TABLE I

ANALYTICAL AND OTHER DATA

	Yield, %	M. p., °C.	Nitrogen, % Calcd.	Found	Chlorine, % Calcd.	Found
$C_6H_5(C_{10}H_7)NCOOC_2H_4N(C_2H_5)_2 \cdot HCl$	66	214–216	7.02	6.87	8.90	9.01
$C_6H_5(C_{10}H_7)NCOOCH(CH_2N(C_2H_5)_2)_2 \cdot HCl$	71	90 (dec.)	..	..	7.34	7.30
$C_6H_5(C_{10}H_7)NCOOC.C_2H_5(CH_2N(CH_3)_2)_2 \cdot HCl$	61	165–167	9.22	9.30	7.78	7 90

pane-2 phenyl-α-naphthylamine-N-carboxylate was a hygroscopic substance. When heated above 80° it gradually softened and decomposed.

Free Base of Diethylaminoethyl Phenyl-α-naphthylamine-N-carboxylate.—Diethylaminoethyl phenyl-α-naphthylamine-N-carboxylate which was first formed as an oil, crystallized after standing for several weeks. When it was recrystallized from light petroleum ether it occurred as colorless prisms which melted at 60–61°.

Anal. Calcd. for $C_{23}H_{26}O_2N_2$: N, 7.73. Found: N, 7.72.

Preparation of Acid Citrate of Diethylaminoethyl Phenyl-α-naphthylamine-N-carboxylate.—To a solution of diethylaminoethyl phenyl-α-naphthylamine-N-carboxylate in dry ether was added exactly one molecular equivalent of anhydrous citric acid, dissolved in a small amount of absolute alcohol. The precipitate which formed was collected on a filter, washed with dry ether and dried *in vacuo* over calcium chloride. It occurred as a colorless, microcrystalline, hygroscopic substance. When it was heated in a melting point tube, it gradually softened and decomposed with effervescence between 50 and 80°.

Anal. Calcd. for $C_{29}H_{34}O_9N_2$: N, 5.02. Found: N, 5.04.

We are indebted to Dr. Hans Molitor of the Merck Institute of Therapeutic Research for a pharmacological investigation of the new compounds. The results of his investigation will be reported in detail elsewhere. However it may be said that all of the new compounds were powerful local anesthetics. For terminal and bloc anesthesia the anesthetic action could be compared with that of a procaine solution of equal strength, whereas the action upon the eye and mucous membrane was somewhat stronger than that of procaine. Test animals tolerated a subcutaneous dose up to 25 mg. per kilo without any marked toxic symptoms. The toxicity by intravenous injection was very high. The new compounds had very marked penetrating powers. When an ointment containing from 5 to 20% of the anesthetic was rubbed into the intact skin of rabbits or guinea pigs, there was induced a degree of anesthesia sufficient to permit major surgical operations (as opening the abdomen or exposing the sciatic nerve). Unfortunately the penetrating action through the human skin was much lower.

Summary

1. Phenyl-α-naphthylcarbamyl chloride has been prepared.

2. Several dialkylaminoalkyl esters of phenyl α-naphthylamine-N-carboxylic acid have been prepared by the condensation of phenyl-α-naphthylcarbamyl chloride and the sodium derivative of the corresponding dialkylaminoalkyl alcohol.

3. The new urethans had a marked local anesthetic action.

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGY, WASHINGTON SQUARE COLLEGE, NEW YORK UNIVERSITY]

1-Xenyl-2-aminopropanol

BY SAMUEL MACHLIS AND KENNETH C. BLANCHARD

Xenylaminopropanol, an analog of norephedrine, has been synthesized with the expectation that it should have a pressor activity of sufficient magnitude to be of pharmacological interest. The synthesis of this substance was easily accomplished as follows: biphenyl was converted to 4-propionylbiphenyl from which the corresponding α-isonitroso derivative was prepared; the latter was then reduced to the desired 1-xenyl-2-aminopropanol which was isolated in the form of its hydrochloride. This salt appears to be stable for an indefinite period although the free base is oxidized immediately by air with the formation of colored products. The 4-propionylbiphenyl was obtained by the interaction of biphenyl with propionyl chloride in the presence of aluminum chloride, a reaction erroneously claimed by Willgerodt and Scholtz[1] to yield 3-propionylbiphenyl. The remaining steps of the synthesis require no comment as the methods employed were essentially those devised by Hartung and Munch[2] for the synthesis of norephedrine and its derivatives.

Through the couresty of Drs. Co Tui and Frank Calderone of the University and Bellevue Medical

(1) Willgerodt and Scholtz, *J. prakt. Chem.*, [2] **81**, 396 (1910).
(2) Hartung and Munch, THIS JOURNAL, **51**, 2262 (1929).

College a preliminary pharmacological examination of the xenylaminopropanol hydrochloride, has been made. Its pressor action as determined by intravenous injection in the dog is approximately one-third that of ephedrine hydrochloride but the solubility of the synthetic product is too low to cause this substance to be of any pharmacological interest.

Experimental

4-Propionylbiphenyl.—This was obtained in essentially quantitative yield by the interaction of biphenyl with a slight excess of propionyl chloride in the presence of aluminum chloride and carbon disulfide as directed by Willgerodt and Scholtz[1] for the preparation of 3-propionylbiphenyl. The crude product was recrystallized twice from ligroin and once from chloroform, from which it separated as lustrous plates of m. p. 97°.

Contrary to Willgerodt and Scholtz who record a melting point of 89°, the product obtained in this reaction is 4-propionylbiphenyl and not 3-propionylbiphenyl, for upon oxidation with hot aqueous permanganate only 4-phenylbenzoic acid is formed.

α-Bromo-4-propionylbiphenyl.—Bromine (12 g.) was added dropwise to a continuously stirred solution of 15 g. of 4-propionylbiphenyl in 180 cc. of glacial acetic acid at such a rate that only a slight accumulation of bromine occurred in the mixture. After all the bromine had been added, the mixture was heated to 45° for one hour to complete the reaction and then poured into 1 liter of ice water. The separated product was recrystallized from alcohol; m. p. 79°, yield 75%. The product was apparently identical with the α-bromo-4-propionylbiphenyl prepared in another manner by Collet.[3]

α-Isonitroso-4-propionylbiphenyl.—During the course of two hours 37 g. of freshly distilled *n*-butyl nitrite was added dropwise to a continuously stirred solution of 60 g. of 4-propionylbiphenyl in 600 cc. of anhydrous ether through which a current of dry hydrogen chloride was bubbled continuously. The gas current and stirring were continued for another four hours and the mixture then left overnight. The isonitroso compound was extracted from the reaction mixture with an excess of 2 *N* sodium hydroxide and the alkaline extract poured into a mixture of an excess of concentrated hydrochloric acid with sufficient crushed ice to prevent the temperature from rising above 15°. The isonitroso derivative, which separated immediately, was twice recrystallized from warm chloroform as microscopic needles of m. p. 176°, yield 43.5 g. (63.7%).

Anal. Calcd. for $C_{15}H_{13}O_2N$: N, 5.86. Found, N, 6.01.

1-Xenyl-2-aminopropanol Hydrochloride.—The isonitroso compound (6.1 g.), dissolved in 400 cc. of absolute alcohol containing 3 moles of hydrogen chloride, was added to 2.7 g. of palladiumized charcoal prepared as described by Hartung[4] and reduced with hydrogen at 35 lb. pressure in a Burgess-Parr apparatus. In six hours 89% of the theoretical quantity of hydrogen was taken up. The catalyst mass was removed by filtration and the alcoholic solution evaporated to dryness *in vacuo*. The residue was washed with ether to remove the unchanged isonitroso compound and recrystallized first from dilute hydrochloric acid and then from alcohol, yield 3.6 g. (63%) of minute glistening white plates with m. p. 235° dec.; approximate solubility in water at 25°, 0.25 g. per 100 cc.

Anal. Calcd. for $C_{15}H_{18}NOCl$: C, 68.4; H, 6.79; N, 5.50. Found: C, 68.2; H, 6.83; N, 5.31.

Attempts to isolate and characterize the free base were abandoned since upon alkalinization of a solution of 1-xenyl-2-aminopropanol hydrochloride, the precipitated colorless base rapidly underwent oxidation, assuming a yellow color which quickly passed through orange to a deep red.

Summary

1. 1-Xenyl-2-aminopropanol hydrochloride has been synthesized.

2. The pressor activity of this substance is approximately one-third that of ephedrine hydrochloride.

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(3) Collet, *Compt. rend.*, **125**, 306 (1897).

(4) Hartung, THIS JOURNAL, **50**, 3370 (1928).