

Anal. Calcd. for $C_{11}H_{13}O_2N_2Cl$: N, 11.64. Found: N, 11.66.

(B) With α -Naphthyl Isocyanate.—The above procedure was used; yield 1.5 g. after four days; m. p. 195–196°; a mixed melting point with the product of reaction (A) was 165–170°. A mixed melting point with the product prepared by the following method showed no depression.

Anal. Calcd. for $C_{16}H_{15}O_2N_2Cl$: N, 9.64. Found: N, 9.74.

One gram of the urea derivative from α -naphthyl isocyanate and morpholine⁷ was dissolved in 25 ml. of glacial acetic acid and 5 ml. of water, and cooled to 0°. With stirring, 6 g. of commercial bleaching solution was added dropwise over a period of one-half hour. The solution was then warmed slowly to room temperature and finally heated to 60°. The crude product was precipitated by the addition of 60 ml. of water, filtered, and washed with water until free of acid. Recrystallization from aqueous alcohol gave a product melting at 195°.

N-Bromomorpholine.—The reaction of equivalent quantities of sodium hypobromite solution and morpholine at 0° yielded a bright yellow solid with a very pungent odor. This compound decomposed completely within ten hours to a red, paste-like mixture, containing both needles of morpholine hydrobromide (m. p. 204°), and orange prisms of an unidentified material (m. p. 117–119°). Attempted recrystallization of the latter resulted in its decomposition. This viscous mass gradually became dark brown and very hard.

Anal. Calcd. for C_4H_8ONBr : N, 8.44. Found: N, 8.29.

N-Cyanomorpholine.—The method of Slosson⁸ was employed. The yield from 9.8 g. of potassium cyanide and 18.1 g. of N-chloromorpholine was 6.2 g. of a colorless oil, b. p. 123–124° at 18 mm.

Anal. Calcd. for $C_4H_8ON_2$: N, 24.99. Found: N, 24.38.

The same compound was formed in essentially quantitative yield by treating two moles of morpholine with one of cyanogen bromide in ethereal solution.⁹

N,N,N',N'-Bis-(oxydiethylene)-guanidine, O(C₄H₈)₂NC(NH)N(C₄H₈)O.—Three grams of N-cyanomorpholine and 9 g. of morpholine hydrobromide were heated for thirty minutes in an oil-bath at 155–165° (method of v. Braun¹⁰). The cold melt was treated with 2.2 g. of sodium hydroxide in 30 ml. of water and steam distilled to remove unreacted morpholine. The residue in the still-pot was cooled to 0°, made strongly alkaline, and extracted immediately with three 25-ml. portions of ethyl ether. Removal of the ether, after desiccation over anhydrous potassium carbonate, left an oil that soon solidified. Fractional crystallization from commercial ethyl ether gave colorless plates containing one molecule of ethyl alcohol; m. p. 116–117°.

Anal. Calcd. for $C_6H_{17}O_2N_3 \cdot C_2H_5OH$: N, 17.13. Found: N, 17.17, 17.23.

N-Hydroxymorpholine.—A 30% solution of hydrogen peroxide (22.7 g.) was added slowly to 17.4 g. of morpholine. Initially, only a small amount of heat was evolved, but if the mixture was permitted to stand at room temperature for about thirty minutes a very vigorous reaction took place. Considerable gas was evolved and an undesirable darkening occurred. To avoid this, the solution was cooled in an ice-bath for five to six hours, the oxidation then proceeding smoothly. Vacuum distillation of the reaction mixture yielded 1.1 g. of a colorless, viscous oil, b. p. 100–102° at 16 mm. The major portion of the product remained as a brown residue in the distilling flask.

(7) Henry and Dehn, *THIS JOURNAL*, **71**, 2298 (1949).

(8) Slosson, *Am. Chem. J.*, **29**, 302 (1903).

(9) D'Alelio and Pyle, U. S. Patent 2,375,628, May 8, 1945.

(10) v. Braun, *Ber.*, **42**, 2039 (1909).

Anal. Calcd. for $C_4H_7O_2N$: N, 13.59. Found: N, 13.56.

N-Hydroxymorpholine is readily soluble in water and in ether. It rapidly reduces silver nitrate solution.

DEPARTMENT OF CHEMISTRY

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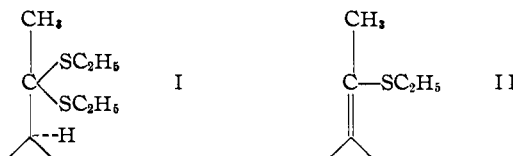
Desulfuration of the 20-Thioenol Ether of Pregnenolone

BY ROGER W. JEANLOZ

A recent report of the desulfuration of the 3-thioenol ether of a Δ^4 -3-ketosteroid¹ to give a sulfur-free product in which the double bond is reduced prompts us to publish similar findings for the 20-thioenol ether of pregnenolone.

Reaction between 5-pregnen-3 β -ol-20-one acetate and ethyl mercaptan in the presence of zinc chloride and anhydrous sodium sulfate leads to a crystalline mixture which cannot be purified by crystallization or chromatography. Analysis indicates the presence of approximately 35% of the 20-diethyl mercaptol (I) and 65% of a 20-thioenol ether (II). The location of the double bond can be assumed to be in position 17,20 by analogy with the Δ^{17} -enol-20-acetate.²

Hydrogenolytic-desulfuration of the crystalline mixture of I and II with a fully active Raney nickel, prepared according to the method of Mozingo,³ affords in yield of 82% 5-pregnen-3 β -ol acetate, recently prepared by Huang-Minlon.⁴ This compound was characterized by saponification and Oppenauer oxidation to 4-pregnen-3-one.⁵



Experimental^{1,6,7,8}

Mixture of 20-Thioenol Ethyl Ether and 20-Diethylmercaptol of 5-Pregnen-3 β -ol-20-one Acetate (I and II).—To a solution of 200 mg. of 5-pregnen-3 β -ol-20-one acetate in 12 ml. of ethyl mercaptan was added 600 mg. of freshly fused zinc chloride and 600 mg. of anhydrous sodium sulfate. The mixture was kept overnight at 5°. The ethyl mercaptan was removed *in vacuo*, water added, and the mixture extracted with ether. The ethereal solution was washed twice with 2 N sodium hydroxide, three times with water, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was crystallized from meth-

(1) Rosenkranz, Kaufmann and Romo, *THIS JOURNAL*, **71**, 3689 (1949).

(2) Fieser and Huang-Minlon, *ibid.*, **71**, 1840 (1949).

(3) Mzingo, Wolf, Harris and Folkers, *ibid.*, **65**, 1013 (1943); "Organic Syntheses," **21**, 15 (1949).

(4) Huang-Minlon, *ibid.*, **71**, 3301 (1949).

(5) Marker and Lawson, *ibid.*, **61**, 586 (1939).

(6) All the melting points were determined on the Kofler micro melting point apparatus.

(7) The rotations were observed in a 2-dm. tube of 2.5 ml. capacity.

(8) The microanalyses were carried out by Dr. K. Ritter, Basle, Switzerland.

anol whereby 305 mg. of crystals was obtained, m. p. 97–104°. Repeated recrystallization from methanol-ether served to raise the melting point to 104–107°. Chromatography on alumina provided fractions eluted with petroleum ether, petroleum ether-benzene and benzene, which after recrystallization from methanol melted between 97° and 110° over a range of several degrees.

Anal. Calcd. for $C_{27}H_{44}O_2S_2$: C, 69.78; H, 9.54; S, 13.80. Calcd. for $C_{26}H_{38}O_2S_2$: C, 74.58; H, 9.51; S, 7.96. Found: C, 73.14; H, 9.37; S, 9.62.

5-Pregnen-3 β -ol Acetate.—Two hundred milligrams of the above crystalline mixture (m. p. 104–107°) was dissolved in 20 ml. of absolute ethanol and after adding about 2 g. of Raney nickel prepared according to Mazingo, *et al.*,³ was refluxed for five hours. The catalyst was filtered and washed several times with hot ethanol and then with acetone. The combined filtrate and washings were evaporated *in vacuo* and the residual oil was recrystallized from methanol or acetone affording 135 mg. (82%) of elongated prisms, m. p. 151–152°. This melting point was not depressed on mixing with an authentic sample of 5-pregnen-3 β -ol acetate,⁹ m. p. 147–149.5°; $[\alpha]^{20}_D$ –60° (c, 0.8 in chloroform).

Anal. Calcd. for $C_{28}H_{46}O_2$: C, 80.18; H, 10.53. Found: C, 80.60; H, 10.55; O, 10.16, 10.03.

The above acetate was saponified with methanolic potassium hydroxide to form 5-pregnen-3 β -ol, m. p. 136–137°. The mixture with an authentic sample⁹ (m. p. 133–134°) melted at 133–135°; $[\alpha]^{20}_D$ –57° (c, 0.95 in chloroform).

Anal. Calcd. for $C_{27}H_{44}O$: C, 83.39; H, 11.33. Found: C, 83.64; H, 11.31.

4-Pregnen-3-one.—Sixty-five milligrams of the above pregnenol was dried by evaporating a solution of this material in dry benzene and redissolved in 1.5 ml. of dry benzene. Dry acetone (0.75 ml.) and 75 mg. aluminum *t*-butylate were added and the mixture was heated in a sealed tube for twelve hours on the water-bath. After cooling, the mixture was dissolved in a large amount of ether and the solution was washed twice with 2 *N* hydrochloric acid, twice with 2 *N* sodium carbonate, three times with water, and dried over anhydrous sodium sulfate. After evaporation, the crystalline residue was purified by chromatography on alumina. Elution with mixtures of benzene-petroleum ether afforded 52 mg. of needles (80%), which after recrystallization from methanol melted at 96–98°. The 2,4-dinitrophenylhydrazones melted after recrystallization from ethanol 196–198°. Marker and Lawson⁵ reported, respectively, 90° and 198°.

(9) This compound was obtained through the courtesy of Professor Fieser's laboratory.

WORCESTER FOUNDATION FOR
EXPERIMENTAL BIOLOGY

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A New Preparation of 1,3-Dichloro-2,4,6-trinitrobenzene¹

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Boyer, Spencer and Wright⁴ described the synthesis of 2,4,6-trinitrochlorobenzene by the reaction of phosgene on dry pyridinium picrate. The application of this technique for the synthesis of 1,3-dichloro-2,4,6-trinitrobenzene (chloropicryl chloride) was unsuccessful and resulted

once in a violent detonation when the dry pyridinium salt of 2,4,6-trinitroresorcinol (styphnic acid) was treated with phosgene under elevated pressure. However, it was found that if phosgene was introduced into an acetone suspension of pyridinium styphnate, chloropicryl chloride was obtained in 70% yield. The effect of different experimental conditions on the conversion of pyridinium styphnate to chloropicryl chloride was observed. The highest yield was obtained when at least three moles of phosgene were used per mole of pyridinium styphnate. The solvent used exerted a profound influence on the reaction. When acetone or methyl ethyl ketone was used, good conversions could be obtained; however, no chloropicryl chloride was formed when dioxane or benzene was employed. The reaction was carried out in the temperature range 30–60° with good results; at higher temperatures the side reactions with phosgene and ketone solvents became excessive and it was difficult to isolate the chloropicryl chloride. The purification step involved the separation of chloropicryl chloride from a mixture containing acetone, pyridinium styphnate, pyridinium chloride, pyridinium chloropicate (formed in the reaction) and the reaction product of acetone with phosgene.

In the course of the investigation it was found that pyridinium styphnate could be prepared containing either one or two moles of pyridine per mole of styphnic acid depending on the method of preparation. The salt containing two moles of pyridine is relatively unstable and loses pyridine on heating to form the more stable mono-pyridinium salt.⁵

Experimental

Preparation of 1,3-Dichloro-2,4,6-trinitrobenzene.—A suspension of 279.5 g. (0.86 mole) of pyridinium styphnate in two liters of acetone was prepared in a three-necked flask equipped with thermometer, stirrer and gas inlet tube. The mixture was heated to 35° and held at this temperature by cooling while 295 g. (2.97 moles) of phosgene was introduced over a period of 8.8 hours. The solution was allowed to come to 23° and stand for twenty-two hours. It was then placed in a separatory funnel attached to a flask of boiling water through which steam was passed. The solution was run into this flask at a rate such that the acetone solvent distilled over as fast as it was introduced. When all of the solvent had been stripped off in this manner, the residue in the flask was cooled and the crystalline material which had formed was filtered off and dried. This material was then leached with several portions of warm benzene. The residue from the benzene leaching process amounted to 26 g. containing a mixture of pyridinium styphnate and pyridinium chloropicate. The benzene extract was evaporated to dryness to give chloropicryl chloride. This was further purified by recrystallization from a mixture containing equal parts of ethanol and chloroform. A total of 166.5 g. (68.5%) was obtained, m. p. 126.5–127°; lit. value⁶ 128°.

The α -naphthylamine addition compound melted at 125–127°; lit. value⁶ 125–127°. Treatment of chloropicryl chloride with gaseous ammonia in alcohol gave 2,4,6-

(1) Abstracted from a thesis by Arthur A. Harban, submitted to the Faculty of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August, 1948.

(2) Present address: General Aniline and Film Corp., New York, N. Y.

(3) Present address: Standard Oil Company, Whiting, Ind.

(4) Boyer, Spencer and Wright *Can. J. Research*, **24B**, 200 (1946).

(5) Hoo, Mah and Sah, *Science Repts. Natl. Tsinghua Univ.*, **2**, 151 (1933).

(6) Sudborough and Picton, *J. Chem. Soc.*, **89**, 591 (1906).