Anal. for xylitol pentapropionate: Calcd. for $C_{20}H_{32}O_{10}$: C, 55.54; H, 7.46. Found: C, 55.2; H, 7.44.

Anal. for xylitol pentabutyrate: Calcd. for $C_{25}H_{42}O_{10}$: C, 59.74; H, 8.42. Found: C, 59.5; H, 8.38.

Preparation of Xylitol Pentalaurate, Pentamyristate, Pentapalmitate, and Pentastearate.—These esters were prepared by reaction of xylitol with the appropriate acid chloride in the presence of pyridine. The acid chlorides were prepared by the method of Ralston[5] from Eastman acids.

To a solution of 5.0 g. (0.033 mole) of xylitol in 150 g. of dry pyridine, 0.2 mole of acid chloride was added in small portions at a time and the reaction mixture was heated on a steam-bath for four hours under anhydrous conditions. The mixture was extracted with toluene and the toluene extract was washed successively with 3% potassium hydroxide, 3% hydrochloric acid, and distilled water. The extract was decolorized with carbon, and the solvent was removed *in vacuo*, yielding the ester as a solid residue. Yields of 88, 84, 95, and 95% were obtained for the pentalaurate, pentamyristate, pentapalmitate and pentastearate, respectively. Xylitol pentalaurate and pentamyristate were most conveniently purified by recrystallization from 4 parts of acetone at −15°. The palmitic and stearic acid esters were conveniently recrystallized from acetone or toluene at −20°.

(5) Ralston, THIS JOURNAL, **61**, 1019 (1939).

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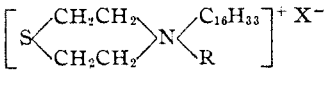
Invert Soaps. Thiomorpholinium Salts[1]

BY WILLIAM F. HART AND JOSEPH B. NIEDERL

Studies of the morpholine types of "invert soaps"[2] have been extended to the corresponding sulfur analogs. Recognizing the importance of a "cetyl" group in bacteridical "invert soaps"[3] N-cetylthiomorpholine was studied first. This compound was prepared by condensing cetylamine with mustard gas utilizing the methods of H. T. Clarke[4] and W. E. Lawson and E. E. Reid[5] as follows:

$$C_{16}H_{33}NH_2 + (ClCH_2CH_2)_2S \xrightarrow[C_2H_5OH]{\Delta\ Na_2CO_3} S<(CH_2CH_2)_2>NC_{16}H_{33}$$

The above tertiary amine upon treatment with appropriate alkyl halides and sulfates was then converted into the respective quaternary thiomorpholinium salts of the "simple invert soaps" types:



R: methyl, ethyl, propyl, benzyl
X: Cl, Br, I, CH_3SO_4-, $C_2H_5SO_4$-

Experimental

N-Cetylthiomorpholine.—Seventy-six grams of cetylamine (b. p. 325° uncor.) was dissolved in 120 ml. of absolute alcohol and 34 g. of anhydrous sodium carbonate added. Fifty grams of mustard gas was then added, and the solution was refluxed for eight hours. The warm solution was filtered to remove inorganic salts, which were washed twice with hot absolute alcohol. The combined alcohol extracts were distilled *in vacuo* to remove the solvent. The residue was then taken up in an excess of dry ether, and saturated with dry hydrogen chloride. The hydrochloride was filtered off and washed repeatedly with dry ether and with acetone. The free base was obtained by taking up the hydrochloride in a concentrated potassium hydroxide solution and extracting with ether. The combined ether extracts were dried over solid potassium hydroxide pellets, and the solvent removed by distillation. The free base was purified by recrystallization from ether.

The picrate was prepared by adding an equal volume of a saturated aqueous solution of picric acid to an aqueous solution of the hydrochloride. This was purified by one recrystallization from alcohol.

Quaternary Thiomorpholinium Salts.—The methiodide and ethiodide were prepared by refluxing N-cetylthiomorpholine the free base with a slight excess of methyl and ethyl iodide, respectively, for three hours, allowing the excess alkyl iodide to evaporate spontaneously at the end of that period. The products were then taken up in warm ethyl acetate in which thiothiomorpholinium iodides are soluble, cooled, filtered, and recrystallized from the same solvent.

The *n*-propyl bromide and benzyl chloride quaternary salts were prepared by refluxing the free base with an equivalent amount of the alkyl halide in toluene solution for six hours, distilling the solvent *in vacuo*, washing with dry acetone, and finally recrystallizing from ethyl acetate.

The alkyl sulfates were prepared by refluxing for four hours equivalent quantities of the free base and the respective di-alkyl sulfates, dimethyl and diethyl sulfate, in half the total volume of dry benzene.

TABLE I

Compound	Formula	M. p., °C. (uncor.)	Analyses, % N Calcd.	Found
N-Cetylthiomorpholine	$C_{20}H_{41}NS$	78	4.27	4.35
Hydrochloride	$C_{20}H_{42}NSCl$	162	3.82	3.93
Picrate	$C_{26}H_{44}O_7N_4S$	112	10.06	10.15
Methiodide	$C_{21}H_{44}NSI$	244	2.98	3.05
Ethiodide	$C_{22}H_{46}NSI$	205	2.90	3.02
n-Propyl bromide	$C_{23}H_{48}NSBr$	173	3.10	3.13
Benzyl chloride	$C_{27}H_{48}NSCl$	166	3.08	3.12
Methosulfate	$C_{21}H_{47}NS_2O_4$	210 dec.	3.08	3.15
Ethosulfate	$C_{24}H_{51}NS_2O_4$	Oil	2.90	2.97

Acknowledgment.—The authors desire to express their appreciation to the Commanding Officer of Edgewood Arsenal for the mustard gas used in this work, and to the Chemical Division of Armour and Company for technical cetylamine.

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(1) Presented before the Division of Organic Chemistry at the New York City meeting of the American Chemical Society, September, 1944.

(2) J. B. Niederl and co-workers, THIS JOURNAL, **63**, 1476 (1941); **66**, 840 (1944).

(3) R. Kuhn, *Ber.*, **73**, 1080, 1095, 1100, 1105, 1109 (1940).

(4) H. T. Clarke, *J. Chem. Soc.*, **101**, 1583 (1912).

(5) W. E. Lawson and E. E. Reid, THIS JOURNAL, **47**, 2821 (1925).

The Preparation of the Trityl Ether of Propylene Glycol

BY NANCY GREEN AND MELVIN W. GREEN

During recent years, propylene glycol has been introduced into many types of pharmaceutical preparations and in fact standards governing its purity have been introduced into the National

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
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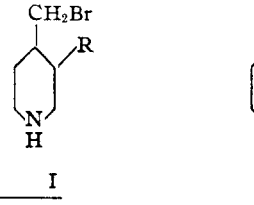
The Stability of 1-Nitrosopiperidine to Ethyl Sodiomalonate

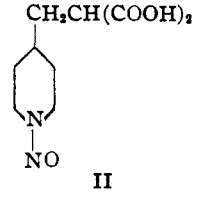
BY C. F. KOELSCH

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.