added a solution of 229 mg. of picric acid[6] in 3.0 ml. of hot absolute ethanol. After cooling, the yellow crystalline product was collected by filtration, washed, and dried (weight 335 mg.).

The material was recrystallized from absolute ethanol (150 ml./g.). After one or two days, there were obtained sheaves of yellow needles, dry weight 221 mg. (56%) m.p. 177–181° (gradually turns to dark viscous liquid).

*Anal.* Calcd. for $C_{14}H_{15}N_5O_9$: C, 42.32; H, 3.81. Found: C, 41.97; H, 3.66.

*4-Aminomethyl-3-hydroxy-2-methyl-5-pyridinemethanol dipicrate (pyridoxamine dipicrate).* (A) To pyridoxamine free base (84 mg.) in 6 ml. of boiling ethanol was added a solution of 229 mg. of picric acid[6] in 5 ml. of hot ethanol. The yellow precipitate was collected, washed, dried, and recrystallized from absolute ethanol (220 ml./g.), giving 139 mg. (44%) of glistening yellow leaflets, m.p. 189–192° (gradually changes to dark liquid). The reported[5] (capillary) melting point is 201° (dec.).

This picrate when recrystallized from water separates in the form of long yellow needles.

(B) In an attempted preparation of pyridoxamine thiourea picrate, a solution of 964 mg. of pyridoxamine dihydrochloride, 583 mg. of anhydrous potassium thiocyanate, and 336 mg. of sodium bicarbonate, in 5.0 ml. of water was boiled 10 min. A solution of 1.01 g. of picric acid[6] in 20 ml. of boiling water was then added. The yellow crystals which separated on cooling were collected, washed, and dried (weight 1.3 g.). The material was recrystallized from water (57 ml./g.), giving 1.15 g. (dry weight) of long yellow needles, consisting of starting material dipicrate. The melting behavior was identical with that of the product in Part A (above).

*Anal.* Calcd. for $C_{20}H_{19}N_8O_{16}$: C, 38.34; H, 2.90; N, 17.88. Found: C, 38.23; H, 2.71; N, 17.56.

*3-Hydroxy-2-methyl-4-ureidomethyl-5-pyridinemethanol picrate (pyridoxurea monopicrate).* To 336 mg. of pyridoxamine free base was successively added 162 mg. of potassium cyanate, 5.0 ml. of water, and 0.33 ml. of 6*M* hydrochloric acid, with stirring. The resulting mixture was heated to boiling, giving a clear solution, which was boiled under reflux for an additional 10 min.

A 458 mg. portion of crystalline picric acid[6] was added all at once, and the mixture boiled for 5 min. On cooling, there separated yellow crystals, which were collected by filtration, washed with two 5-ml. portions of water, and dried, giving 750 mg. (85%) of crude product.

For analysis, a portion of this material was recrystallized from absolute ethanol (175 ml./g.). After 24 hr. a good recovery was obtained of long yellow needles, m.p. 198–203° (dec.). (It was later found that 50% ethanol, 37 ml./g., is a more convenient crystallizing solvent.).

*Anal.* Calcd. for $C_{15}H_{16}N_6O_{10}$: C, 40.91; H, 3.66; N, 19.09. Found: C, 41.05; H, 3.41; N, 18.59.

From the mother liquors on standing there separated yellow prisms, which have not yet been characterized.

*3-Hydroxy-2-methyl-4-ureidomethyl-5-pyridinemethanol hydrochloride (pyridoxurea monohydrochloride).* A 1.55-g. portion of the urea picrate was dissolved in 10.0 ml. of 6*M* hydrochloric acid, and the solution extracted twice with 25 ml. portions of benzene. The acidic aqueous phase was separated, and vacuum distilled to dryness. The residue was recrystallized from 1:1 absolute ethanol–methanol, and dried, giving 560 mg. (64%) of colorless needles, m.p. 205–208° (dec.).

*Anal.* Calcd. for $C_9H_{14}ClN_3O_3$: C, 43.64; H, 5.70; Found: C, 43.62; H, 5.87.

*5-Acetoxymethyl-3-hydroxy-2-methyl-4-ureidomethylpyridine hydrochloride (pyridoxurea 5-O-acetate monohydrochloride).* To 440 mg. of the above urea picrate there was added 2.05 ml. of a 2.44*M* solution of hydrogen chloride[3] in glacial acetic acid, with stirring. Within a few minutes the yellow crystals changed into a nearly colorless oil. The mixture was allowed to stand for 24 hr., and 5.0 ml. of benzene was then added, with stirring.

After 30 min. the yellowish crystals were removed by filtration and washed repeatedly with additional 5 ml. portions of benzene until colorless. The crude vacuum-dried (over sodium hydroxide) product weighed 2.5 mg. and melted with decomposition at 190–210°.

To the product in 5.4 ml. of boiling absolute ethanol (slight residue) was added sufficient water (5–10 drops) to give a clear (yellow) solution. On cooling there was obtained 86 mg., dry weight (30%), of flat colorless needles, m.p. 200–208 (dec.).

For analysis this material was again recrystallized, from 95% ethanol, giving sheaves of colorless needles, m.p. 203–206° (dec.).

*Anal.* Calcd. for $C_{11}H_{16}ClN_3O_4$: C, 45.60; H, 5.57; N, 14.50. Found: C, 45.50; H, 5.42; N, 14.40.

A sample when tested for phenolic hydroxyl with ferric chloride gave an immediate deep red brown color (positive test). A control test on pyridoxamine dihydrochloride gave a similar color. An additional control test on 3-amino-5-aminomethyl-4-ethoxymethyl-2-methylpyridine[7] (which has no phenolic group) did not give any color.

The infrared spectrum (determined with a Perkin-Elmer Model 21 Recording Spectrophotometer, using a potassium bromide pellet) showed a strong absorption maximum at 1730 cm.$^{-1}$. This peak presumably represents the stretching vibration of the ester carbonyl group,[8] and is missing in the spectrum of the nonacetylated urea hydrochloride (II.HCl). A comparison spectrum on pyridoxamine dihydrochloride itself likewise had no absorption maximum in this region.

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(6) The commercial picric acid used presumably contains up to 10% of added water; it is unfortunate that the manufacturers seldom, if ever, specify on the label the added water content of this reagent.

(7) S. A. Harris and K. Folkers, *J. Am. Chem. Soc.*, 61, 1245 (1939).

(8) Although acylation of a urea primary amino group is sometimes possible, we believe that the strongly acidic conditions here used would prevent amine acylation, and at the same time would favor esterification. Under strongly acidic conditions acyl groups, even if originally attached to nitrogen, tend to migrate to oxygen.

## Some Sulfones of the Anthraquinone Series

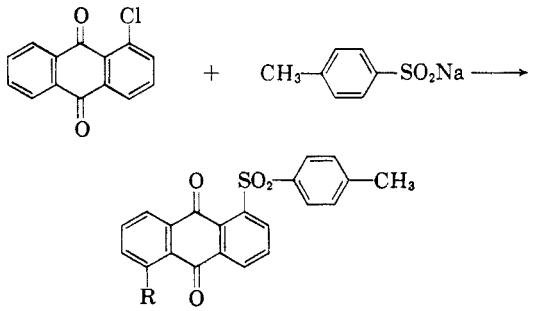
ERWIN KLINGSBERG

*Received December 18, 1958*

Anthraquinonyl sulfones are usually prepared by oxidation of the corresponding thioethers, which are obtainable from haloanthraquinones, either di-

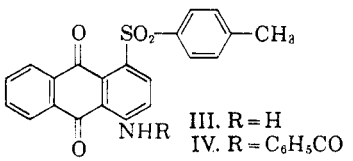
rectly or *via* the mercaptans. The reaction of a haloanthraquinone with an alkali sulfinate, to give the sulfone in one step, has apparently never been tried.

1-Chloroanthraquinone did, in fact, react smoothly with sodium *p*-toluenesulfinate in refluxing diethylene glycol monoethyl ether to give the sulfone (I). 5-Benzamido-1-chloroanthraquinone reacted similarly to give II, though in poorer yield.



I. R = H
II. R = $NHCOC_6H_5$

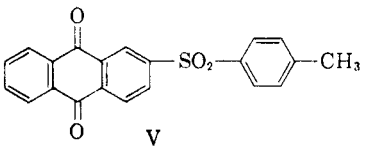
With 4-benzamido-1-chloroanthraquinone, results were not very reproducible, although it was possible to isolate the debenzoylated sulfone (III) in rather poor yield; this could be benzoylated to IV.



III. R = H
IV. R = $C_6H_5CO$

The sulfone group is removed by syrupy phosphoric acid, converting III to 1-aminoanthraquinone.

As would be expected, 2-chloro derivatives proved less reactive. 2-Chloro-3-anthraquinonecarboxylic acid gave a poor yield of the decarboxylated sulfone (V), while 2-chloroanthraquinone gave a



V

reaction mixture containing unchanged starting material and sulfone (V). The latter was not isolated but was identified by infrared comparison with the pure compound.

*Ultraviolet and visual spectra.* Table I gives wave lengths and molecular extinction coefficients for all absorption peaks shown by these sulfones in the visual and ultraviolet range, measured in methylene dichloride. The positions of the peaks of highest wave length were then correlated (Table II) by the recent method of Labhart.[1] In his analysis, the energy difference between the ground state and the first excited state, considered as a function of the nature and position of the substituents, is expanded in a Taylor series through the square terms. This gives rise to two sets of parameters, of which the ring position parameters are called $\alpha$'s and the substituent parameters, $b$'s. In this way, Labhart made fairly accurate wave-length computations for anthraquinone derivatives containing no more than two substituents.

TABLE I

VISUAL AND ULTRAVIOLET ABSORPTION[a]

| Sulfone | Band 1 | | Band 2 | | Band 3 | |
|---|---|---|---|---|---|---|
| | $\lambda_{max}$ | $\epsilon$ | $\lambda_{max}$ | $\epsilon$ | $\lambda_{max}$ | $\epsilon$ |
| I | 325 | 4500 | 255 | 39,000 | ... | ... |
| II | 425 | 6800 | 252 | 44,000 | ... | ... |
| III[b] | 448 | 4940 | 306 | 11,500 | 248 | 38,100 |
| IV | 400 | 4600 | 310 | 22,700 | 265 | 40,400 |
| V | 325 | 6600 | 258 | 49,000 | ... | ... |

[a] The spectra were measured at 10 mg./l. concn. in dichloromethane, the visual with a modified Hardy-type and the ultraviolet with a Cary recording spectrophotometer. [b] Shoulder at 275 m$\mu$ ($\epsilon$ = 15,600).

TABLE II

FIRST ABSORPTION MAXIMA

| Sulfone | $\lambda_{max}$ (m$\mu$) | | $\Delta$E (eV) | |
|---|---|---|---|---|
| | Found | Calcd. | Found | Calcd. |
| I[a] | 325 | ... | 3.83 | ... |
| II | 425 | 414 | 2.92 | 3.00 |
| III | 448 | 462 | 2.77 | 2.68 |
| IV | 400 | 410 | 3.10 | 3.02 |
| V | 325 | 325 | 3.82 | 3.82 |

[a] The calculation of the parameter $b$ = −0.03 for the *p*-toluenesulfonyl group is based on this compound; this value is used in turn to compute $\lambda_{max}$ and $\Delta$E for the remaining compounds.

Table II shows the moderately successful predictions of the first absorption peaks for these sulfones; it might be said that they do not constitute a very severe test of Labhart's equation, inasmuch as the *p*-toluenesulfonyl group does not affect absorption very strongly. Its feebly hypsochromic influence is reflected in the low negative value of −0.03 for its parameter, which causes the square terms to vanish in the energy expansion. Nevertheless, it is interesting to incorporate these compounds in the Labhart scheme, which was naturally based almost exclusively on the far commoner bathochromic substituents. It is of the nature of this scheme that each addition to it multiplies the scope of its predictive power.

## EXPERIMENTAL[2]

*1-(p-Toluenesulfonyl)anthraquinone* (I). A mixture of 2.4 g. (0.010 mole) 1-chloroanthraquinone and 2.0 g. (0.011 mole) sodium *p*-toluenesulfinate in 75 ml. of diethylene glycol monoethyl ether was stirred for 5 hr. at 180–190° and then cooled and diluted with water, giving 2.8 g. (78%

(1) H. Labhart, *Helv. Chim. Acta*, **40**, 1410 (1957).

(2) Melting points are corrected.

yield) of yellow solid, m.p. 248–251°. (Additional product was obtainable by further dilution.) Crystallization from acetic acid or xylene raised the m.p. to 257–258°.

*Anal.* Calcd. for $C_{21}H_{14}O_4S$: C, 69.6; H, 3.9; S, 8.8. Found: C, 69.4; H, 3.6; S, 8.8.

*5-Benzamido-1-(p-toluenesulfonyl)anthraquinone* (II). 5-Benzamido-1-chloroanthraquinone crystallized from acetic acid as orange-yellow needles, m.p. 221.5–222.5°.

*Anal.* Calcd. for $C_{21}H_{12}ClNO_3$: C, 69.7; H, 3.3; Cl, 9.8; N, 3.9. Found: C, 69.8; H, 3.4; Cl, 9.8; N, 3.7.

A mixture of 1.8 g. (5.0 mmol.) 5-benzamido-1-chloroanthraquinone and 1.0 g. (5.6 mmol.) sodium *p*-toluenesulfinate in 25 ml. of diethylene glycol monoethyl ether was stirred under reflux for 7 hr. in an oil bath at 195–200°, cooled partially, diluted with about 3 ml. of water, cooled to room temperature, and filtered. The orange-yellow product was crystallized from 40 ml. xylene, giving a yield of 1.40 g. (58%) with m.p. 257–260°. Crystallization from acetic acid or xylene raised the m.p. to 259–260°.

*Anal.* Calcd. for $C_{28}H_{19}NO_5S$: C, 69.8; H, 4.0; N, 2.9; S, 6.6. Found: C, 69.7; H, 3.7; N, 3.2; S, 6.8.

*4-Amino-1-(p-toluenesulfonyl)anthraquinone* (III). 4-Benzamido-1-chloroanthraquinone crystallized from acetic acid as yellow needles of m.p. 234.5–236°.

*Anal.* Calcd. for $C_{21}H_{12}ClNO_3$: C, 69.7; H, 3.3; Cl, 9.8; N, 3.9. Found: C, 69.5; H, 3.5; Cl, 9.9; N, 3.9.

A mixture of 5.0 g. (0.014 mole) 4-benzamido-1-chloroanthraquinone, 3.0 g. (0.017 mole) sodium *p*-toluenesulfinate, and 50 ml. of diethylene glycol monoethyl ether was stirred and refluxed for 16 hr., cooled slightly, diluted with 5 ml. of water, cooled to room temperature, and filtered. The product was washed with a little methanol and crystallized from 500 ml. of xylene, giving 2.6 g. (50%) of orange solid, m.p. 254–259°. Crystallization from acetic acid raised the m.p. to 260–261°.

*Anal.* Calcd. for $C_{21}H_{15}NO_4S$: C, 66.9; H, 4.0; S, 8.5. Found: C, 67.2; H, 3.8; S, 8.6.

As with others of these sulfones, yields were lower on larger runs. On 5 hr. refluxing in sirupy phosphoric acid, this product is converted to 1-aminoanthraquinone, identified by m.p., analysis, and formation of the benzoyl derivative.

The *N*-benzoyl derivative (IV) of the sulfone was prepared by 3 hr. refluxing with benzoyl chloride in *o*-dichlorobenzene. It crystallized from acetic acid in fine yellow needles, m.p. 273–275°.

*Anal.* Calcd. for $C_{28}H_{19}NO_5S$: C, 69.8; H, 4.0; N, 2.9; O, 16.6; S, 6.6. Found: C, 70.0; H, 4.0; N, 2.8; O, 16.5; S, 6.7.

*2-(p-Toluenesulfonyl)anthraquinone* (V). A mixture of 2.9 g. (0.010 mole) 2-chloro-3-anthraquinonecarboxylic acid and 6.0 g. (0.034 mole) sodium *p*-toluenesulfinate in 75 ml. of diethylene glycol monoethyl ether was stirred under reflux for 24 hr. in an oil bath at 190–195°. After cooling, dilution with water, and filtration, the product was crystallized from 30 ml. of acetic acid containing 4 ml. of water, giving 0.95 g. (26% yield) yellow solid, m.p. 194–205°. Further crystallization from acetic acid alternating with mixed amyl alcohols gave 0.60 g. (17% yield) of white product, m.p. 211.5–212.5°. It was insoluble in ammonium or sodium hydroxide.

*Anal.* Calcd. for $C_{21}H_{14}O_4S$: C, 69.6; H, 3.9; S, 8.8. Found: C, 69.5; H, 3.8; S, 8.8.

A mixture of 2.4 g. (0.010 mole) 2-chloroanthraquinone and 2.0 g. (0.011 mole) sodium *p*-toluenesulfinate in 75 ml. of diethylene glycol monoethyl ether, stirred and refluxed at 185–195° for 5 hr., gave 2.1 g. yellow solid, m.p. approximately 175–190°, unchanged upon crystallization first from acetic acid and then from ethylene glycol monomethyl ether. The presence of the sulfone in the mixture was indicated by a prominent infrared absorption band at 1143 cm.$^{-1}$, which is in the region characteristic of sulfone absorption,[3] and is also shown by the pure sulfone but not by 2-chloroanthraquinone.

Elementary analysis for chlorine and sulfur was in agreement with a mixture containing 47% sulfone and 53% 2-chloroanthraquinone.

*Anal.* Calcd. for 47% $C_{21}H_{14}O_4S$ and 53% $C_{14}H_7ClO_2$: Cl, 7.7; S, 4.1. Found: Cl, 7.9; S, 4.1.

When the reaction was run for 24 hr. with a 3:1 mole ratio of sodium *p*-toluenesulfinate to 2-chloroanthraquinone, a chlorine-free mixture was obtained, again too low in sulfur content for the sulfone.

*Acknowledgments.* The author is indebted to F. C. Dexter for visual and ultraviolet absorption data, to Miss J. L. Gove for infrared data, and to O. E. Sundberg and his associates for microanalyses.

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(3) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, 2d. ed., J. Wiley & Sons, Inc., New York, 1958, p. 361.

## Nitrosation of α-Aceto-γ-butyrolactone. Isolation of an *O*-Acetyloximino Intermediate

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In the course of some synthetic work in the amino acid field we had occasion to prepare α-oximino-γ-butyrolactone (IV). When this preparation was carried out by the method of Feofilaktov and Onishchenko,[1] a procedure which involves the reaction of nitrous acid with α-aceto-γ-butyrolactone (I), an intermediate compound, not previously described by the Russian workers, was isolated. This white, crystalline product (m.p. 89–90°) is sensitive to solvolytic action and thus is slowly hydrolyzed in the presence of moisture to form the desired α-oximino-γ-butyrolactone (IV) with the liberation of acetic acid. Hydrolysis with dilute hydrochloric acid readily converts this intermediate compound to IV in 68% yield.[2]

From similar experiments, Sudo and co-workers[3] and also Reppe and co-workers[4] reported the isolation of an intermediate compound (m.p. 88°) which appears to be identical to the one described above. These investigators assumed that this compound was α-aceto-α-nitroso-γ-butyrolactone (II). The compound isolated in our laboratory showed infrared absorption bands at 5.98μ and 8.50μ. The presence of these bands, which were interpreted as corresponding to a C=N grouping and to

(1) V. Feofilaktov and A. Onishchenko, *J. Gen. Chem. (U.S.S.R.)*, **9**, 304 (1939); *Chem. Abstr.*, **34**, 378 (1940).

(2) Gas evolution was observed during the course of this hydrolysis. It is possible that some of the lactone is opened and the resulting α-oximino (or α-keto) acid undergoes decarboxylation to produce β-hydroxypropionaldehyde or the corresponding oxime.

(3) R. Sudo, Y. Akiyama, T. Kato, and M. Ohta, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **74**, 1009 (1953); *Chem. Abstr.*, **49**, 6829 (1955).

(4) W. Reppe and co-workers, *Ann.*, **596**, 164 (1955).