stability may overrule the slight increase in electronegativity found on going from bromine (2.8 on Pauling's scale) to chlorine (3.0), it does not appear capable of surmounting the large increase in electronegativity found in fluorine (4.0).

Experimental

The benzodifluorochloride used had the following properties: $n^{24.7}D$ 1.4622, $d^{26.2}{}_4$ 1.2397; molar refractivity calcd. 35.59, found 36.03.

First order rate constants for hydrolysis in 50% (by volume) aqueous acetone, determined as described previously,[3] yielded the following results

at 36°, $k = (0.0830 \pm 0.0023) \times 10^{-4}$ min.$^{-1}$
at 45°, $k = (0.2232 \pm 0.0023) \times 10^{-4}$ min.$^{-1}$
at 60°, $k = (0.9880 \pm 0.0048) \times 10^{-4}$ min.$^{-1}$
at 30°, $k = 0.0419 \times 10^{-4}$ min.$^{-1}$ (extrapolated from the data above to facilitate comparisons with Table I, reference 3)

The average activation energy was 21.2 kcal./mole.

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The Determination of the Relative Affinities of a Series of Specific Substrates from their Respective K_S and k_3 Values[1]

BY DAVID S. HOGNESS AND CARL NIEMANN[2]

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For the systems

$$E_f + S_{1f} \underset{k_{2\cdot1}}{\overset{k_{1\cdot1}}{\rightleftarrows}} ES_1 \xrightarrow{k_{3\cdot1}} E_f + P_f \qquad (1.1)$$

$$E_f + S_{2f} \underset{k_{2\cdot2}}{\overset{k_{1\cdot2}}{\rightleftarrows}} ES_2 \xrightarrow{k_{3\cdot2}} E_f + P_f \qquad (1.2)$$

where $K_{S_1} = (k_{2.1} + k_{3.1})/k_{1.1}$ and $K_{S_2} = (k_{2.2} + k_{3.2})/k_{1.2}$ it has been argued[3-5] that $k_{2.1}/k_{1.1} > k_{2.2}/k_{1.2}$ when $K_{S_1} > K_{S_2}$ and $k_{3.1} < k_{3.2}$, thus implying that in certain cases it is possible to order the relative affinities of a series of specific substrates solely on the basis of their respective K_S and k_3 values. While this conclusion was at one time accepted by workers in this Laboratory[6] it is now recognized that the argument is fallacious and that an unambiguous ordering of affinities cannot be achieved by the above procedure. That this latter conclusion is correct is apparent from the fact that $k_2/k_1 = K_S(1 + k_3/k_2)^{-1}$ and that

$$\frac{k_{2.1}/k_{1.1}}{k_{2.2}/k_{1.2}} = \frac{K_{S_1}}{K_{S_2}}\left(\frac{1 + k_{3.2}/k_{2.2}}{1 + k_{3.1}/k_{2.1}}\right) \qquad (2)$$

Thus if no restriction is placed upon the values of $k_{2.1}$ and $k_{2.2}$, except that they be positive, then $k_{2.1}/k_{1.1}$ can be less than, equal to, or greater than $k_{2.2}/k_{1.2}$ regardless of the relative values of K_{S_1} and K_{S_2} and of $k_{3.1}$ and $k_{3.2}$. Since the determination of K_S and k_3 does not give any information relative to the magnitude of k_2 it follows that the evaluation of only these two constants, *i.e.*, K_S and k_3, for two or more specific substrates cannot under any circumstance lead to an unambiguous ordering of their respective enzyme–substrate dissociation constants.

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An Improved Synthesis for α-Methyl-Δ,α,β-butenolide[1,2]

BY WILLIAM H. HOUFF AND HAROLD M SELL

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Introduction

In a study on the effects of inhibition of respiration in germinating seeds by α,β-unsaturated lactones it was necessary to synthesize α-methyl-Δ,α,β-butenolide. The reported method of synthesis,[3] which involves the condensation of formaldehyde and acetone, could not be employed because of the great tendency for butanol-1-one-3 to polymerize to yield other compounds. This note is a report of a modified method which will produce α-methyl-Δ,α,β-butenolide in good yields.

Experimental

1-Chlorobutanone-3.—Into a 3-necked flask equipped with a dropping funnel, stirrer, and downward condenser was placed 32.5 g. (0.3 mole) of 1-chlorobutanol-3. The solution was heated to 125° and a mixture of 60 g. of potassium dichromate in 300 ml. of dilute 1-1 sulfuric acid was added dropwise until the temperature increased and the oxidizing mixture no longer gave the green color of chromous ion. The ketone, as it was formed, was permitted to distil over with the water. The two layers were separated by means of a separatory funnel and the aqueous portion was extracted three times with ether. The product was combined with the ether extracts and the solution was dried over anhydrous sodium sulfate for 12 hours. The ether was distilled off and the fraction distilling at 52–53° at 15 mm. was collected. The yield was 24 g. or 80%.

α-Hydroxy-α-methylbutyrolactone.—To 24 g. (0.22 mole) of 1-chlorobutanone-3 in 100 ml. of water was added 100 ml. of a solution containing 20 g. of potassium cyanide. The solution was cooled to 15° and the 100 ml. of a 25% solution of hydrochloric acid was added slowly with stirring. An additional quantity of 200 ml. of concentrated hydrochloric acid was added and the solution stirred vigorously for four hours. The reaction mixture was extracted continuously with ether in a liquid–liquid extraction unit for eight hours. After drying the ethereal extract over anhydrous sodium sulfate, the ether was removed under vacuum. The crude product distilled with an evolution of hydrogen chloride. The yield of the fraction distilling at 109–110° at 6 mm. was 14 g. or 54%; m.p. of the *p*-nitrobenzoate of the hydroxylactone 161–161.5°, reported[3] m.p. 162°.

α-Methyl-Δ,α,β-butenolide.—The same procedure described by Cavallito, *et al.*,[3] was used. The product distilling at 82° at 7 mm. was collected. The yield was 3.5 g. or 30%; $n^{20}D$ was 1.465.

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