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Julien Crozzolo, Georges Formon, Mickaël Pomes-Hadda, Stefano Aime, Stéphane Jouenne, et al.. Associative and Thermoresponsive Aqueous Polymer Formulations Based on Imine Chemistry. ACS Applied Polymer Materials, 2022, 4 (6), pp.4274-4285. 10.1021/acsapm.2c00239 . hal-03773518

HAL Id: hal-03773518

<https://hal.science/hal-03773518v1>

Submitted on 9 Sep 2022

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Associative and thermoresponsive aqueous polymer formulations based on imine chemistry

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ABSTRACT: Controlling the flow properties of aqueous formulations is essential in fields as diverse as biotechnology, cosmetics, paints, or chemically enhanced oil recovery, to cite a few. This work presents a study of the association, in aqueous solutions, of complementary polyacrylamides carrying amino and aryl aldehyde side-groups. Through free radical polymerization, copolymers with tunable molar masses (M_n ranging from 60 to 370 kg.mol⁻¹), functionality (2 to 17 mol%) and permanent charge degrees (0 to 98 mol%) were obtained. Imine formation was studied on model systems consisting of amino polyacrylamides and a benzaldehyde derivative. It was found that the presence of permanent charges on the amino polyacrylamide does not prevent imine formation, but influences the association degree. In addition, imines were efficiently formed in the presence of NaCl and the dynamic crosslinks proved to be thermoresponsive, with a reversible displacement of the equilibrium towards amine and aldehyde

with increasing temperature. The associative formulations were subsequently studied by rheology. It was shown that the functionality, the charge degree, and the molar mass of the copolymers can be used to rationally manipulate inter-chain association, which proved to be a powerful tool to control the viscosity and rheological profile of the different formulations. Dynamic light scattering was utilized to further study the microstructural dynamics of one of the formulations, showing good agreement with rheology. Finally, taking advantage of the influence of temperature on the imine crosslinks, a thermoresponsive hydrogel was prepared, that undergoes reversible sol-gel transition over multiple heating-cooling cycles between 30 and 80 °C.

KEYWORDS: imine, aqueous formulations, associative polymers, dynamic covalent bonds, thermoresponsive hydrogels

INTRODUCTION

More and more applications require the use of materials capable of adapting to their environment and/or to self-heal when damaged.¹⁻² It is therefore often necessary to design materials that can reorganize or change properties under the effect of stimuli.³⁻⁵ As a result, the field of stimuli-responsive polymers has received considerable interest over the past decade. In the context of organic materials, the static and permanent character of most covalent bonds limits this adaptability. However, several approaches have been developed to modulate the connectivity between polymer chains in order to design stimuli-associative (pH-⁶⁻⁷, redox-,⁸ temperature-,⁹ photo-responsive¹⁰⁻¹¹) and drug delivery systems,^{6,12-13} or self-healing¹⁴⁻¹⁵ and recyclable materials.¹⁶⁻¹⁷ When it comes to associative polymer formulations, reversible physical interactions (H-bonds, π - π interactions, hydrophobic interactions, metal-ligand coordination, macrocyclic

host–guest complexation)¹⁸⁻²³ and dynamic covalent bonds^{4-5,24} have been used to modulate inter-chain associations. The dynamic nature of these interactions allows the system to reorganize and adapt to its environment under certain conditions.

For example, associative systems are a powerful tool to modulate the flow properties of formulations,²⁵⁻²⁷ and in particular aqueous formulations, which is essential in fields as diverse as medicine and biotechnology, cosmetics, paints, or chemically enhanced oil recovery, to cite a few. In the case of chemically enhanced oil recovery for example, which consists in displacing the oil present in the petroleum reservoir by viscosified water, high molar mass polymers suffer from mechanical degradation when they are injected at high flow rate into the rock porous underground.²⁸⁻²⁹ Increasing the viscosity through the association of shorter polymer chains would alleviate this problem.³⁰⁻³¹

In the past thirty years, numerous water-soluble associative polymer systems relying on hydrophobic interactions have been reported.³²⁻³⁶ Among them, hydrophobically-modified polyacrylamides (HMPAM),³⁷⁻³⁸ hydrophobically-modified ethoxylate urethanes (HEUR)³⁹⁻⁴¹ and hydrophobically-modified alkali-soluble emulsions (HASE)⁴²⁻⁴³ have probably been the most extensively studied, with reports detailing the influence of the length, content and structure of the hydrophobic grafts on the rheological properties of the formulations. A number of dynamic covalent chemistries, including imine,^{6,44-45} acylhydrazone,^{18,22,46-47} oxime,⁴⁸ disulfide^{44,47,49} boric and boronic acid⁵⁰⁻⁵² chemistries, or Diels-Alder cycloaddition^{13,53-54} have also been successfully used to design associative polymers in aqueous solutions, largely focusing on reversible, injectable or self-healing hydrogels.

The design of associative polymers relying on dynamic covalent chemistry to control the flow properties of aqueous solutions requires to consider the ease and modularity of synthesis of the

functional polymers, as well as the stability and dynamics of the reversible covalent links. To be of the greatest possible interest, these systems should be easily accessible from a synthetic point of view, impact the viscosity of the formulations at low polymer concentrations, operate without the need to adjust the pH with exogenous compounds and be operational in the presence of salt. Taking into account all these requirements, we aimed at developing associative complementary water-soluble polymers carrying aryl aldehyde and amino side-groups, which can reversibly associate through the formation of imine crosslinks. Such copolymers were synthesized by free radical polymerization (FRP) of acrylamides bearing aryl aldehyde or amine functions with charged and/or neutral commercially available acrylamides, which offers a simple and robust method to directly prepare water soluble copolymers with varying functionality, composition, and molar mass. The influence of the polymer composition, pH, presence of salt and temperature on imine formation was first studied on model aqueous formulations consisting of amino functional polyacrylamides and a water-soluble benzaldehyde derivative. Associative formulations containing the amino and aryl aldehyde functional polyacrylamides were then studied by rheology and dynamic light scattering (DLS). Hydrogels were also prepared from the complementary copolymers, and the aptitude of the system to undergo a thermally induced reversible gel to sol transition was evaluated.

EXPERIMENTAL

Materials

Unless otherwise stated, reagents and solvents were commercially available and used without further purification. *N,N*-Dimethylacrylamide (DMAM, 99%) was purified by passing through a column filled with neutral alumina to remove the inhibitor (monomethyl ether hydroquinone, MEHQ). 2,2'-Azobis(2-methylpropionitrile) (AIBN) was recrystallized twice from methanol.

Methods

Nuclear magnetic resonance (NMR) spectroscopy. ^1H NMR spectra were recorded either at 297, 303 or 353 K on a Bruker AVANCE 400 spectrometer at 400 MHz and referenced to the residual solvent peaks (δ 7.26 for CDCl_3 , δ 4.79 for D_2O). ^{13}C NMR spectra were recorded at 297 K on a Bruker AVANCE 400 spectrometer at 100 MHz and referenced to the residual solvent peaks (δ 77.16 for CDCl_3). When studying the influence of the temperature on imine formation, the formulations were equilibrated at 30 or 80 °C for 15 min before each measurement.

Size exclusion chromatography (SEC). SEC analyses were conducted with a Malvern Omnisec equipment, composed of an Omnisec Resolve for the separation (columns set: Aq. Guard+A3000+A6000+A7000) and an Omnisec Reveal for the detection (refractometer, viscosimeter, static light scattering at 7 and 90° and UV detector). NaNO_3 0.2 mol.L^{-1} was used as the eluent, with 200 ppm amount of NaN_3 as anti-bacterial agent, at a flow rate of 0.8 mL.min^{-1} . Molar masses (M_n and M_w) and dispersities (D) of isolated polymers were obtained by triple detection.

Rheological characterization. Rheological measurements at room temperature were performed on an Anton-Paar MCR302 rheometer equipped with a Peltier system using a cone-plate geometry (diameter 50 mm, angle 2°). Flow curves were obtained for viscous solutions by applying a shear rate from 0.1 to 1000 s^{-1} . Frequency sweep measurements were performed on hydrogels with an angular frequency ranging from 0.1 to 100 rad.s^{-1} and a constant shear strain of 1%. When rheological measurements were performed above room temperature, an oil bath was used to limit the water evaporation.

Dynamic Light Scattering. DLS measurements were performed with a home-made small-angle light scattering setup.⁵⁵ A collimated He-Ne laser (wavelength $\lambda = 632 \text{ nm}$) is used to illuminate

the sample, and an optical setup is used to collect the scattered light on a CMOS camera (Basler acA2000-340km). In particular, the camera records images of the so-called far field speckle field, with different scattering angles, θ , separated in distinct annular regions of the captured image. Each scattering angle is associated to a scattering vector, $q=(4\pi n/\lambda)\sin(\theta/2)$, n being the refractive index of the medium,⁵⁶ which sets the length scale probed by DLS. For each annular region, we process the time fluctuations of the scattered intensity through the time correlation function $g_2(q,\tau)=\langle I(t)I(t+\tau)\rangle_q/[\langle I(t)\rangle_q\langle I(t+\tau)\rangle_q]$, where $I(t)$ is the intensity recorded at time t and $\langle \dots \rangle_q$ denotes averages on pixels belonging to the annular region associated with a specific scattering vector q .⁵⁷

Mass spectrometry. Mass spectra with electronic impact (MS-EI) were recorded on a gas chromatograph–mass spectrometer.

Samples preparation for rheology measurements. All formulations were obtained by preparing solutions of each polymer separately in aqueous solutions of Na_2CO_3 (0.01M) and then mixing the solutions together 24 hours later. Rheological measurements were performed 24 hours, at least, after the preparation of the formulation.

Synthesis

N-tert-Butyloxycarbonyl-N'-acryl-1,2-diaminoethane, 1-Boc. The *tert*-butyloxycarbonyl (Boc) protected *N*-(2-aminoethyl)acrylamide monomer, **1-Boc**, was prepared according to the literature procedure.⁵⁸

***N*-(2-Aminoethyl)acrylamide TFA salt (AEAm-TFA salt), 1.** Monomer **1** was prepared according to the literature procedure.⁵⁸

***N*-(3-Formylphenyl)acrylamide (BenzAm), 2.** 3-Aminobenzaldehyde ethylene acetal (6.00 g, 36.3 mmol, 1.0 eq.) was dissolved in a 1:1 mixture of THF (80 mL) and water (80 mL) in a round-

bottom flask. Sodium hydrogen carbonate (6.10 g, 72.6 mmol, 2.0 eq.) and acryloyl chloride (5.87 mL, 72.6 mmol, 2.0 eq.) were added to the flask at 0-5 °C. The solution was stirred for 4 hours and THF was subsequently evaporated. The aqueous phase was stirred in ethyl acetate (100 mL) for 2 hours and after filtering the solid materials, the ethyl acetate layer was washed with water (100 mL), a saturated sodium bicarbonate solution (100 mL), water (100 mL) and brine (100 mL), and then dried over MgSO₄ for 2 hours. The ethyl acetate layer was filtered and the solvent was removed under reduced pressure, providing 5.29 g (83% yield) of a white solid, corresponding to the targeted BenzAm monomer, **2**. ¹H NMR (CDCl₃, 400 MHz, ppm): δ = 9.99 (s, 1H), 8.08 (s, 1H), 7.96 (dd, 1H, J = 7.9 Hz, J = 1.9 Hz), 7.69 (s, 1H), 7.65 (dt, 1H, J = 7.6 Hz, J = 1.3 Hz), 7.51 (t, 1H, J = 7.8 Hz), 6.48 (dd, 1H, J = 16.9 Hz, J = 1.2 Hz), 6.30 (dd, 1H, J = 16.9 Hz, J = 10.2 Hz), 5.82 (dd, 1H, J = 10.2 Hz, J = 1.2 Hz) (Fig. S1†). ¹³C NMR (CDCl₃, 100 MHz, ppm): δ = 192.3, 164.1, 138.9, 137.1, 130.9, 129.9, 128.7, 126.0, 126.0, 120.7 (Fig. S2†). MS (EI): m/z expected [M]⁺ 175.06, found 175.05.

4-(2,3-dihydroxypropoxy)benzaldehyde (BenzAld), 3. 4-Hydroxybenzaldehyde (6.11 g, 50.0 mmol, 1 eq.) was dissolved in ethanol (30 mL) in a two-neck round-bottom flask. Sodium hydroxide (2.50 g, 62.5 mmol, 1.25 eq.) was dissolved in water (10 mL) and added to the flask. The solution was placed under reflux for 10 minutes and then 3-chloro-1,2-propanediol (5.00 mL, 60.0 mmol, 1.2 eq.) diluted in ethanol (5 mL) was added to the flask. The mixture was placed under reflux for 16 hours. After evaporation of the solvent, water (100 mL) was added and the product was extracted with ethyl acetate (3 × 100 mL). The organic phases were combined, dried over MgSO₄ for 2 hours, filtered, and the solvent was removed under reduced pressure, providing 8.00 g (82% yield) of a white solid, corresponding to the targeted BenzAld, **3**. ¹H NMR (D₂O, 400 MHz, ppm): δ = 9.71 (s, 1H), 7.87 (m, 2H), 7.10 (m, 2H), 4.20 (m, 1H), 4.11 (m, 2H), 3.73

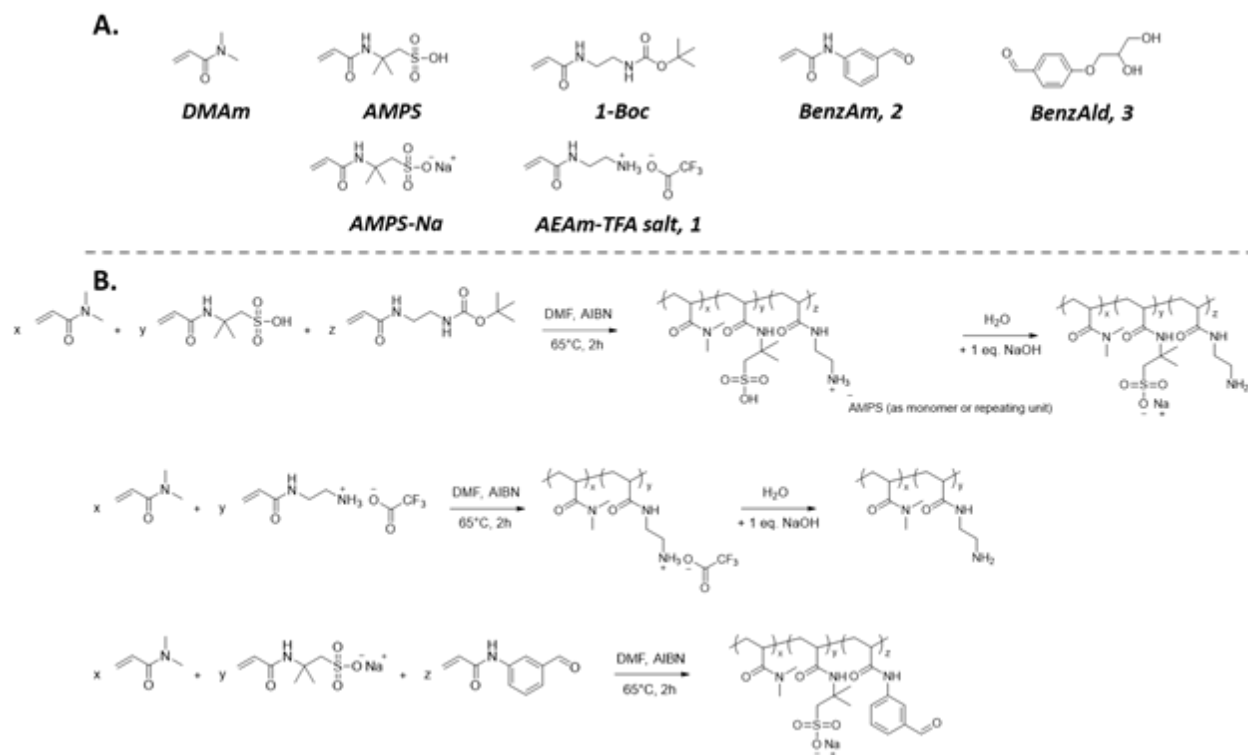
(m, 2H) (Fig. S3†). ^{13}C NMR (D_2O , 100 MHz, ppm): $\delta = 197.3, 166.6, 135.2, 131.8, 117.5, 72.4, 71.6, 64.7$ (Fig. S4†).

General procedure for the synthesis of neutral and charged copolymers carrying benzaldehyde side-groups. In a typical experiment, DMAM (10.4 g, 105 mmol, 900 eq.) and BenzAm, 2, (2.05 g, 11.7 mmol, 100 eq.) were dissolved in DMF (52 mL) in a Schlenk flask. A stock solution of initiator was prepared by dissolving AIBN (192 mg, 1.17 mmol) in DMF (10 mL). The solutions were deoxygenated by bubbling N_2 for 30 min. The Schlenk flask containing the monomer solution was placed in an oil bath thermostated at 65°C . Then, 1 mL of the AIBN stock solution (1 eq. of AIBN) was added to the Schlenk flask and the polymerization was run for 2 hours. At timed intervals, samples were withdrawn via a syringe to follow monomer conversion by ^1H NMR. The polymerization was stopped by placing the flask in an ice–water bath, and the polymer was isolated by successive precipitations into diethyl ether.

General procedure for the synthesis of copolymers carrying amino side-groups. In a typical experiment, DMAM (9.95 g, 100 mmol, 900 eq.) and AEAm-TFA salt, 1, (2.55 g, 11.2 mmol, 100 eq.) were dissolved in DMF (52 mL) in a Schlenk flask. A stock solution of initiator was prepared by dissolving AIBN (183 mg, 1.12 mmol) in DMF (10 mL). The solutions were deoxygenated by bubbling N_2 for 30 min. The Schlenk flask containing the monomer solution was placed in an oil bath thermostated at 65°C . Then, 1 mL of the AIBN stock solution (1 eq. of AIBN) was added to the Schlenk flask and the polymerization was run for 2 hours. At timed intervals, samples were withdrawn via a syringe to follow monomer conversion by ^1H NMR. The polymerization was stopped by placing the flask in an ice-water bath, and the polymer was isolated by successive precipitations into diethyl ether.

General procedure for the synthesis of copolymers carrying amino and sulfonic acid side-groups. In a typical experiment, 2-acrylamido-2-methylpropane sulfonic acid (AMPS) (11.2 g, 54.1 mmol, 900 eq.) and 1-Boc (1.29 g, 6.01 mmol, 100 eq.) were dissolved in DMF (52 mL) in a Schlenk flask. A stock solution of initiator was prepared by dissolving AIBN (98.6 mg, 601 μ mol) in DMF (10 mL). The solutions were deoxygenated by bubbling N₂ for 30 min. The Schlenk flask containing the monomer solution was placed in an oil bath thermostated at 65 °C. Then, 1 mL of the AIBN stock solution (1 eq. of AIBN) was added to the Schlenk flask and the polymerization was run for 2 hours. At timed intervals, samples were withdrawn via a syringe to follow monomer conversion by ¹H NMR. The polymerization was stopped by placing the flask in an ice-water bath, and the polymer was isolated by successive precipitations into acetone.

General procedure for the neutralization of amino functional polyacrylamides. In a typical experiment, poly(DMAm-*co*-AEAm-TFA salt) was dissolved in an aqueous solution containing 1 eq. of NaOH as compared to the ammonium functions. The solution was kept under stirring for 24 hours, before the polymer was isolated by successive precipitations into diethyl ether. The resulting polymer was then solubilized in water and freeze-dried.



Scheme 1. (A) Structure of the monomers used in this study. (B) Synthesis of polyacrylamides carrying amino or aryl aldehyde side-groups.

RESULTS AND DISCUSSION

Synthesis of functional polyacrylamides with amino or aryl aldehyde side-groups

The synthesis of polyacrylamide copolymers containing both hydrophilic and lipophilic monomers can be achieved by FRP, either through micellar polymerization, where a surfactant stabilizes the lipophilic monomer within micelles in an aqueous dispersion, or through a homogeneous copolymerization in an organic solvent or a water-based solvent mixture, in which both monomers are soluble.³⁸ Since micellar polymerization typically leads to an inhomogeneous distribution of the co-monomers along the polymer chain,³⁸ homogeneous copolymerization was selected to prepare the functional polyacrylamides. A preliminary study on the FRP of AMPS with the Boc-protected AEAm, **1-Boc** (Scheme 1A), or with BenzAm, **2**, in a mixture of water and

ethanol indicated that the copolymerization is not statistical under these conditions. A drift of the monomer composition was observed during the copolymerization, both **1-Boc** and **2** being consumed faster than AMPS, yielding copolymers with heterogeneous compositions. However, when AMPS/**1-Boc** and AMPS/**2** copolymerizations were performed in DMF, AMPS, **1-Boc** and **2** displayed similar reactivities, and random copolymers were formed. Under these conditions (DMF, AIBN, 65 °C, $[M]_0 = 20$ wt%, 2 hours of copolymerization, final monomer conversions ranging between 60 and 80 %), a series of functional copolymers with varying functionalities, charge degrees and molar masses could be prepared (Table 1).

Depending on the composition of the targeted polymers, amino functional polyacrylamides were prepared either from **1-Boc**, or from AEAm-TFA salt, **1** (Scheme 1B). Since AMPS is a strong acid, Boc deprotection was observed during the copolymerization of AMPS with **1-Boc** (Figure S5), allowing Boc deprotection and polymerization to be conducted simultaneously. However, when amino functional polyacrylamides free of permanent charges were targeted **1** and DMAm were copolymerized. In every case, a supplementary step was necessary to neutralize the AMPS and/or the ammonium functions. To do so, the amino functional polyacrylamides were solubilized in an aqueous solution containing 1 eq. of NaOH with respect to the functions to be neutralized, before being precipitated into diethyl ether. The resulting copolymers were subsequently solubilized in water and freeze-dried.

When polyacrylamides carrying both aryl aldehyde side-groups and permanent charges were targeted, 2-acrylamido-2-methyl-1-propanesulfonic acid sodium salt (AMPS-Na) (Scheme 1A) was directly copolymerized with **2**, thereby suppressing the need to neutralize the copolymers after their synthesis (Scheme 1B). In this case, the copolymerizations were pushed to full monomer conversion (by extending the duration of the copolymerization) to facilitate the isolation of the

copolymers, since the final copolymers and AMPS-Na are both insoluble in diethyl ether. Copolymers presenting a higher dispersity and a shoulder towards low molar masses in SEC were obtained under these conditions (Table 1 and Figure S6), which is expected when (close to) full monomer conversion is reached in FRP.⁵⁹

This simple, robust, and versatile approach allowed to prepare functional copolymers carrying 2 to 17 mol% of amino or aryl aldehyde side-groups, with charge degrees varying between 0 to 98 mol%, and M_n ranging between 64 and 370 kg.mol⁻¹ (Table 1). The influence of these structural characteristics, as well as experimental parameters such as the temperature, pH and ionic strength, onto both the amine-aryl aldehyde association and the rheological properties of aqueous formulations were subsequently studied.

Table 1. Amino and aryl aldehyde functional polyacrylamides prepared by FRP

Entry	[DMAm] ₀ /[AMPS] ₀ / [1] ₀ or [2] ₀ /[AIBN] ₀ ^a	Functionality (mol%) ^b	Permanent charges (mol%) ^b	<i>M_n</i> (kg.mol ⁻¹) ^c	<i>D</i> ^c	Functions/ chain ^d
P_{NH2}1 ^e	0/980/20/1	2	98	146	1.6	13
P_{NH2}2 ^e	0/900/100/1	10	90	180	1.6	83
P_{NH2}3 ^e	0/9000/1000/1	10	90	340	1.9	156
P_{NH2}4 ^e	0/830/170/1	17	83	210	1.7	170
P_{NH2}5 ^f	450/450/100/1	10	45	117	2.1	74
P_{NH2}6 ^f	430/430/140/1	14	43	136	1.7	125
P_{NH2}7 ^f	675/225/100/1	10	22.5	105	2.0	81
P_{NH2}8 ^g	900/0/100/1	10	0	85	1.4	84
P_{CO}1 ^e	0/900/100/1	10	90	82	4.4	37
P_{CO}2 ^f	450/450/100/1	10	45	91	4.8	57
P_{CO}3 ^f	675/225/100/1	10	22.5	92	3.8	68
P_{CO}4 ^g	980/0/20/1	2	0	64	2.0	13
P_{CO}5 ^g	900/0/100/1	10	0	158	1.5	148
P_{CO}6 ^g	9000/0/1000/1	10	0	370	1.2	347

^a **1-Boc** or AEAm-TFA salt, **1**, for P_{NH2}, and BenzAm, **2**, for P_{CO} polymers. ^b Determined by ¹H NMR. ^c Determined by SEC triple detection. ^d Determined by a combination of SEC triple detection and ¹H NMR. ^e AMPS based copolymers. ^f AMPS/DMAm based terpolymers. ^g DMAm based copolymers.

Thermodynamic study of the association

A thermodynamic study of the association taking place in aqueous solutions between the amino side-groups of various polyacrylamides and a water-soluble benzaldehyde derivative (BenzAld), **3**, (Schemes 1 and S2) was conducted. The methodology developed by Lehn *et al.* was used to measure the reduced equilibrium constant for imine formation, *K'*, in accordance with equations (1) and (2).⁶⁰



$$K' = \frac{K}{[\text{H}_2\text{O}]} = \frac{[\text{RCH}=\text{NR}'][\text{H}_2\text{O}]}{[\text{RCHO}][\text{R}'\text{NH}_2]} \frac{1}{[\text{H}_2\text{O}]} = \frac{[\text{RCH}=\text{NR}']}{[\text{RCHO}][\text{R}'\text{NH}_2]} \quad (2)$$

Imine formation was followed by ^1H NMR, monitoring the aromatic protons of **3** and of the imine (Figure S7). The influence of the pH, temperature, and ionic strength on K' was studied as a function of the charge degree of the amino functional polyacrylamides, while maintaining a stoichiometric balance between amine and aldehyde functions.

Influence of the pH on imine formation. The general features that govern imine formation in aqueous solutions are well known,⁶⁰⁻⁶² notably thanks to the work of Lehn and coworkers,⁶⁰ which correlates the stability of imines with their structure, and shows that the percentage of imine formed between aromatic aldehydes, such as benzaldehyde derivatives, and aliphatic amines is very much dependent on the pH. Imine formation is highly favored for pHs close to, or **greater than** the pKa of the ammonium/amine acid base pair. Indeed, only the neutral form of the amine participates in imine formation. However, the situation could be different for weak polybases, such as the amino functional polyacrylamides used in this study. Unlike molecular weak acids and bases, for which the ionization of individual species occurs independently, the ionization of different sites on a polymer are correlated.⁶³⁻⁶⁴ The number of charged groups, and their distribution, can both affect the pKa of the ionisable units,⁶⁴⁻⁶⁶ and therefore imine formation. For these reasons, we were interested to assess, as a function of the pH, the effect of the charge degree of the functional polyacrylamides onto imine formation.

Functional polyacrylamides carrying 10 mol% of pendant alkyl amines, a weak base, and 0 (**P_{NH2}8**), 45 (**P_{NH2}5**) and 90 mol% (**P_{NH2}2**) of sodium sulfonate moieties, as permanent charges, were synthesized to this aim (Table 1). Formulations at a fixed concentration of amine functions of 20 mmol.L⁻¹ were prepared by mixing the amino functional polyacrylamides with equimolar

quantities of **3** in deuterated water. The pH of the formulations was adjusted to the desired values using NaOD or DCl. A formulation in pure deionized water was also prepared. Imine formation was monitored by ^1H NMR, using equation (3) to link pH and pD.⁶⁷

$$\text{pD} = \text{pH} + 0.4 \quad (3)$$

Table 2. Influence of the pH and ionic strength on imine formation as function of the charge degree of the amino functional polyacrylamide^a

Entry	pH set at	$K' \text{ P}_{\text{NH}_2\mathbf{8}}$ ($\text{L}\cdot\text{mol}^{-1}$)	$K' \text{ P}_{\text{NH}_2\mathbf{5}}$ ($\text{L}\cdot\text{mol}^{-1}$)	$K' \text{ P}_{\text{NH}_2\mathbf{2}}$ ($\text{L}\cdot\text{mol}^{-1}$)
1	3.6	2	2	3
2	7.1	4	2	3
3	10	25	16	16
4	11.6	31	44	47
5	pH not adjusted ^b	20.7 ± 3.8 (10.4) ^c	13.3 ± 2.3 (10.1) ^c	12.3 ± 3.2 (10.1) ^c
6	pH not adjusted ^{b,d}	21.7 ± 5.7	14.3 ± 3.1	13.7 ± 5.5
7	pH not adjusted ^e	20.3 ± 2.3 (10.2) ^c	13.0 ± 2.6 (9.8) ^c	10.3 ± 2.5 (9.9) ^c

^a See Table 1 for polymer characteristics. A stoichiometric ratio between amine and aldehyde functions was used. The concentration of each functional group was set to 20 $\text{mmol}\cdot\text{L}^{-1}$. ^b (Poly)amine and **3** were mixed in pure deionized water. ^c Measured pH of the solutions is reported in brackets. ^d Concentrations in amine and aldehyde functions were set to 12 $\text{mmol}\cdot\text{L}^{-1}$. ^e (Poly)amine and **3** were mixed in an aqueous solution of NaCl (6 $\text{g}\cdot\text{L}^{-1}$).

The association between amino functional polyacrylamides and **3** followed trends similar to small molecule systems reported by Lehn and collaborators.⁶⁰ Imine formation was very limited at both acidic and neutral pH, regardless of the charged content of the polyamine (Table 2, entries 1 and 2). K' values ranged between 2 and 4 at pH 7.1, for example. Raising the pH to 10, *i.e.* slightly below the pK_a of primary alkylamines, yielded a significant increase of the reduced equilibrium constant. Systems composed of polyamines carrying permanent charges ($\text{P}_{\text{NH}_2\mathbf{5}}$ and

P_{NH2}2), displayed a K' of 16 L.mol⁻¹, while the amino functional polyacrylamide free of sodium sulfonate moieties (**P_{NH2}8**) presented a K' of 25 L.mol⁻¹ (Table 2, entry 3). When the pH was further increased to 11.6, *i.e.* approximately 1 point above the pK_a of primary alkylamines, the association constant of the **3/P_{NH2}8** system slightly increased, to reach 31 L.mol⁻¹, while the association constant of systems composed of polyamine carrying permanent charges almost tripled, to reach values of 44 and 47 L.mol⁻¹, with **P_{NH2}5** and **P_{NH2}2**, respectively (Table 2, entry 4). The behavior of amino functional polyacrylamides carrying sodium sulfonate side-groups (**P_{NH2}5** and **P_{NH2}2**) was thus different from that of the amino functional polyacrylamide free of permanent charges (**P_{NH2}8**), for pH values close to the pK_a of the alkylamine function. This difference of behavior likely originates from the conformational transition, from elongated chains to random coils, experienced by the polyacrylamide free of sodium sulfonate moieties, whereas amino functional polyacrylamides carrying sodium sulfonate side-groups (**P_{NH2}5** and **P_{NH2}2**) adopt an elongated conformation regardless of the pH. Interestingly, when amino functional polyacrylamides were mixed with **3** in pure deionized water, *i.e.* without adjusting the pH, the reduced equilibrium constant for all three systems were only slightly lower than to those obtained at pH 10 (Table 2, entries 3 and 5). In that case, a fraction of the amino side groups acts as base and is protonated, leading to an increase of the pH. In addition, decreasing the concentration of associating amine and aldehyde groups down to 12 mmol.L⁻¹ did not affect the measured K' (Table 2, entry 6). These characteristics are highly desirable to design associative systems that can operate at low polymer concentrations, without the need to adjust the pH of the formulation.

Influence of the temperature on imine formation. Modulating the association between aldehydes and amines using temperature could lead to thermoresponsive systems.³ To assess this possibility, the reduced equilibrium constant for imine formation was measured by ¹H NMR at 30

and 80 °C. Three successive cycles of measurements at 30 and 80 °C were performed on a model aqueous formulation containing 20 mmol.L⁻¹ of ethanolamine and **3**, as well as 10 mmol.L⁻¹ of Na₂CO₃. The latter was added to limit CO₂ solubilization at high temperature, which leads to the acidification of the solutions and potential consumption of amines through the formation of carbamates. Increasing the temperature from 30 to 80 °C led to a decrease of K' from 28 to 12 L.mol⁻¹ (Figure 1), which indicates that the equilibrium is displaced towards imine dissociation with increasing temperature. Interestingly, the reduced equilibrium constant measured at 30 °C after two heating-cooling cycles was 29 L.mol⁻¹, indicative of a good thermal reversibility of the imine bond under these conditions. The thermal reversibility of the association was also tested with an amino functional polyacrylamide, **P_{NH2}5**, carrying 10 mol% of pendant amino groups and 45 mol% of sodium sulfonate moieties (Figure 1). A good reversibility of the imine formation was also observed with this system, K' decreasing from 24 to 10 L.mol⁻¹, on the first heating cycle, and from 20 to 11 L.mol⁻¹ on the third (Figure 1).

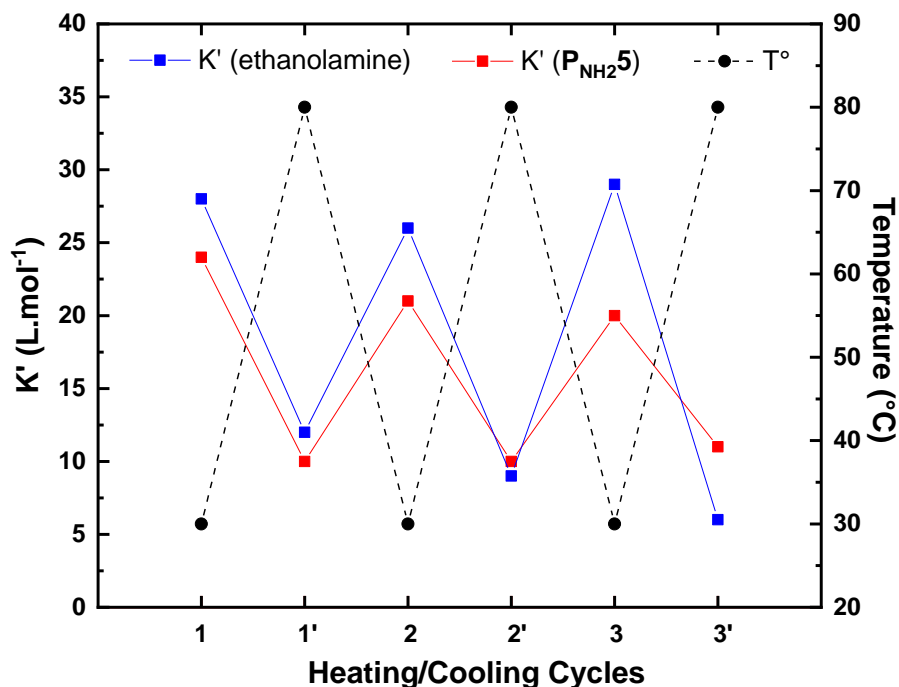


Figure 1. Evolution of K' as a function of temperature for successive heating-cooling cycles between 30 and 80 °C. Aqueous formulations of ethanolamine (blue, $[\text{NH}_2] = 20 \text{ mmol.L}^{-1}$) and polyacrylamide P_{NH_25} (red, $[\text{NH}_2] = 20 \text{ mmol.L}^{-1}$) with a stoichiometric amount of **3** and 10 mmol.L^{-1} of Na_2CO_3 .

Influence of the ionic strength on imine formation. To assess the impact of the presence of salts on imine formation, the amino functional polyacrylamides P_{NH_28} , P_{NH_25} and P_{NH_22} were mixed with equimolar quantities of **3** (20 mmol L^{-1}) in deuterated aqueous solutions containing 6 g.L^{-1} of NaCl (Table 2, entry 7). The K' measured with P_{NH_28} and P_{NH_25} were essentially the same as those obtained in the absence of NaCl (difference of *ca.* 2%, Table 2, entry 5). In the case of the amino functional polyacrylamide carrying 90 mol% of sodium sulfonate moieties, (P_{NH_22}), the measured K' decreased by *ca.* 20%. These results indicate that the presence of NaCl at a concentration of 6 g.L^{-1} has a minimal effect on the association by itself. Yet, it also induces

conformational changes on highly charged polymers, which affects the chemical environment of the amine groups, and thus K' .

Rheological measurements of aqueous formulations

The previous model studies provide some valuable information on the impact of the pH, temperature and ionic strength on the association taking place in water between amino functional polyacrylamides and a benzaldehyde derivative. These parameters should impact to an even larger extent the rheological behavior of formulations incorporating associative polymers, as they will simultaneously affect the conformation, topology, and molar masses of the macromolecular assemblies. To test this assumption, rheological measurements were performed on aqueous formulations containing complementary aryl aldehyde and amino functional polyacrylamides. The influence of structural parameters, *e.g.* the functionality and molar masses of the polymers, and experimental parameters, *e.g.* temperature and ionic strength, were evaluated.

Influence of the charge degree and functionality of the complementary polymers. The charge degree of the complementary copolymers is expected to significantly influence the rheological behavior of the formulations, as it will impact inter-chain association, through electrostatic repulsion, as well as the conformation, and thus the hydrodynamic volume, of both the individual polymer chains and the macromolecular assemblies. Rheological measurements were performed on formulations containing 0.3 wt% of aryl aldehyde functional polyacrylamides, 0.3 wt% of amino functional polyacrylamides and 0.01 M of Na_2CO_3 (Table 3). First, the amino and aldehyde functionality of all polymers was kept constant at 10 mol%, and only the content of permanent charges, *i.e.* repeating units carrying sodium sulfonates moieties, was varied. In a first set of experiments, three formulations in which both complementary polymers contained the same amount of permanent charges were studied (Table 3, **formulations 1-3** and Figure 2, orange to

brown dots). These formulations yielded two distinct rheological behaviors. Formulations in which both functional polymers carried a large amount of permanent charges, *i.e.* 90 or 45 mol%, presented low and constant viscosities ($1 < \eta < 3$ mPa.s) over the entire range of shear rates tested. In sharp contrast, the formulation made of complementary copolymers containing only 22.5 mol% of permanent charges provided a much more pronounced viscosification ($100 < \eta < 10.000$ mPa.s) and a shear thinning behavior. Since all polymers should display an elongated conformation at these charge degrees, we hypothesize that these two distinct behaviors reflect limited inter-chain associations, caused by electrostatic repulsions, when both polymers present high charge degrees.

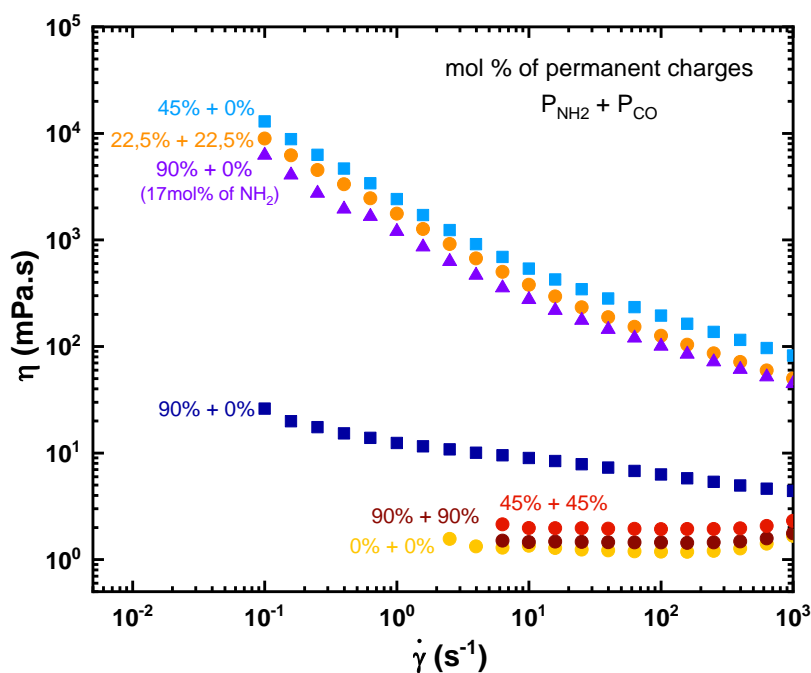


Figure 2. Flow curves of aqueous formulations (10 mmol.L^{-1} of Na_2CO_3) containing complementary amino and aryl aldehyde functional polyacrylamides (10 mol% of functions; 0.3 wt% of each polymer) presenting identical charge degrees (dots), different charge degrees (square), or 17 mol% of amino side-groups (instead of 10 mol%) (triangle).

Table 3. Formulations used to study the flow properties as a function of the charge degree of the complementary polymers

Formulation ^a	Polymers ^b	mol% of permanent charges	mol% of NH ₂ / CO functions	[NH ₂] / [CO] (mM)	R = [NH ₂]/[CO]
1	P _{NH2} 2 / P _{CO} 1	90 / 90	10 / 10	1.38 / 1.34	1.03
2	P _{NH2} 5 / P _{CO} 2	45 / 45	10 / 10	1.89 / 1.82	1.04
3	P _{NH2} 7 / P _{CO} 3	22.5 / 22.5	10 / 10	2.41 / 2.21	1.05
4	P _{NH2} 8 / P _{CO} 5	0 / 0	10 / 10	2.99 / 2.82	1.06
5	P _{NH2} 5 / P _{CO} 5	45 / 0	10 / 10	1.89 / 2.82	0.67
6	P _{NH2} 2 / P _{CO} 5	90 / 0	10 / 10	1.38 / 2.82	0.49
7	P _{NH2} 4 / P _{CO} 5	90 / 0	17 / 10	2.44 / 2.82	0.87

^a Aqueous formulations containing 10 mM of Na₂CO₃; [P_{NH2}] = [P_{CO}] = 0.3 wt%. ^b See Table 1 for polymer characteristics

A second set of experiments was designed to assess the behavior of formulations containing at least a functional polymer free of permanent charges (Table 3, **formulations 4-6** and Figure 2, yellow dots and blue squares). To this aim, an aldehyde functional polyacrylamide carrying 10 mol% of aryl aldehyde function and no permanent charge (0.3 wt%) was mixed with amino functional polyacrylamides carrying 10 mol% of amine functions and 0, 45 or 90 mol% of permanent charge (0.3 wt%). The two rheological behaviors previously observed with complementary copolymers both carrying permanent charges were obtained again, as well as an additional third intermediate regime (Figure 2, navy blue squares). When both functional copolymers did not carry permanent charges (Table 3, **formulation 4** and Figure 2, yellow dots), a low and shear rate independent viscosification was observed ($1 < \eta < 3$ mPa.s). At this low polymer concentration (0.6 wt% overall), the random coil conformation of both functional copolymers coupled to their limited molar mass (M_n of 180 and 158 kg mol⁻¹ for the amino and aldehyde

functional copolymers, respectively) generated limited inter-chain association. The formulation containing the amino functional polyacrylamide carrying 45 mol% of sodium sulfonate groups (Table 3, **formulation 5** and Figure 2, light blue squares) yielded an important viscosification ($100 < \eta < 10.000$ mPa.s) with a shear thinning behavior, as previously observed with complementary copolymers bearing both 22.5 mol% of permanent charges. Interestingly, a third and intermediate regime was observed for the formulation containing the amine functional polyacrylamides carrying 90 mol% of sodium sulfonate groups (Table 3, **formulation 6**). The amino functional polyacrylamides used in the formulations studied so far (Table 3, **formulations 1-6**) all carried 10 mol% of amine functions and were always introduced at a constant weight fraction of 0.3%. However, the AMPS-Na ($229 \text{ g}\cdot\text{mol}^{-1}$) and DMAm ($99.1 \text{ g}\cdot\text{mol}^{-1}$) repeating units have significantly different molar masses. As a result, the amine concentration and the stoichiometric ratio between amine and aldehyde functions varied with the content of permanent charges. They were $1.38 \text{ mmol}\cdot\text{L}^{-1}$ and 0.49, respectively, in the **formulation 6**, against $1.89 \text{ mmol}\cdot\text{L}^{-1}$ and 0.67, respectively, in the **formulation 5** (Table 3). Therefore, the difference of rheological behavior between **formulations 5** and **6** is the result of fewer inter-chain association caused by a lower concentration of amine functions.

To verify this assumption, the neutral aryl aldehyde functional polyacrylamide used in the **formulations 5** and **6** was mixed with an amino functional polyacrylamide carrying 17 mol% of amine functions and 83 mol% of AMPS-Na repeating units (Table 1, **P_{NH2}4** and Table 3, **formulation 7**). The resulting formulation (Fig. 2, purple triangle) displayed a rheological profile very similar to that of **formulation 5**, indicating that amount of charges and functional groups of both complementary copolymers, as well as the stoichiometric ratio between amine and aldehydes

functions, are important parameters that significantly impact the rheological behavior of these associative formulations.

To illustrate the versatility of the associative system to modulate the flow properties of aqueous formulations, the rheological profiles of formulations composed of equimassic fractions of amino functional P(AMPS-Na) (carrying 2, 10 or 17 mol% of amine functions) and aryl aldehyde functional PDMAm (carrying 2 or 10 mol% of aryl aldehyde functions) were compared to that of a non-associative reference formulation, composed of a P(AMPS-Na) homopolymer ($M_w = 209 \text{ kg}\cdot\text{mol}^{-1}$; $D = 2.2$) and a PDMAm carrying 10 mol% of aryl aldehyde functions (Table 4, **formulations 8-12**). As can be seen on the rheological profiles presented in Figure 3, all formulations presented a viscosity of *ca.* 1 mPa.s for polymer concentrations of 0.1 wt% (measured at $\dot{\gamma} = 10 \text{ s}^{-1}$). The non-associative reference formulation (**formulation 8**) and the one presenting the lowest average functionality (**formulation 9**) displayed almost identical rheological profiles up to a polymer concentration of 4 wt%, with viscosities of 9.3 and 8.4 mPa.s, respectively. When further increasing polymer concentration, inter-chain association started to take place in **formulation 9**, which presented a viscosity of 7.800 mPa.s at 8 wt%, more than 400 times higher than the viscosity of the non-associative reference formulation (18.5 mPa.s). By increasing the average functionality of the complementary polymers (**formulations 10-12**, Table 4), the polymer weight fraction at which the inter-association started to take place decreased to 0.3-0.4 wt%, and the increase of viscosity as a function of polymer concentration became much more pronounced (Figure 3).

Table 4. Formulations used to study the flow and the viscoelastic properties of the associative polymers in aqueous solutions, as a function of functionality (8-12) and molar mass (11, 13-14) of the complementary polymers, and of the salinity (15) and temperature (16) of the formulation

Formulation ^a	Polymers ^b	mol% of permanent charges	mol% of NH ₂ / CO functions	R = [NH ₂]/[CO]
8 (ref)	P _{AMPS-Na} / P _{CO5}	100 / 0	0 / 10	-
9	P _{NH21} / P _{CO5}	98 / 0	2 / 10	0.09
10	P _{NH24} / P _{CO4}	83 / 0	17 / 2	4.10
11	P _{NH22} / P _{CO5}	90 / 0	10 / 10	0.49
12	P _{NH24} / P _{CO5}	83 / 0	17 / 10	0.87
13	P _{NH23} / P _{CO5}	90 / 0	10 / 10	0.49
14	P _{NH23} / P _{CO6}	90 / 0	10 / 10	0.49
15 ^c	P _{NH24} / P _{CO5}	83 / 0	17 / 10	0.87
16	P _{NH27} / P _{CO3}	22.5 / 22.5	10 / 10	1.05

^a Aqueous formulations containing 10 mM of Na₂CO₃. ^b See Table 1 for polymer characteristics. ^c Formulation containing 6 g L⁻¹ of NaCl.

For example, the reference formulation and the formulation with the highest average functionality (**formulations 8 and 12**, Table 4), displayed comparable viscosities of 1.2 and 2.0 mPa.s, respectively, at a polymer concentration of 0.3 wt%. However, for a polymer concentration of 0.8 wt%, the viscosity of the associative formulation was 680 times higher than that of the reference formulation, with viscosities of 1 230 and 1.8 mPa.s, respectively. Thus, adjusting the average functionality of the associative system, keeping all other parameters constant, allows to tune the viscosity of the formulation at a given polymer concentration, as well as the viscosity profile as a function of polymer concentration (Figure 3).

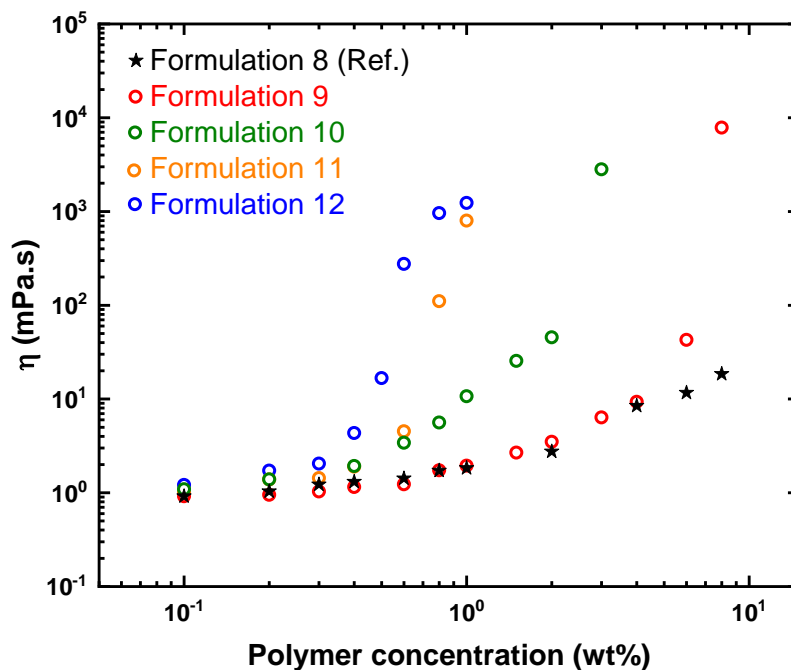


Figure 3. Rheological profiles of formulations composed of aryl aldehyde and amino functional polyacrylamides with varying degrees of functionality (**formulations 9-12**), as well as a non-associative reference formulation (**formulation 8**). Aqueous formulations containing 10 mM of Na_2CO_3 . Viscosity measured at $\dot{\gamma} = 10 \text{ s}^{-1}$.

Influence of the molar mass. The molar mass of the functional polymers is another parameter that can be used to tune the flow properties of associative formulations.^{35,38,68} To study the effect of molar masses on the rheological properties of imine associative systems, aqueous formulations incorporating a P(AMPS-Na) carrying 10 mol% of amine functions, and with a M_n of 180 or 340 $\text{kg}\cdot\text{mol}^{-1}$, (**P_{NH22}** and **P_{NH23}**, respectively), and a PDMAm carrying 10 mol% of aldehyde functions, and with a M_n of 158 or 370 $\text{kg}\cdot\text{mol}^{-1}$ (**P_{Co5}** and **P_{Co6}**, respectively) were prepared. Figure 4 presents the rheological profiles of **formulation 11** (orange circles), consisting of the two “short” complementary polymers, of **formulation 13** (pink circles), composed of the long

polyamine) and the short poly(aldehyde), and of **formulation 14** (green circles), consisting of the two “long” complementary polymers (Tables 1 and 4).

While all three formulations displayed a marked associative character, evidenced by a large increase of the viscosity above a certain polymer concentration, the polymer weight fraction at which the inter-chain association starts to operate clearly depends on the molar masses of the polymers. All three formulations displayed a viscosity comprised between 1 and 1.1 mPa.s at a polymer concentration of 0.1 wt%. However, the viscosity of **formulation 11**, measured at a shear rate of 10 s^{-1} , was 1.9 mPa.s at a polymer concentration of 0.4 wt%, against 272 mPa.s, for **formulation 14**. Increasing polymer concentration led to the formation of a hydrogel for all three formulations, for weight fraction comprised between 0.4 and 0.6 wt% for **formulations 13** and **14**, while a polymer concentration superior to 1 wt% was needed for **formulation 11**. Therefore, modulating the molar masses of the copolymers, while keeping constant their functionality and charge degree, is a simple and efficient way to tune the rheological properties of imine associative formulations.

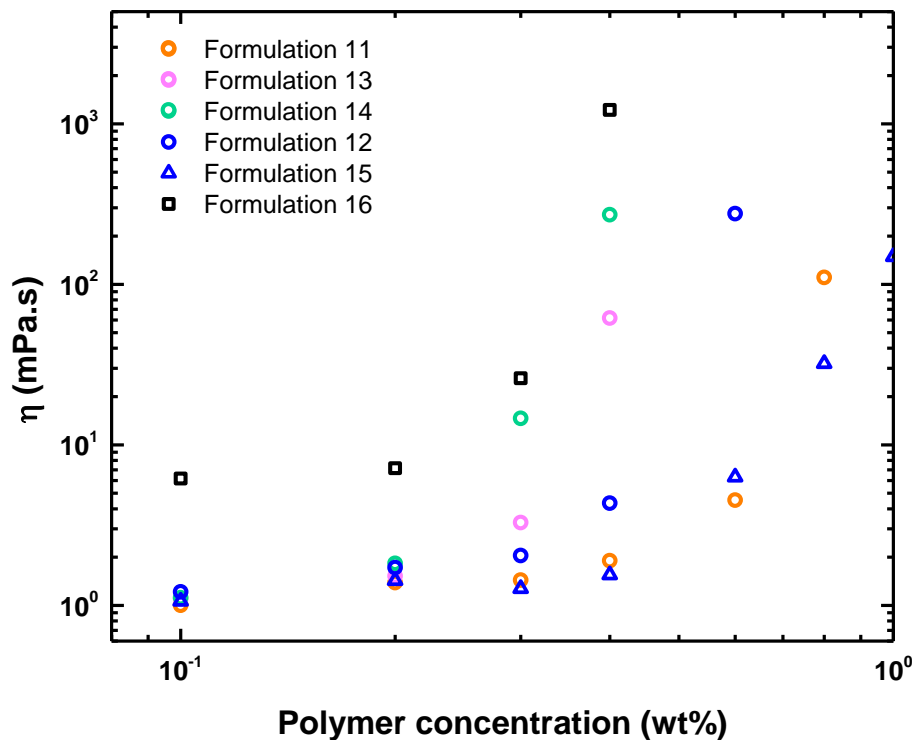


Figure 4. Rheological profiles of formulations composed of aryl aldehyde and amino functional polyacrylamides with varying molar masses (**formulations 11, 13 and 14**), as well as in the absence (**formulation 12**) or presence (**formulation 15**) of NaCl ($6\text{g}\cdot\text{L}^{-1}$). **Formulation 16** was used for light scattering characterization and to evaluate its thermoresponsive behavior. Aqueous formulations containing 10 mM of Na_2CO_3 . Viscosity measured at $\dot{\gamma} = 10\text{ s}^{-1}$.

Influence of the ionic strength. The model study conducted with amine functional polyacrylamides and **3** showed that the presence of NaCl at a concentration of $6\text{ g}\cdot\text{L}^{-1}$ has limited to no effect on imine formation. Therefore, we were interested to compare the rheological profiles of an associative formulation in the presence and in the absence of salt. To this aim, a 10 mM Na_2CO_3 aqueous formulation incorporating the amine functional polyacrylamide **P_{NH2}4** and the aldehyde functional polyacrylamide **P_{CO}5** was studied in the absence and in the presence of $6\text{ g}\cdot\text{L}^{-1}$ NaCl (Table 4, **formulations 12** and **15**; Figure 4 blue circles and blue triangles, respectively).

As can be seen from Figure 4, both formulations displayed very similar behaviors, and the presence of NaCl at a concentration of 6 g.L⁻¹ had only a limited impact on the rheological profiles. The weight concentration at which inter-chain association took place slightly increased in the presence of salt, likely reflecting conformational changes induced by the screening of the electrostatic interactions between ionized side-groups.

Light scattering characterization. To further investigate the chain dynamics of the associative polymers, dynamic light scattering (DLS) was used to evaluate its microstructural behavior. To this effect, **formulation 16** (Table 4) was chosen because its viscosity increased rapidly with concentration (Figure 4, black squares), leading to a hydrogel between 0.4 and 0.5 %wt, as shown in Figure S10. Analyses were carried out at different concentrations, ranging from 0.1 to 0.5 %wt. At the lowest polymer concentrations, 0.1 and 0.2 %wt, the intensity correlation function decays exponentially, as shown in Figure 5A. This behavior is typical of Brownian suspensions, for which $g_2(q,\tau)-1 = \exp(-2Dq^2\tau)$, where q is the scattering vector and D is the diffusion coefficient.⁵⁶ To further confirm the diffusive nature of the microscopic dynamics, we take the natural logarithm of the correlation functions measured at all accessible scattering vectors, and we rescale them by q^2 . We find that all correlation curves collapse on a master curve, proportional to the mean squared displacement $\langle \Delta r^2(\tau) \rangle = 6D\tau$, as shown in Figure 5B. A linear fit to $\langle \Delta r^2(\tau) \rangle$ yields a diffusion coefficient $D = 3.3$ and $1.8 \mu\text{m}^2/\text{s}$ for polymer concentrations of 0.1 and 0.2 %wt, respectively. This is compatible with the diffusion of micron-sized aggregates in a medium with a viscosity slightly above water, as indicated by rheology (Figure 4, black squares). As the polymer concentration is increased to 0.3%, the exponential decay of the correlation function is delayed to longer timescales and is preceded by a slower decay, which is more apparent in Figure 5B. This indicates that on timescales shorter than about 0.2 s the dynamics are sub-diffusive, presumably

hindered by dynamic covalent interactions. For intermediate timescales, between 0.2 and 2 s, a diffusive regime is recovered, with an effective diffusion coefficient $D = 0.3 \mu\text{m}^2/\text{s}$, about 10 times smaller than the one of more dilute samples, in agreement with the increased viscosity measured by rheology (Figure 4, black squares). At even longer timescales, however, we observe that the exponential relaxation of the correlation functions does not lead to a full decay as in the previous cases. Instead, the correlation functions exhibit slower-relaxing tails that no longer scale with q^2 . Such complex dynamics suggest that the aggregates interact, forming transient, large-scale structures that inhibit their diffusive motion.

As the polymer concentration is further increased to 0.4 and 0.5 %wt, the initial, sub-diffusive regime turns into a well-defined plateau, covering a wide range of timescales between the shortest timescales accessed by the experiment (10 ms), and a few hours. The plateau value is lower than 1 and scales again with q^2 . This indicates the existence of a first relaxation mode, which is too fast to be captured and which entails displacements that are constrained to within a finite range, smaller than $1/q$. This is the hallmark of an interconnected network, in which the nodes act as topological constraints for the spontaneous dynamics.⁶⁹ To characterize this network, we use the plateau value measured at all scattering vectors to compute the mean squared displacement, $\delta^2 = -3\ln(g_2-1)/q^2$, of the constrained dynamics. We obtain $\delta^2 = 0.017 \mu\text{m}^2$ and $0.002 \mu\text{m}^2$ for polymer concentrations of 0.4 and 0.5 %wt, respectively. Taking this value of δ as an estimate for the correlation length, ξ , of the network, and assuming that the network elasticity is entropic⁷⁰ we obtain a shear modulus, $G \sim k_B T / \xi^3 = 1.6 \text{ Pa}$ and 40 Pa for the two polymer concentrations, which is in good agreement with direct rheological measurements of 30 Pa for 0.5%wt (Figure S10).

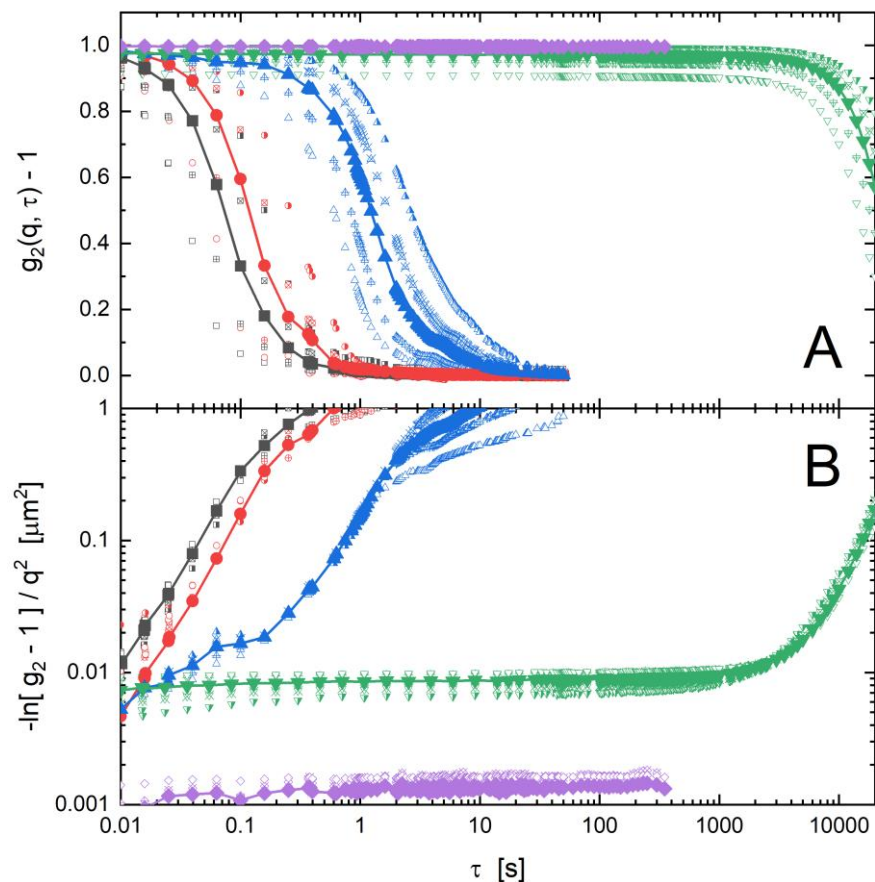


Figure 5. (A) DLS correlation function, $g_2 - 1$, as a function of time delay, τ , for **formulation 16** at polymer concentration 0.1%wt (black squares), 0.2%wt (red circles), 0.3%wt (blue triangles), 0.4%wt (green inverted triangles) and 0.5%wt (purple diamonds). Full symbols are measured at a scattering vector $q = 1.8 \mu\text{m}^{-1}$. For reference, data for four additional scattering vectors is also shown as open, plused, crossed and half-filled symbols ($q = 1, 1.4, 2.4$ and $3.1 \mu\text{m}^{-1}$, respectively). (B) Natural logarithm of the correlation function, rescaled by the scattering vector squared, to highlight the collapse on a q -independent master curve of both Brownian dynamics (black and red data) and constrained network fluctuations (green and purple data).

Thermoresponsiveness. As previously mentioned, the associative systems can lead to hydrogels. The properties of the hydrogels and the polymer concentration at which they are formed are dictated by the molar mass, the functionality and the composition of the complementary amino

and aldehyde functional polyacrylamides. In addition, the thermodynamic equilibrium constant for imine formation is temperature dependent and displaced towards imine dissociation with increasing temperature (Figure 1). The thermoresponsiveness of the associative system was studied on hydrogels, by performing frequency sweeps every 10 °C between 20 and 60 °C (Fig. S9) on a formulation containing 0.5 wt% of the amino functional polyacrylamide **P_{NH2}7**, 0.5 wt% of the aldehyde functional polyacrylamide **P_{CO3}**, and 10 mM of Na₂CO₃ (Table 4, **formulation 16**). Increasing the temperature led to much weaker hydrogels, as evidenced by the significant decrease of both the storage and loss moduli, G' and G'', respectively (Figure S10). For example, the hydrogel displayed a G' and a G'' of 26.4 and 1.4 Pa, respectively, at 20 °C and 0.01 rad.s⁻¹, against 1.7 and 0.4 Pa, respectively, at 60 °C and 0.01 rad.s⁻¹. Unfortunately, measurements could not be performed at higher temperature, as gas bubbles formed above 60 °C, leading to unreliable results. Nonetheless, when the formulation was heated to 80 °C, a liquid solution was unequivocally obtained (Figures S11 and S12).

In order to test the reversibility of the sol-gel transition, **formulation 16** was placed in an open Erlenmeyer flask and maintained at 80 °C overnight. The formulation was then allowed to cool down to room temperature and to rest for three days. Four heating-cooling cycles were performed. Frequency sweeps were performed before the first cycle and after the rest period of each heating-cooling cycle. The viscoelastic properties of the hydrogels were almost unchanged after four temperatures cycles, with a G' and G'' of 27.8 and 0.695 Pa after the fourth temperature cycle, to be compared to a G' and G'' of 29.2 and 0.905 Pa for the pristine hydrogel (at an angular frequency of 0.01 rad.s⁻¹, Figure S13). Therefore, the sol-gel transition proved to be reversible and reproducible over four temperature cycles, exemplifying the thermoresponsiveness and the stability of the system under these conditions (prolonged heating under ambient atmosphere).

CONCLUSIONS

In conclusion, imine dynamic covalent chemistry was used to develop associative aqueous formulations composed of complementary copolymers carrying amino or aryl aldehyde side-groups. The equilibrium constant for imine formation was first studied between amino functional polyacrylamides and a water soluble monofunctional benzaldehyde. The association followed trends similar to small molecule systems, with imine formation being favored for pH values close to, or superior to the pKa of the amino groups. However, different behaviors were observed depending on the presence of permanent charges on the functional polyacrylamides. In addition, thanks to their polybase character, the amino functional polyacrylamides intrinsically buffer the solutions at pH compatible with imine formation, without the need to add an exogenous base. These model studies also indicated that the imine link is thermoresponsive in aqueous solutions, with imine dissociation being favored with temperature. Interestingly, the hydrolysis/condensation equilibrium proved to be reversible over consecutive heating-cooling cycles between 30 and 80 °C. The rheological properties of aqueous solutions were then studied as a function of the functionality, charge degree and molar masses of the complementary copolymers. The inter-chain association operating between the functional polyacrylamides was used to modulate the flow properties of the formulations. It was shown that the amine/aldehyde stoichiometric ratio, the functionality, charge degree, molar masses, and weight fractions of the copolymers are parameters that impact the flow properties of the formulations. For example, the viscosity of the formulations can be changed by more than three orders of magnitude by only varying the charge degree of the copolymers. Dynamic light scattering was also used to characterize the dynamic and structural properties of one associative formulation, obtaining results that were in qualitative and quantitative agreement

with rheology. Taking advantage of the influence of the temperature on the imine equilibrium constant, thermoresponsive hydrogels were designed, which showed a reversible and reproducible sol-gel transition when subjected to heating-cooling cycles between 30 and 80 °C. Therefore, the combination of imine dynamic covalent chemistry and radical polymerization affords a simple, robust and versatile tool to modulate the flow properties of aqueous formulations.

ASSOCIATED CONTENT

Supporting Information. The following files are available free of charge:

Supporting information (PDF) Experimental NMR spectra, additional schemes for synthesis and imine equilibrium and additional information on rheology and gel formation.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

There are no conflicts to declare.

ACKNOWLEDGMENT

We are very grateful to Thomas Aubineau for technical assistance with ^1H NMR experiments, especially measurements conducted in temperatures. We are very grateful to Michel Cloître for

technical guidance and assistance with rheology measurements. We thank TOTAL, ESPCI Paris – PSL and the CNRS for financial support.

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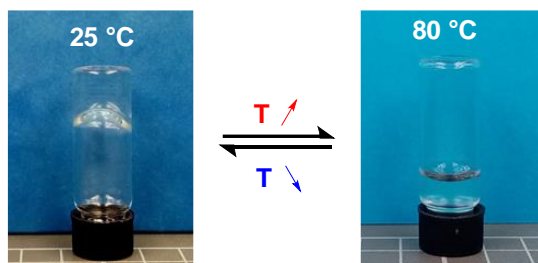
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