanediol diacrylate led to a polymer structurally similar to polyethylene with a low density of in-chain ester and thioether groups. Two different recycling cycles were envisioned (Fig. 130). The first one consists in the hydrolysis, esterification and further step-growth polymerization of the polymer.

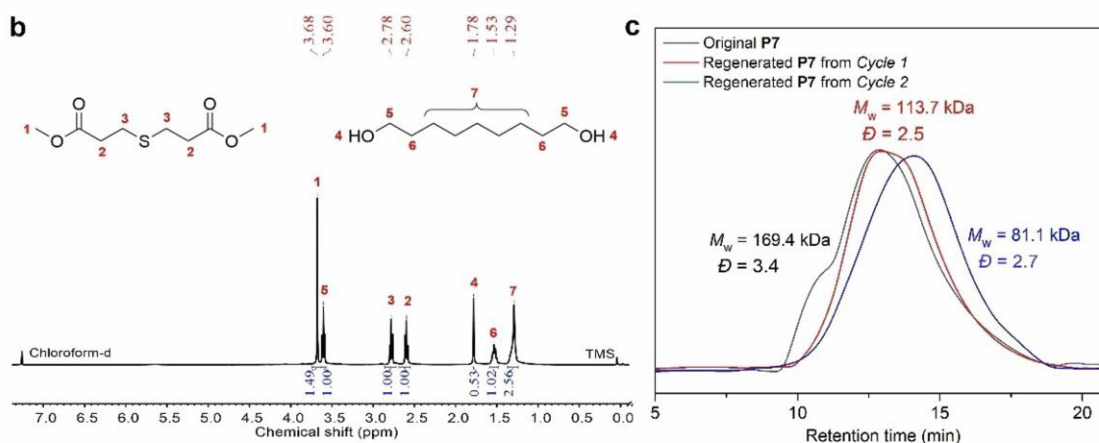
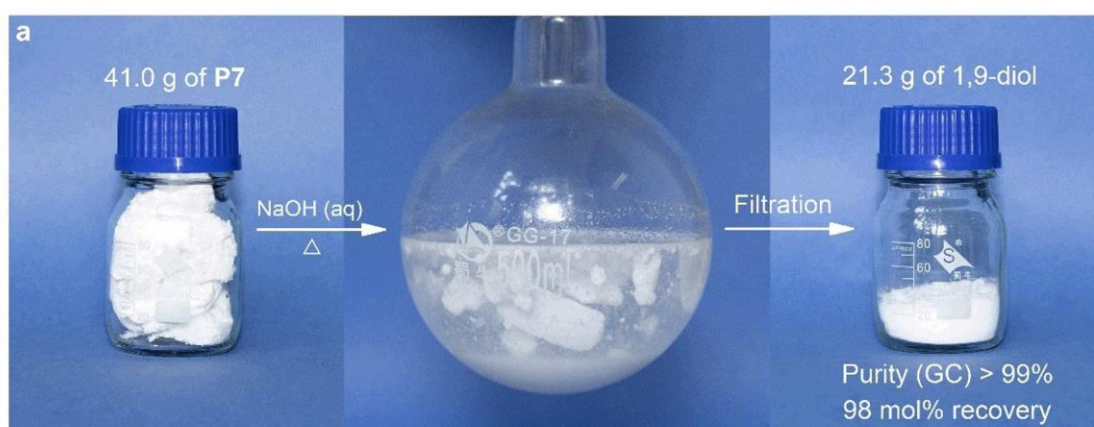
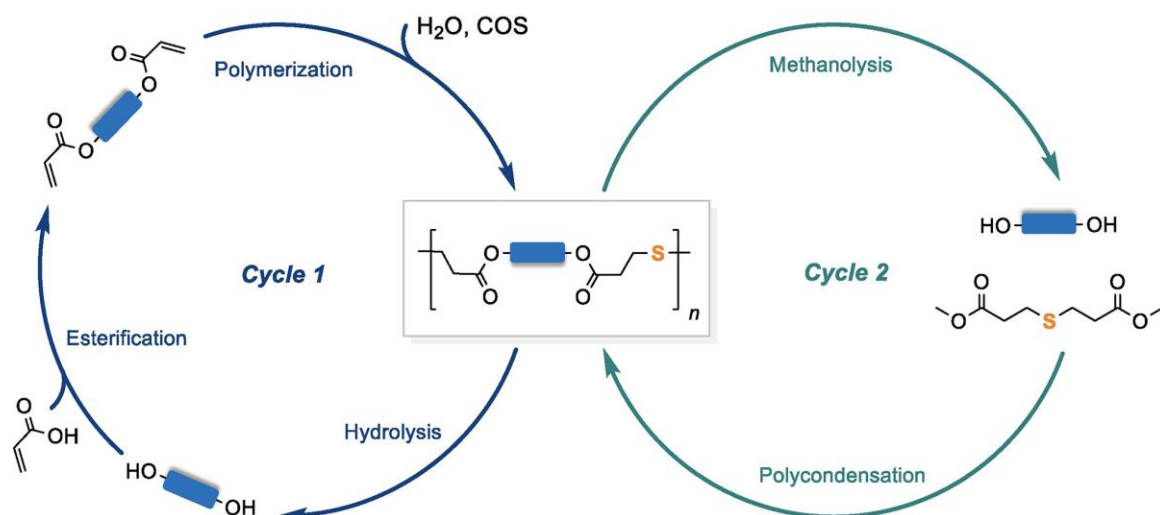


Fig. 130 Recycling routes of the polymers completed through two cycles: Cycle 1 via hydrolysis, esterification, and polymerization; Cycle 2 via methanolysis and polycondensation. a) Images of polymer prepared using the 1,9-nonanediol diacrylate (P7) synthesized on dozens of grams scales, 1,9-diols crystallized from aqueous solution after heating, and 1,9-diols recovered finally. b) 1H NMR spectrum of the product after methanolysis of P7. c) SEC curves

of original P7 and regenerated P7 from Cycles 1 and 2. Reprinted from Ref. [394] with permission.

As an alternative, the polymer could be methanolized for 24 hours at 120 °C with 0.042 mol% titanium(IV) n-butoxide as the catalyst (Fig. 130). This treatment produced a non-volatile equal molar combination of dimethyl 3,3'-thiodipropionate and 1,9-diol after heating to eliminate residual methanol. The combination also included non-volatile titanium(IV) n-butoxide, which can catalyze the subsequent polycondensation process. In both cases, the recycled polymers have the same properties than the pristine materials.

Besides PE mimics, other polymers containing weak bonds were subjected to recycling. Polymers prepared by rROP were very little tested. In 2022, Johnson *et al.*[301] established the first proof-of-concept by preparing a polystyrene containing thioester linkages from the ring-opening of thionolactone DOT. These copolymers were degraded under specific conditions (aminolysis or thiolysis) to give polystyrene oligomers with two thiol functions as chain ends. The simplest route to repolymerization is oxidative oligo-dithiol polymerization. This method is attractive because it is atomically economical and potentially compatible with a wide range of conditions under which the thiol/disulfide redox couple can be used. The use of I₂ as an oxidant in the presence of pyridine as an H-I scavenger enabled rapid and efficient repolymerization to be achieved. Under these conditions, an oligo-dithiol of $M_n = 1.1$ kDa yielded the recycled polymer ($M_n = 12.3$ kDa) in 89% isolated yield. Remarkably, the molar mass distribution of this recycled polymer is almost identical to that of the starting polymer. Based on this finding, the authors were able to establish theoretically that the presence of monofunctional fragments in degradation oligomers derived from end groups of the starting polymer limits the M_n to the value of the original polymer, plus the mass of the cleavage

reagent. Johnson *et al.*[301] finally validated this method on recyclable PS of high molar mass. The deconstruction of a PS of M_w between (240 and 310 kDa) containing 2.5 or 5 mol% DOT by the action of cysteamine yields PS oligomers in yields of over 98% with $M_w = 9.1$ and 4.5 kDa, and dispersities close to 2. Oxidative repolymerization of these crude fragments, without any purification, yielded recycled polymers, in which 68% (212 kDa) and 62% (154kDa) of the M_w of the starting polymers was recovered. These values were improved to 94% (292 kDa) and 116% (287 kDa) if the oligomers were first precipitated in methanol to purify them (Fig. 131).

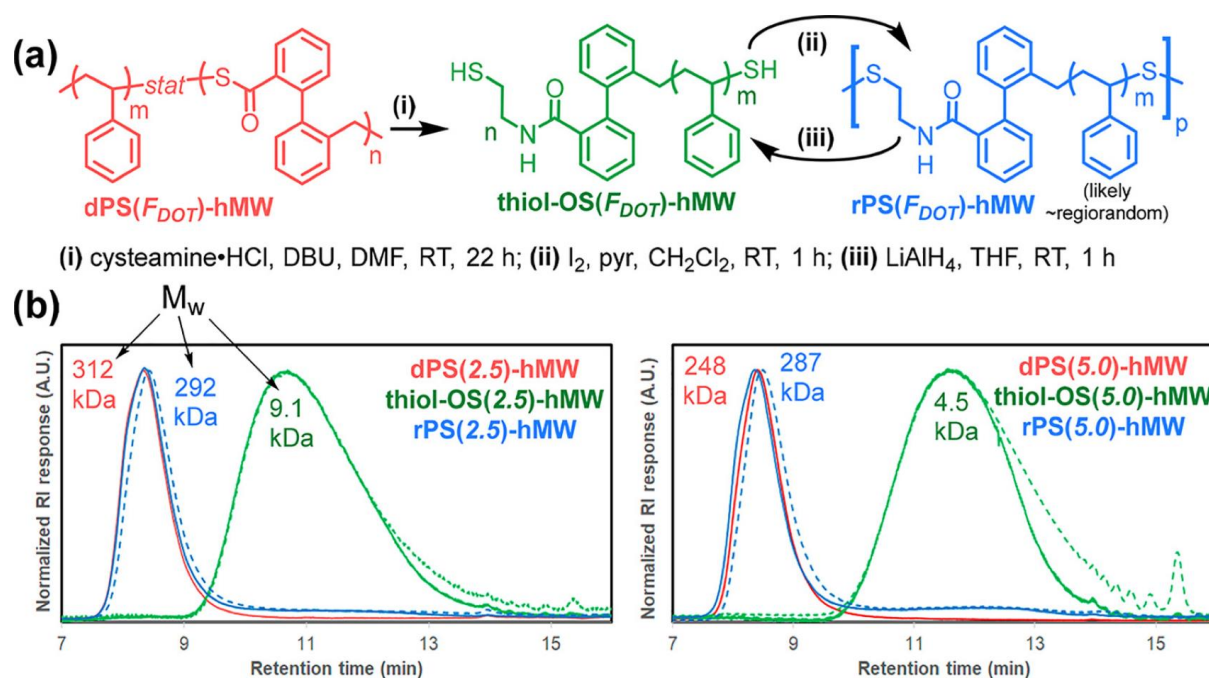


Fig. 131. Circular, high molar mass PS. (a) Synthetic scheme for deconstruction and recycling of high M_w PS. (b) SEC traces for deconstruction/recycling cycles on copolymers with 2.5% and 5% comonomer loading. The dotted green and blue traces are for crude oligomer and the recycled PS obtained from the crude oligomer, respectively. Noted M_w values are those derived from the solid traces (i.e., from purified oligomer). Reprinted from Ref. [301] with permission.

These results show that it is possible to synthesize recyclable PS of high molar mass on the decagram scale under solvent-free polymerization conditions, degrade these polymers into low-mass fragments and repolymerize them under mild conditions to generate recycled PS of almost equivalent molar mass, in excellent yields. To demonstrate circularity, a second deconstruction/reconstruction cycle was carried out, exploiting the reversibility of disulfide bond cleavage. Several common reducers were used to achieve complete degradation of the recycled polymer into an oligomer with a molar mass distribution similar or identical to that of the original oligomers. LiAlH_4 showed that it is possible to retain the fidelity of suitable end groups for a second round of recycling. A second round of oxidative repolymerization yielded a second recycled polymer with an M_w of 180 kDa, or 57% of the original molar mass.

A closed-loop of synthesis and degradation may be generated if the degradation byproduct from the ensuing degradable polymer is polymerizable. Following this approach, an interesting recycling process was proposed by Aoshima *et al.*[510] on the cationic polymerization of vinyl ethers and aldehydes. The alternating copolymerization was presented in section 3.3.1. Indeed, well-defined degradable copolymers were prepared by the copolymerization of benzaldehyde derivatives (BzAs) with vinyl ethers. Because of the acid-labile acetal bond created by the VE-aldehyde sequence, the copolymers are easily decomposed by acid hydrolysis, leading to cinnamaldehyde (CinA) as practically the single hydrolysis products. This degradation product is potentially a conjugated aldehyde that could undergo alternating copolymerization with vinyl ether derivatives. The authors thus showed that at least three cycles could be performed (Fig. 132), each time leading to side-products that is elongated by one more unsaturation. The thermal characteristics of the second and third recycled alternating copolymers were comparable to those of the first generation and the generation number could be deduced from the structure of the degradation product.

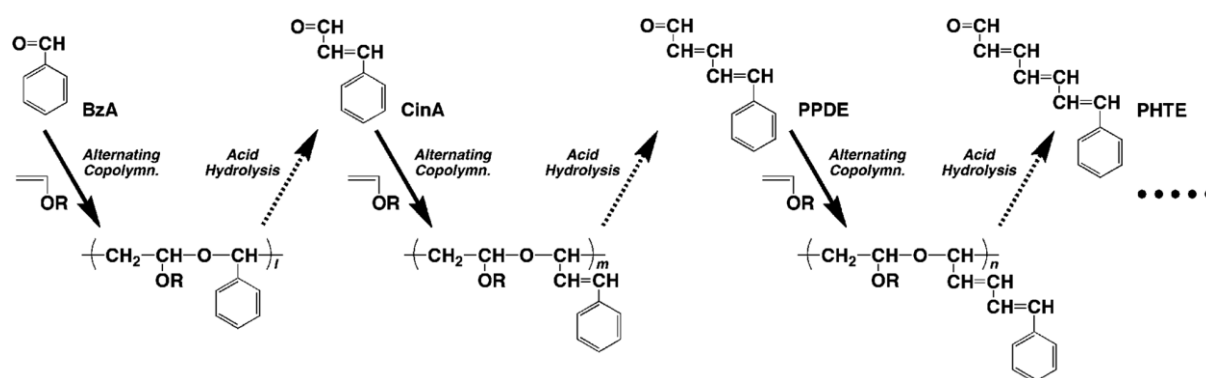


Fig. 132. A novel chemical recycling system consisting of alternating copolymerization of conjugated/aromatic aldehydes with VEs and selective acid hydrolysis of product copolymers. Reprinted from Ref. [510] with permission.

Finally, recycling was also tested for thermosets containing weak/labile bonds. As presented in section 4.3, degradable poly(DCPD) were prepared in combination with 5-20 mol% of **ROMP22**. This led to a thermoset with similar properties than the pristine materials, but the cross-linked materials could be depolymerized selectively in the presence of fluoride anion (TBAF solution). The degradation products of the crosslinked materials are hydroxylated polymers with cyclopentene functionalities that may be recycled (Fig. 133). The soluble samples were examined using SEC and diffusion-ordered spectroscopy. Both techniques revealed an inverse correlation between the amount of weak/labile bonds and degradation product size. Based on SEC, the weight-average molar masses of these samples were 2-8 kDa, that was in good agreement with the average diameter of the degradation products (4 nm) that was determined via DOSY.

The presence of a majority of unreacted cyclopentene substituents and also exchangeable crosslinks with alkenes led the authors to reprocess the degradation products to prepared recycled materials. Samples with comparable stress-strain behavior and elastic moduli (Fig. 133) was achieved by combining the degradation products of the 10% **ROMP22**-doped

material (25 wt%) with fresh DCPD and curing using the same method as for pristine poly(DCPD). The recycled materials furthermore demonstrated comparable native poly(DCPD) ballistic impact resistance. Open-loop recycling was thus obtained.

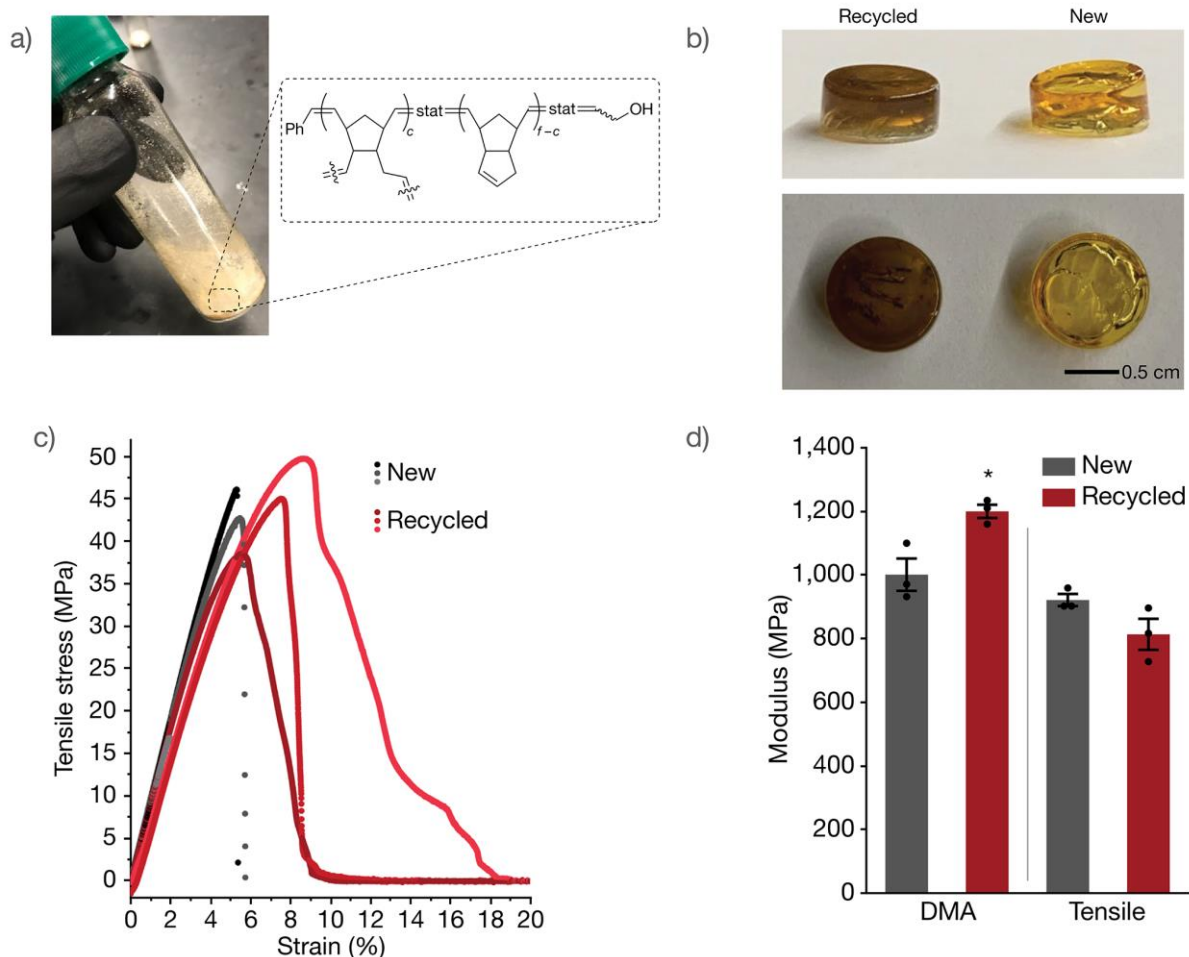


Figure 133. a) Structure of the degraded poly(DCPD) containing **ROMP22** additive. b) Images of representative recycled and new poly(DCPD) samples. c) Stress–strain curves from dogbone-shaped samples of new and recycled poly(DCPD), showing comparable stress–strain curves with increased strain at break for the recycled samples. d) Elastic moduli of native and recycled poly(DCPD), as assessed by DMA and tensile testing. Reprinted from Ref. [51] with permission.

Besides open-loop recycling, Johnson and coll. decided to use the hydroxyl end group functionality of the degraded oligomers to prepare new materials. The presence of allyl alcohol end groups was confirmed by MALDI-TOF analysis of the oligomers and the authors determined that the amount of hydroxyl units per mg of fragments using ^1H NMR. They obtained a value that is close to 85 % of the theoretical value. The reaction of these hydroxy groups with 4,4'-methylenebis-(phenyl isocyanate) was then tested (Fig. 134). Dynamic mechanical analysis (DMA) was used to examine the thermomechanical characteristics of the recycled thermosets and the results were compared to those of the original poly(DCPD) network containing 10 mol% **ROMP23** in order to assess the efficacy of the recycling procedure.

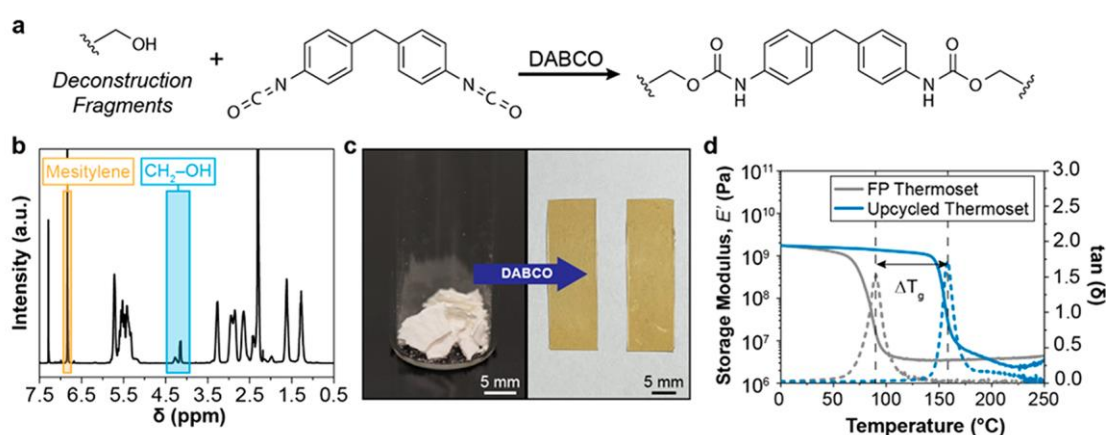


Fig. 134. a) Schematic representation of the incorporation of hydroxyl-rich fragments into a polyurethane network with a diisocyanate, such as 4,4'-methylenebis(phenyl isocyanate) (MDI). b) ^1H NMR spectrum of the fragments obtained after dismantling a thermoset containing 20 mol % **ROMP23** with a mesitylene internal standard. c) Optical images of the deconstruction fragments isolated from a thermoset containing 10 mol% **ROMP23** (left) and the free-standing films obtained after reaction with MDI. d) Traces of the storage modulus and

tan δ obtained during DMA analysis of a frontally polymerized thermoset containing 10 mol % iPrSi-7 and the upcycled polyurethane film. Reprinted from Ref. [108] with permission.

The thermoset cross-linking density is successfully recovered by the film prepared with diazabicyclo[2.2.2]octane (DABCO) as a catalyst. The T_g of this new polyurethane material is 162.4 °C, which is 70 °C higher than that of the original thermoset (92.3 °C), allowing for effective upcycling to produce a material with better properties (Fig. 134). The polyurethane's T_g is even higher than that of any of the studied FROMP copolymers and approaches that of plain poly(DCPD). The hard aromatic urethane linkers that were substituted for the flexible aliphatic silyl ether in the original material's backbone explained these upcycling properties.

In both cases, the recycling properties was possible in the presence of fibers. For example, carbon fiber textiles that could be used to prepare composites for high-performance applications could be quantitatively recovered after being embedded in 10% **ROMP22**-doped poly(DCPD) (see section 4.3.2 Fig. 106f). The similarities between the pristine and recovered carbon fiber's Raman spectra indicate that the mild poly(DCPD) degradation process has no effect on the fiber's composition. These results point to interesting options for recycling thermoset composites.

6. Conclusion

The insertion of weak/labile bonds into the backbone of various polymers appears to be a promising way of meeting current and future environmental challenges, by offering a simple method for producing degradable materials. This approach was applied to all kind of polymers

from water-soluble to thermosets and using all polymerization technique. A low level of labile functions is in many examples sufficient to render the material degradable after use, while maintaining the thermal and mechanical properties of the materials during service. Besides common labile bonds, such as esters, more and more studies were devoted to the introduction of specific groups that are prone to degradation under specific stimuli such as light, mechanic forces, presence of fluoride atoms or enzymes, etc. This makes the materials devoted to specific applications.

While this approach is now well recognized in the community as a promising solution to the problem of plastic pollution, the end-of-life of materials obtained by this method has yet to be developed. In the case of collectable polymers, recycling appears to be the best way of managing and recovering waste. However, only few studies have addressed this issue even if proof of concept were presented and even close-loop recycling example were demonstrated.

Furthermore, as regards non-collectable polymers, and in particular water-soluble polymers, their biodegradation is becoming an essential property in order to limit their impact on the environment as much as possible. However, standardized studies (in particular according to the OECD 301 standard) have been carried out only to a limited extent to date, and therefore remain to be developed for all the materials that have been prepared.

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