Anal. Calcd. for $C_{20}H_{16}ClN_3O_2 \cdot HCl \cdot 1^1/_2H_2O$: C, 56.00; H, 4.70; N, 9.79; Cl^-, 8.28. Found: C, 55.49, 55.28; H, 4.79, 4.91; N, 9.72, 9.79; Cl^-, 8.47, 8.42.

The free base melted at 153–154.5°. *Anal.* Calcd.: C, 65.65; H, 4.41; N, 11.49. Found: C, 64.89; H, 4.42; N, 11.39.

N-[N'-(7-Chloro-4-quinolyl)-N'-methylaminopropyl] phthalimide Hydrochloride.—This homolog was synthesized in the same way and isolated as the sparingly soluble hydrochloride. After recrystallization from hot water, it amounted to 82% of the theoretical yield and melted at 139–141°. Recrystallization from ethanol gave 65% recovery of pure material, m.p. 246–248°, s. 150°.

Anal. Calcd. for $C_{21}H_{18}ClN_3O_2 \cdot HCl \cdot 1\text{–}3/4H_2O$: C, 56.35; H, 5.06; N, 9.21; Cl^-, 7.76. Found: C, 56.36, 56.27; H, 5.58, 5.49; N, 9.29, 9.03; Cl^-, 7.79, 7.90.

The free base melted at 118.5–120.5°.

Anal. Calcd.: C, 66.35; H, 4.78; N, 11.06. Found: C, 66.65, 66.41; H, 4.73, 4.78; N, 11.03, 10.94.

7-Chloro-4-(2-methylaminoethyl)aminoquinoline (III).—This compound was produced by the condensation (2 hr. at 115°) of 4,7-dichloroquinoline and 2-methylaminoethylamine.[8] It was purified by distillation (115°/20 μ), crystallization from benzene, and vacuum sublimation. The yield was approximately 50%, m.p. 110–111.5°.

Anal. Calcd. for $C_{12}H_{14}ClN_3$: C, 61.18; H, 5.98; N, 17.83. Found: C, 61.13, 61.25; H, 6.41, 6.45; N, 17.72, 17.98.

N-[2-[Methyl-(7-chloro-4-quinolyl)]aminoethyl]phthalamic Acid.—A mixture of 60 ml. of water, 72 ml. of *N* sodium hydroxide, 30 ml. of ethanol, and 15 g. (36 mmoles) of *N*-[*N'*-(7-chloro-4-quinolyl)-*N'*-methylaminoethyl]phthalimide hydrochloride (I, $n = 2$) was stirred for 1 hr. while it became homogeneous. Acidification with acetic acid precipitated the product. It weighed 14.5 g. and melted at 174–177° dec. An analytical sample obtained by reprecipitating from an alkaline ethanolic solution with acetic acid melted at 172–174° dec.

Anal. Calcd. for $C_{20}H_{18}ClN_3O_3 \cdot H_2O$: C, 59.75; H, 5.01; N, 10.46. Found: C, 59.25, 59.01; H, 5.17, 5.14; N, 10.52, 10.42.

Acid Hydrolysis of Phthalamic Acid.—A 16.8-g. sample of *N*-[2-[methyl-(7-chloro-4-quinolyl)]aminoethyl]-phthalamic acid was hydrolyzed with 100 ml. of 6 *N* hydrochloric acid by heating on the steam cone overnight, concentrated *in vacuo*, diluted to 100 ml., and 5.5 g. of phthalic acid was removed by filtration. The filtrate was concentrated and diluted with ethanol and ether to precipitate 11.3 g. of base hydrochloride. The crystalline base was isolated in 97% yield and recrystallized several times from hydrocarbon solvents. Both recrystallization and vacuum sublimation gave a melting point of 110–112° not depressed by a sample of 7-chloro-4-(2-methylaminoethyl)aminoquinoline (III).

N-[2-(7-Chloro-4-quinolylamino)ethyl]-N-methylphthalamic Acid.—A 5.9-g. sample of the above material was allowed to react with an equimolar quantity of phthalic anhydride in ethanolic solution. The precipitated product was filtered and reprecipitated from alkaline solution with acetic acid. It weighed 8.3 g. and melted at 250–255°.

Anal. Calcd. for $C_{20}H_{18}ClN_3O_3 \cdot 2H_2O$: C, 57.20; H, 5.27; N, 10.01. Found: C, 57.98; H, 5.88; N, 9.32.

Hydrazine Hydrolysis.—A sample of the phthalimide free base (I, $n = 2$) was refluxed for 2 hr. with an equivalent amount of molar ethanolic hydrazine and gave a product which on recrystallization and sublimation proved to be identical with that from the acid hydrolysis.

(8) The usual method of attachment of an amine to a 4-chloroquinoline; *cf.*, R. M. Peck, R. K. Preston, and H. J. Creech, *J. Am. Chem. Soc.*, **81**, 3988 (1959).

A New Method of Preparation of 2,2'-Biquinoxalines[1]

H. SMITH BROADBENT AND RICHARD C. ANDERSON

Department of Chemistry, Brigham Young University, Provo, Utah

Received January 26, 1962

The synthesis of some 2,2'-biquinolines and 2,2'-bipyridines by catalytic dehydrogenation of the corresponding quinolines and pyridines has been described by prolonged heating of a mixture of the heterocyclic base and 10% by weight of 5% palladium-on-carbon catalyst, usually at a reflux temperature of the base.[2] Modest yields (2–21%) of coupled product were formed by such treatment.

2,2-Biquinoxalines have not been studied extensively, and no generally applicable unambiguous syntheses of compounds of this class have been reported. We have encountered a new method of preparation of 2,2'-biquinoxalines as an outgrowth of an attempt to prepare 2-vinylquinoxaline by heating 2-methylquinoxaline with paraformaldehyde at 160–165° in an autoclave. Under these conditions, a high-melting red-brown crystalline compound was obtained in about 5% yield. This compound was shown to have the molecular formula, $C_{18}H_{14}N_4$, by elemental analysis and molecular weight determination. The structure, 3,3'-dimethyl-2,2'-biquinoxaline, was assigned on the basis of the following observations: (1) Quinoxaline was found to react under the same conditions to give an almost quantitative yield of 2,2'-biquinoxaline (identical with authentic sample). (2) 2,3-Dimethylquinoxaline failed to form a coupled product even upon prolonged heating at 200°. (3) The same products are formed in the absence of paraformaldehyde under otherwise similar conditions. (4) The infrared absorption spectrum of the product from 2-methylquinoxaline exhibits absorption bands in the region characteristic of four adjacent aromatic hydrogens. (5) The ultraviolet absorption spectrum of this compound exhibits absorption maxima at much longer wave length than does the ultraviolet absorption spectrum of 2-methylquinoxaline indicating conjugation between aromatic rings.

Yields of the coupled product from 2-methylquinoxaline were enhanced by heating at higher temperatures. For example a 39% yield of coupled product was obtained by heating at 200° for six hours, whereas only a 5% yield was realized by heating at 160–165° for four hours. Slight catalytic activity was exhibited by 5% palladium-on-carbon

(1) Financial support of this work by a grant (CY-3751) from the National Cancer Institute, U.S. Public Health Service, is gratefully acknowledged.

(2) H. Rapoport, R. Iwamoto, and J. R. Tretter, *J. Org. Chem.*, **25**, 373 (1960).

since a 46% yield of the coupled product was obtained by heating for six hours at 200° in the presence of 2% by weight of the catalyst.

With a related compound, 4-methylquinazoline, we failed to obtain any coupled product upon heating at 200° for four hours in the presence of 2% by weight of 5% palladium-on-carbon.

Experimental

3,3'-Dimethyl-2,2'-biquinoxaline.—2-Methylquinoxaline (50.0 g., 0.347 mole) was placed in a glass liner for a Pendaclave high pressure hydrogenation apparatus, and 1.0 g. of 5% palladium-on-carbon catalyst was added. The mixture was agitated and heated at 200° for 6 hr. The solid reaction mixture was taken up in 200 ml. of hot ethyl acetate and filtered, using suction. The filtrate was cooled in an ice bath and the product was collected by suction filtration. Yield was 16.3 g. of brown-red crystalline material having m.p. 256–258.5°. The filtrate was evaporated and the residue was distilled at reduced pressure, leaving an additional 5.8 g. of product having m.p. 245–252° as residue. Total yield was 22.1 g. (46%). Twenty-three grams of 2-methylquinoxaline was recovered from the vacuum distillation. An analytical sample as long brownish red needles having m.p. 256.5–258.5° was prepared by vacuum sublimation.

Anal. Calcd. for $C_{18}H_{14}N_4$: C, 75.5; H, 4,9; N, 19.6. Found: C, 76.0; H, 4.6; N, 19.6.

Infrared (KBr): 3.20 (w), 3.24(w), 6.20(m), 6.45 (m,sh), 6.52 (s), 6.80 (s), 7.04 (s), 7.30 (w), 7.67 (m), 7.93 (m), 11.76 (m), 12.33 (m), 13.20 (s), 15.32 (m)μ. Ultraviolet ($CHCl_3$): λ_{max} 277 mμ (ϵ38,500), 367 mμ (ϵ12,900), 383.5 mμ (ϵ15,000), 468 mμ (ϵ 5600).

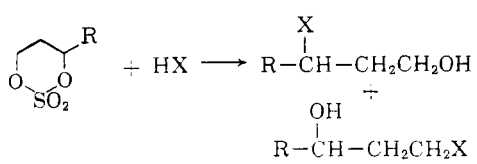
Cleavage of 1,3-Butanediol Cyclic Sulfate with Hydrogen Chloride

JOHN J. MILLER

Rohm & Haas Company, Research Laboratories, Bristol, Pennsylvania

Received January 29, 1962

Reactions of 1,3-diol cyclic sulfates with hydrogen halides have been shown to give 1,3-halohydrins.[1,2] Symmetrical sulfates can provide only one product, but unsymmetrical materials could lead to isomers.



The reactions of 1,3-butanediol cyclic sulfate with hydrogen halides have been described to furnish only 3-halo-1-butanols,[1,2] while similar reactions of hydrogen chloride with 1,3-butanediol or 2-methyloxetane have been shown to provide mixtures of 3-chloro-1-butanol and 4-chloro-2-butanol under a variety of conditions.[3] In no case was one isomer obtained exclusively. A desire for a convenient source of pure 3-chloro-1-butanol stimulated a reinvestigation of the cyclic sulfate–hydrogen chloride reaction.

Reaction of 1,3-butanediol cyclic sulfate with hydrochloric acid was carried out as described.[1] The product, a distillable liquid, exhibited physical properties which were quite similar to those reported for 3-chloro-1-butanol[1,4]; however, vapor phase chromatography indicated that the product was a mixture of two materials in approximately a three to one ratio. Syntheses of 3-chloro-1-butanol and 4-chloro-2-butanol were performed by known methods.[3] Vapor phase chromatographic retention times of these materials demonstrated that the product from the cyclic sulfate reaction was indeed a mixture of 73% 3-chloro-1-butanol and 27% 4-chloro-2-butanol rather than pure 3-chloro-1-butanol.

The corresponding reaction with hydrobromic acid has provided a three component mixture comprised of the isomeric 1,3-bromobutanols and a lower boiling material.

Experimental[5]

Instrument.—A Beckman GC-2 Vapor Fractometer with a 6-ft. column of lac 446 polyester on Chromosorb-W was employed for gas chromatography at 130° with a helium flow of 60 ml./min.

1,3-Butanediol Cyclic Sulfate (I).—The method of Lichtenberger[1] was employed; however, 20% oleum was used in place of 47% material.

A solution of 104 g. of 1,3-butanediol in 600 ml. of chloroform was placed in a 2-l. flask equipped with a stirrer, condenser, thermometer, and dropping funnel. The solution was cooled in an ice bath and the temperature maintained at 0–10° as 1060 g. of 20% oleum was slowly added. After addition, the reaction mixture was kept at ice-bath temperature for 1 hr. and then poured onto ice. The layers were separated and the aqueous layer was extracted with chloroform. The chloroform portions were combined, washed with water, 10% aqueous sodium bicarbonate, and water again. Activated charcoal was added to the chloroform solution and then the solution was filtered, dried, and evaporated leaving 99.5 g. (56% yield) of a clear oil which solidified on cooling. Recrystallization from ether provided white crystals of I, m.p. 44–46° (reported,[1] m.p. 43–44°).

Reaction of I and Hydrochloric Acid.—A mixture of 20 g. of the cyclic sulfate of 1,3-butanediol and 50 ml. of concentrated hydrochloric acid was heated on the steam bath for 40 min. During this time the two layer mixture became homogeneous. The mixture was cooled, 200 ml. of water was added and the solution was extracted with three 100-ml. portions of ether. Washing of the combined ether extracts with 10% aqueous sodium bicarbonate and then with water was followed by drying over magnesium sulfate. Evaporation of the ether left 9 g. of an oil which was distilled *in vacuo* to give 7.5 g. (53%) of a clear liquid, b.p. 70–71°/17 mm., $n^{25}D$ 1.4397.

Anal. Calcd. for C_4H_9ClO: C, 44.25; H, 8.34; Cl, 32.66. Found: C, 44.34; H, 8.16; Cl, 32.25.

(1) J. Lichtenberger and R. Lichtenberger, *Bull. soc. chim. France*, 1002 (1948).

(2) J. Lichtenberger and L. Dürr, *ibid.*, 664 (1956).

(3) S. Searles, Jr., K. A. Pollart, and F. Block, *J. Am. Chem. Soc.*, **79**, 952 (1957).

(4) J. Velhulst, *Bull. soc. chim. Belges*, **40**, 85 (1931).

(5) All boiling and melting points are uncorrected.