

## Poly-(4- and 5-acrylamidosalicylic Acids). Part I. Preparation and Properties †

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Salicylic acid type polymers have been prepared by polymerisation of 4- and 5-acrylamidosalicylic acids. Difficulties in achieving the polymerisation were overcome by prior formation of the salts or borate complexes of the monomers. The characteristics of the polymers and their solubilities in a number of solvent systems have been examined.

FREE-RADICAL polymerisation can be inhibited by species which can interfere with radical formation or chain reactions by a variety of mechanisms. For example, Bovey and Kolthoff<sup>1,2</sup> reported that the free-radical polymerisation of styrene was retarded by 3,5-dinitrobenzoic acid and by benzoquinone. Our attempts to polymerise 4-acrylamidosalicylic acid by various conventional techniques for free-radical polymerisation were non-productive. It therefore appeared that the presence of adjacent hydroxy- and carboxy-groups as substituents on an aromatic nucleus in an olefinic monomer inhibits free radical polymerisation.

However, we have shown that the inhibition can be considerably reduced and probably completely eliminated either by conducting the polymerisation in the presence of sodium ions and hence forming the salt, or in the presence of borate ions [to give polymer (A)]. The boron-11 n.m.r. spectra of salicylic acid (0.75M) in sodium tetraborate solutions (1M in monomeric boron species) at various pH values (Figure 1) showed a peak at  $\delta$  ca. 3.6 p.p.m., corresponding to complexed boron, and a peak at higher shift corresponding to free borate. The latter peak disappeared at pH 9.1 and integrations also showed that all the borate was complexed at this pH (Figure 2). At pH values greater than 10.0, the shift for the uncomplexed borate approached that for the complexed boron; thus it was not possible to distinguish between the two. We therefore considered the poly-

merisation to proceed *via* the borate complex of the monomer (II) to give the borate-complexed polymer (III). Since high yields were obtained, it was considered that complex formation of two monomer molecules with a borate ion, if it did occur, did not cause significant inhibition of the polymerisation.

In the cases where polymerisation was achieved after addition of alkali to the monomer solutions [to give polymer (B) or (C)], it was clear that the pH of the solution was without effect over a wide range. The first and second  $pK_a$  values for salicylic acid are 2.97 and 13.40; whilst these will be modified by the presence of the acrylamide side-chain, we presume that at pH 4.5 and 9.0 the carboxy-group will be ionised. The situation is therefore analogous to that described<sup>1</sup> for 3,5-dinitrobenzoic acid in ionised form, where no inhibition occurred. Since the higher pH used (9.0) was well below the  $pK_a$  value for the ionization of the phenolic hydroxy-group of salicylic acid, we presume that the carboxy-group is predominantly responsible for the inhibition of polymerisation. It was not possible to test polymerisation at very low pH values owing to insolubility of the monomers.

Determination (by drying) of the water contents of samples of poly-(4-acrylamidosalicylic acid) (A) and poly-(5-acrylamidosalicylic acid) (A) which had had all surplus water removed at the pump showed that the gel-like polymers contained 90% water, thus suggesting that they are hydrophilic. Changes in their physical

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<sup>1</sup> F. A. Bovey and I. H. Kolthoff, *J. Amer. Chem. Soc.*, 1948, **70**, 791.

<sup>2</sup> F. A. Bovey and I. M. Kolthoff, *J. Polymer Sci.*, 1950, **5**, 569.

properties were apparent on drying, the 4-acrylamido-derivative becoming off-white and the 5-substituted polymer becoming brown.

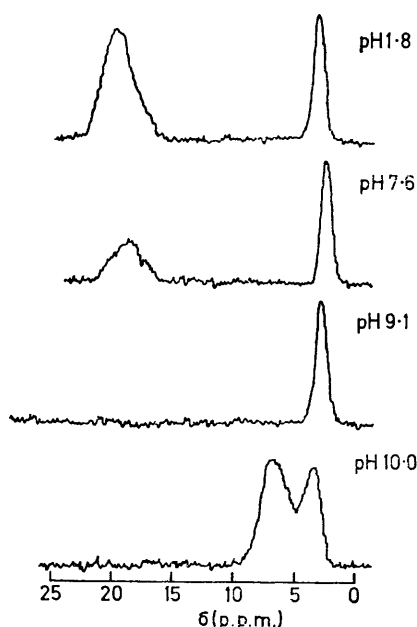


FIGURE 1 Dependence of the  $^{11}\text{B}$  n.m.r. spectrum of salicylic acid (0.75M) in borax solutions (1M in monomeric boron species) upon pH

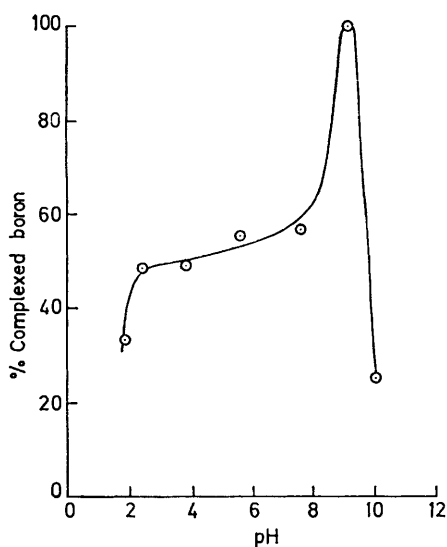
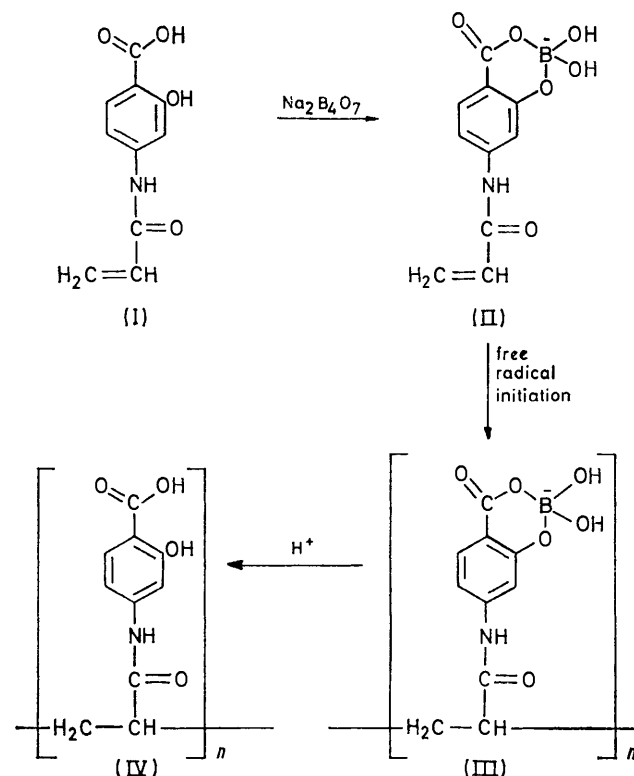


FIGURE 2 Dependence of the percentage of complexed boron upon pH for salicylic acid (0.75M) in borax solution (1M in monomeric boron species)

Values of 1.067 and 1.075 carboxy-groups per molecule of monomer were calculated, from titrations and net weights of duplicate samples of the polymers, for poly-(4- and 5-acrylamidosalicylic acids) (A), respectively. These close agreements with the expected value of unity contribute to the confirmation of a structure of type (IV). The highly anionic nature of the polymers was also demonstrated by the ability of poly-(4-acrylamidosalicylic acid) (A) to interact with and remove

cetyltrimethylammonium cations from solution. The presence of salicylic acid residues was confirmed by the formation of an intense purple precipitate when ethanolic solutions of the polymers were treated with iron(III) chloride solution.

Dialysis of the initial polymer solutions against ionic solutions of various pH values showed that the polymers did not precipitate above pH 3.0. Once precipitated, they were insoluble in distilled water. Both were insoluble in diethyl ether, petroleum (b.p. 80–100, 60–80, or 40–60°), pyridine, benzene, carbon disulphide, n-pentane, chloroform, carbon tetrachloride, dichloromethane, ethyl acetate, n-butanol, and ethanol. However, both polymers were readily dissolved by cold methanol and were also soluble in hot diethylene glycol, ethylene glycol, glycerol, n-butanol, ethanol, and glacial acetic acid. In the case of solutions in glacial acetic acid



the polymers spontaneously precipitated on cooling whereas in all other cases they stayed in solution. The solubilities confirm the hydrophilic nature of the polymers. The poly-(4-acrylamidosalicylic acid) (A) was also soluble in tetrahydrofuran and dioxan whereas the 5-acrylamido-compound was not. This implied that the former polymer was slightly less hydrophilic than the latter.

These polymers, perhaps in a more suitable physical state, hold potential for applications to ion-exchange chromatography of cationic materials, and selective binding of positively charged molecules to form, e.g., insolubilised derivatives of enzymes, proteins, and glycoproteins including immunoglobulins.

## EXPERIMENTAL

**4-Acrylamidosalicylic Acid (I)**—Sodium 4-aminosalicylate (Hopkin and Williams; 40 g, 0.24 mol) dissolved in distilled water (250 ml) was stirred for 1 h. Two separate additions of acryloyl chloride (20 and 10 ml; 0.368 mol) were made, the solution being stirred for 1 h after each addition. Acidification to pH 4.0 with 10N-hydrochloric yielded a grey precipitate which was filtered off and washed with distilled water (500 ml) to give 4-acrylamidosalicylic acid (27.0 g, 57%), m.p. 227–229 °C (from aqueous ethanol),  $\nu_{\max}$  (KBr) 3315 (amide N-H str.), 1680 (acid C=O str.), 1655 (amide C=O str.), and 980  $\text{cm}^{-1}$  (C=C),  $\delta$  ( $\text{CD}_3\cdot\text{OD}$ ) 5.69 (1H, dd,  $J$  ca. 6 and 5 Hz,  $\text{CH}_2=\text{CHC}=\text{O}$ ), 6.18 (2H, m,  $\text{CH}_2=\text{CH}-\text{CO}$ ), 7.0 [1H, dd,  $J$  ca. 9 and 2 Hz, C(5)H], 7.32 [1H, d,  $J$  ca. 3 Hz, C(3)H], and 7.73 p.p.m. [1H, d,  $J$  ca. 8 Hz, C(6)H] (Found: C, 57.7; H, 4.35; N, 6.65.  $\text{C}_{10}\text{H}_9\text{NO}_4$  requires C, 58.0; H, 4.35; N, 6.75%).

**5-Acrylamidosalicylic Acid**.—Similarly 5-aminosalicylic acid (R. N. Emanuel; 40 g, 0.261 mol) gave the 5-acrylamido-compound (25.8 g, 47.6%), m.p. 218–219 °C,  $\nu_{\max}$  (KBr) 3315br (amide N-H str.), 1680 (acid C=O str.), 1655 (amide C=O str.), and 980  $\text{cm}^{-1}$  (C=C),  $\delta$  ( $\text{CD}_3\cdot\text{OD}$ ) 5.63 (1H, dd,  $J$  ca. 6 and 5 Hz,  $\text{CH}_2=\text{CH}-\text{C}=\text{O}$ ), 6.17 (2H, m,  $\text{CH}_2=\text{CH}-\text{C}=\text{O}$ ), 6.83 [1H, d,  $J$  ca. 9 Hz, C(3)H], 7.62 [1H, dd,  $J$  ca. 9 and 4 Hz, C(4)H], and 8.08 p.p.m. [1H, d,  $J$  ca. 3 Hz, C(6)H] (Found: C, 57.5; H, 4.5; N, 6.5.  $\text{C}_{10}\text{H}_9\text{NO}_4$  requires C, 58.0; H, 4.35; N, 6.75%).

**Poly-(4-acrylamidosalicylic Acid) (A) (IV)**.—Use of an ethanolic solution of 4-acrylamidosalicylic acid and azobisisobutyronitrile, ammonium persulphate, or benzoyl peroxide as initiator, or a solution in ethylene glycol and irradiation with a Hanovia u.v. lamp all failed to induce polymerisation.

*N*-Acrylamidosalicylic acid (15 g) and disodium tetraborate (9.36 g) were dissolved in distilled water (180 ml), the pH was adjusted to 9.0 with 10N-sodium hydroxide, and a solution of azobisisobutyronitrile (150 mg) in ethanol (50 ml) was added. The resulting solution was heated at 80 °C for 48 h and then diluted with distilled water (200 ml). 5N-Hydrochloric acid was added to precipitate the white polymer. The precipitate was washed with distilled water ( $10 \times 1$  l) by decantation and the wet material was then evaporated *in vacuo* with methanol ( $4 \times 250$  ml) to remove any remaining borate as methyl borate. After a final wash with water by decantation (250 ml) the polymer was stored as a suspension in distilled water; yield 11.4 g (76%),  $\nu_{\max}$  (KBr) 1680–1650br  $\text{cm}^{-1}$  (acid and amide C=O str.),  $\delta$  ( $\text{CD}_3\cdot\text{OD}$ ) 1.8–2.4br (3H,  $\text{CH}_2\cdot\text{CH}$ ), 6.85br

[1H, C(5)H], 7.13br [1H, C(3)H], and 7.55br p.p.m. [1H, C(6)H].

**Poly-(5-Acrylamidosalicylic Acid) (A)**.—Similarly 5-acrylamidosalicylic acid (15.0 g) gave a pale pink polymer (14.2 g, 94%),  $\nu_{\max}$  (KBr) 1680–1650br  $\text{cm}^{-1}$  (acid and amide C=O str.),  $\delta$  ( $\text{CD}_3\cdot\text{OD}$ ) 1.8–2.4br (3H,  $\text{CH}_2\cdot\text{CH}$ ), 6.60br [1H, C(3)H], 7.40br [1H, C(4)H], and 7.85br p.p.m. [1H, C(6)H].

**Poly-(4- and 5-acrylamidosalicylic Acids) (B)**.—The acrylamidosalicylic acids (1 g) were polymerised as described for polymers (A) but borate was excluded, the pH of the monomer suspensions being adjusted to pH 9.0 with 10N-sodium hydroxide. The precipitation and washing procedures were carried out as before to yield the white poly-(4-acrylamidosalicylic acid) (B) (0.80 g, 80%) and the pink poly-(5-acrylamidosalicylic acid) (B) (0.90 g, 90%).

**Poly-(4- and 5-acrylamidosalicylic Acids) (C)**.—These polymers were prepared as described for polymers (B), the pH of the monomer suspension being adjusted to pH 4.5 before polymerisation; yields 0.94 g (94%) and 0.90 g (90%), respectively.

**Determination of Acid Groups**.—Samples (2 ml; ca. 100 mg) of the polymers (A) dissolved in methanol (20 ml) were titrated (phenolphthalein) with 0.1M-sodium hydroxide.

**Interaction of Poly-(4-acrylamidosalicylic Acid) with Cetyltrimethylammonium Bromide**.—Duplicate samples (50 mg) of poly-(4-acrylamidosalicylic acid) were suspended in distilled water (1.0 ml) and the pH was adjusted to 7.0 with sodium hydroxide. After centrifugation and removal of the supernatant, the polymer was treated with a solution of cetyltrimethylammonium bromide (100  $\mu\text{g ml}^{-1}$ ; 2.0 ml). After shaking and centrifugation, assay<sup>3</sup> of the supernatant with Solochrome Green V150 (I.C.I. Organics Division) showed that all cetyltrimethylammonium cations had been removed from solution.

**Solubility of the Polymers**.—The polymer (2 ml; 100 mg) was added to the solvent (10 ml) and the mixture was shaken for 10 min at room temperature. If the sample was insoluble, the mixture was heated in a water-bath to 100 °C with continuous shaking for 10 min. If the sample dissolved, the solution was cooled rapidly in an ice-bath to see whether precipitation occurred.

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<sup>3</sup> A. S. Jones, *Nature*, 1963, **199**, 280.