Experimental[5]

Hydroxamic Acids.—All of these intermediates were prepared by the usual method of treating the methyl or ethyl ester of the appropriate organic acid with salt-free hydroxylamine and were identified through their reported melting points which are indicated in parentheses: acetohydroxamic acid, m.p. 87–88° (88°[6]); caprohydroxamic acid, m.p. 63–64° (64°[7]); laurohydroxamic acid, m.p. 93–94° (94°[7]); adipohydroxamic acid, m.p. 164–165° (165–165.5°[8]); γ-glutamohydroxamic acid, m.p. 151–152° (155°[9]); cyclohexanecarbohydroxamic acid, m.p. 132–133° (132[10]); benzohydroxamic acid, m.p. 127–128° (from 124° to 131°[11]); *o*-aminobenzohydroxamic acid, m.p. 147–149° (148°[12]); and nicotinohydroxamic acid, m.p. 164–165° (165°[13]).

Catalytic Hydrogenolysis of Hydroxamic Acids (Table I).—All of the hydroxamic acids indicated in the preceding paragraph were converted to the corresponding amide by the same general procedure. The hydrogenolysis of laurohydroxamic acid will be described as a representative example. A mixture of 4.0 g. of laurohydroxamic acid and about 1 g. of Raney nickel in 75 ml. of ethanol was shaken in a Parr hydrogenation apparatus under 50 p.s.i. of hydrogen pressure for a total of about 3 hr. The time required for essentially complete hydrogenolysis of the different compounds varied as indicated in Table I. The course of the reaction was determined by examining an aliquot sample of the reaction mixture for its ability to produce a visible violet color with ferric chloride reagent.[14] When the ferric chloride test became negative, the catalyst was filtered and the filtrate was reduced to about one-third volume *in vacuo*. Upon addition of water, the amide which precipitated was dried *in vacuo* over sodium hydroxide pellets to yield 3.24 g. of product, m.p. 101–102°. The identity of the compound was determined by a mixture melting point using a 50:50 mixture of the isolated material and a sample of lauryl amide to give a mixture which melted at 101–102°.

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[5] All melting points are uncorrected and were determined using the capillary technique in a liquid bath. The authors are indebted to J. T. Lee for the elemental analysis.

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The Acid-catalyzed Hydrolysis of (−)-2-Octyl Ethyl Methylphosphonate

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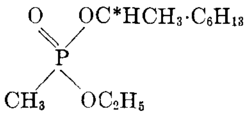
The hydrolysis of esters of alkylphosphonic acids has been studied in some detail,[2] and, although the alkaline hydrolysis undoubtedly proceeds by a nucleophilic attack on the phosphorus atom with subsequent P—O fission, the mechanism of acid-catalyzed hydrolysis is less clearly defined. The O^{18} studies on trimethylphosphate[3] are not entirely unambiguous and in any case, the mechanisms for phosphate and phosphonate hydrolysis are not necessarily the same. The acid-catalyzed hydrolysis of optically active di(2-octyl) ethylphosphonate has been studied[4] and the alcohol produced shown to be mainly racemic with a slight retention of configuration, in agreement with the postulated alkyl–oxygen fission mechanism.

Unfortunately, the actual rates of hydrolysis and optical activity change were not determined, but the optical activity of the octanol-2 measured after extraction at the end of a prolonged hydrolysis and the rate of racemization of optically active octanol-2 under the hydrolysis conditions is not stated. Furthermore, in acid solution both alkyl groups are hydrolyzed, the alcohol could be produced in either reaction, and the mechanisms need not necessarily be the same.

Since the rate of hydrolysis of secondary alkyl ester groups is about 25-fold faster than that of primary alkyl ester groups,[2] a mixed ester could overcome this problem and so (−)-2-octyl ethyl methylphosphonate (I) was prepared by the reaction of (−)-2-octyl methylphosphonochloridate[5] with ethanol in the presence of a base.



I

The rate of acid-catalyzed hydrolysis was measured acidimetrically and the change in optical activity determined simultaneously. The optical activity of the octanol-2 liberated was also determined after extraction and distillation. The rate of racemization of (−)-octanol-2 was measured under the conditions used in the hydrolysis experiment and shown to be only one fifth the rate of the ester hydrolysis, so that changes in configuration subsequent to hydrolysis can be ignored. The results (Table I and Fig. 1) show that the rate of acid production and rate of change of optical activity are equal and the alcohol isolated is almost racemic with a slight retention of configuration. This confirms the view of Gerrard, Green, and Nutkins[4] that alkyl-oxygen fission occurs without simultaneous attack on the carbon atom by a water molecule, which would give inversion of configuration. The mechanism must involve a carbonium ion, unless both P—O and C—O

TABLE I

THE HYDROLYSIS OF (−)-2-OCTYL ETHYL METHYLPHOSPHONATE IN *N* $PhSO_3H$ IN 50% DIOXANE AT 100°

Time, hr.	N_t[a]	k_1 (acid production)	$\alpha\alpha$ [a]	k_1 (racemization)
0	20.62	...	−1.20	...
0.5	20.78	0.188	....	...
1	20.90	.176	−1.10	0.100
2	21.15	.180	−0.85	.173
3	21.32	.172	....	...
4	21.52	.180	− .49	.220
7	...	...	− .35	.177
11	...	...	− .16	.183
96 (∞)	22.37	...	0	...
		average k_1 = 0.179		average k_1 = 0.171

[a] See Experimental for explanation of symbols.

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[1] Present address: Research and Engineering Division, Monsanto Chemical Co., St. Louis 66, Mo.

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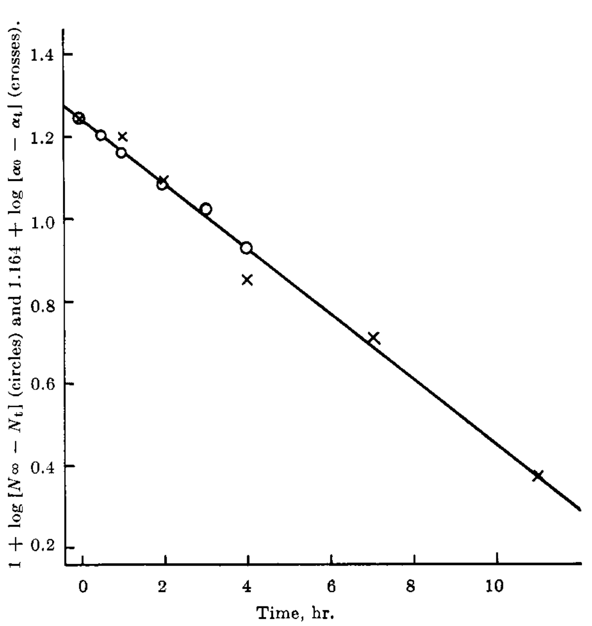

Fig. 1.—First-order kinetic plot of titrimetic and polarimetric data for acid-catalized hydrolysis of (−)-2-octyl ethyl methylphosphate. From the slope of the graph, $k_1 = 0.183$ hr.$^{-1}$.

fissions can occur, the latter reaction involving nucleophilic assistance from a water molecule (the $A_{AL}2$[6] or $A''2$[7] mechanism), which seems unlikely.

Experimental

Materials.—Dioxane was purified by refluxing with hydrochloric acid to hydrolyze any acetals, adding an excess of solid potassium hydroxide, decanting, drying over sodium, and finally distilling from over fresh sodium.

Optically active octanol-2 was prepared by fractional crystallization of the brucine salts of the phthalic acid monoester, followed by hydrolysis and distillation.[8]

(−)-2-Octyl methylphosphonochloridate was prepared in 79% yield by the reaction between (−)-octanol-2 and methylphosphonic dichloride in the presence of triethylamine in ether at 0°.[4] Specific gravity, 1.036; $[\alpha]^{18}\text{D}$ −12.65° (from octanol-2, $[\alpha]^{20}\text{D}$ −9.95°.)

Anal. Calcd. C, 47.7; H, 8.8; Cl, 15.7. Found: C, 48.1; H, 8.6; Cl, 15.7.

(−)-2-Octyl Ethyl Methylphosphonate.—A 22.6-g. sample (0.1 mole) of (−)-2-octyl methylphosphonochloridate was added slowly with agitation to 16.0 ml. (0.1 mole) of diethylaniline and 30.0 ml. (0.5 mole) of anhydrous ethanol. The reaction mixture was then heated on a boiling water bath for 0.5 hr. The semisolid pasty mass was allowed to cool and then shaken with 300 ml. of dry petroleum ether (b.p. 40–60°). The solid was removed by filtration and washed with more petroleum ether. The solvent was removed from the combined filtrate and washings and the residual oil distilled under reduced pressure; yield, 20.0 g. (85%), b.p. 73–74°/(0.2 mm.); specific gravity, 0.945; $[\alpha]^{18}\text{D}$ −11.87° (from alcohol $[\alpha]^{20}\text{D}$ −9.95°).

Anal. Calcd. C, 55.7; H, 10.5. Found: C, 54.8; H, 10.5.

An attempt to prepare the same compound by the reaction of octanol-2 with ethyl methylphosphonochloridate in the presence of a tertiary base was unsuccessful, probably due to the slow reaction with the octanol-2 which was recovered unchanged.

Kinetic and Optical Activity Measurements.—The ester (2.36 g.) was dissolved in 100 ml. of N benzenesulfonic acid in 50% aqueous dioxane (v./v.) to give a 0.1 M solution of ester. Five-milliliter aliquots were removed with pipets and placed in glass ampoules and sealed. The ampoules were placed in an agitated oil bath maintained at 100.2°, and ampoules were removed for analysis at suitable time intervals. The formation of acid was determined by rapidly cooling the ampoule and titrating the contents against 0.25 N sodium hydroxide using methyl red indicator. The change in optical activity was determined by placing the cooled contents of ampoules in the 2-dm. polarimeter tube and measuring the rotation at the sodium "D" line.

The velocity constants for the acid production and optical activity change were determined using the equations,

$$k_1 = \frac{2.303}{t} \cdot \log\left\{\frac{N_\infty}{N_\infty - N_t}\right\} \quad \text{and } k_1 = \frac{2.303}{t} \cdot \log \left\{\frac{\alpha_0}{\alpha_0 - \alpha_t}\right\}$$

where N_t is the volume of 0.25 N sodium hydroxide required to neutralize a 5-ml. reaction mixture at time t, and α_t is the optical rotation of the reaction mixture observed in a 2-dm. tube at time t, and also from the graph of log $(N\alpha - N_t)$ or log $(\alpha_0 - \alpha_t)$ *vs.* time, $k_1 = -2.303 \times$ slope of the graph.

The optical activity of the alcohol produced was also measured after isolation; 10 g. of ester was heated with 50 ml. of 1 N benzenesulfonic acid in 50% aqueous dioxane at 100° for 6 hr. in a large sealed ampoule. The ampoule was cooled; the contents made slightly alkaline with sodium hydroxide and immediately extracted twice with ether. The ether solution was dried over anhydrous magnesium sulfate and the solvent removed. The residue was distilled in a microfractionation unit to give 3.0 g. (55%) of octanol-2, b.p. 175–180° (lit. b.p. 178–179°), $[\alpha]^{20}\text{D}$ −0.84° (the octanol-2 used in the ester preparation had $[\alpha]^{20}\text{D}$ −9.95°).

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The Addition of Phosgene to Carbodiimides

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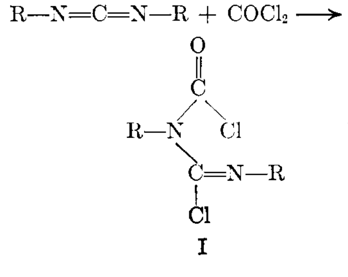
It is well known that carboxylic acids add to carbodiimides[2] and recently acetyl chloride was shown to do so,[3] although the products are unstable and tend to decompose to the starting compounds. We have found that phosgene, which has not previously been reported as taking part in addition reactions with cumulative double bonds,[4] also adds readily to aliphatic and aromatic carbodiimides to give N,N′-disubstituted chloroformamidine-N-carbonyl chlorides (I), which are remarkably stable as illustrated by their distillation in vacuum without decomposition.



I

a. R = *n*-butyl
b. R = cyclohexyl
c. R = *o*-tolyl

The structure of the 1:1 addition products was established by elementary analysis and infrared spectroscopy. The infrared spectra of I show C=O absorption at 5.73–5.75 μ and a C=N absorption at 5.98–6.0 μ.

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(1) To whom inquiries should be directed.

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