oxide. The reduction product was precipitated from the filtered and cooled solution with acetic acid. After boiling in alcohol in the presence of animal charcoal, crystallization was effected by concentrating the solvent; yield 0.5 g.

On recrystallization from alcohol the amino acid separated in long orange-yellow needles melting at 273–274° (dec.) with sintering at 268°.

It is easily soluble in dilute sodium hydroxide, moderately in alcohol, chloroform, ether and hot water but difficultly soluble in hot benzene. The solution in concd. sulfuric acid shows green fluorescence.

Anal. Calcd. for $C_{14}H_{10}O_2N_2$: C, 70.59; H, 4.20. Found: C, 70.36; H, 4.37.

The monohydrochloride gives black-violet leaflets from dilute hydrochloric acid, decomposing at 245–250°. It is soluble in alcohol and water with violet-red color.

Anal. Calcd. for $C_{14}H_{10}O_2N_2 \cdot HCl \cdot {}^1/_2H_2O$: C, 59.26; H, 4.23. Found: C, 59.27; H, 4.77.

Summary

5-Nitrodiphenylamine-2,2′-dicarboxylic acid, on ring closure, yields 1-nitroacridone-4-carboxylic acid as a chief product.

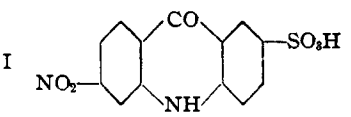
TOKYO, JAPAN RECEIVED SEPTEMBER 27, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF KITASATO INSTITUTE]

Sulfonation of 6-Nitroacridone

BY KONOMU MATSUMURA

6-Nitroacridone-2-sulfonic acid, I can be prepared by the action of fuming sulfuric acid on the



I

corresponding nitroacridone. Contrary to expectation, the sodium salt of this new acid yields with phosphorus oxychloride or pentachloride the corresponding acridone sulfonyl chloride, while sodium acridone-2-sulfonate is converted to 9-chloroacridine-2-sulfonyl chloride.[1]

The assumed 2-position of the sulfonic acid group in I was confirmed as follows:

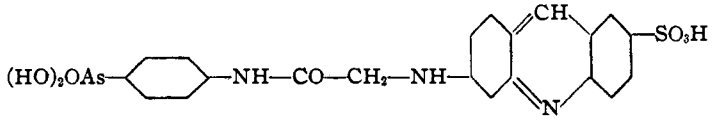
II. Acridone-2-sulfonic acid was prepared from the nitroacridone sulfonic acid by reduction of the nitro group, followed by removal of the amino group through diazotizing. The product so obtained, on admixture with an authentic sample,[1] showed no depression in melting point.

III. Synthesis of 6-nitroacridone-2-sulfonic acid was effected as follows: *p*-nitro-*o*-chlorobenzoic acid was condensed with sulfanilic acid by the method of Polaczek,[2] the reaction product was treated with phosphorus oxychloride and the resultant acridone sulfonyl chloride was hydrolyzed to the corresponding sulfonic acid.

IV. The same nitroacridonesulfonic acid was synthesized by the interaction of 5-nitrodiphenylamine-2-carboxylic acid and fuming sulfuric acid.

The identity of preparations I, III and IV was established by the constant melting point of admixed samples.

By the interaction of sodium ω-chloroacetaminophenyl-*p*-arsinate and sodium 6-aminoacridine-2-sulfonate, 6-arsacetinylaminoacridine-2-sulfonic acid (V) was made.



V

This compound was shown to be trypanocidally ineffective when tested with recurrent fever on mice.[3]

Experimental

Sodium 6-Nitroacridone-2-sulfonate.—6-Nitroacridone (20 g.) in fuming sulfuric acid (20%, 100 g.) was allowed to stand at room temperature for several hours until a sample dissolved completely in water, the mixture was poured into ice water, sodium hydroxide (21 g. in 500 cc. of water) was added and the sodium salt was precipitated from the filtered solution with hydrochloric acid (yield 27.7 g. or 97.2%).

Crystallized from water, it forms yellow needles with two moles of water, being unaltered at 360°. It is readily soluble in hot dilute sodium carbonate and cold dilute sodium hydroxide with red color but almost insoluble in alcohol, dilute hydrochloric acid or salt solution.

Anal. Calcd. for $C_{13}H_7O_6N_2SNa$: C, 45.61; H, 2.05; Na, 6.73. Found: C, 45.03; H, 2.55; Na, 6.62.

6-Nitroacridone-2-sulfonic Acid.—Prepared from its sodium salt through the barium salt, it crystallized from

(1) Matsumura, THIS JOURNAL, **57**, 1535 (1935).

(2) Polaczek, *Roczniki Chem.*, **15**, 565 (1935); *Chem. Zentr.*, **108**, 2355 (1936).

(3) I am indebted to Dr. Yamamoto of this Institute for the biological test.

dilute sulfuric acid in yellow thin plates which decompose to tar at 325–352°. It is easily soluble in water and alcohol.

Anal. Calcd. for $C_{13}H_8O_6N_2S$: C, 48.75; H, 2.50. Found: C, 48.73; H, 3.09.

Disodium Salt.—This salt crystallizes from 2% sodium hydroxide in violet-red needles containing 3.5 moles of water and undergoes partial hydrolysis in aqueous solution to the yellow monosodium salt.

Anal. Calcd. for $C_{13}H_6O_6N_2SNa_2$: Na, 12.64. Found: Na, 11.83.

p-Toluidine salt gives yellow leaflets from alcohol, m. p. 318–320° (dec.).

Anal. Calcd. for $C_{13}H_8O_6N_2S \cdot C_7H_9N$: C, 56.21; H, 3.98. Found: C, 56.05; H, 4.29.

6-Nitroacridone-2-sulfonyl Chloride.—A mixture of sodium 6-nitroacridone-2-sulfonate (1 g.), phosphorus pentachloride (4 g.) and toluene (6 cc.) was refluxed for three hours and after evaporation to dryness under reduced pressure, the residue was treated with ice-cold sodium bicarbonate solution; yield 0.9 g.

It forms yellow prisms from a benzene–nitrobenzene mixture (2:1), m. p. 289° (dec.).

Anal. Calcd. for $C_{13}H_7O_5N_2SCl$: C, 46.09; H, 2.07. Found: C, 46.77; H, 2.56.

The sulfamide was obtained on treating the cooled acetone solution of the sulfonyl chloride with ammonia, in the form of yellow prisms, being unaltered at 360°. It is sparingly soluble in the usual organic solvents, but easily soluble in dilute sodium hydroxide.

Anal. Calcd. for $C_{13}H_9O_5N_3S$: C, 48.90; H, 2.82. Found: C, 49.00; H, 3.22.

The Methyl Ester.—Yellow prisms from methanol, with no definite melting point.

Anal. Calcd. for $C_{14}H_{10}O_6N_2S$: C, 50.30; H, 2.99. Found: C, 50.18; H, 3.02.

Sulfonation of 5-Nitrodiphenylamine-2-carboxylic Acid.—The method was similar to that of the sulfonation of 6-nitroacridone; the yield of sodium 6-nitroacridone-2-sulfonate was 77.7% of the theoretical.

Anal. Calcd. for $C_{13}H_7O_6N_2SNa$: C, 45.61; H, 2.05. Found: C, 45.54; H, 2.59.

The *p*-toluidine salt gave orange-yellow plates from alcohol, the m. p. 318–320° (dec.) of which remained constant for a sample admixed with authentic *p*-toluidine salt of 6-nitroacridone-2-sulfonic acid.

Sodium 5-Nitro-4'-sulfonate-diphenylamine-2-carboxylic Acid.—A mixture of *p*-nitro-*o*-chlorobenzoic acid (10.1 g.), sulfanilic acid (10.5 g.), potassium carbonate (6.9 g.), copper powder (0.1 g.) and water (14 cc.) was kept at 115–120° for eight hours and then the cooled solution was made alkaline with sodium hydroxide.

After treatment with animal charcoal, the desired diphenylamine derivative, along with *p*-nitrobenzoic acid, was precipitated from the hot filtrate with hydrochloric acid. The nitrobenzoic acid was extracted with ether and the residue was dissolved in 100 cc. of dilute sodium carbonate. The hot solution, on saturation with sodium chloride, gave a thick paste of brown-orange needles, which was dissolved in hot water (50 cc.) and precipitated with hydrochloric acid; yield 4.8 g. of the sodium salt, m. p. 281–286° (dec.). It forms reddish-orange needles from alcohol, m. p. 291–292° (dec.).

Anal. Calcd. for $C_{13}H_9O_7N_2SNa \cdot 0.5H_2O$: C, 42.28; H, 2.71; Na, 6.23. Found: C, 42.38; H, 2.93; Na, 6.37.

The free acid was prepared through the barium salt. It separates in orange-red needles with four moles of water from dilute hydrochloric acid (5%) and in yellow needles from ether, m. p. 176–177° (dec.).

Anal. Calcd. for $C_{13}H_{10}O_7N_2S$: C, 46.15; H, 2.96. Found: C, 46.23; H, 3.47.

The barium salt gives orange-red needles containing 1.5 moles of water from hot water and being unaltered at 360°.

Anal. Calcd. for $C_{13}H_8O_7N_2SBa$: Ba, 29.02. Found: Ba, 28.72.

The monosodium salt was refluxed with phosphorus oxychloride and the resultant nitroacridonesulfonyl chloride (m. p. 290°) was hydrolyzed by heating with ten times its weight of water at 130° for three hours into nitroacridonesulfonic acid. The *p*-toluidine salt crystallizes from alcohol in orange-yellow plates the melting point, 318–320°, of which is not lowered by admixture with the corresponding salt of the sulfonation product of 6-nitroacridone.

6-Aminoacridone-2-sulfonic Acid.—A mixture of sodium 6-nitroacridone-2-sulfonate (15 g.), stannous chloride (51 g.), concd. hydrochloric acid (150 cc.) and glacial acetic acid (300 cc.) was well triturated, then warmed at 80° for two hours, filtered on cooling and washed repeatedly with dilute hydrochloric acid and finally with water; yield 11.7 g. (92% of the theoretical). Recrystallized from water, it is obtained in light yellow leaflets, being unaltered at 360°, readily soluble in dilute sodium bicarbonate and exhibiting intense blue fluorescence in concentrated sulfuric acid.

Anal. Calcd. for $C_{13}H_{10}O_4N_2S$: C, 53.79; H, 3.45. Found: C, 53.90; H, 3.68.

6-Hydrazinoacridone-2-sulfonic Acid.—6-Aminoacridone-2-sulfonic acid (0.2 g.), dissolved in concd. sulfuric acid (8 g.), was diazotized with powdered sodium nitrite (0.1 g.) in the cold.

The solution when poured into ice water deposited red orange needles. The diazonium salt was digested with stannous chloride (1 g.) in hydrochloric acid (1.5 cc.).

The hydrazinosulfonic acid thus formed was dissolved in dilute sodium carbonate and then precipitated with hydrochloric acid in the form of yellow needles melting at 350° (dec.).

Anal. Calcd. for $C_{13}H_{11}O_4N_3S$: C, 51.15; H, 3.61. Found: C, 50.86; H, 3.92.

Acridone-2-sulfonic Acid.—6-Aminoacridone-2-sulfonic acid (0.4 g.) was diazotized as described above. The diazo compound was dissolved in 50 cc. of alcohol and the solution was refluxed for two hours. After evaporation of the solvent and repeated recrystallization of the residue from dilute hydrochloric acid, the purified product was obtained in the form of yellow prisms melting at 318° and identified by comparison in the usual way with an authentic sample of acridone-2-sulfonic acid; yield 50 mg.

Anal. Calcd. for $C_{13}H_9O_4NS$: C, 56.73; H, 3.27. Found: C, 56.52; H, 3.56.

6-Aminoacridine-2-sulfonic Acid.—To the hot solution of 6-aminoacridone-2-sulfonic acid (6 g.) in sodium hydroxide (10%, 9 g.) and water (120 cc.), sodium amalgam (5%, 60 g.) was added. The mixture was shaken gently at 80° for two hours. The filtered hot solution on acidifying with hydrochloric acid deposited prismatic needles of pink color; yield 5.5 g. It forms brownish-orange rods from water, being unaltered at 360° and soluble in hot water and hot alcohol with green fluorescence. The almost colorless solution in concentrated sulfuric acid shows intense greenish-blue fluorescence. This compound is rather sensitive to heat especially in alkaline solution.

Anal. Calcd. for $C_{13}H_{10}O_3N_2S$: C, 56.93; H, 3.65. Found: C, 56.95; H, 3.77.

The sodium salt gives yellow thick plates from water. It is soluble in water and alcohol with green fluorescence.

Anal. Calcd. for $C_{13}H_9O_3N_2SNa$: Na, 7.77. Found: Na, 7.15.

6-Carboxymethylaminoacridine-2-sulfonic Acid.—A solution of 6-aminoacridine-2-sulfonic acid (0.55 g.), monochloroacetic acid (0.2 g.) and hydrated sodium carbonate (0.6 g.) in water (8 cc.) was refluxed for two hours and gave, on acidifying with hydrochloric acid, aggregates of violet-red fibrous needles (0.4 g.) which turned to tar at 345–360°.

Anal. Calcd. for $C_{15}H_{12}O_5N_2S$: C, 54.22; H, 3.61. Found: C, 54.32; H, 4.08.

***p*-Chloroacetylaminophenyl-arsinic Acid.**—A mixture of *p*-aminophenyl-arsinic acid (1.1 g.) and chloroacetyl chloride (0.9 g.) was warmed at 70° for a few minutes and poured on cooling into water. The reaction product was dissolved in sodium carbonate and precipitated with hydrochloric acid in colorless plates, m. p. 295–296° (dec.). It is readily soluble in methanol but insoluble in water.

Anal. Calcd. for $C_8H_9O_4NClAs$: C, 32.72; H, 3.07. Found: C, 33.00; H, 3.38.

6-Arsacetinylaminoacridine-2-sulfonic Acid.—A solution of 6-aminoacridine-2-sulfonic acid (0.5480 g.) and *p*-chloroacetylaminophenyl-arsinic acid (0.5720 g.) in sodium hydroxide (10%, 1.6 g.) was warmed at 70–80° for three hours and acidified with hydrochloric acid on cooling. The solid was digested with warm water, washed with water and then with methanol; yield 0.75 g.

The substance crystallizes in dark red prisms, turning to tar at 340–360°. It is soluble in dilute sodium carbonate and insoluble in alcohol and acetone. The yellow solution in concd. sulfuric acid exhibits green fluorescenee.

Anal. Calcd. for $C_{21}H_{16}O_7N_3SAs$: C, 47.46; H, 3.39. Found: C, 47.33; H, 4.02.

I hereby thank Professor Hata for his interest in the work.

Summary

Fuming sulfuric acid acts upon 6-nitroacridone as well as 5-nitrodiphenylamine-2-carboxylic acid to give 6-nitroacridone-2-sulfonic acid.

TOKYO, JAPAN RECEIVED OCTOBER 5, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE ROYAL VETERINARY AND AGRICULTURAL COLLEGE]

Amine Catalysis of the Ketonic Decomposition of α,α-Dimethylacetoacetic Acid

BY KAI JULIUS PEDERSEN

It has been found by Widmark and Jeppsson[1] and by Ljunggren[2] that the ketonic decomposition of acetoacetic acid

$$CH_3COCH_2COOH \longrightarrow CH_3COCH_3 + CO_2$$

is catalyzed by primary amines when the *p*H of the solution is kept within certain limits. In more acid and in more alkaline solution the amines do not catalyze. The influence of the acidity of the medium is explained by assuming that the reaction takes place either between the neutral amine and the undissociated acetoacetic acid, or between the positive aminium ion and the acetoacetate ion.

It is the object of this paper to examine more closely the amine catalysis of the decomposition of β-keto carboxylic acids. Instead of acetoacetic acid there was used α,α-dimethylacetoacetic acid, whose uncatalyzed decomposition has been studied in earlier papers.[3,4] The two amines aniline and *o*-chloroaniline were chosen as catalysts. Experiments were carried out at 24.97 and 34.93° in aniline–anilinium chloride buffer solutions and in *o*-chloroaniline–*o*-chloroanilinium chloride buffer solutions. To all the solutions had been added enough sodium chloride to make the total salt concentration 0.150 *N*.

We denote the undissociated dimethylacetoacetic acid by HA, the uncharged amine by B, and the total concentration of the reacting substance by $x \equiv (HA) + (A^-)$. According to the Swedish investigators[1,2] we may interpret the decomposition in the amine buffer solutions as

(1) E. M. P. Widmark and C. A. Jeppsson, *Skand. Arch. Physiol.*, **42**, 43 (1922).

(2) G. Ljunggren, "Katalytisk Kolsyreavspjälkning ur Ketokarbonsyror," Dissertation, Lund, 1925.

(3) K. J. Pedersen, THIS JOURNAL, **51**, 2098 (1929).

(4) K. J. Pedersen, *ibid.*, **58**, 240 (1936).