Formulary.[1] In addition, this compound is so widely used as a plasticizing, solubilizing and stabilizing agent in so many technical fields that means of positively identifying it and differentiating it from other glycols are needed. In this laboratory the trityl (*i. e.*, triphenylmethyl) ether has been synthesized and found valuable for such a purpose because it is easily prepared and has a sharp and characteristic melting point.

Experimental.—The method of Seikel and Huntress[2] for the ditritylation of glycols was employed. Heat 1 g. of propylene glycol and 7.2 g. of trityl chloride together with 10 cc. of pyridine under a reflux for one hour on a steam-bath. Dissolve the resultant ether in about 125 cc. of acetone, stir well with a small portion of activated carbon and filter. Unless separating the propylene glycol from aqueous mixtures, the reagents and glycol need not be rendered especially anhydrous. As the acetone spontaneously evaporates large transparent crystals form which become opaque on heating in a drying oven at 100°. The trityl ether was recrystallized to a constant melting point. The following data were obtained:

TABLE I

TRITYL ETHER OF PROPYLENE GLYCOL

		Analyses,[b] %			
		Carbon		Hydrogen	
Formula	M. p.,[a] °C.	Calcd.	Found	Calcd.	Found
$C_{41}H_{36}O_2$	176.5–177.0	87.82	87.68	6.47	6.50
			87.57		6.49

[a] 76 mm. immersion, uncorrected. [b] Microanalyses by Carl Tiedke, New York.

(1) National Formulary, 7th ed., Supplement 3, 1943, p. 7.

(2) Seikel and Huntress, THIS JOURNAL, **63**, 593–595 (1941).

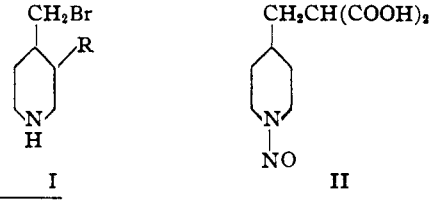
LABORATORY OF THE AMERICAN PHARMACEUTICAL ASSOCIATION
WASHINGTON, D. C. RECEIVED JULY 5, 1944

The Stability of 1-Nitrosopiperidine to Ethyl Sodiomalonate

BY C. F. KOELSCH

Certain unpublished observations have indicated that 4-bromomethylpiperidine (I, R = H) undergoes cyclization so rapidly that it cannot be used to alkylate ethyl malonate. This cyclization can be prevented by acylating the nitrogen atom; 1-benzoyl-4-bromomethylpiperidine is a crystalline solid that is easily purified, and has been used for alkylation.[1] It is not anticipated, however, that homologs of I (R = alkyl) will yield crystalline benzoyl derivatives.

It has now been found that nitrosation also affords a serviceable method for removing the basic properties of a piperidine nitrogen atom. The method will probably be useful in reactions involving homologs of I, for even oily nitroso derivatives can be isolated in a state sufficiently pure for use in subsequent reactions.



I II

(1) Koelsch, THIS JOURNAL, **65**, 2460 (1943).

No published data were found to indicate whether or not nitrosamines would be stable toward ethyl sodiomalonate. But when a mixture of 0.1 mole each of ethyl malonate and nitrosopiperidine was boiled for four hours in 30 ml. of alcohol containing 0.1 mole of sodium ethoxide, no reaction took place.[2] Eighty-five per cent. of the original mixture (b. p. 95–108° at 23 mm.) was recovered. Both components could not be separated unchanged, but saponification, etc., gave 12.4 g. of calcium malonate (identified by quantitative analysis), and 7.3 g. of nitrosopiperidine, b. p. 106–108° at 23 mm. (identified by conversion to 1-aminopiperidine and 1-benzalaminopiperidine).

The following experiments illustrate an application of the method to synthesis. A solution of 4.2 g. of 4-methoxymethylpiperidine hydrobromide in 22 ml. of 47% hydrobromic acid was boiled for six hours, and the excess hydrobromic acid was then removed (water-bath) under reduced pressure. The crystalline residue was dissolved in 10 ml. of water, mixed with 1.7 g. of sodium nitrite in 5 ml. of water, and warmed to 80°. The oily precipitate was taken up in ether, washed with dilute sodium carbonate, and then freed of solvent and water at 100° under reduced pressure. The residue (3.2 g., 80%) was crude 4-bromomethyl-1-nitrosopiperidine, a bright yellow oil which became viscous but did not crystallize in a freezing mixture.

The crude nitroso compound was boiled for two hours with a solution of 0.7 g. of sodium and 5 g. of ethyl malonate in 10 ml. of alcohol, and then dilute acetic acid was added. The product was removed with ether, freed of solvent, and boiled for ten minutes with 3 g. of sodium hydroxide in 25 ml. of water. The undissolved part (0.6 g.) crystallized from ether in the form of faintly yellow prisms, m. p. 108–109°; the substance showed a positive Liebermann test, and analysis indicated that it was **ethyl bis-(1-nitrosopiperidyl-4-methyl)-malonate.**

Anal. Calcd. for $C_{19}H_{32}N_4O_6$: C, 55.4; H, 7.8. Found: C, 55.2; H, 7.7.

By acidification and twelve ether extractions of the saponified part, there was obtained **1-nitrosopiperidyl-4-methylmalonic acid (II)** (2.8 g., 79%), nearly colorless prisms from ethyl acetate–benzene. The compound gave no Liebermann test, was easily soluble in water, sintered at 141° and melted at 145° with foaming.

Anal. Calcd. for $C_9H_{14}N_2O_5$: C, 47.0; H, 6.1. Found: C, 47.0; H, 6.3.

The malonic acid (0.7041 g.) lost 0.1373 g. (calcd. 0.1345 g.) when it was heated at 160° for fifteen minutes. The residual **1-nitrosopiperidine-4,β-propionic acid** was easily soluble in ether, benzene, and warm water. From ether–ligroin it formed white nodules, m. p. 84–86°. The acid gave no true Liebermann test; a solution in sulfuric acid containing phenol became blue when it was warmed, then pink when diluted and pale yellow when it was made basic.

Anal. Calcd. for $C_8H_{14}N_2O_3$: C, 51.6; H, 7.5. Found: C, 51.7; H, 7.3.

A solution of 100 mg. of the propionic acid in 1.5 ml. of hydrochloric acid was mixed with 100 mg. of cuprous

(2) The present result is of interest in comparison with the finding that nitroso-β-anilino ketones [Jones and Kenner, *J. Chem. Soc.*, 363 (1933)] and nitroso-α-anilino ketoximes, but not nitroso-α-anilino ketones [Earl and Hazelwood, *ibid.*, 374 (1937)] react with alkaline β-naphthol yielding phenylazo-β-naphthol. The present result is of some additional interest in that it is not in harmony with an early suggestion [v. Pechmann, *Ber.*, **25**, 3199 (1892)] as to the mechanism of the coupling reactions of aromatic diazonium compounds.

chloride,[3] warmed until no more nitric oxide was evolved (five minutes), and then distilled to dryness under reduced pressure. The residue was dissolved in 8 ml. of water and treated with excess sodium hydroxide. The mixture was boiled, copper oxide was removed, and the filtrate was shaken with 100 mg. of benzoyl chloride. Acidification gave a white precipitate which crystallized from toluene in the form of colorless prisms (100 mg., 71%), m. p. 149–150° alone or mixed with an authentic sample[1] of 1-benzoylpiperidine-4,β-propionic acid.

The author thanks Mr. Stanley T. Rolfson for the analyses reported in this paper.

(3) Jones and Kenner, *J. Chem. Soc.*, 711 (1932).

SCHOOL OF CHEMISTRY
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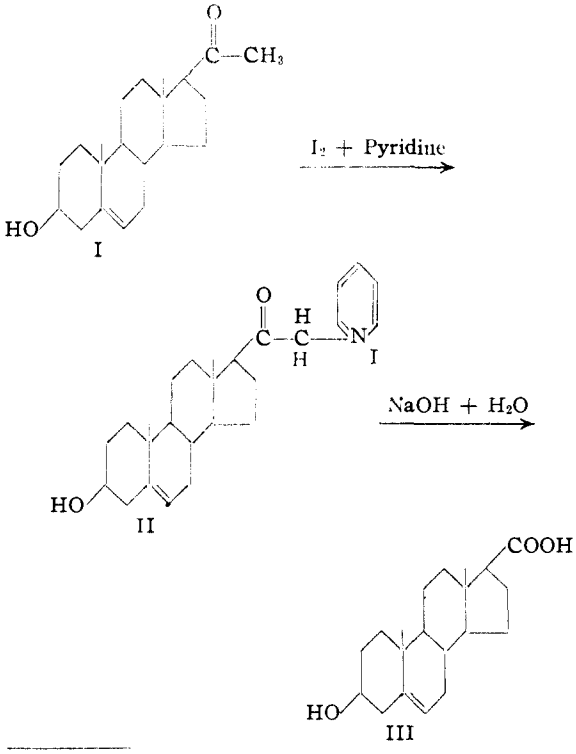
Preparation of 21-Pyridinium-3-β-hydroxy-5-pregnene-20-one Halides and 3-β-Hydroxy-5-androstene-17-carboxylic Acid

BY L. CARROLL KING

In a recent paper from this Laboratory the preparation of substituted β-ketoalkylpyridinium iodides by reaction of ketones with iodine and pyridine was reported.[1] This reaction has now been extended to 3-β-hydroxy-5-pregnene-20-one (I), which gave 21-pyridinium-3-β-hydroxy-5-pregnene-20-one iodide (II) in 50% yield. Alkaline decomposition of (II) or of the corresponding perchlorate yielded 93% of crude 3-β-hydroxy-5-androstene-17-carboxylic acid (III) from which the pure methyl ester was obtained (83% yield from II). The main reactions may be formulated as



(1) King, THIS JOURNAL, **66**, 894 (1944).

Reich and Reichstein[2] obtained compounds of type II when a 21-halo-3-β-hydroxy-5-pregnene-20-one was treated with pyridine.

Experimental[3]

21-Pyridinium-3-β-hydroxy-5-pregnene-20-one Iodide (II).—A solution containing 3.12 g. of 3-β-hydroxy-5-pregnene-20-one in 75 ml. of pyridine was treated with 2.56 g. of iodine in a manner previously described.[1] The resulting relatively insoluble pyridinium iodide was separated from pyridine hydroiodide and crystallized from methanol; yield 3.053 g.; m. p. 248–250°.

Anal. Calcd. for $C_{26}H_{36}INO_2$: C, 59.91; H, 6.91. Found: C, 59.50; H, 6.83.

21-Pyridinium-3-β-hydroxy-5-pregnene-20-one Perchlorate.—This substance was prepared from the above pyridinium iodide as previously described.[1] The product was crystallized from methanol and apparently contains water of crystallization; m. p. 255–260° dec.

Anal. Calcd. for $C_{26}H_{36}ClNO_6 \cdot {}^1/_2H_2O$: C, 62.07; H, 7.37. Found: C, 62.12; H, 7.04.

Methyl 3-β-Hydroxy-5-androstene-17-carboxylate.—To a suspension of 656 mg. of the above pyridinium iodide (II), or a corresponding quantity of the perchlorate, in water or 50% ethyl alcohol, 0.5 g. of sodium hydroxide was added. The mixture was heated for two hours on the steam-bath, acidified and the acidic fraction isolated. The crude 3-β-hydroxy-5-androstene-17-carboxylic acid, yield 400 mg., was of a light tan color and melted at 255–270°. On recrystallization from methanol or dioxane the melting point increased to 270–275°. The total crude product was then dissolved in methanol, a few drops of acetyl chloride added and the reaction mixture heated one hour. The methyl ester was recovered and crystallized from methanol: yield 332 mg.; m. p. 174–177°.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.83; H, 9.70. Found: C, 75.69; H, 9.37.

The above methyl 3-β-hydroxy-5-androstene-17-carboxylate was converted to the benzoate, m. p. 204–206°, and to the acetate, m. p. 153–154°.

(2) Reich and Reichstein, *Helv. Chim. Acta*, **22**, 1124 (1939).

(3) All melting points were observed on a Fisher–Jones melting point block. Carbon and hydrogen analyses by T. S. Ma.

CHEMISTRY DEPARTMENT
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS RECEIVED JUNE 5, 1944

NEW COMPOUNDS

ω-Nitro-3-vinyl-pyrene

In the manner described for the preparation of nitrostyrene,[1] equimolecular amounts of 3-pyrene-aldehyde and nitromethane were condensed in the presence of methyl-alcoholic sodium hydroxide solution. Hydrochloric acid precipitated the ω-nitro-3-vinyl-pyrene as red crystals, which after recrystallization from a mixture of acetone and benzene had m. p. 177°.

Anal. Calcd. for $C_{18}H_{11}O_2N$: C, 79.1; H, 4.0. Found: C, 78.6; H, 3.9.

Alcoholic alkali gives a yellow solution, but the substance is not satisfactory as an indicator.

DEPARTMENT OF ORGANIC CHEMISTRY
HEBREW UNIVERSITY
JERUSALEM, PALESTINE ELIAHU BOGRACHOV
RECEIVED JUNE 12, 1944

(1) "Organic Syntheses," Coll. Vol. I, p. 413.