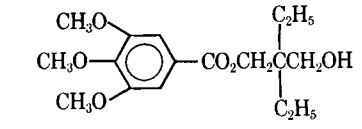
Preparation of 2,2-Diethyl-3-(3,4,5-trimethoxybenzoyloxy)propyl Carbamate

By JOSEPH SAM*

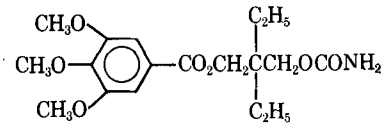
The preparation of the 3,4,5-trimethoxybenzoate of 2,2-diethyl-1,3-propanediol, and the conversion of the ester to the carbamate are described.

THE USEFUL depressant properties of propanediols (1) and the presence of the 3,4,5-trimethoxybenzoyl group in the rauwolfia alkaloids (2) prompted the preparation of a hybrid involving the two groups.

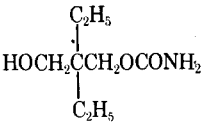
The esterification of an excess of 2,2-diethyl-1,3-propanediol with 3,4,5-trimethoxybenzoyl chloride provided the mono ester, I. The treatment of I



I



II



III

with phosgene, followed by ammonolysis yielded the mixed ester-carbamate, II. Compound II also was prepared by the esterification of 2,2-diethyl-3-hydroxypropyl carbamate (III).

Preliminary pharmacological studies in mice demonstrated that compounds I and II exhibit mild central nervous system depressant properties.

EXPERIMENTAL[1]

2,2-Diethyl-3-hydroxypropyl-3,4,5-trimethoxybenzoate—A mixture of 46 Gm. (0.2 mole) of 3,4,5-trimethoxybenzoyl chloride, 53 Gm. (0.4 mole) of 2,2-diethyl-1,3-propanediol, and 300 ml. of toluene was refluxed for 7 hr. The mixture was cooled and washed with a 5% sodium carbonate solution. The toluene solution was dried over anhydrous sodium sulfate and then distilled to yield 25 Gm. (39%) of product, b.p. 193–196° (0.2 mm.).

Anal.—Calcd. for $C_{17}H_{26}O_6$: C, 62.6; H, 8.03. Found: C, 62.0; H, 7.88.

2,2-Diethyl-3-(3,4,5-trimethoxybenzoyloxy)propyl Carbamate—*Method A*—A solution of 17.5 Gm. (0.1 mole) of 2,2-diethyl-3-hydroxypropyl carbamate (3, 4) and 23 Gm. (0.1 mole) of 3,4,5-trimethoxybenzoyl chloride in 300 ml. of benzene was refluxed for 3 hr. and then cooled. The benzene solution was washed with water and 5% sodium bicarbonate, respectively, and then dried over anhydrous sodium sulfate. Distillation of the solvent and crystallization of the residual material from a mixture of benzene and *n*-hexane gave 15 Gm. (41%) of light brown solid, m.p. 110–118°. Recrystallization from benzene gave product, m.p. 124.5–126°.

Anal.—Calcd. for $C_{18}H_{27}NO_7$: C, 58.5; H, 7.37. Found: C, 58.3; H, 7.41.

Method B—The procedure (5) described for the preparation of carbamates of aryl glycerol ethers was followed using the same molar ratios of reactants. From 3.3 Gm. (0.01 mole) of 2,2-diethyl-3-hydroxypropyl-3,4,5-trimethoxybenzoate there was obtained 0.4 Gm. (10%) of product which was washed with petroleum ether (b.p. 60°) and recrystallized from benzene; m.p. 124.5–126°. A mixed melting point with the product obtained by method *A* showed no depression.

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[1] All melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected.

Keyphrases

2,2-Diethyl-3-(3,4,5-trimethoxybenzoyloxy) propyl carbamate—synthesis
Esterification and ammonolysis—reactions
Pharmacological screening—CNS depressant activity