The Phenylation of Nitroparaffins[1,2]

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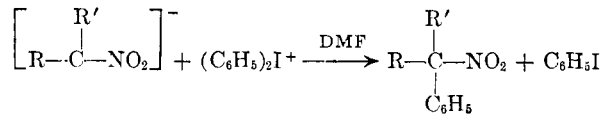
The reaction of nitroparaffin salts with diphenyliodonium tosylate in N,N-dimethylformamide (DMF) takes place smoothly at room temperature and gives α-phenylnitroparaffins.



Since, thanks to the efforts of Beringer and his students,[3] a variety of diaryliodonium salts have now become accessible, this represents not only a new but also a useful reaction. The yields listed in Table I refer to pure products and, since no systematic study was made to arrive at optimum conditions, they are minimal. The salt of the only α-nitro ester studied, ethyl α-nitrocaproate, reacted less rapidly than any of the nitroparaffins and in this instance a temperature of 55° was employed.

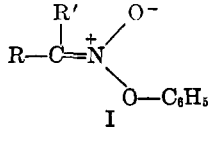
TABLE I

REACTION OF DIPHENYLIODONIUM TOSYLATE AND NITROPARAFFIN SALTS IN DMF

Salt of[a]	Product	Yield, %
1-Nitropropane	1-Phenyl-1-nitropropane	62
2-Nitropropane	2-Phenyl-2-nitropropane	56
2-Nitrobutane	2-Phenyl-2-nitrobutane	69
2-Nitroöctane	2-Phenyl-2-nitroöctane	54
Nitrocyclohexane	1-Phenyl-1-nitrocyclohexane	58
Ethyl α-nitrocaproate	Ethyl α-phenyl-α-nitrocaproate	58

[a] Sodium salts used in all instances except for the 2-nitropropane experiment; there the lithium salt was employed.

The salts of aliphatic nitro compounds are ambident anions and, therefore, phenylation at oxygen to give nitronic esters (I) is a real possibility, especially since alkylation usually occurs at oxygen.[4] It is of interest, then, that phenyl nitronic esters were not found.



I

Experimental[5]

Preparation of Diphenyliodonium Tosylate.—In a 1-l. flask cooled in an ice bath were placed 107 g. (0.50 mole) of potassium iodate, 90 ml. (0.50 mole) of benzene, and 200 ml. of acetic anhydride. A solution of 100 ml. of acetic anhydride and 225 ml. of concentrated sulfuric acid was added in the course of *ca.* 2 hr. to the stirred mixture while maintaining the temperature below 10°. The reaction mixture was stirred for *ca.* another hour and then the ice bath was removed and the mixture stirred for an additional 20 hr. The product was poured onto *ca.* 350 g. of ice and the resulting suspension was extracted twice with 100-ml. portions of ethyl ether. The aqueous phase was diluted with an equal volume of water and a solution of 80 g. (0.53 mole) of sodium iodide in 1 l. of water was added slowly. The precipitated diphenyliodonium iodide was removed by filtration.

The moist iodide was suspended in 750 ml. of methanol and to this was added, with vigorous stirring, 58.0 g. (0.25 mole) of silver oxide and 85.0 g. (0.50 mole) of *p*-toluenesulfonic acid monohydrate. After stirring overnight, the solids were removed by filtration and the filtrate vacuum evaporated (below 50°) to dryness. The residue was dissolved in 1.2 l. of chloroform and the solution was extracted with 5% aqueous sodium hydroxide until the aqueous phase remained alkaline. The chloroform layer was washed twice with water, dried over anhydrous sodium sulfate, filtered, and the solvent removed *in vacuo* (room temp.) to yield diphenyliodonium tosylate, m.p. 176–181°. The salt was recrystallized from 1.5 l. of hot acetonitrile giving 100 g. (44%) of material, m.p. 181–184° dec. (lit.,[6] m.p. 178–181°).

Anal. Calcd. for $C_{19}H_{17}IO_3S$: C, 50.45; H, 3.76; S, 7.08; I, 28.10. Found: C, 50.24; H, 3.97; S, 7.00; I, 27.99.

Preparation of the Salts of Nitro Compounds.—The alkali metal salts were prepared by addition of the nitro compounds in *ca.* 10% excess, to standardized absolute ethanolic solutions of the alkali ethoxide. When, as was usually the case, the salts were soluble in alcohol they were precipitated by dilution with either petroleum ether (b.p. 35–37°) or anhydrous ethyl ether. The salts, after collection on a sintered glass funnel, were dried in a vacuum desiccator over phosphorus pentoxide and paraffin wax. The neutralization equivalents, determined by potentiometric titration in absolute ethanol with standard ethanolic picric acid, agreed within 3% of the calculated values. Yields ranged from 75 to 90%. The salts were used within 24 hr. since dry alkali metal salts of nitro compounds are capable of decomposing explosively if heated or subjected to mild shock.[7]

Preparation of 2-Phenyl-2-nitroöctane.—This exemplifies the procedure for phenylating secondary nitro compounds. Diphenyliodonium tosylate (9.04 g., 20 mmoles) was added to a magnetically stirred suspension of 3.62 g. of the sodium salt of 2-nitroöctane in 15 ml. of dry DMF (distilled from calcium hydride) contained in a 50-ml. flask. After 22 hr.[8] the reaction was 95% complete as shown by titration of an aliquot for residual base. The reaction mixture was then poured into 100 ml. of ice–water and the aqueous phase was saturated with sodium chloride and extracted with five 40-ml. portions of petroleum ether (b.p. 35–37°). The combined petroleum ether layers were extracted twice with 10 ml. of 10% aqueous sodium hydroxide and then washed with four 25-ml. portions of water. The solution was dried over anhydrous sodium sulfate after which the solvent and most of the iodobenzene were removed *in vacuo* at room temperature. The residual liquid was dissolved in an equal volume of petroleum ether (b.p. 35–37°) and passed through a column of Merck's basic alumina. Elution with the petroleum ether washes the residual iodobenzene off the column and when this process is completed, elution with benzene–petroleum ether (1:4) washes the phenylated nitroöctane off the column. The pure nitro compound was obtained by vacuum evaporation of the benzene–petroleum ether solution at room temperature; yield 2.53 g. (54%) of a colorless liquid, $n^{20}D$ 1.5053, which is analytically pure (Table II) and which exhibits strong nitro absorption in the infrared at 6.50 μ.

Preparation of 1-Phenyl-1-nitropropane.—This, because it involves the salt of a primary nitroparaffin, required modified conditions. Preliminary experiments using equivalent amounts of nitroparaffin salt and iodonium salt gave relatively complex mixtures of products which presumably are derived from the salt of the monophenylated nitro compound. In keeping with this assumption it was found that these by-products were absent when 10 moles of 1-nitropropane were present.

To a suspension of the sodium salt of 1-nitropropane (2.22 g., 20 mmoles), 20 ml. of dry DMF and 1-nitropropane (18 ml., 203

(1) Paper XX in the series, "The Chemistry of Aliphatic and Alicyclic Nitro Compounds." For the previous paper in this series, see N. Kornblum, W. D. Gurowitz, H. O. Larson, and D. E. Hardies, *J. Am. Chem. Soc.*, **82**, 3099 (1960).

(2) Sponsored by the U. S. Army Research Office (Durham).

(3) F. M. Beringer, S. A. Galton and S. J. Huang, *J. Am. Chem. Soc.*, **84**, 2819 (1962), and earlier papers in that series.

(4) N. Kornblum and P. Pink, *Tetrahedron*, in press.

(5) Analyses are by Galbraith Microanalytical Laboratories, Knoxville, Tenn., and by Dr. C. S. Yeh and Mrs. T. M. Eikeri, Purdue University.

(6) F. M. Beringer, R. A. Falk, M. Karniol, I. Lillien, G. Masullo, M. Mausner, and E. Sommer, *J. Am. Chem. Soc.*, **81**, 342 (1959).

(7) H. B. Hass, E. B. Hodge, and B. M. Vanderbilt, *Ind. Eng. Chem.*, **28**, 339 (1936).

(8) With the other secondary nitroparaffin salts reaction times of 1–3 hr. sufficed.

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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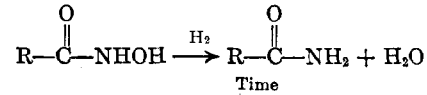
Metallic reduction of various hydroxamic acids to yield the corresponding amide derivatives has been reported[2]; however, controlled catalytic hydrogenolysis of hydroxamic acids to yield the corresponding amides has not been described adequately in the available literature.[3] Recently, as a part of 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.