The structure IId which has three substituents on one side of the planar cyclopropane ring would be a comparatively unstable one, and in the following discussion it will be assumed that the isomer with this structure has not been isolated. The carbonyl stretching frequencies in the infrared spectra (in Nujol) of the two isomers melting at 135° and 169° are located, respectively, at 1674 and 1670 cm.$^{-1}$. Table I shows that the maximum in the ultraviolet absorption spectrum of the isomer melting at 169° occurs at the higher wave length and has the larger extinction coefficient. This suggests that it should be the "*trans*" compound.

TABLE I[a]

ULTRAVIOLET ABSORPTION MAXIMA OF THE ISOMERS OF II

Melting Point	Solvent	Concentration	λ Max., Mμ	$\epsilon \times 10^{-3}$
135°	95% ethanol	2.1×10^{-5}	261.0	18.80
	Abs. ethanol	4.213×10^{-5}	262.7	20.30
169°	95% ethanol	2.19×10^{-5}	264.0	21.70
	Abs. ethanol	4.258×10^{-5}	263.5	22.10

[a] All spectra were obtained on a Beckman Model D Spectrophotometer.

In the case of this cyclopropane, "*trans*" means that the phenyl (electron donor in this case) and *p*-bromobenzoyl (electron acceptor) groups are on opposite sides of the plane of the cyclopropane ring. However, this is true in both structures, IIa and IIb. The nitro group is also an electron acceptor and will conjugate with a *trans* phenyl group as in IIa in competition with the aroyl group. Structure IIb with the nitro group in a noncompetitive position *cis* to the phenyl group is probably the compound melting at 169°. In this case the isomer melting at 135° can be either IIa or IIc. The other possibility, considered to be less likely, is that structure IIa represents the isomer melting at 169° and the 135° compound is IIc.

The former conclusion, *i.e.*, the 169° compound is best represented as IIb and the 135° isomer is either IIa or IIc, is supported by other chemical and physical evidence reported by Smith and Holly.[10]

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3-Isoxazolidone

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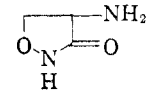
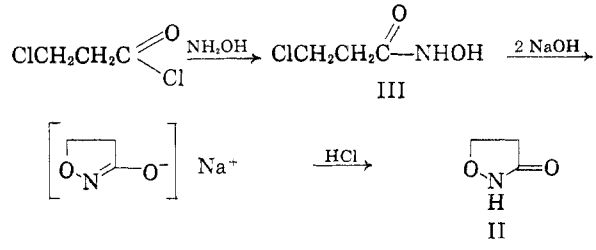
Received September 27, 1956

Cycloserine has been shown to be D-4-amino-3-isoxazolidone (I)[1,2] and a synthesis has been reported.[3] The synthesis of I involved the cyclization of an α-substituted β-halopropionohydroxamic acid. In order to determine the conditions necessary for this reaction, the preparation of a simple analog, 3-isoxazolidone (II),[4] was first undertaken.



I

β-Chloropropionohydroxamic acid (III) was prepared by the reaction of β-chloropropionyl chloride with aqueous hydroxylamine at −10°. The resulting acid (III) gave a red-violet color with ferric chloride.[5] Treatment of III with two equivalents of aqueous sodium hydroxide at 50° gave a solution of *ca.* *p*H 9. An aliquot of this solution after acidification failed to give a color with ferric chloride, showing that the hydroxamic acid was no longer present. Neutralization of the solution with one equivalent of acid yielded 3-isoxazolidone (II). The compound is a crystalline solid which, after reaction with hydroxylamine, gives a red-violet color with ferric chloride. This indicates that 3-isoxazolidone reacts with hydroxylamine in a manner similar to that of a lactone[5] to give a hydroxamic acid (probably 3-aminoxypropionohydroxamic acid).



III

II

EXPERIMENTAL[6]

β-Chloropropionohydroxamic acid. Hydroxylamine hydrochloride (27.5 g.) was dissolved in 167 ml. of 2.5*N* sodium hydroxide and the solution was cooled to −10°. To this solution, β-chloropropionyl chloride (25.0 g.) was added dropwise with stirring. The temperature was maintained at −5° to −10° during the addition and for 30 min. longer. The resulting solution was extracted with four portions of butanol and the combined extracts were dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue solidified on cooling. The solid was extracted with several portions of refluxing ether, and the extracts were combined and concentrated to a small volume. The crystalline precipitate that separated was redissolved in ether and

(1) Kuehl, Wolf, Trenner, Peck, Howe, Hunnewell, Downing, Newstead, Buhs, Putter, Ormond, Lyons, Chaiet, and Folkers, *J. Am. Chem. Soc.*, **77**, 2344 (1955).

(2) Hiddy, Hodge, Young, Harned, Brewer, Phillips, Runge, Stavely, Pohland, Boaz, and Sullivan, *J. Am. Chem. Soc.*, **77**, 2345 (1955).

(3) Stammer, Wilson, Holly, and Folkers, *J. Am. Chem. Soc.*, **77**, 2346 (1955).

(4) After this work had been completed the cyclization of ethyl 3-aminoxypropionate with alkali to 3-isoxazolidone (isolated as the potassium and silver salts) was reported (ref. 2).

(5) Feigl, *Spot Tests II*, Elsevier Publishing Co., Houston, Tex., 1954, pp. 170–171.

(6) Analyses by R. N. Boos and associates; infrared spectrum by R. W. Walker. Melting points were determined on a Kofler micro hot stage.

Darco was added. The mixture was filtered, concentrated, and cooled giving 10.6 g. of β-chloropropionohydroxamic acid, m.p. 104–106°. This compound gives an intense red-purple color with aqueous ferric chloride.[5] A sample was recrystallized for analysis, m.p. 106–107°.

Anal. Calc'd for $C_3H_6ClNO_2$: C, 29.2; H, 4.9; N, 11.3. Found: C, 29.7; H, 5.1; N, 11.1.

3-Isoxazolidone. One gram of β-chloropropionohydroxamic acid was dissolved in 150 ml. of water, 16.5 ml. of 1*N* sodium hydroxide (a slight excess over two equivalents) was added, and the solution was warmed to 50°. The reaction was complete after 5 min. as shown by the fact that an aliquot of the solution after acidification did not give a color with aqueous ferric chloride. The solution was concentrated to 5 ml. under reduced pressure, 8.2 ml. of 1*N* hydrochloric acid was added, and the resulting solution was evaporated to dryness under reduced pressure. The crystalline residue was extracted with ethanol. Evaporation of the ethanol left 0.70 g. of a crystalline residue which was extracted with three 100-ml. portions of boiling ether. The ether extracts were combined and concentrated to 20 ml. On cooling, 3-isoxazolidone separated as a white crystalline solid m.p. 68–70°; wt. 0.38 g. Recrystallization did not raise the melting point. The compound did not give a color with ferric chloride. However, when hydroxylamine was added first,[7] a positive test for a hydroxamic acid was obtained. The infrared spectrum in the solid state showed absorption in the 3–4 μ region, a broad absorption band at 5.8–6.0 μ and a strong 6.1 μ band. In solution (chloroform) it showed absorption at 3–4 μ and a strong band at 5.9 μ. The sample for analysis was sublimed *in vacuo*, m.p. 69–69.5°.

Anal. Calc'd for $C_3H_5NO_2$: C, 41.4; H, 5.8; N, 16.1, eq. wt. 87.1. Found: C, 41.9; H, 5.9; N, 16.6; eq. wt. 88.4.

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(7) The method of Boxer and Everett [*Anal. Chem.*, **21**, 670 (1949)] for the determination of total penicillins was used.

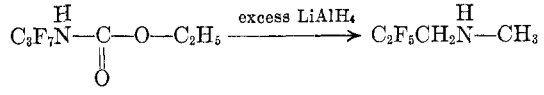
Reduction of *N*-Perfluoroalkyl Urethans with Lithium Aluminum Hydride

RALPH L. DANNLEY AND ROBERT G. TABORSKY[1]

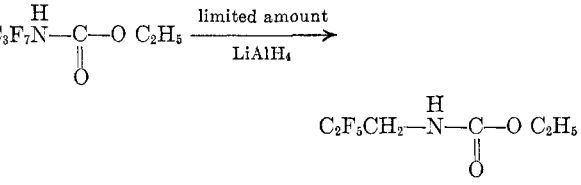
Received Sept. 11, 1956

The reduction of simple N-alkyl urethans to the corresponding methylalkylamines by means of lithium aluminum hydride has been reported by several authors.[2] The present work was undertaken to determine the behavior of N-perfluoroalkyl urethans with the same reagent.

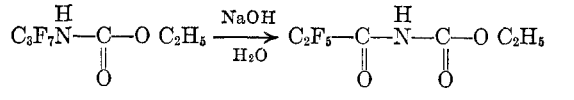
Since the reaction of perfluoroalkyl isocyanates with excess lithium aluminum hydride has been found[3] to produce 1,1-dihydroperfluoroalkylmethylamines, treatment of the corresponding urethans with an excess of the same reducing agent might be expected to give the identical amine products. This has now been confirmed, for the reaction of an excess of lithium aluminum hydride with ethyl N-*n*-perfluoropropylcarbamate and ethyl N-*n*-perfluoroheptylcarbamate produced the corresponding 1,1-dihydroperfluoroalkylmethylamines in yields of 60% and 51%, respectively.



Treatment of an N-perfluoroalkyl urethan with only a limited quantity of the hydride provided a competitive reaction in which only the most susceptible of the available functional groups could undergo reduction. Under these conditions it has been found that ethyl N-perfluoropropylcarbamate gives the corresponding N-1,1-dihydroperfluoroalkyl urethan in 63% yield. Therefore, the hydride reacts with the fluorine atoms alpha to the nitrogen in preference to the carbethoxyl group.



The hydrolysis of ethyl N-*n*-perfluoropropylcarbamate was attempted as a synthesis of ethyl N-perfluoropropionylcarbamate, a by-product in the reduction of the urethan. It was found that mild aqueous alkaline hydrolysis of the urethan gave an essentially quantitative yield of ethyl N-*n*-perfluoropropionylcarbamate.



This again emphasizes the susceptibility to displacement reactions of the fluorine atoms alpha to nitrogen. This type of reactivity has previously been observed[4] in the treatment of these urethans with alcohol.

EXPERIMENTAL

Reagents. Ethyl N-*n*-perfluoropropylcarbamate and ethyl N-*n*-perfluoroheptylcarbamate were prepared by treating the appropriate isocyanates with stoichiometric quantities of alcohol.[4] Ethereal solutions of lithium aluminum hydride were prepared in a Soxhlet apparatus and standardized by measuring the hydrogen evolved upon addition to butanol.

Ethyl N-Perfluoropropylcarbamate reduction with excess lithium aluminum hydride. A solution of 25 g. (0.0973 mole)

(1) From the thesis to be submitted by Robert G. Taborsky to the Graduate School of Western Reserve University in partial fulfillment of the requirements for the Doctor's degree.

(2) (a) Wessely and Swoboda, *Monatsh.*, **82**, 621 (1951); (b) Karrer and Nicolaus, *Helv. Chim. Acta.*, **35**, 1581 (1952); (c) Haggis and Owen, *J. Chem. Soc.*, 389 (1953); (d) Bruchhausen and Knabe, *Arch. Pharm.*, **287**, 601 (1954); (e) Dannley, Lukin, and Shapiro, *J. Org. Chem.*, **20**, 92 (1955); (f) Knabe, *Arch. Pharm.*, **288**, 469 (1955).

(3) Dannley, Taborsky, and Lukin, *J. Org. Chem.*, **21**, 1318 (1956).

(4) Dannley and Lukin, *J. Org. Chem.*, **21**, 1036 (1956).