5-Chloro-2-phenylbenzothiazole.—When the above benzal derivative was refluxed in glacial acetic acid solution and the product separated as described in the similar cases above, the only pure compound isolated was the 5-chloro-2-phenylbenzothiazole, m. p. 138.5–139° (corr.), whose properties coincided entirely with those ascribed to this compound by Lankelma and Knauf;[10] yield, 52%.

The first crude product which separated in this reaction melted at 127–130°, and its melting point was raised to 138.5–139° (corr.) by crystallization from a mixture of petroleum ether and ether. Lankelma and Sharnoff[4] give the melting point of 5-chloro-2-phenylbenzothiazoline as 127°, so that even this crude product must have been mainly the thiazole.

When refluxed for four hours with alcohol, the zinc benzalamino derivative gave a 55% yield of the thiazole. Even refluxing with petroleum ether slowly converted the zinc benzalamino derivative into the thiazole, although the quantity formed, even after twelve hours of heating, was but small.

(10) Lankelma and Knauf, THIS JOURNAL, **53**, 311 (1931).

Summary

1. It is shown that anils are intermediate products in the formation of benzothiazoles from aromatic aldehydes and *o*-aminothiophenol.

2. Zinc *o*-aminothiophenolate can be condensed directly with aromatic aldehydes to crystalline bright-colored anil zinc salts of the general formula $(RCH{=}NC_6H_4S)_2Zn$, which yield 2-R-benzothiazoles when boiled for a few minutes in glacial acetic acid solution.

3. *o*-Aminophenyl disulfide likewise forms anils with aromatic aldehydes. These anils yield the 2-R-benzothiazoles readily when mixed with their parent aldehyde and refluxed in xylene solution.

4. Analogous results are recorded using 4-chloro-2-aminothiophenol as initial material.

NEW YORK, N. Y. RECEIVED JUNE 4, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF KITASATO INSTITUTE]

Sulfonation of Acridone

BY KONOMU MATSUMURA

Concerning the formation of acridones by the dehydration of phenylanthranilic acid and its derivatives with sulfuric acid,[1] a search of the literature reveals that on prolonged heating certain substituted phenylanthranilic acids give a low yield of the desired acridone.[2] Since no statement is recorded regarding the other reaction products, it appeared desirable to examine this reaction further.

In the present paper it is reported that acridone is best prepared by heating a solution of phenylanthranilic acid in concentrated sulfuric acid at 85° for one-half hour and that on further heating sulfonation occurs. Results are summarized in the tables.

TABLE I

REACTION BETWEEN PHENYLANTHRANILIC ACID AND CONCENTRATED SULFURIC ACID

Subs., g.	15	15	15	30
H_2SO_4, g.	150	150	150	450
Reaction time, min.	30	45	90	120
Temp., °C.	85	85	100	100
Acridone, g.	13.5	11.8	4.8	0.05
Acridone-2-sulfonic acid, g.			11.5	39.3
Acridone-4-sulfonic acid, g.				0.9

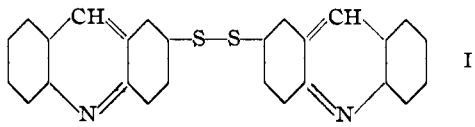
(1) Graebe and Lagodzinski, *Ber.*, **25**, 1734 (1892).

(2) Ullmann, *Ann.*, **355**, 312 (1907); Matsumura, THIS JOURNAL, **49**, 813 (1927).

Evidence that the sulfonic acid of m. p. 318° isolated predominantly may be acridone-2-sulfonic acid and the other sulfonic acid of m. p. 268° isolated in a minute amount may be acridone-4-sulfonic acid, was obtained in the following way. The attempted condensation of sulfanilic acid with *o*-chlorobenzoic acid either in amyl alcohol or in aqueous solution failed and hence direct identification by a synthetic method which leaves no doubt as to the constitutions was not attained. Therefore application of alkali fusion, which is reliable on the basis of the assumption that group migration does not occur during the reaction, was adopted as a method of establishing orientation. On fusion with alkali, the sulfonic acid of m. p. 318° was found to give 2-hydroxyacridone and the sulfonic acid m. p. 268° to give 4-hydroxyacridone, respectively, both hydroxyacridones being identified by comparison with authentic specimens of synthetic material. Therefore, in acridone, sulfonation appears to follow the same course as does nitration.[3]

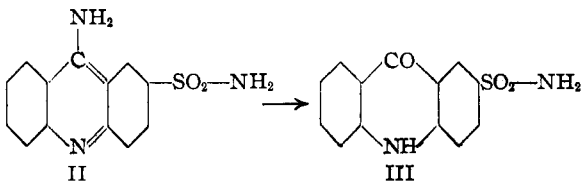
With the use of acridone-2-sulfonic acid as starting material, diacridyl-2,2′-disulfide (I) could be made while attempts to prepare 9-aminoacridine-2-sulfonic acid failed. 9-Chloroacridine-

(3) Lehmstedt, *Ber.*, **64**, 2381 (1931).



I

2-sulfonyl chloride, obtained by the reaction of phosphorus pentachloride on sodium acridone-2-sulfonate, on amidation gave 9-aminoacridine-2-sulfamide (II) which, however, on hydrolysis with either mineral acid or alcoholic potassium hydroxide yielded acridone-2-sulfamide (III) in accordance with the scheme



II III

and acridone-2-sulfamide on further hydrolysis gave acridone-2-sulfonic acid, showing that, in this compound, the amino group in the 9-position is more susceptible to hydrolytic reagents than the sulfamide group in the 2-position.

This unusual lability of the 9-amino group especially in the presence of mineral acid may be attributable to the presence of the negative sulfamide group in the 2-position.

Efforts to obtain 9-chloroacridine-2-sulfonic acid, which appeared likely to provide a convenient material for 9-aminoacridine-2-sulfonic acid, were unsuccessful; 9-chloroacridine-2-sulfonyl chloride on treatment with alcohol at room temperature gave 9-chloroacridine-2-sulfonic acid ethyl ester, while hot alcohol or alcoholic potassium hydroxide at room temperature gave ethyl-acridone-2-sulfonate.

Experimental

Acridone-2-sulfonic Acid.—A solution of phenylanthranilic acid (30 g.) in concentrated sulfuric acid (450 g.) is heated in a water-bath from 50–100° (one-half hour), kept at this temperature for two hours with occasional shaking, and after cooling poured into 3 liters of ice water. Next day, the separated solid is removed by filtration and from it on further working 0.05 g. of acridone (m. p. 354–355°) is isolated.

The filtrate, on removal of the major part of excess sulfuric acid by means of barium carbonate, and concentrating, gave a yield of 39.3 g.

It crystallizes from dilute hydrochloric acid (5%) or sulfuric acid (6.5%) as yellow prisms with a mole of water of crystallization, m. p. 318° with foaming.

It is easily soluble in water and fairly so in alcohol with intense bluish-violet fluorescence, but insoluble in ether. The aqueous solution gives a blue color reaction with congo red. The solution either in concentrated sulfuric acid or in alcoholic alkali exhibits yellowish-green fluorescence.

Anal. Calcd. for $C_{13}H_9O_4NS \cdot H_2O$: H_2O, 6.14. Found: H_2O, 6.78. Calcd. for $C_{13}H_9O_4NS$: C, 56.73; H, 3.27; N, 5.09; S, 11.64. Found: C, 56.88; H, 3.54; N, 5.37; S, 11.64.

The neutral barium salt forms light yellow prisms from water, m. p. >360°.

Anal. Calcd. for $C_{26}H_{16}O_8N_2S_2Ba \cdot 4H_2O$: H_2O, 9.52. Found: H_2O, 9.10. Calcd. for $C_{26}H_{16}O_8N_2S_2Ba$: Ba, 20.04. Found: Ba, 19.02.

Acridone-4-sulfonic Acid.—The filtrate from 2-sulfonic acid on working up gives 0.9 g. of 4-sulfonic acid. Its solution in dilute hydrochloric acid (10%) coagulates to a gel on cooling, but on concentrating turns to yellow needles, m. p. 268°.

It is a little more easily soluble in solvents than the 2-isomer and gives exactly the same color reactions as does the latter.

Anal. Calcd. for $C_{13}H_9O_4NS \cdot H_2O$: H_2O, 6.14. Found: H_2O, 6.31. Calcd. for $C_{13}H_9O_4NS$: C, 56.73; H, 3.27; N, 5.09. Found: C, 56.98; H, 3.49; N, 5.20.

The neutral barium salt forms aggregates of light yellow needles from water, m. p. >360°.

Anal. Calcd. for $C_{26}H_{16}O_8N_2S_2Ba \cdot 3H_2O$: H_2O, 7.30. Found: H_2O, 7.51. Calcd. for $C_{26}H_{16}O_8N_2S_2Ba$: Ba, 20.04. Found: Ba, 19.62.

Alkali Fusion of Acridone-2-sulfonic Acid.—A mixture of acridone-2-sulfonic acid (1 g.), potassium hydroxide (10 g.) and water (5 cc.) placed in an iron pot, is gradually heated in a metal bath to 300° (bath temperature) and kept at that temperature for ten minutes with constant stirring until the initial yellow mass becomes brownish-red paste. The reaction mass, on cooling, is dissolved in water, filtered and acidified. The separated yellow solid (0.55 g.), after crystallization from alcohol, then from acetic acid (50%), affords glistening flat needles of brownish-yellow color, m. p. 343–345° (dec.) with preliminary darkening at 315°.[4] It has the same properties as an authentic specimen of 2-hydroxyacridone made from 4'-ethoxyphenylanthranilic acid by the method of Borsche.[5]

Anal. Calcd. for $C_{13}H_9O_2N$: C, 73.93; H, 4.27; N, 6.64. Found: C, 74.20; H, 4.31; N, 6.26.

2-Methoxyacridone.—2-Hydroxyacridone (1 g.) prepared by the alkali fusion is treated with dimethyl sulfate (1.6 cc.) in sodium hydroxide solution (0.4 g. of sodium hydroxide in 10 cc. of water) at room temperature. The product, after crystallization from acetic acid (50%) and then from alcohol, forms glistening yellow prisms, melting at 274–276° alone or on admixture with the specimen of synthetic material.[6]

Anal. Calcd. for $C_{14}H_{11}O_2N$: C, 74.67; H, 4.89; N, 6.22. Found: C, 74.81; H, 5.02; N, 6.35.

Alkali Fusion of Acridone-4-sulfonic Acid.—The fusion is carried out in exactly the same manner as that described for 2-sulfonic acid, yielding 0.7 g. from 1 g. of 4-sulfonic acid.

(4) Ullmann gives m. p. 345–350° for his product; Ullmann and Kipper, *Ann.*, **355**, 346 (1907).

(5) Borsche, Runge and Trautner, *Ber.*, **66**, 1315 (1933).

(6) Borsche gives m. p. 263–265° for his product (Ref. 5).

Crystallized from alcohol and then from dilute acetic acid (80 cc. of glacial acetic acid and 40 cc. of water), it gives brown-yellow needles, m. p. 300° with preliminary darkening at 294°.

It showed no depression of melting point on admixture with the authentic specimen of 4-hydroxyacridone made from 2'-ethoxyphenylanthranilic acid by a known method.[7]

Anal. Calcd. for $C_{13}H_9O_2N$: C, 73.93; H, 4.27; N, 6.64. Found: C, 73.87; H, 4.53; N, 6.44.

Acridine-2-sulfonic Acid.—A solution of acridone-2-sulfonic acid monohydrate (15 g.) in water (300 cc.) is treated with sodium amalgam (4%, 150 g.) for five hours at 80° until complete disappearance of fluorescence and filtered from mercury. The clear brown colored filtrate, on acidification with hydrochloric acid, acquires a dark greenish violet color possibly on account of being admixed with quinhydrone salt (on concentrating on a water-bath dihydroacridine-2-sulfonic acid is separated in the form of colorless needles of m. p. >350° which, when perfectly dry, are fairly stable in contact with air). Without isolating the dihydro compound, on addition of concentrated aqueous solution of ferric chloride hydrate (30 g.) to the acidic solution, a yellow crystalline paste results which dissolves on warming at 80° for one-half hour and crystallizes on cooling.

It forms gold-yellow centimeter-long flat needles from dilute hydrochloric acid (1%), m. p. >360°; yield, 9.85 g. (75% of the theoretical).

It is easily soluble in hot water with green fluorescence, difficultly in cold, and sparingly in hot alcohol. The aqueous solution gives a blue color reaction with congo red. The solution in concentrated sulfuric acid gives intense green fluorescence.

Anal. Calcd. for $C_{13}H_9O_3NS \cdot H_2O$: H_2O, 6.50. Found: H_2O, 6.92. Calcd. for $C_{13}H_9O_3NS$: C, 60.23; H, 3.47; N, 5.41. Found: C, 60.01; H, 3.68; N, 5.49.

The **neutral barium salt** forms bundles of long yellowish needles, m. p. >360°.

Anal. Calcd. for $(C_{13}H_8O_3NS)_2Ba \cdot 6H_2O$: H_2O, 14.19. Found: H_2O, 14.29. Calcd. for $(C_{13}H_8O_3NS)_2Ba$: Ba, 21.02. Found: Ba, 20.43.

Acridine-2-sulfonyl Chloride.—A mixture of sodium acridine-2-sulfonate (1.65 g.), phosphorus pentachloride (6.6 g.) and toluene (10 cc.) is refluxed for three hours and evaporated under a diminished pressure to dryness. The product is triturated with ice-cold sodium bicarbonate solution and crystallized from benzene; yield, 1.5 g.

It forms yellow prismatic needles from benzene, m. p. >357°. It is insoluble in water, but readily soluble in cold chloroform and less easily in cold benzene.

Anal. Calcd. for $C_{13}H_8O_2NClS$: C, 56.22; H, 2.88; Cl, 12.79. Found: C, 56.51; H, 3.50; Cl, 12.58.

The **sulfamide** gives yellowish-white prisms from alcohol, m. p. 258°. It is insoluble in ether but soluble in benzene, chloroform and dilute sodium hydroxide solution.

Anal. Calcd. for $C_{13}H_{10}O_2N_2S$: C, 60.47; H, 3.88; N, 10.85. Found: C, 60.66; H, 4.21; N, 10.76.

The **hydrochloride** gives yellow needles from dilute hydrochloric acid, m. p. 278° (dec.). It hydrolyzes in water.

Anal. Calcd. for $C_{13}H_{10}O_2N_2S \cdot HCl$: HCl, 12.39. Found: HCl, 12.77.

9-Chloroacridine-2-sulfonyl Chloride.—This compound is prepared in the same manner as was acridine-2-sulfonyl chloride; yield, 4.75 g. from 6.5 g. of starting material. It gives yellow prisms from benzene, m. p. 165–167°. It is readily soluble in chloroform, less soluble in ether and almost insoluble in petroleum ether.

Anal. Calcd. for $C_{13}H_7O_2NCl_2S$: C, 50.00; H, 2.24; Cl, 22.76. Found: C, 50.33; H, 2.72; Cl, 22.42.

Amidation of 9-Chloroacridine-2-sulfonyl Chloride.—A mixture of 9-chloroacridine-2-sulfonyl chloride (3 g.), copper acetate (0.5 g.), and absolute alcohol (60 cc.) is saturated with ammonia at 0°, heated at 135° (18 atm. pressure) for three hours, and then alcohol removed by evaporation. The residue is triturated with dilute hydrochloric acid (5%), filtered and dried on a porous plate. It is extracted with cold water. The undissolved matter (0.9 g.) proved to be acridone-2-sulfamide. It forms lustrous plates of light yellow color from alcohol, decomposing at 353–360°. It is easily soluble in dilute sodium hydroxide solution with green fluorescence.

Anal. Calcd. for $C_{13}H_{10}O_3N_2S$: C, 56.93; H, 3.65; N, 10.22. Found: C, 57.13; H, 3.52; N, 10.46.

The aqueous extract on addition of sodium carbonate deposits yellow resinous precipitates which soon turn to prisms on warming for several minutes on a water-bath; yield, 1.85 g.

9-Aminoacridine-2-sulfamide gives yellow prisms from alcohol, m. p. 298° (dec.). It is soluble in alcohol, concentrated sulfuric acid and dilute sodium hydroxide solution with green fluorescence, respectively. On refluxing with alcoholic potassium hydroxide solution (15%) for thirty-eight hours or hydrochloric acid (20%) for one hour, it gives acridone-2-sulfamide in almost theoretical yield.

Anal. Calcd. for $C_{13}H_{11}O_2N_3S$: C, 57.14; H, 4.03; N, 15.38. Found: C, 57.35; H, 4.23; N, 15.14.

The **hydrochloride** gives yellow prisms from dilute hydrochloric acid, m. p. 318° (dec.). The aqueous solution on heating at 100° for one-half hour affords an appreciable amount of acridone-2-sulfamide.

Anal. Calcd. for $C_{13}H_{11}O_2N_3S \cdot HCl$: C, 50.40; H, 3.88. Found: C, 50.87; H, 3.93.

Ethyl 9-chloroacridine-2-sulfonate is prepared on treatment of 9-chloroacridine-2-sulfonyl chloride with alcohol at room temperature. The product forms light yellow prisms from acetone, m. p. 254–255° (dec.). It is soluble in alcohol but insoluble in benzene, chloroform and dilute alkali.

Anal. Calcd. for $C_{15}H_{12}O_3NSCl$: C, 55.99; H, 3.73. Found: C, 55.47; H, 3.57.

Ethyl acridone-2-sulfonate is prepared on treatment of 9-chloroacridine-2-sulfonyl chloride either with alcoholic potassium hydroxide solution at room temperature and evaporation in a desiccator over sodium hydroxide in vacuum or with alcohol at its boiling temperature. It gives yellowish white prisms from alcohol, decomposing at 255°.

Anal. Calcd. for $C_{15}H_{13}O_4NS$: C, 59.41; H, 4.29. Found: C, 59.58; H, 4.11.

(7) Matsumura, THIS JOURNAL, **49**, 816 (1927); Ullmann and Kipper, *Ann.*, **355**, 345 (1907).

TABLE II

ACRIDINE THIO DERIVATIVES

No.	Compound	Form	Solvent	M. p., °C.
I	Acridyl-2-benzoylmercaptan[a]	Light yellow lustrous plates	Alcohol (70%)	178–179
II	Acridyl-2-mercaptan[b]	Greenish-yellow prisms	.....	120–130
III	Diacridyl-2,2′-disulfide[c]	Light yellow lustrous plates	Ethyl acetate	245–246
IV	Dihydrochloride of III	Orange-yellow needles	HCl (2%)	255 (dec.)

No.	Solubility	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
I	Org. solv.	$C_{20}H_{13}ONS$	76.19	76.16	4.13	4.16
II	Org. solv. and in dil. NaOH	$C_{13}H_9NS$	73.93	72.85	4.27	4.13
III	C_6H_6, $CHCl_3$, difficultly in EtOH	$C_{26}H_{16}N_2S_2$	74.29	74.33	3.81	3.95
IV	Hydrolyzes in water	$C_{26}H_{16}N_2S_2 \cdot 2HCl$	63.29	63.05	3.65	3.96

[a] Yield, 74% of the theoretical. [b] Hydrolysis is effected by six hours of refluxing instead of one hour. This compound could not be obtained pure, for the ethereal solution of carefully dried material, on evaporation in a desiccator (vacuum) over sodium hydroxide gave a product which was altogether insoluble in dilute sodium hydroxide. [c] Yield, the theoretical.

The thioacridines listed in Table II are prepared according to the procedure described by Edinger for the preparation of thioquinoline.[8]

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

(8) Edinger, *Ber.*, **41**, 937 (1908).

Summary

Sulfuric acid acts upon phenylanthranilic acid to form acridone-2-sulfonic acid together with a small amount of acridone-4-sulfonic acid.

TOKYO, JAPAN RECEIVED APRIL 15, 1935

[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORIES OF THE UNIVERSITY OF FLORIDA]

The Preparation of Certain Acyl and Benzenesulfonyl Derivatives of *o*-Aminophenol

BY LAWRENCE H. AMUNDSEN AND C. B. POLLARD

In the purification of a sample of *o*-benzenesulfonaminophenyl benzenesulfonate[1] a small quantity of a different compound was isolated. From its composition it appeared to be the tribenzenesulfonyl derivative of *o*-aminophenol. This has been confirmed by synthesis. In view of the failure of attempts by Tingle and Williams[2] to obtain the corresponding tribenzoyl compound, we have reinvestigated the problem and have developed a satisfactory procedure for the purpose.

Experimental

N-Potassium Salt of *o*-Benzenesulfonaminophenyl Benzenesulfonate.—This salt crystallized while a hot solution of 75 g. of the free compound[1] in 500 cc. of 10% potassium hydroxide was allowed to cool. After several recrystallizations from 25 parts of alcohol the yield was 79%; m. p. 220° (not sharp and varies with rate of heating).

Anal. Calcd. for $C_{18}H_{14}KNO_5S_2$: N, 3.28; S, 15.00; K, 9.15. Found: N, 3.29; S, 14.65; K, 9.54.

It is soluble in hot water, ethyl alcohol, β-hydroxyethyl ether and dioxane; insoluble in ethyl ether, benzene and hexane.

(1) Pollard and Amundsen, THIS JOURNAL, **57**, 357 (1935).
(2) Tingle and Williams, *Am. Chem. J.*, **37**, 51 (1907).

Acyl and benzyl derivatives were prepared by heating with the corresponding chlorides in dioxane. The data relating to these preparations are shown in Table I; the products are, in general, soluble in acetone, benzene, chloroform, dioxane and hot alcohol; insoluble in ether and hexane.

TABLE I

N-ACYL-*o*-BENZENESULFONAMINOPHENYL BENZENESULFONATES

Acyl, etc.	Hours heated	Yield, %	M. p., °C.	Analyses, % Calcd. N	Calcd. S	Found N	Found S
Acetyl	5	74	115–116	3.25	14.87	3.23	14.83
Benzoyl	4.5	87	125.5–126	2.84	13.00	2.57	12.94
Benzenesulfonyl	1.5	89	164–164.5	2.65	18.17	2.66	17.80
Benzyl	16	52	144.5–145.5	2.92	13.38	2.90	13.23

***o*-Dibenzoylaminophenyl Benzoate.**—A solution of 15 g. of *o*-benzoylaminophenyl benzoate and 10 g. of benzoyl chloride in 30 cc. of nitrobenzene was boiled under reflux for twelve hours. The product crystallized on cooling. After recrystallization from either alcohol, acetone or toluene it melted at 170.5–171.5°. The yield was 43.5%. When amyl ether was employed as solvent the yield was 72.5%.

Anal. Calcd. for $C_{27}H_{19}NO_4$: N, 3.33. Found: N, 3.31.

In the course of the work three other new derivatives of *o*-aminophenol were prepared. Data relating to them are