H, 2.59, 2.52; S, 10.50, 10.82. Since bis-(*p*-nitrophenyl) sulfoxide is reported[3] to melt at 173° additional evidence for the identity of our product was sought. We, therefore, heated a sample of it with fuming nitric acid and obtained a substance melting at 254–255° (259–260° cor.), which checks well with the melting point 254° reported by Witte[3] for bis-(*p*-nitrophenyl) sulfone.

N-(γ-Acetamidopropyl)-*p*-nitrobenzenesulfonamide.—This compound was prepared from N-acetyltrimethylenediamine[4] by the same procedure used for the previous compound except that the solid that was filtered off from the reaction mixture was crystallized directly from water.

N⁴-Acetyl-N¹-(β-acetamidoethyl)-sulfanilamide.—A mixture of 8.16 g. (0.08 mole) of N-acetylethylenediamine,[2] 22.8 g. (0.096 mole) of N-acetylsulfanilyl chloride, 10.08 g. (0.12 mole) of sodium bicarbonate, 80 cc. of water, and 200 cc. of chloroform was shaken mechanically for seven hours. The solution then was filtered and the solid product recrystallized.

N¹-(β-Acetamidoethyl)-sulfanilamide.—A solution of 2.8 g. (0.01 mole) of N-(β-acetamidoethyl)-*p*-nitrobenzenesulfonamide in 75 cc. of 95% ethanol was shaken at room temperature with 0.1 g. of Raney nickel catalyst and hydrogen under three atmospheres pressure. The mixture was centrifuged, the clear solution then was evaporated to dryness, and the residue was purified by crystallization.

N⁴-Acetyl-N¹-(γ-acetamidopropyl)-sulfanilamide.—A mixture of 5.8 g. (0.05 mole) of N-acetyltrimethylenediamine,[4] 11.7 g. (0.05 mole) of N-acetylsulfanilyl chloride, 6.2 g. (0.075 mole) of sodium bicarbonate, 32 cc. of water and 25 cc. of chloroform was shaken mechanically for seven hours and the solid product was filtered off.

N¹-(γ-Acetamidopropyl)-sulfanilamide.—A solution of 1.5 g. (0.005 mole) of N-(γ-acetamidopropyl)-*p*-nitrobenzenesulfonamide in 75 cc. of 95% ethanol was shaken for twenty-four hours under a pressure of three atmospheres of hydrogen with 0.1 g. of Raney nickel catalyst promoted with a trace of Adams platinum oxide catalyst. The mixture was centrifuged and the clear solution was evaporated to dryness to obtain the product.

N,N′-Trimethylenebis-(*p*-nitrobenzenesulfonamide).—A solution of 0.741 g. (0.01 mole) of trimethylenediamine[5] in 10 cc. (0.06 mole) of 6 *N* sodium hydroxide was cooled in an ice-bath and 4.432 g. (0.02 mole) of *p*-nitrobenzenesulfonyl chloride was added. The mixture was shaken for an hour, acidified and filtered. The solid was dissolved in sodium hydroxide solution, precipitated with hydrochloric acid, filtered, and crystallized. The other N,N′-alkylenebissulfonamides were prepared by substantially the same procedure. Tetramethylenediamine was used in the form of its dihydrochloride, so with it the quantity of sodium hydroxide was increased to 0.08 mole. These substances are all very insoluble and therefore require relatively large volumes of solvents for recrystallization. Even then they go into solution slowly.

Summary

Some sulfanilyl and related derivatives have been prepared from ethylenediamine, trimethylenediamine, and tetramethylenediamine.

(3) Witte, *Rec. trav. chim.*, **51**, 299 (1932).

(4) Aspinall, THIS JOURNAL, **62**, 2160 (1940).

(5) Amundsen and Malentacchi, *ibid.*, **67**, 493 (1945).

STATEN ISLAND, NEW YORK RECEIVED OCTOBER 30, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

Some Basic Barbituric Acid Derivatives

BY JOHN H. GARDNER,[1] FRANK H. BOPP[2] AND ROBERT F. PRINDLE[3]

Some time ago, Guggenheim pointed out that barbituric acid derivatives must have at least one acidic hydrogen if they are to have hypnotic activity.[4] Those with one N-hydrogen replaced by an alkyl group are characterized by a shorter duration of activity. It seemed of interest to prepare some of these compounds in which an N-hydrogen has been replaced by a basically substituted alkyl group to determine whether such a product would be an effective hypnotic. While a few such compounds have been described,[5] no pharmacological properties have been reported. In this investigation, we have prepared the β,4-morpholine-ethyl derivatives of barbital and of amytal. The first of these was subjected to a preliminary pharmacological examination by Mr. L. W. Rowe of Parke, Davis and Co. He found no evidence of hypnotic action in white mice, guinea pigs or dogs.

(1) Present address: J. T. Baker Chemical Co., Phillipsburg, N. J.

(2) Present address: American Can Co., Maywood, Ill.

(3) Present address: Strong Cobb & Co., Cleveland, Ohio.

(4) M. Guggenheim, "Festschrift Emil Barell," F. Hoffmann-LaRoche and Co., Basel, 1936, p. 171.

(5) E. Gryszkiewicz-Trochimowski, *Arch. Chem. Farm.*, **2**, 1 (1934).

Experimental

β,4-Morpholine-ethylurea.—A mixture of 8.4 g. of β,4-morpholine-ethylamine and 7.9 g. of nitrourea in 40 cc. of alcohol was warmed gently. The reaction soon started and proceeded without further heating until the evolution of gas was complete. The mixture was then boiled for a few minutes and most of the alcohol evaporated on the steam-bath. On cooling, the product crystallized; yield 6.1 g. (53.5%), m. p. 173–174° from alcohol.

Anal. Calcd. for $C_7H_{15}O_2N_3$: N, 24.28. Found: N, 24.55, 24.73.

5,5-Diethyl-1-(β,4-morpholine-ethyl)-barbituric Acid Hydrochloride.—Condensation of 5.2 g. of β,4-morpholine-ethylurea and 6.5 g. of ethyl diethylmalonate was carried out in a solution of 2.8 g. of sodium in the smallest amount of absolute alcohol. The mixture was boiled five hours, cooled, diluted with water, made just acid to congo red, and most of the alcohol removed on the steam-bath by a current of air. The residue was extracted with ether. On standing for several days, the aqueous solution deposited long, white needles. These were filtered off and additional crystals obtained by chilling the mother liquor; yield 3.85 g. (38.5%), m. p. 255–256° from alcohol.

Anal. Calcd. for $C_{14}H_{23}O_4N_3.HCl$: N, 12.59; Cl, 10.95. Found: N, 12.98, 12.39; Cl, 11.10, 10.78.

5-Ethyl-5-iso-amyl-1-(β,4-morpholine-ethyl)-barbituric Acid Hydrochloride.—In a similar manner, ethyl ethyl-iso-amylmalonate was condensed with β,4-morpholine-ethylurea; yield 38%, m. p. 90–92°.

Anal. Calcd. for $C_{17}H_{29}O_4N_3.HCl$: N, 11.18. Found: N, 11.14, 11.02.

Summary

The 1-(β,4-morpholine-ethyl) derivatives of barbital and amytal have been prepared. The former has been found ineffective as a hypnotic.

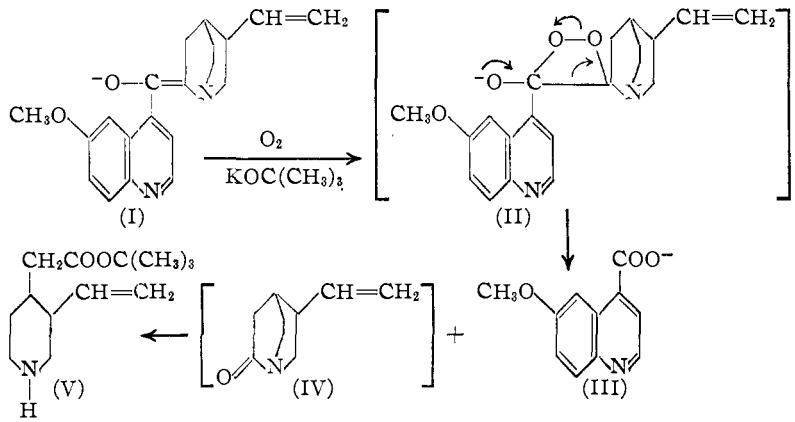
PHILLIPSBURG, N. J. RECEIVED DECEMBER 11, 1945

[CONTRIBUTION FROM CHANDLER LABORATORY, COLUMBIA UNIVERSITY]

The Autoxidation of Quininone[1]

BY W. E. DOERING AND J. D. CHANLEY

In the course of several experiments in which quininone was handled as its sodium or potassium derivative (I), we observed the occasional formation of quininic acid (III) in variable amounts. Woodward[2] suggested that the acid had been formed by the action of air on the enolate ion from quininone, and was able to isolate 50% of the theoretical amount of quininic acid and 10% of unchanged quininone from a reaction mixture obtained by passing air for three hours through a boiling solution of potassium enolate in benzene.[3]



In following up our initial observations, we have found that under certain conditions the oxidative cleavage of quininone is very rapid, and have been able to ascertain the fate of both halves of the original molecule. When a solution of quininone in *t*-butyl alcohol is shaken at room temperature with oxygen under two atmospheres pressure, the absorption of one mole of oxygen is complete in two to five minutes, the reddish orange color of the enolate being discharged and the temperature of the solution rising about twenty degrees. Quininic acid is isolated in 92% of the theoretical amount and identified by conversion to its methyl ester.

The other fragment from the cleavage of quininone has been found to be meroquinene *t*-butyl ester (V) isolated in 58% of the theoretical amount. The structure of the liquid ester follows from several observations. Analysis and titration confirm the empirical formula. A positive reaction with nitrous acid demonstrates the presence of a secondary amino group. Hydrolysis with acid gives meroquinene, and transesterification with ethanol forms the ethyl ester of meroquinene, identified as its hydrochloride.

The remarkable rate of the autoxidation is due to the presence of tertiary butoxide ion.[4] In neutral *t*-butyl alcohol, quininone is stable to oxygen, 70% of the starting material being recovered after shaking for a week, whereas in the presence of added potassium *t*-butoxide, quininone is oxidized completely in a few minutes. The difference in behavior may be ascribed to the fact that quininone is present in potassium *t*-butoxide solution as its potassium salt (I) and that this resonating anion is oxidized much more rapidly than either the keto or the enol form of quininone.[5]

The literature contains isolated references to the autoxidation of ketones. A majority of autoxidative cleavages we have been able to find involve the neutral compound and require either long periods of time or high temperatures or both for completion.[6,7] Kohler[6] has shown that the enol is oxidized a great deal more rapidly than the ketone. In several other examples in which alkali was present during the oxidation, it was not stated whether alkali accelerated the reaction or not.[8]

(1) The work was carried out under Government Contract WPB-191 between the Office of Production Research and Development and the Division of War Research, Columbia University.

(2) Woodward, private communication.

(3) Woodward, Wendler and Brutschy, THIS JOURNAL, **67**, 1425 (1945)

(4) The role of peroxide catalysts in the reaction has been acknowledgedly left uninvestigated.

(5) The difference is the more surprising since quininone alone shows mutarotation and is therefore in labile equilibrium with the enol form.

(6) Kohler, *Am. Chem. J.*, **36**, 177 (1906); Kohler and Thompson, THIS JOURNAL, **59**, 887 (1937).

(7) Fortey, *J. Chem. Soc.*, **75**, 871 (1899); Salway and Kipping, *ibid.*, **95**, 166 (1909); Fuson, Byers and Rabjohn, THIS JOURNAL, **63**, 2639 (1941); Fuson, Maynert and Shenk, *ibid.*, **67**, 1939 (1945); Fleming, German Patent 583,704, Sept. 12, 1933; German Patent 597,973, June 2, 1934; Becker, German Patent 732,236, Jan. 28, 1943; Prückner, U. S. Patent 2,341,288, Feb. 8, 1944.

(8) Zinin, *Chem. Zentr.*, **42**, 211 (1871); Miller and Rohde, *Ber.*, **25**, 2095 (1892); Bogdanowska, *ibid.*, **25**, 1271 (1892); Graebe and Gfeller, *Ann.*, **276**, 12 (1893); Graebe and Jequier, *ibid.*, **290**, 199 (1896).