Experimental[2]

Dimetalated Diphenylethane.—The glycol dimethyl ether used as reaction medium was purified by refluxing over sodium under nitrogen until the blue sodium ketyl was formed when benzophenone was added. The dimethyl sulfate was purified by shaking with half-saturated aqueous sodium carbonate, drying with sodium sulfate and distilling to retain the fraction, b. p. 71.5° (10 mm.).

A solution of 27.0 g. (0.15 mole) of *trans*-stilbene in 300 cc. glycol dimethyl ether added over two to five hours to a stirred three-necked flask containing rigorously pure nitrogen and 13.8 g. (0.60 atom) of sodium wire or 4.16 g. (0.60 atom) of lithium wire suspended in 125 cc. of glycol dimethyl ether. Reaction was then completed by thirty minutes of subsequent stirring. The heat of reaction was small.

Reaction with Sulfur.—When 5 cc. (0.0021 mole) of the blue-green disodiumdiphenylethane solution was added to 2 g. of sulfur under nitrogen, the color changed to cherry red and the solution became warm. Subsequent processing yielded 0.3 g. of stilbene, m. p. 122°. Regeneration of stilbene was 75% of the theoretical amount.

Reaction with Arsenic Trichloride.—To 28 cc. (0.034 mole) of arsenic trichloride under nitrogen was added 5 cc. of the blue-green disodiumdiphenylethane solution. The solution turned black and became very warm. Hydrolysis with water and subsequent steam distillation yielded 0.18 g. (45%) of regenerated stilbene, m. p. 122°.

Electrolysis of Disodiumdiphenylethane Solution.—Forty ml. of the disodiumdiphenylethane solution was transferred under oxygen-free conditions to a 100-ml. test-tube equipped with a mercury cathode at the bottom (area 4 sq. cm.) and a 50-mesh platinum gauze anode (16 sq. cm.) 7 cm. above the cathode. A current of 3 milliamp. at 3 volts was passed for two hours. The solution was then drained off, the mercury washed with dry glycol dimethyl ether and filtered through a pin hole into water. Titration of the water solution with 0.2 *N* sulfuric acid showed no alkalinity present.

Reaction with Dimethyl Sulfate.—The reaction of disodium- or dilithiumdiphenylethane with methyl sulfate was very slow at −40°, but faster when the reaction mixture was held at 15–20° by a water-bath. To the stirred blue-green solution from 27 g. of stilbene was added 27.4 cc. (0.29 mole) of dimethyl sulfate in 150 cc. of glycol dimethyl ether over one hour. This bleached the solution to a pale lilac color. The reaction mixture was then filtered to remove excess metal as well as the metal sulfate. The filtrate was distilled under 10 mm. to remove excess glycol dimethyl ether. The dry residue was treated with water and ether; evaporation of the ether left 32.5 g. of crude product which was dissolved in benzene. Bromine was then added until a permanent brown color resulted. After vacuum evaporation of the benzene, the residue was steam distilled to remove the diphenylbutanes from nonvolatile stilbene dibromide. Collection in ether of the diphenylbutanes in the distillate gave a solution which on vacuum evaporation yielded 29.6 g. of diphenylbutanes or 93%.

Separation of the diphenylbutanes was effected by ethanol crystallization. Solution of the 29.6 g. of product in 25 cc. of boiling ethanol yielded 6 g. of *meso*-2,3-diphenylbutane, m. p. 124° on cooling. A further 0.5 g. was obtained by concentration of the mother liquors. The remaining liquid isomer weighed 20.2 g. and distilled at 130–140° (10 mm.). The ratio of the *meso* isomer yield (6.5 g.) to that of the impure *dd,ll* isomer (19.5 g.) is 1:3 whether the metal is lithium or sodium.

Summary.—The yield of *dd,ll* and *dl,ld*-2,3-diphenylbutane is the same when either disodium or dilithiumdiphenylethane is treated with dimethyl sulfate. No transport can be detected when disodiumdiphenylethane is electrolyzed in glycol dimethyl ether.

CHEMICAL LABORATORY
UNIVERSITY OF TORONTO
TORONTO, CANADA

RECEIVED NOVEMBER 2, 1946

(2) All melting points corrected against known standards.

Studies in the Quinoline Series. VII. 2-Dihydroxystyrylquinolines

BY ALICE G. RENFREW

Trypanocidal action has characterized certain 2-styrylquinolines especially when tested as quaternary salts.[1] Because the methylenedioxy group is frequently found in alkaloids and because both methylenedioxyphenyl[2] and catechol[3] structures influence physiological action in some cases, these modifications of the styryl group were utilized in the present study.

Experimental

2-(3,4-Dihydroxystyryl)-4-chloro-6-methoxyquinoline.—The condensation of 2-methyl-4-hydroxy-6-methoxyquinoline with piperonaldehyde was carried out by refluxing for twenty-four hours in acetic anhydride.[4] The condensation product was a tan powder, initially obtained as an oil because of the presence of piperonaldehyde. Extraction with ether and with aqueous alkali removed residual reactants, yield, 50%. A small sample, crystallized from pyridine, melted at 306°. This base, suspended in concentrated hydrochloric acid, forms an orange salt.

The preparation of the 4-chloro derivative was carried out by gently refluxing the above piperonal-quinoline condensation product with five volumes of phosphorus oxychloride; at the same time two chlorine atoms are introduced in the methylene group of the 3,4-methylenedioxystyryl nucleus.[5] For complete reaction it was found advantageous to use enough phosphorus oxychloride to permit rapid solution of the 4-carbostyril at refluxing temperature.

When the excess phosphorus oxychloride was decomposed in ice-water, and partially neutralized with alkali, a bright orange hydrochloride separated.

Anal. Calcd. for $C_{19}H_{12}NO_3Cl_3 \cdot HCl$: Cl, 31.91. Found: Cl, 32.0.

After prolonged treatment with aqueous carbonate, the above chloro-compound was converted to 2-(3,4-dihydroxystyryl)-4-chloro-6-methoxyquinoline; m. p. 173°, on recrystallization from 100 volumes of alcohol.

Anal. Calcd. for $C_{18}H_{14}NO_3Cl$: N, 4.28; Cl, 10.85. Found: N, 4.38; Cl, 11.09.

2-(3,4-Dihydroxystyryl)-4-amino-6-methoxyquinoline.—Replacement of the 4-chloro substituent by an amino group was carried out in the usual manner with ammonia in phenol. The 4-amino derivative, liberated from the hydrochloride, was not very soluble in ether or chloroform, but was crystallized from thirty volumes of hot absolute alcohol. The product was a tan solid; m. p. 205°, yield, 54%.

Anal. Calcd. for $C_{18}H_{16}N_2O_3$: N, 9.1. Found: N, 8.8.

2-(3,4-Dihydroxystyryl)-4-thiocresyl-6-methoxyquinoline, CC975.[6]—The condensation of thiocresol with 2-(3,4-dihydroxystyryl)-4-chloro-6-methoxyquinoline was carried out in refluxing chloroform.[7] The reaction product

(1) Browning, Cohen, Ellingworth and Gulbranson, *Proc. Roy. Soc.* (London), **100B**, 293 (1926). Findlay, "Recent Advances in Chemotherapy," The Blakiston Company, Philadelphia, Pa., 1939.

(2) Bruckner and Fodor, *Ber.*, **71**, 541 (1938).

(3) Barger and Dale, *J. Physiol.*, **41**, 19 (1910); Hartung, *Chem. Rev.*, **9**, 389 (1931).

(4) Shaw and Wagstaff, *J. Chem. Soc.*, 77 (1933).

(5) Fittig and Remsen, *Ann.*, **159**, 129 (1871); "Ortho-, Meta-, and Para-hydroxybenzalrhodanines and 3,4-Dihydroxybenzalrhodanine as Possible Reagents for Inorganic Analysis," T. E. Robbins, Thesis, University of Georgia, 1939; "Organic Syntheses," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 549.

(6) CC indicates the identification number assigned to the compound, for test purposes, by the Chemotherapy Center for Tropical Diseases under the National Research Council.

(7) Renfrew, THIS JOURNAL, **68**, 1433 (1946).

crystallized as a hydrochloride. The white, powdery base was dissolved in two volumes of chloroform and could be precipitated with ether; m. p. 150°, yield 50%.

Anal. Calcd. for $C_{25}H_{21}NO_3S$: S, 7.71. Found: S, 7.55.

2-(3,4-Methylenedioxystyryl)-4-acetylamino-6-methoxyquinoline, CC974.—Piperonaldehyde was condensed with 2-methyl-4-amino-6-methoxyquinoline in the presence of acetic anhydride. The deeply-colored condensation product was purified by converting the base to an orange-colored hydrochloride in alcohol; this salt was collected on a filter and again converted to a base. 2-(3,4-Methylenedioxystyryl)-4-acetylaminoquinoline is a tan solid, melting at 234°; it is difficultly soluble in ether, readily in chloroform, and moderately soluble in alcohol.

Anal. Calcd. for $C_{21}H_{18}N_2O_4$: N, 7.73. Found: N, 7.61.

Acknowledgment.—The author wishes to express appreciation to Dr. L. H. Cretcher and to Dr. O. F. Hedenburg for helpful discussion.

DEPARTMENT OF RESEARCH IN PURE CHEMISTRY
MELLON INSTITUTE
PITTSBURGH 13, PENNSYLVANIA
RECEIVED NOVEMBER 12, 1946

2-Aminofluorene

BY JOHN R. SAMPEY AND E. EMMET REID

In the Diels[1]–Kuhn[2] method for the preparation of 2-aminofluorene ten times the calculated amount of zinc is used. Conditions have now been found whereby the amount of zinc can be reduced to one-third, or, if the time of reduction is doubled, to one-sixth of this amount.

Procedure.—To a suspension of 30 g. of 2-nitrofluorene in 820 ml. of 95% alcohol and 180 ml. of water are added 10 g. of crystalline calcium chloride in 15 ml. of water, 10 ml. of glacial acetic acid and 50 g. of zinc dust. The mixture is refluxed vigorously for four hours in an oil-bath and, while hot, filtered with suction. The residue is washed with 50 ml. of hot 80% alcohol and the filtrate and washings poured into 2 liters of cold water. The precipitate recrystallized from boiling 50% alcohol (yield 80–90%), melted at 127° (uncor.).

With mossy or 10-mesh granular zinc appreciable amounts of orange-yellow azo and azoxy compounds are formed which are not reduced even after the addition of the required amount of zinc dust.

(1) Diels, *Ber.*, **34**, 1758–1768 (1901).
(2) Kuhn, *Org. Syn.*, **13**, 74–76 (1933).

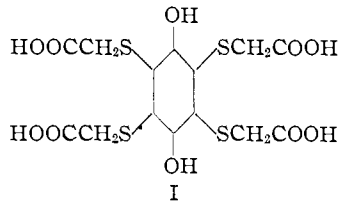
FURMAN UNIVERSITY
GREENVILLE, SOUTH CAROLINA
BALTIMORE, MARYLAND
RECEIVED NOVEMBER 8, 1946

The Interaction of Thiols and Quinones[1]

BY MAXWELL SCHUBERT

In connection with some chemotherapeutic work being carried out at this Laboratory the chemistry of the interaction of quinones and thiols came under consideration. Preliminary experiments led to the isolation of two easily prepared and previously undescribed kinds of compounds. As it is unlikely that this work will be further pursued here, these compounds are now presented and their relation to known compounds pointed out.

If a mole of thioglycolic acid is added to a mole of quinone suspended in water, there results the white crystalline hydroquinone tetrathioglycolic acid, I.



I

This compound on oxidation with nitric acid yields the corresponding red quinone. The quinone on reduction with thioglycolic acid regenerates the hydroquinone. That I represents the structure of the product described is shown by the fact that the same compound results from the action of excess thioglycolic acid on chloranil.

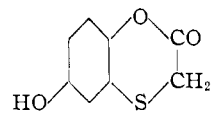
The formation of I from thioglycolic acid and quinone probably results from a sequence of reactions in which quinone adds thioglycolic acid to form a thio substituted hydroquinone which is then oxidized by excess benzoquinone to a thio substituted quinone. This pattern of reaction is repeated until the quinone is completely substituted. The over-all effect is

$$4Q + 4HSR \longrightarrow I + 3H_2Q$$

where R represents —CH_2COOH and Q represents quinone.

Thus, only a quarter of the original quinone could appear in the final product, the other three quarters being used to oxidize the intermediate hydroquinones. On the basis of this scheme, the yield of I recovered after recrystallization was 30%, and the hydroquinone recovered, also after recrystallization, was 63% of that calculated.

Snell and Weissberger[2] in a study of the reaction of thiols and quinones reviewed the older literature. They isolated mono and bis-thio derivatives of quinone and hydroquinone and explained the formation of the bis compounds on the basis of the first steps of the above scheme. Specifically, with thioglycolic acid, they isolated hydroquinone monothioglycolic acid as the lactone.



This compound has also been isolated from our reaction mixture after separation of the hydroquinone derivative, I. Whether the mono or the tetrathioglycolic acid derivative of hydroquinone is formed predominantly seems to depend on the conditions of mixing the components. For example, if a suspension of the quinone in water is added to an aqueous solution of thioglycolic acid,

(1) The work described in this note was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and New York University.

(2) Snell and Weissberger, THIS JOURNAL, **61**, 450 (1939).