Hydrogenation of Spartioidine and Seneciphylline.—A solution of 5.815 mg. of seneciphylline in ethanol absorbed 1.70 cc. of hydrogen at 27.5° and 748.6 mm. This is equivalent to 3.88 moles of hydrogen per mole of alkaloid.

A solution of 5.595 mg. of spartioidine in ethanol absorbed 1.72 cc. of hydrogen at 27.5° and 744.0 mm. This is equivalent to 4.07 moles of hydrogen per mole of alkaloid.

The ethanolic solution of the product of hydrogenation of spartioidine was evaporated to dryness at reduced pressure, the residual oily material was thoroughly dried and its infrared spectrum determined. Bands for a carboxyl group (zwitterion) at 1580 cm.$^{-1}$, for an ester carbonyl at 1730 cm.$^{-1}$ and for a salt-structure at 2340 cm.$^{-1}$ were present. An aqueous solution of the product of hydrogenation of spartioidine had a *p*H value close to neutrality, which did not change after the addition of Dowex 50. This test has been used previously with success for the determination of the inter- or intra-molecular character of salt-like compounds.[10]

Hydrolysis of Spartioidine.—Alkaline hydrolysis of 30 mg. of the alkaloid by the usual procedure followed by separation of the acidic and basic fragments yielded retronecine, identified by its infrared spectrum, melting point and a melting point of a mixture with an authentic sample.

(10) R. Adams and M. Gianturco, THIS JOURNAL, **78**, 4464 (1956).

URBANA, ILLINOIS

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Quinone Imides. XLII. Orientation of Adducts from Substituted *p*-Quinonedimethanesulfonimides

BY ROGER ADAMS AND M. D. NAIR[1]

RECEIVED AUGUST 14, 1956

Addition of thiophenol and benzenesulfinic acid to 2-chloro-*p*-quinonedimethanesulfonimide gives 2-chloro-5-phenylmercapto-*p*-phenylenedimethanesulfonamide and 5-benzenesulfonyl-2-chloro-*p*-phenylenedimethanesulfonamide, respectively. Addition of hydrogen chloride to 2-phenylmercapto-*p*-quinonedimethanesulfonamide results in 5-chloro-2-phenylmercapto-*p*-phenylenedimethanesulfonamide. The 2-benzenesulfonyl-*p*-quinonedimethanesulfonimide, on the other hand, does not give an hydrogen chloride adduct with 1,2,4,5-orientation; by analogy with the corresponding reaction in the benzenesulfonimide series, this compound is assigned a 1,2,3,4-orientation.

Addition of thiophenol and benzenesulfinic acid to 2-chloro-*p*-quinonedibenzenesulfonimide resulted in adducts with 1,2,4,5-orientation[2,3] and addition of hydrogen chloride to 2-phenylmercapto-*p*-quinonedibenzenesulfonimide also yielded 5-chloro-2-phenylmercapto-*p*-phenylenedibenzenesulfonamide.[3] With the strongly electron-attracting benzenesulfonyl group, however, addition of hydrogen chloride resulted in an adduct with 1,2,3,4-orientation.[4]

The orientation in addition of reagents to quinone diimides has been shown to be dependent in part on the character of the groups on the imide nitrogens. The benzoyl and benzenesulfonyl groups had markedly different effects. This suggested a comparison of two sulfonyl groups, one containing an aromatic and the other an aliphatic residue. A few typical addition reactions of *p*-quinonedimethanesulfonimides have now been studied. Thiophenol and benzenesulfinic acid added to 2-chloro-*p*-quinonedimethanesulfonimide (I) to give adducts with identical orientations, since the thiophenol adduct II on oxidation with hydrogen peroxide gives the benzenesulfinic acid adduct III. The orientation of groups in these adducts was shown to be 1,2,4,5 by an unequivocal synthesis. 2-Chloro-5-phenylmercapto-*p*-phenylenediamine (IV)[5] was tetramethanesulfonated to V, oxidized to the benzenesulfonyl derivative VI, and one methanesulfonyl group removed from each nitrogen by means of aqueous alkali, to give III.

(1) An abstract of a portion of a thesis submitted by M. D. Nair to the Graduate College of the University of Illinois, 1956, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

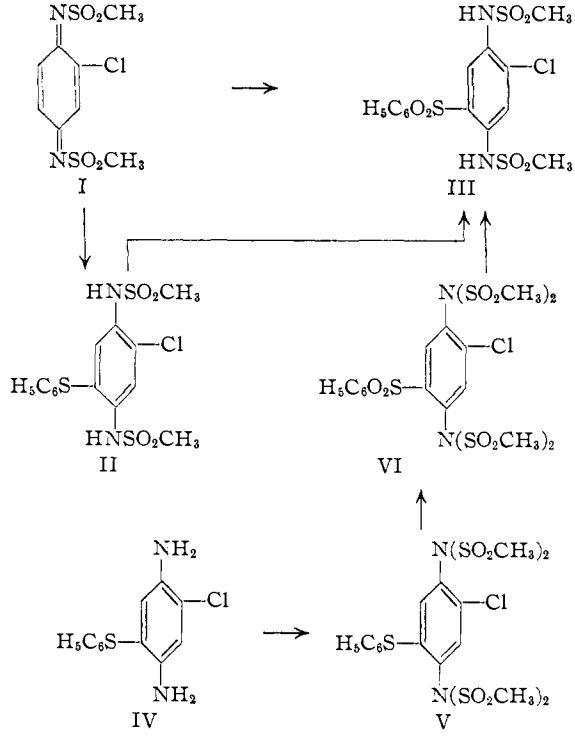
(2) R. Adams, E. F. Elslager and T. E. Young, THIS JOURNAL, **75**, 663 (1953).

(3) R. Adams and T. E. Young, *ibid.*, **75**, 3235 (1953).

(4) R. Adams, T. E. Young and R. W. P. Short, *ibid.*, **76**, 1114 (1954).

(5) R. Adams and M. D. Nair, *ibid.*, **78**, 5932 (1956).

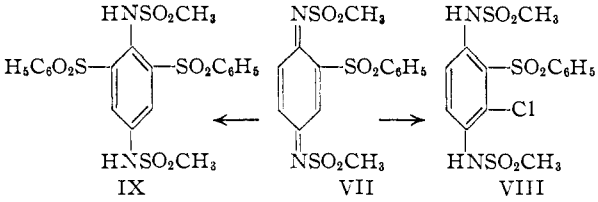
Addition of hydrogen chloride to 2-phenylmercapto-*p*-quinonedimethanesulfonimide also resulted in formation of II. These orientations are identical to those observed in the dibenzenesulfonimide series indicating that alteration of the substituted function of the sulfonimide groups does not have any profound effect on the orientation of adducts.



2-Benzenesulfonyl-*p*-quinonedimethanesulfonimide added hydrogen chloride to give an adduct

which does not have a 1,2,4,5-orientation since it was not identical with the 1,2,4,5-adduct unequivocally synthesized. Of the other two possible orientations, the compound is assigned a 1,2,3,4-orientation (VIII) by analogy with the reaction in the benzenesulfonimide series.

Addition of benzenesulfinic acid to 2-benzenesulfonyl-*p*-quinonedimethanesulfonimide was accomplished in acetic acid solution. The structure of the adduct was not established but is probably 1,2,4,6 as shown in IX by analogy with the addition reaction in the dibenzenesulfonimide series. Attempts to hydrolyze this adduct to the diamine



IX VII VIII

with constant boiling hydrochloric acid or 1:1 sulfuric acid were unsuccessful.

Acknowledgment.—The authors are indebted to Mr. J. Nemeth and Mrs. M. Benassi for the microanalyses and to Mr. J. Brader for the determination and interpretation of the infrared spectra.

Experimental

2-Chloro-5-phenylmercapto-*p*-phenylenedimethanesulfonamide.—A solution of 1.0 g. of 2-chloro-*p*-quinonedimethanesulfonimide[6] in 30 ml. of dioxane was added to a solution of 0.7 ml. of thiophenol in 20 ml. of dioxane containing 3 drops of concentrated sulfuric acid. There was an immediate transient pink color. The mixture was allowed to stand at room temperature for 24 hours and poured into cold water. The product was separated by filtration, washed and dried to give 1.3 g. (88%) of white powder. Three recrystallizations from glacial acetic acid gave white plates, m.p. 218–219°. The compound did not depress the melting point of 2-chloro-5-phenylmercapto-*p*-phenylenedimethanesulfonamide.

5-Benzenesulfonyl-2-chloro-*p*-phenylenedimethanesulfonamide. Method A.—To a suspension of 0.55 g. of 2-chloro-*p*-quinonedimethanesulfonimide in 20 ml. of glacial acetic acid was added 0.6 g. of sodium benzenesulfinate. The mixture was shaken well and heated on a water-bath for 10 minutes. The color faded to a very pale yellow. The volume of the solution was reduced to 10 ml. and 10 ml. of water added. The product was separated, washed and dried to give 0.9 g. (99%) of white solid. Recrystallization from glacial acetic acid and finally from ethanol gave white needles, m.p. 200.5°.

Anal. Calcd. for $C_{14}H_{15}ClN_2O_6S_3$: C, 38.31; H, 3.44; N, 6.38. Found: C, 38.60; H, 3.40; N, 6.10.

Method B.—A mixture of 0.5 g. of 2-chloro-5-phenylmercapto-*p*-phenylenedimethanesulfonamide, 2 ml. of 30% hydrogen peroxide and 30 ml. of glacial acetic acid was heated under reflux for 2 hours, cooled and poured into cracked ice and water. After allowing to stand at room temperature for one hour, the solution was filtered and the residue dried to give 0.35 g. (66%) of white product. Recrystallization from ethanol gave white needles, m.p. 199.5°, identical with the product obtained by method A.

Anal. Calcd. for $C_{14}H_{15}ClN_2O_6S_3$: C, 38.31; H, 3.44. Found: C, 38.50; H, 3.37.

N′,N′,N″,N″-Tetramethanesulfonyl-2-chloro-5-phenylmercapto-*p*-phenylenediamine.—A mixture of 0.25 g. of 2-chloro-5-phenylmercapto-*p*-phenylenediamine,[5] 0.35 ml. of methanesulfonyl chloride and 10 ml. of reagent pyridine was allowed to stand at room temperature for 48 hours. The color had changed to red and some crystals separated. The solution was poured into cracked ice and hydrochloric acid which precipitated a white solid. When filtered and dried it weighed 0.45 g. (83%). It was recrystallized from dimethylformamide–water mixture to give white needles, m.p. 270.5–271°.

Anal. Calcd. for $C_{16}H_{19}ClN_2O_8S_5$: C, 34.07; H, 3.57; N, 4.96. Found: C, 34.37; H, 3.67; N, 4.95.

5-Benzenesulfonyl-2-chloro-*p*-phenylenedimethanesulfonamide.—A mixture of 0.25 g. of N′,N′,N″,N″-tetramethanesulfonyl-2-chloro-5-phenylmercapto-*p*-phenylenediamine, 1 ml. of 30% hydrogen peroxide and 20 ml. of glacial acetic acid was heated under reflux for one hour, then cooled and poured into cold water, which precipitated a white product. Filtration yielded 0.25 g. (95%) of white crystals. After one recrystallization from acetic acid, the product, m.p. 306°, was hydrolyzed.

The compound was heated with 8% aqueous sodium hydroxide for a few minutes, cooled, filtered and neutralized with acetic acid. The precipitate thus obtained was recrystallized from ethanol to give white needles, m.p. 199.5–200°. It did not depress the melting point of the benzenesulfinic acid adduct of 2-chloro-*p*-quinonedimethanesulfonimide and their infrared spectra are identical.

2-Phenylmercapto-*p*-quinonedimethanesulfonimide.—To a mechanically stirred suspension of 1.5 g. of 2-phenylmercapto-*p*-phenylenedimethanesulfonamide[6] in 20 ml. of glacial acetic acid was added in one lot 1.85 g. of lead tetraacetate. The mixture turned blood red in color. It was stirred for one hour, 5 drops of ethylene glycol added and the solution stirred for 10 minutes more. The precipitate was filtered and dried to give 1.3 g. (88%) of red crystals, m.p. 180–183°. No satisfactory solvent was found for purification. It was used directly in the addition reactions.

5-Chloro-2-phenylmercapto-*p*-phenylenedimethanesulfonamide.—To a solution of 1.0 g. of 2-phenylmercapto-*p*-quinonedimethanesulfonimide[6] in 60 ml. of reagent chloroform was passed a current of hydrogen chloride for 2 hours during which time the color faded to a very pale yellow. The solution was evaporated to dryness and the yellow oily residue heated with 20 ml. of ethanol. On cooling a white precipitate separated. It weighed 0.4 g. The filtrate on standing deposited another 0.2 g. bringing the total yield to 0.6 g. (55%). It was recrystallized from glacial acetic acid to give white needles, m.p. 219.5–220°.

Anal. Calcd. for $C_{14}H_{15}ClN_2O_4S_3$: C, 41.32; H, 3.71; N, 6.88. Found: C, 41.60; H, 3.66; N, 6.59.

2-Benzenesulfonyl-*p*-quinonedimethanesulfonimide.—To a mechanically stirred suspension of 4.0 g. of 2-benzenesulfonyl-*p*-phenylenedimethanesulfonamide in 50 ml. of glacial acetic acid was added 4.5 g. of lead tetraacetate. The solution turned yellow in 5 minutes. After stirring at room temperature for 90 minutes, 2 ml. of ethylene glycol was added and stirring continued for 10 minutes more. The precipitate, which was collected and dried, weighed 3.1 g. (78%). Two recrystallizations from glacial acetic acid gave beautiful yellow crystals, m.p. 201° dec.

Anal. Calcd. for $C_{14}H_{14}N_2O_6S_3$: C, 41.78; H, 3.50; N, 6.96. Found: C, 42.09; H, 3.63; N, 6.75.

The infrared spectrum of this compound shows a band at 1575 cm.$^{-1}$ corresponding to the C=N (str.) of the imide.

2-Benzenesulfonyl-3-chloro-*p*-phenylenedimethanesulfonamide.—Into a solution of 1.2 g. of 2-benzenesulfonyl-*p*-quinonedimethanesulfonimide in 60 ml. of dry, reagent chloroform was passed a current of hydrogen chloride. The color turned to a pale yellow in 5 sec. but did not show any further change. The solution was allowed to stand at room temperature for 12 hours and then evaporated to dryness. The residue was triturated with 10 ml. of ethanol and filtered. The precipitate weighed 0.48 g. Concentration of the filtrate gave an additional 0.3 g. of product bringing the total yield to 0.78 g. (60%). Two recrystallizations from ethanol yielded needles, m.p. 224–225°.

Anal. Calcd. for $C_{14}H_{15}ClN_2O_6S_3$: C, 38.31; H, 3.44; N, 6.38. Found: C, 38.50; H, 3.36; N, 6.18.

2,X-Dibenzenesulfonyl-*p*-phenylenedimethanesulfonamide.—To a suspension of 0.75 g. of 2-benzenesulfonyl-*p*-quinonedimethanesulfonimide in 15 ml. of glacial acetic acid was added in one lot 0.3 g. of sodium benzenesulfinate. The slurry was shaken and warmed on the steam-bath for one hour. A small amount of white precipitate separated. This was collected by filtration and to the filtrate was added

(6) R. Adams and W. P. Samuels, THIS JOURNAL, **77**, 5383 (1955).

15 ml. of water which caused precipitation of a white product. The combined fractions were recrystallized from ethanol to give white crystals, m.p. 201.5–202°. The total yield was 0.8 g. (77%).

Anal. Calcd. for $C_{20}H_{20}N_2O_8S_4$: C, 44.06; H, 3.70; N, 5.14. Found: C, 44.09; H, 3.82; N, 4.95.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE NATIONAL INSTITUTES OF HEALTH]

Quinol Intermediates in the Oxidation of Phenols and Their Rearrangements[1]

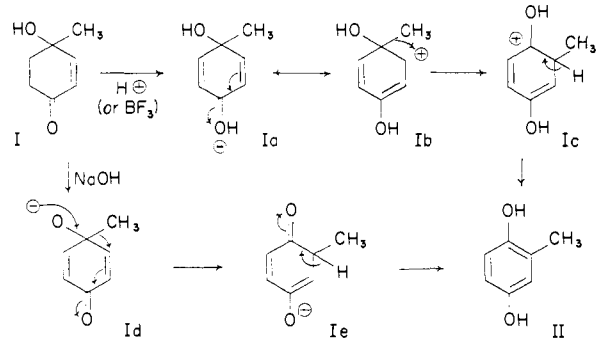
BY SIDNEY GOODWIN AND BERNHARD WITKOP

RECEIVED APRIL 5, 1956

The *p*-quinols and their O-acetates obtained from *p*-cresol, methyl *p*-hydroxyphenylacetate and 6-hydroxytetralin were rearranged to derivatives of hydroquinone under aqueous acidic or basic conditions and to resorcinols under the conditions of the Thiele reaction or by the use of boron trifluoride in ether. The rearrangements are pictured as acyloin shifts, and mechanisms are proposed for the alternate alkyl or acyloxy migrations. Homogentisic acid (XVII) was shown to be the product of the action of alkali on 4-carbomethoxymethyl-4-acetoxy-2,5-cyclohexadien-1-one (XVI). The *o*-quinoid diacetate XX yielded the triacetate of 5-methylpyrogallol (XXI) under the conditions of the Thiele reaction. The implications of these rearrangements are discussed in connection with biological oxidation mechanisms.

The oxidation of *p*-alkylated phenols with peracids in acidic solution[2] leads to alkylhydroquinones. Under neutral conditions the labile intermediates in this reaction can be isolated,[3] namely *p*-alkylquinols, originally obtained by the anionotropic, acid-catalyzed *inter*molecular rearrangement[4,5] of *p*-alkylhydroxylamines.[6] The analogy of these rearrangements to the metabolic sequence tyrosine → homogentisic acid was recognized by several investigators[7,8]; however, attempts to prepare the intermediate quinol in this series failed.[8–10] In this paper the preparation and various rearrangements of a number of free and O-acetylated simple mono- and bicyclic quinols as well as of the quinol precursor of homogentisic acid are described following up a preliminary communication published several years ago.[11]

p-Toluquinol (I) and the homologous xyloquinol have been rearranged by the action of aqueous acid and by aqueous alkali.[6,12]



The rearrangements can best be pictured as vinylogous acyloin shifts.[13] Normally an α-hydroxyketone (or aldehyde) by the action of acid or base[14,15] is converted to the isomeric α-hydroxyketone with concomitant interchange of the oxygen functions and migration of one alkyl group. The quinols will not stop at this stage (Ie or Ic) but aromatize to hydroquinones. Such rearrangements are of importance in the biosynthesis of isoleucine and valine and in the formation of uranes in the metabolism of 17-hydroxy-20-ketosteroids.[16]

Whereas gentle acetylation of *p*-toluquinol with ketene (see Experimental) leads to the O-acetate III, which is more easily prepared by the action of lead tetraacetate on *p*-cresol,[17] rearrangement to the liquid cresorcinol diacetate VII occurs under the conditions of the Thiele reaction (acetic anhydride with concd. sulfuric acid). The same cresorcinol diacetate VII is obtained from the quinol acetate III in the Thiele reaction. Since the methyl group migrates more readily than a hydroxyl group, under Thiele conditions acetylation of the tertiary hydroxyl group of I[18] by acetylium ion probably precedes attack of the ion on the carbonyl oxygen followed by migration of the tertiary acetoxyl group (IV → V with acetoxyl instead of $-OBF_3^-$). Whereas the ordinary Thiele reaction proceeds with *external* addition of acetoxyl ion,[19] the cresorcinol diacetate VII arises probably by an

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