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Bio-based poly(ester-*alt*-thioether)s synthesized by organo-catalyzed ring-opening copolymerizations of eugenol-based epoxides and *N*-acetyl homocysteine thiolactone

Simon Le Luyer,^a Baptiste Quienne,^b Matthieu Bouzaid,^a Philippe Guégan,^a Sylvain Caillol^b and Nicolas Illy^{a,*}

^a Sorbonne Université, CNRS, Institut Parisien de Chimie Moléculaire, Equipe Chimie des Polymères, 4 place Jussieu, F-75005 Paris, France.

^b ICGM, Univ Montpellier, CNRS, ENSCM, Montpellier, France.

Corresponding Author

* Nicolas Illy: Phone 33 (0)1 44275513 E-mail: nicolas.illy@sorbonne-universite.fr

ABSTRACT

The anionic alternating ring-opening copolymerizations of three bio-based aromatic monomers, eugenol glycidyl ether (EGE), dihydroeugenol glycidyl ether (DEGE) and vanilin glycidyl ether (VGE), were carried out with renewable *N*-acetyl homocysteine thiolactone (NHTL) using benzyl alcohol and 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP) as initiating system. This polymerization is a rare example of eugenol-based monomers used to synthesize linear polyesters. Alternating poly(ester-*alt*-thioether)s are obtained with number-average molar masses M_n ranging from 1.1 to 10.8 kg mol⁻¹ and dispersities as low as 1.20. The copolymer structures were carefully characterized by ¹H, ¹³C, COSY, HSQC, ¹H-¹⁵N NMR. It was found that the alternate copolymers were obtained selectively under different monomer feed ratios. In addition, the use of EGE and VGE monomers allows the preparation of multi-functional poly(ester-*alt*-thioether) respectively bearing allyl or aldehyde groups in each repeating unit. The copolymers display only clear glass transition temperatures higher than ambient temperature. This alternating copolymerization method offers a new chemical pathway for the valorization of bio-based aromatic compounds and expand the scope of renewable polyesters.

INTRODUCTION

Eugenol (4-allyl-2-methoxyphenol) is a commercially-available bio-based phenol that can be extracted from numerous essential oils,^{1,2} such as clove oil, nutmeg, cinnamon, basil, bay leaf, tulsi or pepper or synthesized by the allylation of naturally-occurring guaiacol.³ This valuable compound can alternatively be obtained by depolymerization of abundant lignin. The rise of increasingly efficient chemical or enzymatic depolymerization processes will likely establish eugenol as an economically realistic feedstock with a relatively low market price in a near future.⁴⁻⁷ This biocompatible compound has found numerous applications in areas such as cosmetics, fragrance and pharmaceuticals.⁸ For example, it has been widely used in dental materials for its antibacterial, analgesic and anti-inflammatory properties.^{9,10} Eugenol is also intensively investigated as a feedstock for the development of functional polymer materials. Eugenol and eugenol-derived compounds, such as isoeugenol, dihydroeugenol or vanillin, are potential natural substitutes for rigid aromatic monomers.⁴ For example, two common pathways allow the preparation of eugenol-containing epoxide monomers. First, Eugenol glycidyl ether (EGE) has been synthesized by reacting the phenolic hydroxyl group of eugenol with epichlorhydrin (glycidylation), a chemical that can be produced from renewable glycerin, for example according to the Epicerol® technology of TechnipFMC.^{11,12} EGE has been used as reactive diluent in order to lower the viscosity of epoxy resin formulation and extend onset of network formation without changing the glassy phase modulus.¹³ Secondly, epoxydized eugenol has been prepared in high yield by epoxidation of the eugenol allyl group.¹⁴

Numerous research papers are dealing with the preparation of various eugenol-containing thermosets. For example, eugenol derivatives containing more than one epoxy group are excellent non-toxic building blocks candidates for the substitution of the endocrine disrupting diglycidylether of bisphenol A (DGEBA) in the preparation of epoxy thermosets. The resulting networks often exhibit excellent thermo-mechanical properties similar to the ones from petroleum-based DGEBA counterparts.¹⁴ Alternatively, eugenol derivatives, such as glycidyl ether eugenol or allyl-etherified eugenol derivatives, have been cured in the presence of multi-functional thiols by simultaneous thiol-

ene / thiol-epoxy click reactions.¹⁵⁻¹⁸ Glycidyl ether eugenol was also used to prepare hybrid non-isocyanate polyurethane thermosets.¹⁹ Ultimately, a large variety of structurally diverse eugenol-containing thermosets displayed various promising properties, such as high thermal stability^{20, 21} low electric permittivity and flame retardancy,²² or antibacterial properties.²³

Although eugenol-based monomers have been mostly incorporated in thermosetting polymers, some research works have reported the synthesis of linear thermoplastic polymers. Several examples can be found where Eugenol derivatives have been used in step growth polymerizations, resulting in various polymer backbone natures, such as aromatic polyesters,²⁴ poly(ester-thioether)s,²⁵ polycarbonates,²⁶ or poly(anhydride)s.²⁷ However, polycondensation reactions only enable a limited control of the polymer structure with high dispersities and no control of the chain ends. Eugenol-based monomers have been scarcely used in chain-growth polymerization. The use of eugenol allyl bond directly as polymerizable group is rather uncommon. High-dispersity copolymers of ethylene and eugenol with antibacterial properties were prepared by coordination polymerization using a palladium aryl sulfonate catalyst.²⁸ Alternatively, eugenol was functionalized with other polymerizable groups, such as alkyne or methacrylate groups. Polyacetylenes bearing eugenol lateral substituents were synthesized by coordination polymerization of a monomer obtained by the reaction of propargyl chloride with eugenol.²⁹ The free-radical (co)polymerization reaction of eugenyl methacrylate or ethoxyeugenyl methacrylate has been reported for the preparation of orthopedic and dental cements.⁹ For conversion higher than 10%, insoluble networks were obtained due to the additional involvement of eugenol allyl group in the radical polymerization. Eugenol-containing methacrylate monomers were also used in suspension radical polymerization technique to prepare oil-absorbent or aldehyde containing microspheres.^{30, 31} In those cases as well, the cross-linking was made possible by the presence of the allyl bond. Polymeric nanoparticles of the Poly(DMA-co-EMA) with antibacterial and adhesion properties were synthesized by free radical precipitation polymerization of dopamine methacrylamide and eugenyl

methacrylate.¹⁰ Recently, Molina-Gutiérrez et al. studied the free radical homopolymerization of eight eugenol-derived (meth)acrylate monomers in toluene.³²

All these previously reported polymerizations of eugenol-derived monomers were poorly controlled and led to ill-defined polymer chains. Up to date, the use of eugenol as the building block for the preparation of well-defined polymers has been rarely reported. Only two examples of ring-opening copolymerization of eugenol-based epoxide monomers have also been reported. Hu et al. demonstrated that eugenol glycidyl ether could copolymerize with carbonyl sulfide to afford sustainable poly(monothiocarbonate) having a high refractive index and potential application as optical materials.³ Very recently, a series of promising 100% bio-based polyesters has been prepared by the alternating ring-opening copolymerization of eugenol glycidyl ether with cyclic anhydrides.³³ The authors have also demonstrated that the pendant allyl groups provided an additional versatility for further functionalization and the resultant polyesters backbone was potentially biodegradable. However, this method provides a limited control over the polymerization and requires high temperatures and the use of chromium complex catalysts.

Well-defined polyesters originated from renewable resources are very attractive materials for the preparation of environmentally-friendly and potentially biodegradable products. Our group recently reported the synthesis of well-defined poly(ester-*alt*-thioether) by organo-catalyzed anionic ring-opening copolymerization of N-acetyl homocysteine thiolactone (NHTL) and various epoxides under mild conditions. NHTL is commercially-available at relatively low cost and can be synthesized from renewable resources. Thus, the resulting poly(ester-*alt*-thioether)s are partially bio-based. In this paper, we report the synthesis of fully bio-based poly(ester-*alt*-thioether)s by the alternating AROP of NHTL with eugenol glycidyl ether (EGE), dihydroeugenol glycidyl ether (DEGE) and vanillin glycidyl ether (VGE). This study was conducted to assess the feasibility of this polymerization pathway with such biobased monomers under different experimental conditions. In particular, the

influence of the initial monomer ratio has been carefully studied. And the copolymer structures and thermal properties have been carefully characterized.

DISCUSSION

Table 1. Experimental conditions and molecular characteristics of poly(thioether-*alt*-ester)s synthesized by alternating ring-opening polymerization of bio-based NHTL with eugenol and vanillin epoxide derivatives using benzyl alcohol and BEMP as initiating system.

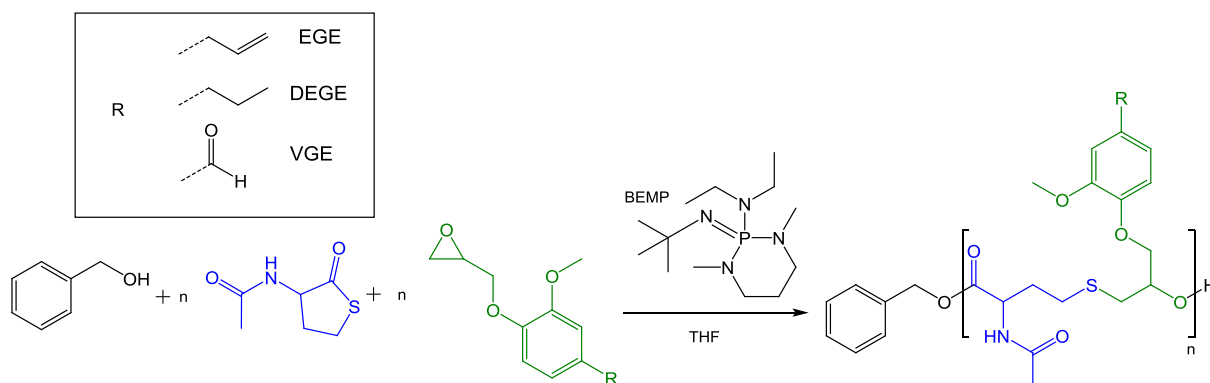
Run	Epoxide	Solvent	ROH ^a :BEMP:NHTL ^b :Epoxide	T° [°C]	Time [h]	Cv NBTL [%]	Cv Epo [%]	M _{n, th} [g mol ⁻¹]	M _{n, NMR} [g mol ⁻¹]	M _{n, SEC} ^c [g mol ⁻¹]	Đ
1	-	THF	1:1:25:0	55	24	-	-	-	-	-	-
2	DEGE	THF	1:1:0:25	55	24	-	-	-	-	-	-
3	EGE	THF	1:1:0:25	55	24	-	-	-	-	-	-
4	VGE	THF	1:1:0:25	55	24	-	-	-	-	-	-
5	DEGE	-	1:1:24:23	100	1	90	89	7850	8035	3550	2.12
6	DEGE	THF	1:1:23:22	55	5.5	88	90	7600	7500	4400	1.47
7	DEGE	THF	1:1:23 ^d :23	55	24	68	64	5750	6400	4000	1.49
8	EGE	THF	1:1:23:23	55	17	97	93.5	8500	7600	4300	1.60
9	DEGE	THF	1:1:12:12	55	2.25	91	89	4350	4300	3400	1.28
10	DEGE	THF	1:1:47:47	55	46.5	84	90	15100	15800	6200	1.39
11	EGE	THF	1:1:50:46	45	7	77	89	14680	14550	5650	1.67
12	EGE	THF	1:1:54:50	40	24	92	99	18950	11100	10800	1.34
13	DEGE	THF	1:1:17.6:8.6	55	2	43	92	2950	2550	2400	1.20
14	DEGE	THF	1:1:35:17	55	23	45	92	6180	6250	4100	1.20
15	EGE	THF	1:1:32:16	55	6	49	96	5600	5485	3900	1.31
16	DEGE	THF	1:1:17:35	55	6	95	46	6250	5900	2250	1.42
17	EGE	THF	1:1:16:33	55	6	99	48	6200	5500	1150	1.44
18	DEGE	-	1:1:35:18	100	2	52	100	6800	7100	4600	1.82
19	VGE	THF	1:1:23:25	55	4	73	89	5750	6200	2700	1.77
20	VGE	THF	1:1:24:24	55	4	75	82	6300	5100	2350	1.71
21	VGE	THF	1:1:50:44	45	23	56	69.5	10300	10750	2600	1.54

^a ROH = benzyl alcohol.

^b [NHTL]₀ = 1.05 mol.L⁻¹.

^c Determined by SEC (THF, 40°C, poly(methyl methacrylate) standards).

^d [NHTL]₀ = 0.72 mol.L⁻¹.



Scheme 1. Synthesis of poly(thioether-*alt*-ester)s synthesized by alternating ring-opening polymerization of bio-based NHTL with eugenol and vanillin epoxide derivatives using benzyl alcohol and BEMP as initiating system.

Question Montpellier : Faut-il écrire une ou deux phrase sur la synthèse du DEGE et de l'EGE ou faut-il juste citer une précédente publication ? DEGE and EGE have been synthesized according to .REF

DEGE and EGE have been synthesized according to Ecochard *et al.* procedure (ref19) with a supplementary purification step by flash chromatography to obtain highly pure monomers for the ring-opening polymerization.

As reported in Table 1, no homopolymerization of NHTL (Table 1, run 1), DEGE (Table 1, run 2), EGE (Table 1, run 3) and VGE (Table 1, run 4) occurred in THF at 55°C using benzyl alcohol - BEMP as initiating system. These results are in agreement with our previous work.³⁴ A first copolymerization attempt between NHTL and DEGE was carried out in the bulk at 100°C with a [OH]:[BEMP]:[NHTL]:[Epoxide] = 1:1:24:23 ratio (Table 1, run 5). No extensive drying protocol was applied to the monomers: NHTL was used as received from Sigma-Aldrich and DEGE was only dried under vacuum after its synthesis. The water contents of THF and the monomers was determined by coulometric Karl Fischer titrations, showing that monomers contained significant amounts of water (Table S1). In addition, all the reactants and the solvent were introduced under air in the polymerization reactor. It is interesting to note that although the reaction was performed without taking any special precautions, almost full monomer conversions were obtained after only 1 h (an example of monomer conversion calculation using reaction mixture ¹H NMR is given in Figure S4).

The experimental number-average molar mass (M_n) determined by ^1H NMR end-group analysis is in excellent agreement with the theoretical one, demonstrating a quantitative initiation by benzyl alcohol. However, the M_n determined by SEC (Figure 1.A, blue trace) is far lower than the theoretical one and the dispersity is high ($\mathcal{D} = 2.12$). This phenomenon has been previously found for the alternating ring-opening copolymerization of thiolactone with epoxides and was explained by undesired chain transfer reactions to water molecules and by transesterification reaction between the propagating alcoholate species and the ester groups of the main chain.^{34, 35} In order to reduce the occurrence of side reactions, one solution is to add solvent and to decrease the reaction temperature.

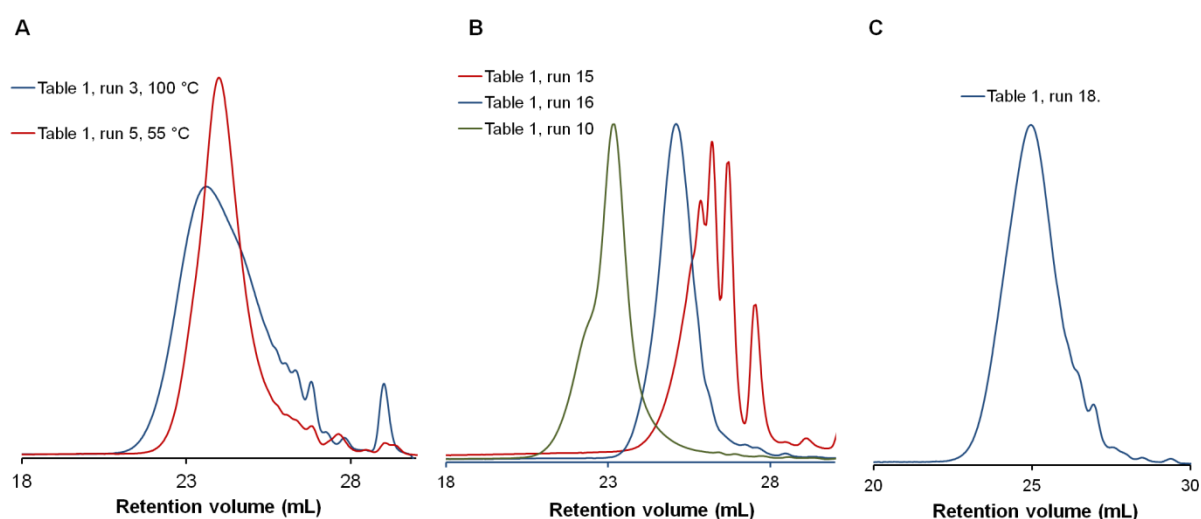


Figure 1. A) SEC profiles in THF of poly(NHTL-*alt*-DEGE) initiated by benzyl alcohol-BEMP synthesized in the bulk at 100 °C (blue trace), in THF at 55 °C (red trace); B) SEC profiles in THF of poly(NHTL-*alt*-EGE) initiated by benzyl alcohol-BEMP in THF at 55 °C using a [OH]:[BEMP]:[NHTL]:[Epoxide] equal to 1:1:16:33 (red trace, Table 1, run 17), to 1:1:32:16 (blue trace, Table 1, run 15) and to 1:1:54:50 (green trace, Table 1, run 12); C) SEC profile in THF of poly(NHTL-*alt*-VGE) initiated by benzyl alcohol-BEMP synthesized in THF at 55 °C (Table 1, run 20).

Thus, a NHTL-DEGE copolymerization with an identical reactant ratio was performed in THF at 55 °C (Table 1, run 6). As expected, a longer reaction time was required to reach similar monomer conversions. Compared to the polymerization in the bulk, the resulting copolymer exhibits a lower molar mass distribution (Figure 1.A). A better agreement is also observed between the theoretical and experimental molar masses, even if a mass discrepancy is still present. The same reaction was

performed at lower monomer concentration, but no significant improvement could be noticed (Table 1, run 7). A copolymerization between NHTL and EGE was performed under the same reaction conditions leading to comparable results (Table 1, run 8). The obtained copolymers were characterized by ^1H , ^{13}C , COSY and HSQC NMR and display spectroscopic data consistent with the ring-opened alternating structures. All signals could be assigned and are provided directly on the spectra in Figures 2 and S5-S7 for poly(NHTL-*alt*-DEGE) and Figures S8-S11 for poly(NHTL-*alt*-EGE). After polymer purification by dialysis, using a membrane with a cutoff value of 1000 Da, the signals associated with the protons of benzyl alcohol initiator are still observed. For all the copolymers produced by the copolymerization of NHTL with DEGE or EGE, the NHTL/DEGE or NHTL/EGE unit ratios were found to be very close to 1/1 and no conspicuous signals assignable to ether linkage can be observed. In addition, the intensity of the signals corresponding to the -CHR- of oxirane units in alpha position of ester groups (at 5.28 ppm for poly(NHTL-*alt*-DEGE) and at 5.29 ppm for poly(NHTL-*alt*-EGE)) correspond to the values expected for strictly alternating structures. The presence of alternating units were further supported by the ^{13}C NMR spectrum of poly(NHTL-*alt*-EGE) (Figure S9), where no characteristic resonance of the ether linkages in the range of 75–85 ppm was observed. The NH of the lateral acetamido groups have very large ^1H NMR signals between around 6.6 and 7.6 ppm as demonstrated by ^1H - ^{15}N HSQC NMR spectrum in Figure S12.

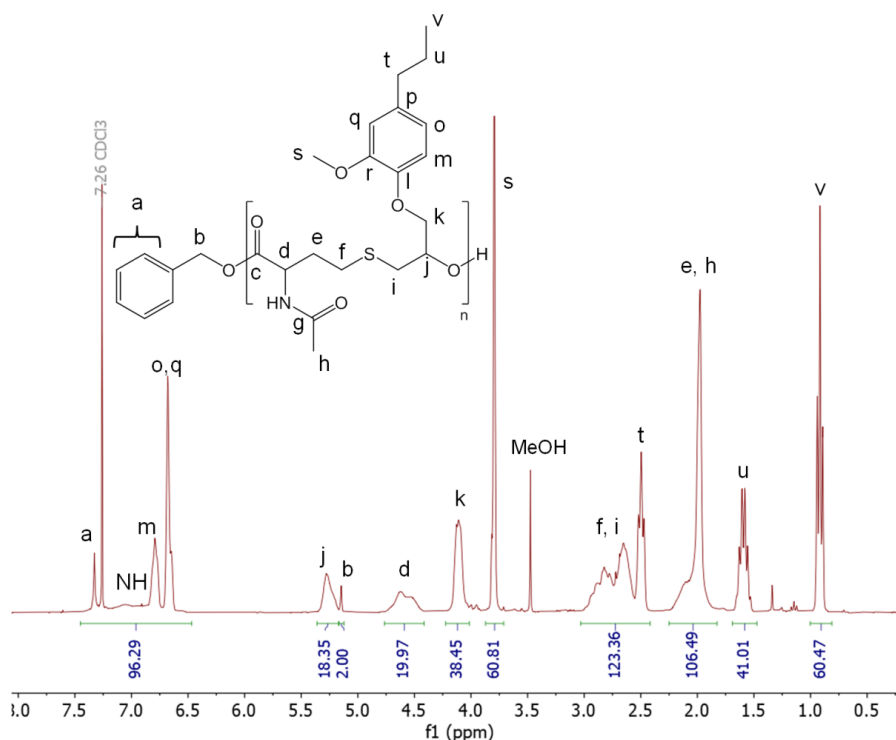


Figure 2. ^1H NMR spectrum of poly(NHTL-*alt*-DEGE) in CDCl_3 at 25°C (Table 1, run 6).

The effect of feed ratio of the two monomers on the copolymer structures was analyzed. For all the copolymerization reactions of NHTL with DEGE or EGE that were performed with stoichiometric amounts of thiolactone and epoxide, the final monomer conversions of both monomers are equal (Table 1, runs 5-12). In the case of the copolymerization of 23 equivalents of NHTL with 23 equivalents of DEGE at 55°C (Table 1, run 7), the conversions of both monomers were plotted against reaction time in Figure 3.A. As expected for strictly alternating copolymerization, they increased equally throughout the polymerization. When the copolymerization of NHTL and oxiranes were performed under different feed ratios (Table 1, runs 13-18), the molar consumptions of both monomers remained strictly equal as shown in Figures 1.B and 1.C. The nature of the monomer in excess does not interfere with the alternating mechanism. However, when alternating copolymerizations were carried out in the presence of a large excess of oxiranes (Table 1, run 16 and 17), lower M_n and higher Đ were obtained compared to alternating copolymerizations having similar targeted M_n but which were performed in the presence of a large excess of thiolactone (Table 1, run 14 and 15). For the alternating copolymerization of NHTL with EGE, the SEC profiles in the presence

of an excess of EGE (red trace) or an excess of NHTL (blue trace) have been superimposed in Figure 1.B.

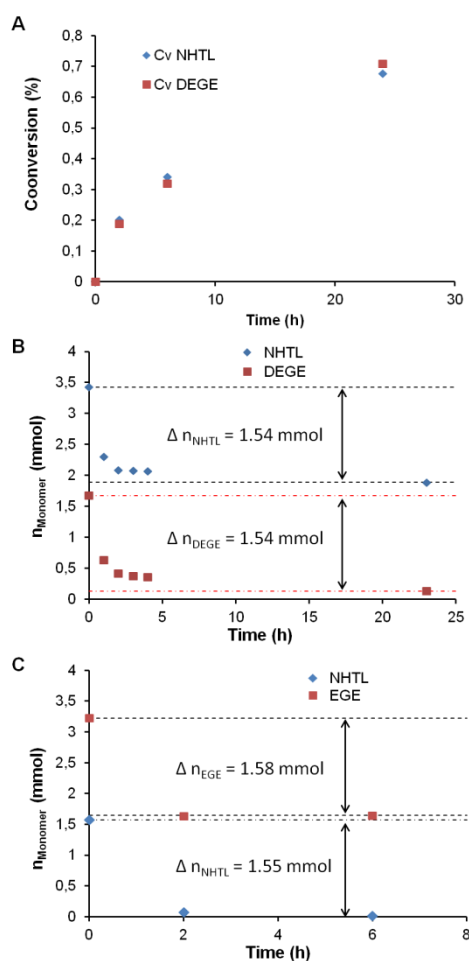


Figure 3. A) Time-conversion of the copolymerization of equivalent amounts of NHTL (2.22 mmol) and DEGE (2.20 mmol) using benzyl alcohol-BEMP as initiating system (0.97 mmol) in THF at 55°C (Table 1, run 7); B) Monomer amounts as a function of time of the copolymerization of NHTL (3.42 mmol) and DEGE (1.67 mmol) using benzyl alcohol-BEMP as initiating system (0.97 mmol) in THF at 55°C (Table 1, run 14); C) Monomer amounts as a function of time of the copolymerization of NHTL (1.57 mmol) and EGE (3.22 mmol) using benzyl alcohol-BEMP as initiating system (0.97 mmol) in THF at 55°C (Table 1, run 17).

In order to increase the M_n of the copolymers, X_n values of 100 were targeted (Table 1, runs 10-12). In all cases, the experimental M_n determined by SEC were significantly lower than the theoretical ones. Nevertheless, M_n higher than 10 000 $\text{g}\cdot\text{mol}^{-1}$ was achieved for the copolymerization of NHTL and EGE performed at 40°C in the presence of a slight excess of NHTL (Table 1, run 12).

Lastly, the copolymerization of vanillin glycidyl ether (VGE) was carried out using 1:1:25:25 (Table 1, runs 19 and 20) or 1:1:50:44 (Table 1, run 21) $[\text{OH}]_0:[\text{BEMP}]_0:[\text{NHTL}]_0:[\text{Epoxide}]_0$ ratios. VGE is a very promising bio-based monomer due to the presence of an aldehyde moiety on the aromatic ring. The synthesis of polymers bearing multiple aldehyde lateral substituents is of particular interest for further postpolymerization modification based on a large variety of chemical reactions under mild conditions.^{36, 37} However, the synthesis of polymer chains bearing highly reactive aldehyde lateral substituent by anionic polymerization remains challenging and usually requires protection and deprotection steps.³⁸ The copolymerization of NHTL and VGE occurred without functional protection. The structure of poly(NHTL-*alt*-VGE) was verified by FTIR and NMR spectroscopy (Figures 4 and S13-S16). The ^1H NMR spectrum in Figure S13 clearly shows the signal of the aldehyde proton at 9.8 ppm, the same shift as the one of the monomer (Figure S3). The integration area ratio of aldehyde proton vs the aromatic methoxy group in vanillin unit was 1.00:3.26 (to compare with 1.00:3.13 for the monomer) illustrating the essential absence of side-reaction on the aldehyde functionalities. The stability of the aldehyde groups can also be seen by the presence of the NMR peak at 190.99 ppm corresponding to the carbonyl in the ^{13}C and HSQC NMR spectra (Figures S14 and S15). In addition, the FTIR spectrum shows a carbonyl band at 1677 cm^{-1} (Figure 4e), a value in agreement with α , β -unsaturated aldehydes, which is also visible in the FTIR spectrum of the monomer at 1682 cm^{-1} (Figure 4d).³⁹ However for all the copolymerization with VGE, only low molar-mass polymer chains ($\leq 2700\text{ g}\cdot\text{mol}^{-1}$) have been measured by SEC (Figure 1.C). According to the technical data sheet of commercial VGE, its epoxy content is only 0.0040 eq/g while the theoretical value is 0.0048 eq/g for pure VGE. Thus, aromatic alcohols resulting from unmodified vanillin could act as additional initiator during the polymerization and strongly limit the achievable M_n .

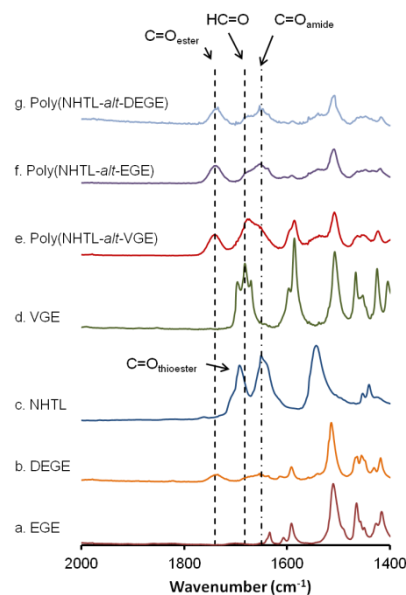


Figure 4. ATR-FTIR analysis of: a) EGE; b) DEGE; c) NHTL; d) VGE; e) Poly(NHTL-*alt*-VGE) (Table 1, run 19); f) Poly(NHTL-*alt*-EGE) (Table 1, run 8); g) poly(NHTL-*alt*-DEGE) (Table 1, run 6).

Table 2. Thermal properties of the alternating copolymers.

Entry	Run	Chemical nature	$T_{d,10\%}$ [°C] ^a	T_{dm} [°C] ^b	T_g [°C]	Char yield (%)
1	Table 1, run 5	poly(NHTL- <i>alt</i> -DEGE)	285	310	31	8.9
2	Table 1, run 6	poly(NHTL- <i>alt</i> -EGE)	283	302	28	11.9
3	Tables 1, run 17	poly(NHTL- <i>alt</i> -VGE)	273	288	46	24.5
4	-	poly(NHTL- <i>alt</i> -PhGE) ^c	286	313	35	9.7

^a Decomposition temperature after 10% weight loss.

^b Decomposition temperature at maximum degradation rate (derivative thermogravimetry).

^c Results from Illy et al.

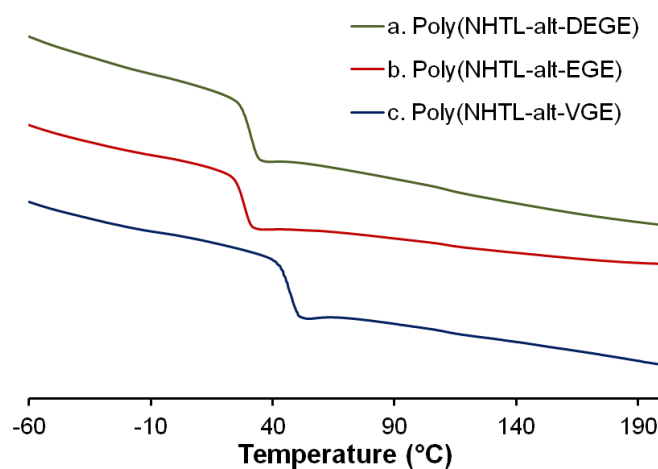


Figure 5. DSC curves of second heating scans at 10 °C/min: a) poly(NHTL-*alt*-DEGE); b) poly(NHTL-*alt*-EGE) and c) poly(NHTL-*alt*-VGE).

TGA and TGA derivative curves of poly(NHTL-*alt*-DEGE), poly(NHTL-*alt*-EGE) and poly(NHTL-*alt*-VGE) are shown in Figures S17-S19. The thermal properties (decomposition temperature after 10% weight loss and decomposition temperature at maximum degradation rate) are outlined in Table 2. All the copolymers exhibit single-step narrow degradation curves with $T_{d,10\%}$ in the range 273-285 °C. The substituent change on the aromatic group does not obviously change the thermal stability of the polymers. The low molar mass of poly(NHTL-*alt*-VGE) has probably to be taken into account when considering the slightly lower $T_{d,10\%}$. The good thermostability of the bio-based alternating copolymers is similar to the one of poly(NHTL-*alt*-PhGE), an alternating copolymer synthesized using petro-based phenyl glycidyl ether (PhGE).³⁴ More generally, similar degradation temperatures have been observed for polymers containing thioether bonds in their backbone, suggesting that carbon-sulfur bond is the weakest linkage in the structure.^{26, 40} The remaining residual weights of poly(NHTL-*alt*-DEGE) and poly(NHTL-*alt*-EGE) at 600°C are equal to 8.0 and 11.9 %, respectively. Linear aliphatic sections are known to decompose almost completely compared to double bonds and aromatic sections under the same TGA conditions.²⁵ The difference between the char yields is consistent with the presence of an allyl group in para position of the aromatic ring in the case of EGE instead of a propyl group in the case of DEGE. In comparison, poly(NHTL-*alt*-VGE) has a higher char yield (24.5 %), more than twice the value of the other alternating copolymers, which is probably due to thermal cross-linking reaction between aromatic aldehyde and aromatic groups.⁴¹ The thermal behaviors of the copolymers were studied by DSC at a 10°C min⁻¹ heating and cooling rate. The second heating DSC curves measured from -60 to 200°C are shown in Figure 5, and the corresponding thermal data are summarized in Table 2. All copolymers are amorphous with no indication of melting temperatures (up to 200 °C), exhibiting clear glass transition temperatures T_g . Melting temperatures were not expected since achiral monomers (epoxides and thiolactone) and initiating system were employed. In addition, the existence of methoxy group on the aromatic ring is detrimental to the structural symmetry. The T_g of poly(NHTL-*alt*-DEGE) ($T_g = 31^\circ\text{C}$) and poly(NHTL-*alt*-EGE) ($T_g = 28^\circ\text{C}$) are slightly lower than the one of poly(NHTL-*alt*-PhGE) ($T_g = 35^\circ\text{C}$). The presence of substituents on

the aromatic rings could increase the steric hindrance and interfere with the formation of hydrogen bonds between amide and carbonyl groups. On the contrary, poly(NHTL-*alt*-VGE) has a higher T_g (46°C) due to the presence of aromatic aldehydes, which are polar groups and thus, can participate to the formation of hydrogen bonds and dipole-dipole interactions.

CONCLUSION

This study introduces a new family of thermoplastic polymers based on sustainable phenols, one of the most abundant bio-based feedstock on earth. A series of fully renewable linear poly(ester-*alt*-thioether)s were synthesized via the alternating ring-opening copolymerization of NHTL with eugenol-based epoxides using benzyl alcohol-BEMP as initiating system. The polymerization process is organo-catalyzed and atom-economical, it occurs in the presence of moisture and air at moderate temperatures from readily accessible monomers. Copolymers with strictly alternating structures, moderate molar masses and rather low dispersities are obtained in high yields. These alternating copolymers are amorphous materials with T_g higher than ambient temperature. In addition, it is worth noting that the copolymerization develops a facile approach for synthesizing allyl- or aldehyde-functionalized bio-based polyesters without any protection/deprotection steps. Poly(NHTL-*alt*-EGE) and poly(NHTL-*alt*-VGE) scaffolds are reactive platforms that could be further functionalized using a wide range of mild chemical reactions. In particular, the ability to control VGE polymerization is currently under investigation, as we believe that this kind of biobased copolymers bearing multiple aldehydes is particularly promising for bioconjugation or hydrogel formation.

EXPERIMENTAL PART

Materials. Phosphazene base 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP) solution (1.0 mol.L⁻¹ in hexane, Sigma-Aldrich), benzyl alcohol (99.8 % anhydrous, Sigma-Aldrich), DL-*N*-Acetylhomocysteine thiolactone (98%, Sigma-Aldrich), eugenol (99

%, Sigma-Aldrich), dihydroeugenol (99 %, Sigma-Aldrich), epichlorohydrin (99 %, Sigma-Aldrich), benzyltriethylammonium bromide (99 %, Sigma-Aldrich) and vanillin glycidyl ether (Specific Polymers) were used as received. Vanillin monoglycidyl ether. THF was dried with an MBRAUN MB SPS-800 solvent purification system under nitrogen.

Instruments. ^1H , ^{13}C NMR and ^1H - ^{15}N HSQC spectra were recorded in CDCl_3 or CD_3COCD_3 using a Bruker 400 MHz NMR spectrometer. IR spectra were collected using a Perkin-Elmer Spectrum1000 FTIR infrared spectrometer with a diamond ATR probe. Size Exclusion Chromatography Experiment (SEC) were carried out on three PL gel Mixed-C $5\mu\text{m}$ columns ($7,5 \times 300$ mm; separation limits: 0,2 to $2000 \text{ kg}\cdot\text{mol}^{-1}$) maintained at 40°C and sample Viscotek GPCmax delivery module and 2 modular detectors: a Viscotek 3580 differential refractive index (RI) detector and a Shimadzu SPD20-AV diode array UV detector. THF was used as the mobile phase at a flow rate of $1 \text{ mL}\cdot\text{min}^{-1}$, toluene was used as a flow rate marker. All polymers were injected ($50 \mu\text{L}$) at a concentration of $5 \text{ mg}\cdot\text{mL}^{-1}$ after filtration through a $0.45 \mu\text{m}$ pore-size membrane. The OmniSEC 4.6.2 software was used for data acquisition and analysis. Number-average molar masses (M_n), weight-average molar masses (M_w) and dispersities were determined by SEC with a calibration curve based on poly(methyl methacrylate) standard, using the RI detector. The thermal decomposition was evaluated by thermogravimetric analysis (TGA) using a TA Q50 apparatus. Data were collected using a $20^\circ\text{C}/\text{min}$ ramp to 600°C . The experiment was run under a stream of nitrogen. DSC measurements were carried out using a TA DSC Q2000 calibrated with indium standard. Sample (ca 15 mg) was placed in an aluminum cell and initially cooled at -70°C . Two heating ($10 \text{ K}\cdot\text{min}^{-1}$) - cooling ($10 \text{ K}\cdot\text{min}^{-1}$) cycles were then applied in the -70 to 200°C temperature range.

General copolymerization procedure. The copolymerization was carried out according to the following typical procedure. 0.3435 g of NHTL (2.157 mmol), 0.5023 g of DEGE (2.260 mmol) and 1.0 mL of THF were introduced into a polymerization tube fitted with a natural rubber folding skirt stoppers. Then, $10 \mu\text{L}$ of benzyl alcohol (0.097 mmol) and $100 \mu\text{L}$ of BEMP solution (0.100 mmol)

were added through the septum using microsyringes. Then, the reaction mixture was stirred at 55 °C and left to react for the required period of time. The progress of the reaction was monitored by removing samples from the polymerization reactor through a septum at various reaction times for ¹H NMR analyses. After removing residual monomers and solvent by rotary evaporation, the polymer was dissolved in methanol and dialyzed in cellulose ester membrane (Repligen Spectra/Por 6 dialysis tubing, flat width = 45 mm, molecular cutoff = 1 kDa) against methanol for 24 hours. After removing the solvent under vacuum at 50 °C a white solid was obtained. Yield: 85 %. Deviations from this general procedure are summarized in Table 1.

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