

Studies on 5-Aminosalicylaldehyde Derivatives. II.¹⁾ Reduction
of 5-(*p*-Sulfophenylazo)salicylaldehyde through Poly(5-
nitrilosalicylidene) to 5-Aminosalicylaldehyde
Derivatives

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Derivatives of 4-aminosalicylaldehyde over a wide range have been synthesized and characterized for medical purposes by several workers²⁾ in recent years. Only a few derivatives of 5-aminosalicylaldehyde have, however, been studied. In the previous paper,¹⁾ it was reported that the attempted synthesis of 5-aminosalicylaldehyde (II) by the reduction of 5-(*p*-sulfophenylazo)salicylaldehyde (I)

1) Part I: M. Tanaka, This Bulletin, **37**, 1210 (1964).

2) For instance, T. Ikeda, S. Hirai, M. Ishikawa and M. Yoshioka, *Ann. Repts. Shionogi Research Lab.*, **1** (1953); A. A. Goldberg and H. A. Walkerm, *J. Chem. Soc.*, **1954**, 2540; R. Justoni, R. Pessina and C. Pirola, *Chem. Abstr.*, **47**, 6944 (1953); Ch. Gausser and P. Rumpf, *Helv. Chim. Acta*, **37**, 437 (1964).

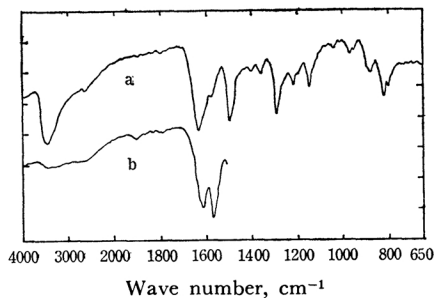


Fig. 1. Infrared spectra of poly(5-nitrilosalicylidene).

a, KBr disk

b, Hexachlorobutadiene mull method.

R₂: a. $-\text{CH}=\text{CH}-$, b. $-\text{CH}_2\text{CH}_2-$, c. $-\text{C}_6\text{H}_4-$

gase *et al.*³⁾ By an analogous method, propionic, isobutyric, caproic, and benzoic anhydrides, as well as succinic, maleic, and phthalic anhydrides, also gave the corresponding 5-acylamino-salicylaldehydes (IV) as well as cyclic dicarbonylamino-salicylaldehydes (V). The red substance (III) was cleaved also by phenylhydrazine and yielded 5-aminosalicylaldehyde phenylhydrazone (VI), which was identified by its infrared spectrum and by a mixed-melting-point determination with an authentic sample prepared by the method of Weil *et al.*⁴⁾ and Oddo *et al.*⁵⁾ Similarly, the reaction of III with hydrazine hydrate gave bis(5-aminosalicylaldehyde)azine.

From the facts mentioned above, the red substance (III) was confirmed to be poly(5-nitrilosalicylidene). As this substance is readily cleaved by acid anhydrides or by hydrazines, the synthesis of some 5-aminosalicylaldehyde derivatives may be facilitated by this new route through the polymer.

Experimental

The Infrared Spectra. The infrared spectra were measured with a Hitachi IR spectrophotometer, model EPI-S2.

Sodium Salt of 5-(*p*-Sulfophenylazo)salicylaldehyde (I). This salt was prepared by Tummely's method.⁶⁾

Found: C, 42.80; H, 3.60; N, 7.48; Na, 5.93%. Calcd for $C_{13}H_9O_5N_2Na \cdot 2H_2O$: C, 42.83; H, 3.60; N, 7.69; Na, 6.31%.

Poly(5-nitrilosalicylidene) (III). To a stirred solution of 3.8 g of sodium salt of I and 1.6 g of sodium hydroxide in 100 ml of water, 3.8 g of sodium hydrosulfite were added at 60–70°C. The precipitate was collected and washed thoroughly with water. Reddish powder, insoluble in various solvents; yield, 1.16 g (85%).

Found: C, 70.64; H, 4.15; N, 11.72%. Calcd for C_7H_5ON : C, 70.58; H, 4.23; N, 11.76%.

Cleavage of Poly(5-nitrilosalicylidene) by Acid Anhydrides. Poly(5-nitrilosalicylidene) (0.01 mol) (III) was heated with acid anhydride (0.05–0.1 mol) containing a small amount of pyridine (0.1 ml) until it dissolved. The temperatures are listed in Table I.

3) Y. Kuwayama and H. Ichibagase, *Yakugaku Zasshi*, **78**, 659 (1958).

Subsequent treatment was altered according to the kind of acid anhydride.

a) The reaction mixture was distilled under diminished pressure to remove an excess of acid anhydride and pyridine. The residue was then dissolved in a solution of sodium hydroxide (1.33 g) in water (100 ml), and acetic acid (3.5 ml) was added, after which the mixture was evaporated under diminished pressure.

b) The reaction mixture was poured into 150 ml of hot water and boiled for an hour. After cooling, the aqueous solution was neutralized with alkali, and the mixture was evaporated under diminished pressure.

c) The reaction mixture was poured into 150 ml of hot water and boiled for an hour. The hot mixture was filtered, and the precipitate was washed with hot water.

The residue obtained by these treatments was extracted with hot benzene or ethyl alcohol and recrystallized from the solvent specified in Table 1.

5-Aminosalicylaldehyde Phenylhydrazone. To 1.19 g of III, 5 g of phenylhydrazine were added. The mixture was then warmed on a water bath. After cooling, the precipitate was collected, washed with ethyl alcohol, and recrystallized from benzene. Yellowish needles. Mp 165–165.5°C.

Found: C, 68.73; H, 5.76; N, 18.61%. Calcd for $C_{13}H_{13}ON_3$: C, 68.70; H, 5.77; N, 18.49%.

Bis(5-aminosalicylaldehyde)azine. A mixture of 1.19 g of III with 5 g of hydrazine hydrate (80%) was slightly warmed on a water bath. After cooling, the reaction mixture was poured into dilute acetic acid. The precipitate was then collected, washed with ethyl alcohol, and recrystallized from dimethylformamide. Mp over 300°C. Yellow powder.

Found: C, 62.44; H, 5.36; N, 20.36%. Calcd for $C_{14}H_{14}O_2N_4$: C, 62.21; H, 5.22; N, 20.73%.

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4) H. Weil, M. Traun and S. Marcel, *Chem. Ber.*, **55**, 2664 (1958).

5) G. Oddo and A. Giacalone, *Gazz. Chim. Ital.*, **58**, 290 (1928).

6) E. Tummely, *Ann.*, **251**, 180 (1889).