2 ml. of ether cooling to −4° and adding 0.5 g. of ethyl chlorocarbonate. The solid (m.p. 94.6–97°) decomposed upon standing. Mixed melting point determinations showed it to be identical with the derivative prepared from the reduction of fumaric acid.

Reduction of Fumaric Acid.—In a manner similar to the above, 0.2 mole of fumaric acid was reduced with 0.5 mole of lithium aluminum hydride to 2-butene-1,4-diol in 78% yield. Titration of a sample of the product with bromine in chloroform indicated that the unsaturated diol was 98.1% pure.

Reduction of acrylic acid was also carried out as in the previously described reactions. The yield of allyl alcohol (68.3%) was obtained from 0.283 mole of acid and 0.35 mole of the hydride. The derivative of the alcohol (m.p. 67.8–68.6°) prepared by treatment with phenyl isocyanate was shown by mixed melting point determination to be identical with an authentic sample.

Reduction of Propiolic Acid.—The reduction of the triple bond acid was carried out as described above, using 0.285 mole of acid and 0.35 mole of lithium aluminum hydride. Allyl alcohol was produced in 85% yield as an azeotrope boiling at 78–81°. Mixed melting point determinations of the phenylurethan derivative showed no depression when mixed with an authentic sample.

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The Rate of Reaction of Cyclopentyl Chloride with Potassium Iodide in Acetone[1]

BY F. G. BORDWELL AND GLENN D. COOPER

In a recent investigation of the reduction of sulfones by lithium aluminum hydride,[2] it was observed that five-membered ring sulfones are reduced at a much faster rate than open-chain sulfones. One possible formulation of this reaction is displacement of the oxygen by attack of aluminohydride ion (AlH_4^-) on sulfur. It, therefore, seemed worthwhile to determine whether or not cyclopentyl halides showed enhanced reactivity as compared to open-chain secondary halides in displacement reactions. The remarkable inertness of cyclohexyl halides and the current interest in the effect of ring size on halide reactivity[3] afforded additional incentives.

Cyclopentyl bromide reacts readily with sodium iodide in acetone,[4a] and with a variety of other nucleophilic reagents,[4b] but the rates of these reactions have not been measured. Accordingly, the rate of reaction of cyclopentyl chloride with potassium iodide in acetone at 58.5° was determined; $k_{58.5°} = 7.0 \times 10^{-3}$ liter mole^{-1} hr.$^{-1}$. The rates of this reaction for five methylalkylcarbinyl chlorides were reported by Conant and Hussey[5]; the k values obtained at 60° ranged between 3.4×10^{-3} and 17.2×10^{-3}.[6] It is apparent that the rate of reaction of cyclopentyl chloride with potassium iodide in acetone is comparable with that of open-chain secondary chlorides.

Experimental

The rates were measured by the method of Conant and Kirner.[7] Cyclopentyl chloride was prepared from cyclopentanol and concentrated hydrochloric acid; b.p. 111° (750 mm.), $n^{20}D$ 1.4500; literature[4a] b.p. 111–112°, $n^{25}D$ 1.4485.

Rate at $t = 58.5 \pm 0.05°$

Time, hr.	Reacted, %	$k \times 10^3$
72	9.6	7.1
120	16.1	7.0
236	27.2	6.8
	Average	7.0

The solution was only very faintly colored by iodine after 236 hours.

The rate of reaction of isopropyl chloride, measured for comparison, was $k_{58.5°} = 2.8 \times 10^{-3}$; Conant and Hussey[5,6] obtained $k_{60°} = 3.4 \times 10^{-3}$.

(1) This investigation was supported by the Office of Naval Research under Contract No. N7onr-45007.

(2) Bordwell and McKellin, THIS JOURNAL, **73**, 2251 (1951).

(3) Brown, Fletcher and Johannesen, *ibid.*, **73**, 212 (1951).

(4) (a) Rogers and Roberts, *ibid.*, **68**, 843 (1946); (b) Loevenich, Utsch, Moldrickx and Schaefer, *Ber.*, **62B**, 3084 (1929).

(5) Conant and Hussey, THIS JOURNAL, **47**, 476 (1925).

(6) These are values of k. The values reported by Conant and Hussey are for $0.4343k$.

(7) Conant and Kirner, THIS JOURNAL, **46**, 232 (1924).

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Fluoroacetylcholine Bromide and Some Other Choline Ester Salts

BY THOMAS R. BLOHM

The striking differences between the parasympathomimetic activities of acetylcholine and its chloro-[1] and bromo-substitution[2] products could be due either to the electronegative character of these halogens, or the size of their atoms compared to hydrogen. Since fluorine more nearly approaches hydrogen in size while retaining high electronegativity, it was thought to be of interest to prepare fluoroacetylcholine. Interest in this compound also stems from the ability of fluoroacetic acid to block the Krebs cycle.[3]

In addition to fluoroacetylcholine bromide, the syntheses of trichloroacetylcholine perchlorate, dichloroacetylcholine perchlorate, fluoroacetylcholine perchlorate and β-bromoethyl fluoroacetate are described.

Preliminary pharmacological data on rabbits indicate that these choline esters are much less active than acetylcholine in their parasympathomimetic effects when given by the intravenous route.

Experimental

Fluoroacetyl Chloride.—This intermediate was prepared by the method of Gryskiewicz-Trochimowski, Sporzynski and Wnuk[4] using fluoroacetic acid, benzotrichloride and zinc chloride. This method was found to be definitely superior to methods using phosphorus pentachloride, inasmuch as preparations made with this reagent were found to contain phosphate—yielding contaminants even after careful fractionation. Fluoroacetic acid was prepared from the sodium salt (90%, Monsanto) and 100% H_2SO_4, similarly to the procedure of Saunders and Stacey.[5]

β-Bromoethyl Fluoroacetate.—Five grams (0.040 mole) of freshly distilled ethylene bromohydrin was dissolved in 25 ml. of dry benzene and added to 5.0 g. (0.052 mole) of fluoroacetyl chloride, also dissolved in 25 ml. of dry benzene in a 100-ml. round-bottomed flask. The mixture was refluxed on a boiling water-bath for one hour; the benzene

(1) R. R. Renshaw and J. C. Ware, THIS JOURNAL, **47**, 2989 (1925).

(2) D. Glick, *J. Biol. Chem.*, **130**, 530 (1939).

(3) G. R. Bartlett and E. S. G. Barron, *ibid.*, **170**, 67 (1947); G. Kalnitsky and E. S. G. Barron, *Arch. Biochem.*, **19**, 75 (1948); W. B. Elliott and G. Kalnitsky, *J. Biol. Chem.*, **186**, 487 (1950).

(4) Gryskiewicz-Trochimowski, Sporzynski and Wnuk, *Rec. trav. chim.*, **66**, 413 (1947).

(5) B. C. Saunders and G. V. Stacey, *J. Chem. Soc.*, **58**, 1777 (1948).