TABLE II

PHENYLATED NITRO COMPOUNDS

Compound	$n^{20}D$	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
2-Phenyl-2-nitropropane	1.5204	65.40	65.20	6.76	6.90	8.48	8.49
2-Phenyl-2-nitrobutane	1.5206	67.04	66.91	7.26	7.30	7.82	7.82
2-Phenyl-2-nitroöctane	1.5053	71.49	71.28	8.94	9.07	5.96	6.02
1-Phenyl-1-nitrocyclohexane	[a]	70.24	70.04	7.32	7.28	6.83	6.73
Ethyl 2-Phenyl-2-nitrocaproate	1.5033	63.40	63.25	7.17	7.27	5.28	5.39
1-Phenyl-1-nitropropane	1.5159	65.40	65.59	6.76	6.88	8.48	8.74

[a] M.p. 51.0–52.5°.

mmoles) in a 50-ml. flask was added diphenyliodonium tosylate (9.04 g., 20 mmoles). After 1 hr. the reaction mixture was poured into 150 ml. of ice–water saturated with sodium chloride. The suspension was extracted five times with 50-ml. portions of petroleum ether (b.p. 35–37°), the combined extracts were washed twice with water, dried over anhydrous sodium sulfate, and the drying agent removed by filtration. The solvent, the 1-nitropropane, and the major portion of the iodobenzene were removed *in vacuo* at room temperature. The residue was chromatographed on Merck's silicic acid[9] yielding 2.04 g. (62%) of 1-phenyl-1-nitropropane, $n^{20}D$ 1.5159, which is analytically pure (Table II) and which exhibits strong nitro group absorption at 6.45 μ.

Preparation of Ethyl 2-Phenyl-2-nitrocaproate.—Diphenyliodonium tosylate (18.04 g., 40 mmoles) was added to a magnetically stirred solution of the sodium salt of ethyl 2-nitrocaproate (8.36 g., 40 mmoles) in 30 ml. of DMF at 55°. The reaction is 96% complete after 6 hr. at this temperatre. The reaction mixture was then poured into 150 ml. of ice–water. The water layer was saturated with sodium chloride and extracted with five 50-ml. portions of petroleum ether (b.p. 35–37°). The extracts were each washed with 25 ml. of water, combined, and dried over anhydrous sodium sulfate. The solvent and a portion of the iodobenzene were removed *in vacuo* at room temperature. The residue was dissolved in petroleum ether (b.p. 35–37°) and chromatographed on Merck's silicic acid. The residual iodobenzene was eluted with petroleum ether. Ethyl 2-phenyl-2-nitrocaproate, 6.16 g. (58% yield), was obtained on elution with 30% benzene–70% petroleum ether. Last traces of solvent were removed at *ca.* 1 mm. giving analytically pure material (Table II). The infrared spectrum shows strong nitro group absorption at 6.45 μ.

Preliminary experiments[10] using diphenyliodonium chloride and the lithium salt of 2-nitropropane in methanol, and in water, showed that these solvents are much less useful than DMF. In DMF these salts reacted to give 2-phenyl-2-nitropropane in *ca.* 50% yield.

Acknowledgment.—We thank Dr. Paul Haberfield for several preliminary experiments and the Commercial Solvents Corporation for generous gifts of several nitroparaffins.

(9) The product is decomposed by chromatographing on basic alumina.
(10) By Dr. Paul Haberfield.

Catalytic Hydrogenolysis of Hydroxamic Acids to Amides

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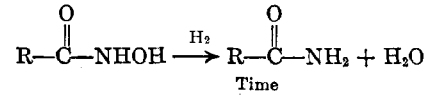
Metallic reduction of various hydroxamic acids to yield the corresponding amide derivatives has been reported[2]; however, controlled catalytic hydrogenolysis of hydroxamic acids to yield the corresponding amides has not been described adequately in the available literature.[3] Recently, as a part of a structural study of a reaction product formed by the interaction of glutamic acid and hydroxylamine in the presence of an enzyme from *Escherichia coli*, a reaction product, which appeared to be a hydroxamate of glutamic acid on the basis of elemental analysis, was found to undergo hydrogenolysis in the presence of Raney nickel catalyst to form glutamine.[4] Although the utility of such a conversion may not be of wide spread interest since the amides usually are more easily obtained through other routes, it was considered desirable to determine the scope of this type of hydrogenolysis reaction. Accordingly, a number of hydroxamic acids were prepared by conventional means and treated with hydrogen gas in the presence of Raney nickel catalyst. It was observed that, in each of the examples studied, the desired amide could be obtained directly from the corresponding hydroxamic acid in good yield. The variety of substituent groupings studied is indicated in Table I, and range from simple aliphatic analogs to cycloaliphatic, aromatic, and heterocyclic derivatives. The yields of the amides produced varied from 76 to 96%, even though no effort was made to determine optimum reaction conditions in each case.

TABLE I

SYNTHESIS OF AMIDES FROM HYDROGENOLYSIS OF HYDROXAMIC ACIDS



R Amide produced	Time required for reaction, hr.	Yield, %
Acetamide	1.25	96
Capramide	1.0	85
Lauramide	3.0	97
Adipamide	1.5	76
L-Glutamine	3.0	80[a]
Cyclohexanecarboxamide	3.0	81
Benzamide	18.0	78
o-Aminobenzamide	12.0	82
Nicotinamide	20.0	84

[a] Yield determined by microbial assay using *Streptococcus lactis*, unpublished technique, J. M. Ravel and W. Shive.

(1) Rosalie B. Hite Predoctoral Fellow, 1962–1963.
(2) C. Gastaldi, *Gazz. chim. ital.*, **54**, 512 (1924).
(3) F. Mathis, *Bull. soc. chim. France*, D9 (1953), refers to a study of the reduction of gluconohydroxamic acid in the presence of nickel catalyst to yield a mixture of gluconamide and ammonium gluconate which was described by F. Mathis, *These Sciences* (Paris) (1952).
(4) F. Pettit and W. Shive, unpublished data.

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°.

(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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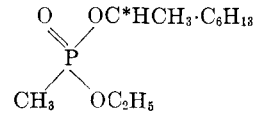
The hydrolysis of esters of alkylphosphonic acids has been studied in some detail,[2] and, although the alkaline hydrolysis undoubtedly proceeds by a nucleophilic attack on the phosphorus atom with subsequent P—O fission, the mechanism of acid-catalyzed hydrolysis is less clearly defined. The O^{18} 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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