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Dispersive Effects in Chemomechanical Reactions with Polyallylamine-Derived Hydrogels

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Volume changes of polyallylamine-derived hydrogels crosslinked with glutaraldehyde are determined with a large variety of effector compounds. Monocarboxylic effectors lead to smaller contractions, in contrast to dicarboxylate structures, which allow more effective non-covalent crosslinking between the positively charged nitrogen centers of the polymer backbone. Electroneutral compounds lead to negligible changes, whereas effectors with either a large *p*-moiety like in naphthoic acid or phenyl derivatives with polarizable substituents induce large contractions. This finding is in line with significant contributions of van der Waals interactions between the effectors within the hydrogel. Chemomechanical differences between regioisomeric effectors such as *p*- and *o*-nitrobenzoic acid are in agreement with independent results of dispersive interactions in related complexes. The volume decrease corresponds almost entirely to the gravimetrically determined water content of the gels. The acidity profile shows a strong contraction above pH 10, which is consistent with the known p*K* value of such polyamines. NMR spectra of the gels indicate strong binding of the effectors by line broadening, which is significant only for the chemomechanically active compounds.

Introduction

Chemomechanical polymers which exhibit volume changes upon selective stimulation by external effector substances hold much promise for applications such as drug release systems,[1] artificial muscles and sensor devices.[2] Gels derived from polyallylamine have until now rarely been investigated with the aim of selectively triggered intelligent materials. As with many chemomechanical polymers mostly the volume change as a function of pH and temperature with PAA hydrogels[3] or of corresponding polyelectrolyte multilayer films[4] was studied, also with the help of FT-IR spectroscopy. With such multilayer films the pH at which the films were prepared had a strong influence on the pH-dependent swelling behaviour in solution, with discontinuous swelling transitions when the assembly pH was above 8.5. Ion-specific swelling of such gels has been demonstrated, showing evidence also for deswelling in the presence of small anions.[5] Sudden collapse of such gels was observed by exposure to sodium salts of various organic acids, to a lesser degree with NaCl and NaI, which showed gradual volume transitions.[6] The association of hydrophobic counterions such as benzenesulfonate with in PAA solutions was studied by viscosity and NMR measurements.[7] Little is known about the structure of PAA-derived materials. With small-angle X-ray scattering (SAXS) a single broad peak was observed not with inorganic ions, but, e.g., with sodium *p*-styrenesulfonate; the peak shifted towards lower angles with increasing size of the counterion.[6] The kinetics of contraction with PAA-derived polyelectrolyte multilayers were found to be strongly influenced by the type of polyanions.[4]

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Results and Discussion

The PAA-derived gel was obtained as described in the literature from commercially available PAA (MW = 60,000) by crosslinking with glutaraldehyde (GA).

pH Effects

In solutions with a moderate ionic strength the crosslinked PAA gel exhibits a strong expansion at pH values below 10, with a 6.2-fold volume increase from pH 3.5 to 12 (see Figure 1). This is in line with the known p*K* value of 9.7[8] and due to protonation of the nitrogen centers, which leads both to repulsion between the polymer chain, but in particular due to the uptake of water for solvation of the cationic centers and the simultaneously imported counter-anions. It has been observed already with gels de-

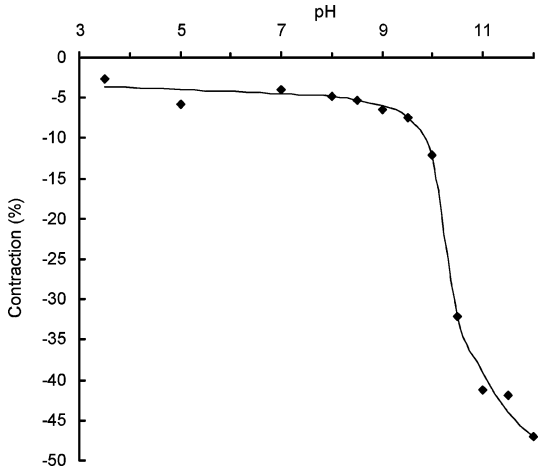
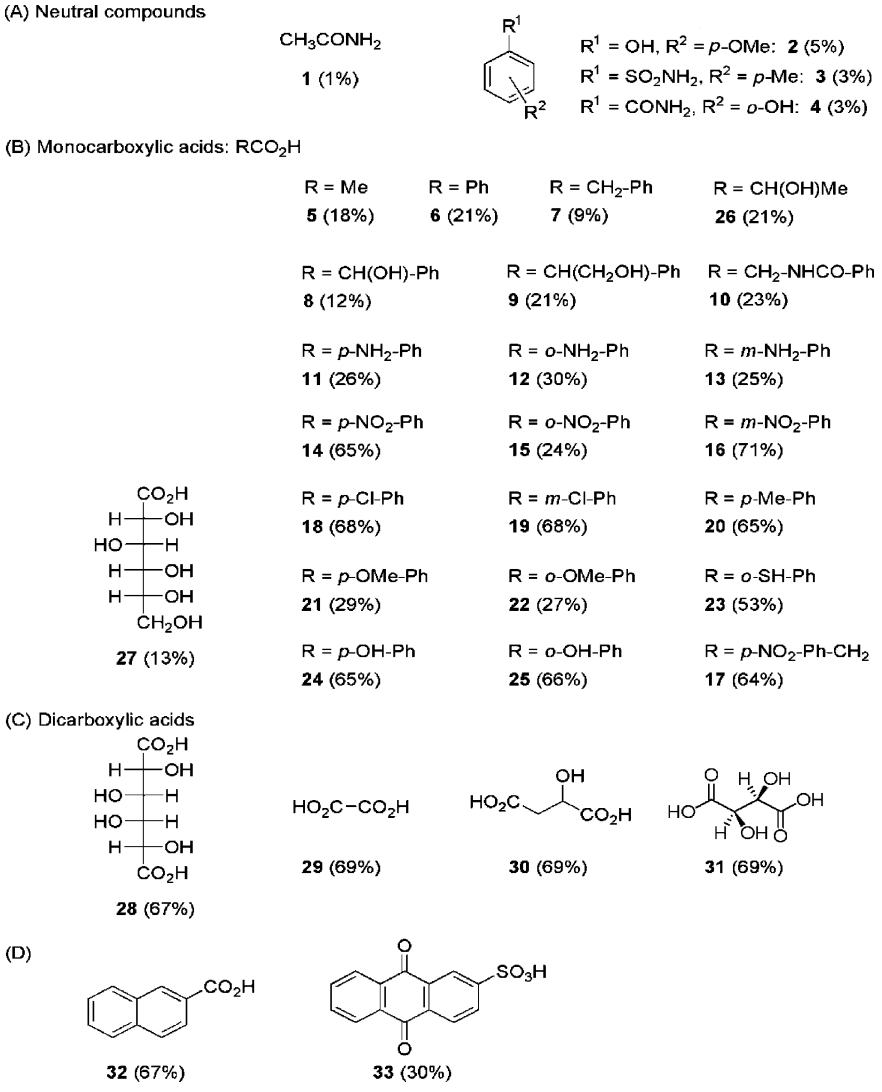


Figure 1. pH-Profile of contraction of PAA in the presence of 10 mM NaCl; % indicates the contraction in one dimension, decreasing with change of pH from 3→11.

rived from polyethylenimine (PEI) that the volume contraction corresponds exactly to the water loss.[9] As observed recently with a chitosan hydrogel even stronger acids tend to loose crosslinking ability at low pH, as there are less free anions for the cation-anion interactions.[10] It should be stressed that other polyamine gels show opposite to the PAA gel expansion at lower pH, due to uptake of water and anions accompanying formation of ammonium ions in the polymer. With PAA this effect is strongly counteracted by non-covalent crosslinking with by the anions which are taken up simultanously with protonation.

Stimulation by Organic Compounds

Volume changes in the presence of different compounds in 10 mM concentration were observed at pH 7 with the PAA gel in the hydrochloride form (Scheme 1). As with other ionic gel materials[2] electroneutral effector com-



Scheme 1. Size changes of the PAA-derived gel in the hydrochloride form, induced by organic compounds (all at 10 mM concentration, at pH 7; % contraction in one dimension of the polymer particle).

pounds such as simple phenoles, amides etc. do not lead to significant volume changes. Simple anions such as acetate can replace the chloride and lead to moderate contraction. The effect of mono-anionic effectors, however, does not significantly exceed that of an increased ionic strength *I*, as 10 mM sodium chloride already leads to 17% contraction (all size change numbers are given for change in one dimension). Non-covalent crosslinking between the cationic polymer backbones is the reason for the larger effect of phosphate, and in particular of di-anions, which trigger up to 69% contraction (Figure 2, a). The different activity of the glucose oxidation products mucic and D-gluconic acid can be used to demonstrate with suitable containers capped with PAA gels the release of compounds which are colored for visibility reasons (see electronic supporting information).

The presence of aromatic residues leads to a remarkably enhanced contraction, which increases from 20% size reduction to 60% and more with additional substituents at the phenyl rings. Naphthyl- instead of phenyl-carboxylic acid also triggers contraction by 67%, which must be ascribed to the significant stacking between the aromatic units within the gel network (see Figure 2, d). The enhanced effect by increased strength of crosslinking can be understood as a result of interactions between the substituents and neighboring phenyl groups (Figure 2, b). Related van der Waals or stacking effects are obviously responsible for the enhanced effects of aryl – in comparison to aliphatic effectors; these have been quantified for substituents of high polarizibility in analyses with porphyrin complexes.[11] The substituent effect depends on the position of the substituent, thus allowing the distinction between *o*- and *p*- or *m*-nitrobenzoic acid. That the dispersive contribution of nitro groups in *o*-position is diminished as result of steric hindrance with the vicinal carboxylate group (Figure 2, c) has also been established in the investigation with porphyrin complexes.[11] Additional binding effects can be due to cation–π interactions between the ammonium centers and the polarizable guest moieties. Small effects are seen with amino acids, surprisingly similar with glycin and phenylalanin, with a contraction of similar magnitude as triggered by acetic acid. The volume decrease corresponds almost entirely to a loss of water; thus the gravimetrically determined water content changed from 99% to 45% after exposure of the gel to 10 mM of *p*-nitrobenzoic acid. The volume changes can be controlled also by host compounds which may compete with the polymeric gel host for complexation of different effectors. Thus, in the presence of β-cyclodextrin, which by itself exerts only small contraction, 1-admantantyl carboxylate triggers much smaller contraction (Table S2). The reduction of the chemomechanical effect roughly parallels the known complexation strength of the effector molecules by cyclodextrin.

Concentration Dependence and Possible Cooperativity Effects

The effector concentration–contraction profiles are characterized by distinct discontinuity, reaching a plateau at about 0.5 mM concentration for naphthoic acid; the presence of amino acids such as Gly and Phe has a negligible influence (Figure 3). With related hydrogels derived from polyamines it has been demonstrated that the critical concentration for reaching a maximum volume change is a function of the gel particle size, as the full occupation of all available binding sites requires only a small excess of effector molecules in the surrounding medium as long as the

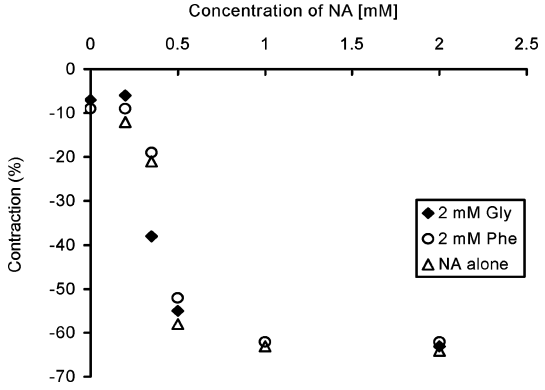


Figure 3. Concentration–contraction profile with 2-naphthoic acid (NA, **32**) as effector at pH 7; the presence of 2 mM amino acids shows no difference, indicating absence of cooperativity.

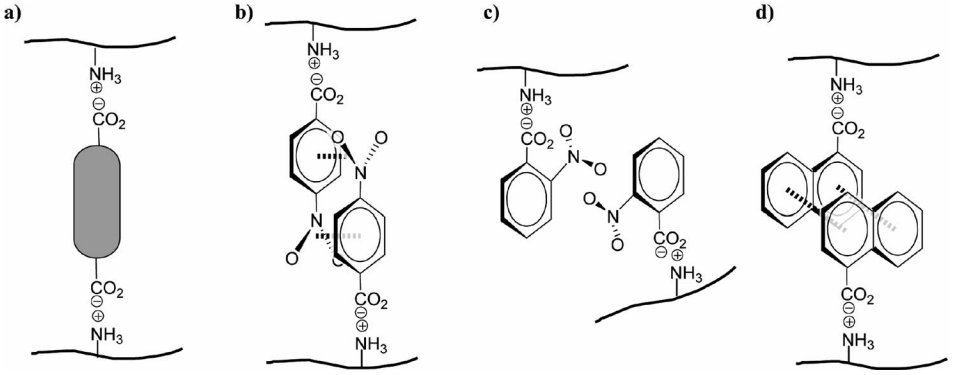


Figure 2. Non-covalent crosslinking in a PAA-derived hydrogel by (a) dicarboxylic acids; (b) *p*-nitrobenzoic acid; (c) *o*-nitrobenzoic acid (no interaction with aryl groups, see text); (d) stacking of naphthyl groups.

affinity is large enough to bind most of the effector molecules, independent of their concentration.[12] It can be assumed that at the plateau concentration all binding sites are occupied, due to the much higher concentration of effector in comparison to the binding sites.

The kinetics of contraction (Figure 4) show as expected a rate increase with increased effector concentration. The profiles cannot be fitted to a simple rate law: the effector diffusion into the core the gels becomes slower in the course of contraction, which necessarily leads to more compact or dense packing of the network. For these reasons there is also a quite fast reaction until about 17% contraction, depending on the effector concentration.

In contrast to results with e.g. hydrogels derived from polyethyleneamine (PEI)[9] the PAA gels showed no positive cooperativity if exposed simultaneously to two different effectors, such as naphthoic and amino acid (Table S1, Figure 3). Instead, a reduced contraction is observed, which likely is the result of competition between the two effector compounds.

NMR Spectroscopy

MAS NMR spectra (Figure 5) show that addition of *o*-nitrobenzoic acid, which affects the gel size only to a small degree, barely shifts the polymer signals: the guest signals remain also remarkably narrow, indicating high mobility inside the polymer network. In contrast, *p*-nitrobenzoic acid as guest leads to considerable signal broadening, and to the appearance of an additional signal around 1.3 ppm, in line with its higher chemomechanical activity. Naphthoic acid, which has a similar contraction effect like *p*-nitrobenzoic acid, shows in the NMR spectrum even larger line broaden-

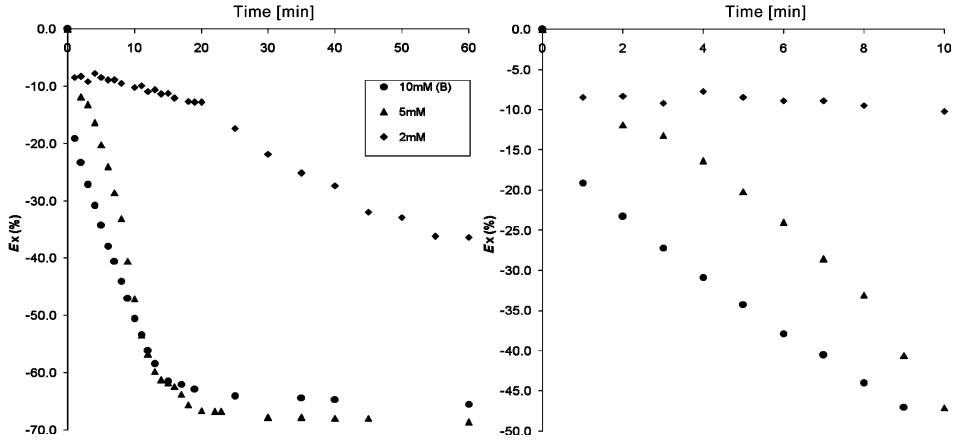


Figure 4. Kinetics of contraction of the PAA gel in the presence of *p*-nitrobenzoic acid at pH 7.0 (pH adjusted with NaOH).

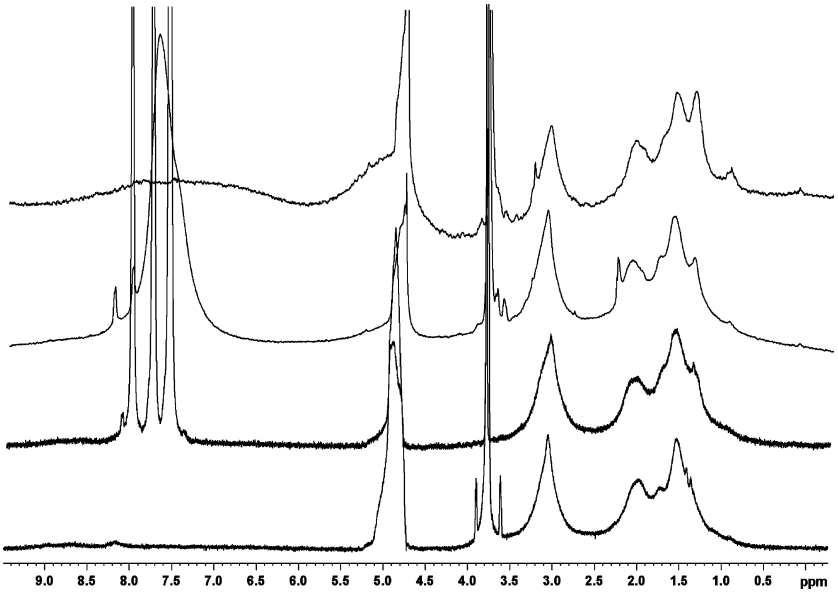


Figure 5. MAS ^{1}H NMR of PAA gels at pH 7 in the presence of 10 mM 2-naphthoic acid (upper trace), 10 mM *p*-nitrobenzoic acid (second trace), 10 mM *o*-nitrobenzoic acid (third trace), and PAA itself (lower trace).

ing, and a stronger signal at the same position as in the spectrum with *p*-nitrobenzoic acid, again indicating a strong interaction. An increase in temperature from 298 to 318 and up to 338 K did show significant line narrowing, e.g., in the presence of 10 mM 2-naphthoic acid at pH 7, in line with the increased mobility of the guest in the polymer network. Since the polymer backbone signals showed almost no shape changes their broad signals must be due to the inhomogenity of the structure, with many overlapping signals.

Experimental Section

All chemicals were commercially available and used without further purification (**27**: D-gluconic acid, **30**: racemic DL-malic acid, **31**: L-tartaric acid).

300 mg of PAA hydrochloride (Alta Aesar, $MW \approx 60{,}000$) was dissolved in 3 mL of water to give a 1.75 M solution; 0.5 mL of this solution was vigorously stirred, and different amounts of glutaraldehyde (GA) were added dropwise with molar ratios of PAA monomer to GA of 1:0.015, 1:0.03, 1:0.06, 1:0.09 and 1:0.12. After 3 min, the magnetic stirrer was removed and the solution left standing at room temperature overnight. The resulting gels were cut into cylinders with 4 mm diameter (thickness about 2 mm), and kept in water (with frequent exchange of the aqueous phase by fresh water). After 3 days no significant further swelling was observed.

Contractions at pH 11 (NaOH solution) occurred faster, and volume changes triggered by different effectors were larger with lower concentrations of cross-linker, but gels became this way too soft for handling. Therefore, the mechanically most stable gel, which had a 1:0.12 molar ratio of PAA monomer to GA, was employed for further investigation. A swollen gel disc was cut into small squares, e.g. 2.0×2.0 mm with 1.0 mm thickness, and the gel pieces were immersed into different effector solutions. The effector concentration always exceeded the amino group concentration in the gel by orders of magnitude (typically the amino group concentration from a gel particle of $2 \times 2 \times 1$ mm swollen gel is in 0.5 mM effector solution 0.5 mM $\times$ 1 mL = 0.50×10^{-6} M, in the presence of, for instance, 0.5 mM effector).

The sizes of the gel pieces and their changes were measured as described previously[9] with a measuring microscope and CCD camera coupled to a Personal Computer with suitable software. NMR measurements were performed with a Bruker DRX 500 MHz system under magic-angle spinning with neat gel pieces.

Supporting Information (see also the footnote on the first page of this article): Table S1 with contraction data of the PAA-derived gel as a function of 2-naphthoic acid concentration. Table S2 with contraction data of PAAm gels in the presence of β-cyclodextrin and different carboxylate anions.

Acknowledgments

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