

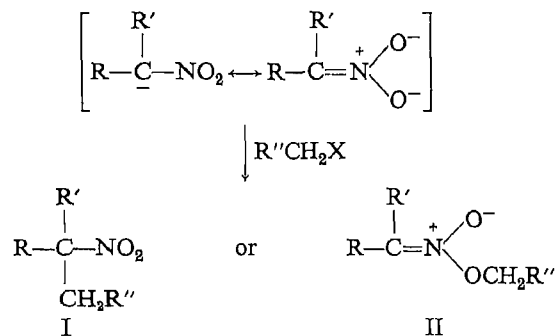
THE LEAVING GROUP AS A FACTOR IN THE ALKYLATION OF THE 2-NITROPROPANE ANION^{1,2}

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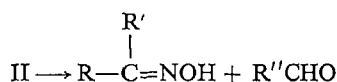
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Abstract—The course of the reaction of the lithium salt of 2-nitropropane with $p\text{-O}_2\text{N}-\text{C}_6\text{H}_4-\text{CH}_2\text{X}$ is governed by the nature of X. Thus, with p -nitrobenzyl chloride a 95 % yield of the carbon alkylate (IV) is obtained whereas the use of p -nitrobenzyl iodide results in an 81 % yield of p -nitrobenzaldehyde.

THE anion derived from an aliphatic nitro compound is capable of covalency formation at either carbon or oxygen, i.e., it is an ambident anion.³



While the carbon alkylation product (I) is stable, the nitronic ester (II) is never isolated; instead the carbonyl compound and oxime are obtained and it is generally assumed that they arise from the nitronic ester.⁴



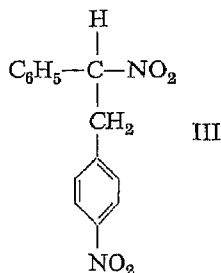
¹ This research was supported by a grant from the U.S. Army Office (Durham).

² Paper IV in the series, *The Chemistry of Ambident Anions*.

³ N. Kornblum and R. Seltzer, *J. Amer. Chem. Soc.* **83**, 3668 (1961).

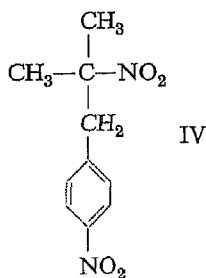
⁴ L. Weisler and R. W. Helmkamp, *J. Amer. Chem. Soc.* **67**, 1167 (1945); H. B. Hass and M. L. Bender, *Ibid.* **71**, 1767, 3482 (1949).

Reactions of the salts of nitro compounds with aliphatic,⁵ allylic⁶ and benzylic halides^{4, 7, 8} usually produce carbonyl compounds and, in fact, serve as a means of preparing aldehydes and ketones^{5, 6, 9}. However, even though these reactions routinely yield carbonyl compounds, instances are known in which the result is carbon alkylation. Thus, Weisler and Helmkamp⁴ found that *p*-nitrobenzyl chloride reacts with the sodium salt of phenylnitromethane to give a 37% yield of the carbon alkylate (III).



An even more striking example of carbon alkylation has been reported by Hass and Bender.⁴ They treated the sodium salt of 2-nitropropane with benzyl chloride, and with *p*-substituted benzyl halides which had as substituents CH₃, Br,

$\text{CH}_3\text{OC}(=\text{O})$, $\text{CH}_3\text{C}(=\text{O})$, CN, CF₃, and $\text{N}^+(\text{CH}_3)_3$, whereupon the corresponding benzaldehydes were produced in 68–77% yields and no carbon alkylate was obtained. However, with *p*-nitrobenzyl chloride an 83% yield of the carbon alkylate (IV) was isolated along with a 1% yield of *p*-nitrobenzaldehyde.



It now has been found that the uniqueness of the *p*-nitrobenzyl system depends not only on the *p*-nitro group but also, and in a dramatic way, on the leaving group. For example, whereas *p*-nitrobenzyl chloride gives 95% carbon alkylation, the use of *p*-nitrobenzyl iodide results in 81% oxygen alkylation; Table 1

⁵ S.V. Lieberman, *J. Amer. Chem. Soc.* **77**, 1114 (1955).

⁶ M. Montavon, H. Lindlar, R. Barbet, R. Ruegg, G. Ryser, G. Saucy, P. Zeller and O. Isler, *Helv. Chim. Acta* **40**, 1250 (1957).

⁷ C. Nenitzescu and D. Isacescu, *Ber. Dtsch. Chem. Ges.* **63**, 2484 (1930).

⁸ J. Thurston and R. Shriner, *J. Org. Chem.* **2**, 183 (1937).

⁹ H.B. Hass and M.L. Bender, *Org. Syntheses* **30**, 99 (1950).

The leaving group as a factor in the alkylation of the 2-nitropropane anion summarizes our findings. Such dependence of the reaction course on the nature of the leaving group has not been demonstrated before, either in the alkylation of nitroparaffin salts, or in the alkylation of any other ambident anions.

TABLE 1. NATURE OF REACTION OF $p\text{-O}_2\text{NC}_6\text{H}_4\text{CH}_2\text{X}$ WITH THE LITHIUM SALT OF 2-NITROPROPANE IN DMF AT -16° AS A FUNCTION OF X^a

X	C, %	O, %
NMe ₃ ^b	93	0
Cl	95	1
OTos	40	32
Br	17	65
I	9	81

^a All yields refer to pure products isolated except for the % O in runs employing the tosylate, bromide and iodide; here the aldehyde yields are by gas chromatography and are ca. 10–15% higher than the yields of pure *p*-nitrobenzaldehyde 2,4-dinitrophenylhydrazone isolated.

^b At 25° .

EXPERIMENTAL^{10, 11, 12}

All alkylation reactions were conducted under nitrogen.

Dimethylformamide (DMF) was stored over calcium hydride and rectified from calcium hydride under red press; b.p. $70^\circ/6$ mm.

2-Nitropropane was washed with aqueous sodium bicarbonate, with water and then dried, first over sodium sulfate and then over Drierite. It was then rectified from a pot containing boric acid (Mallinckrodt Analytical Reagent); n_D^{20} 1.3941; lit. n_D^{20} 1.3941;¹³ b.p. $60^\circ/100$ mm.

p-Nitrobenzyl chloride, bromide, and iodide purified by recrystallization; m.p. $71\text{--}72^\circ$, $98\text{--}99^\circ$ and $127\text{--}128^\circ$ respectively.

p-Nitrobenzyl tosylate was prepared by treating the bromide with ca. 5 % excess silver tosylate¹⁴ in acetonitrile (Fisher Certified Reagent). The reaction mixture was stirred for 3 hr and then allowed to stand overnight. The precipitated silver bromide was removed and the filtrate evaporated to dryness under red press. In the process more AgBr precipitated. Upon recrystallization from boiling carbon tetrachloride, *p*-nitrobenzyl tosylate was obtained; m.p. $100\text{--}101^\circ$, lit¹⁵ 105° .

p-Nitrobenzyl trimethyl ammonium bromide. *p*-Nitrobenzyl bromide, 10.8 g (0.05 mole), was dissolved in 200 ml acetone (dried over calcium chloride) in a flask fitted with a Dry Ice condenser protected by a drying tube. Trimethylamine was bubbled through the magnetically stirred solution. After ca. 15 min, crystals appeared but the amine was bubbled in for a period of 4 hr. The white crystals were collected by filtration, washed with dry acetone and dried overnight *in vacuo*. The crystals contained only 90 % of the theoretical amount of bromide

¹⁰ Analyses are by Dr. C. S. Yeh, Mrs. B. Groten and Mrs. V. Keblys, Purdue University, and Galbraith Microanalytical Laboratories, Knoxville, Tenn.

¹¹ The infrared absorption spectra were determined on a Perkin-Elmer Model 21 spectrophotometer by Mrs. M. Dilling, Purdue University.

¹² All m. p. are uncorrected.

¹³ Commercial Solvents Technical Data Sheet No. 23, 1954.

¹⁴ N. Kornblum, W. J. Jones and G. G. Anderson, *J. Amer. Chem. Soc.* **81**, 4113 (1959).

¹⁵ J. Kochi and G. S. Hammond, *J. Amer. Chem. Soc.* **75**, 3443 (1953).

ion but further drying for 4 hr at 80° *in vacuo* gave material m.p. 220–222° (decomp). (Found: Br, 29.0, 29.2. $C_{10}H_{15}N_2OBr$ requires: Br, 29.1 %). The picrate has m.p. 193–195°; lit¹⁶ 194°.

The Lithium salt of 2-nitropropane. Lithium wire cut into pieces, freed of its oil coating by washing with low boiling pet ether, was weighed under hexane (3.47 g, 0.50 mole) and transferred to a 1 l. flask containing ca. 500 ml absolute ethanol and immersed in an ice bath and fitted with a condenser protected by a drying tube containing potassium hydroxide. A vigorous reaction ensued and the mixture was maintained at gentle reflux; when complete, the contents were cooled to room temp and a solution of 46 g (0.52 mole) 2-nitropropane in ca. 50 ml absolute ethanol added. If the lithium wire employed did not have a shiny surface, a small amount of white precipitate sometimes appeared and after addition of the 2-nitropropane, any precipitate was immediately removed by filtration. The solution was distilled *in vacuo* at a temp below 40°, the residue, still containing some ethanol, was broken up with a spatula and the flask evacuated by an oil pump and maintained at room temp for ca. 1 hr. The solid was then pulverized using a flattened glass rod; no effort being made to exclude air. The flask was again evacuated at room temp for ca. 1 hr; the fine white powder then repulverized and finally subjected to the vacuum of an oil pump for 12 hr. (Found: Li, 7.15. $C_3H_6NO_2Li$ requires: Li, 7.31 %). The purity of the salt was also determined by potentiometric titration for base in absolute ethanol using a picric acid solution in ethanol. This procedure was used to check the purity of each batch of lithium salt and a low analysis was improved by additional pulverizing and evacuating.

Reaction of p-nitrobenzyl iodide with the lithium salt of 2-nitropropane in DMF at –18°

To a solution of 26.30 g (0.10 mole) *p*-nitrobenzyl iodide, in 200 ml DMF at –18°, 19.00 g (0.20 mole) lithium salt of 2-nitropropane dissolved in 200 ml DMF at –18° was added, the solution turning red. After ca. 2 hr at –18°, the product was poured into ca. 1400 ml cold water, acidified with acetic acid and repeatedly extracted with benzene. The extracts, after being washed with water, were dried over sodium sulfate and evaporated *in vacuo* leaving 17.94 g of a light green solid; which was taken up in benzene and diluted to 100 ml (Solution A). A 50 ml aliquot of Solution (A), when chromatographed on basic alumina using benzene, gave 1.0 g (9 % yield) 2-methyl-2-nitro-1-(*p*-nitrophenyl)-propane (IV); m.p. 63.5–65°, lit¹⁷ 65–66°.

As determinations of *p*-nitrobenzaldehyde yields gave low values, presumably, because of condensation with 2-nitropropane, it was established that 1-(*p*-nitrophenyl)-2-nitro-2-methyl propanol-1 could be reconverted to *p*-nitrobenzaldehyde in ca. 95 % yield by a short treatment with base and, accordingly, the amount of oxygen alkylation was determined as follows: a 10 ml aliquot of Solution (A) was evaporated *in vacuo*, the residue dissolved in 50 ml absolute ethanol and added to a solution of 5 g potassium hydroxide in 25 ml water and 25 ml 95 % ethanol. After 10 min at room temp the basic solution was poured into cold water, sodium chloride added, and the mixture extracted with benzene. The extracts, after washing with water, were evaporated *in vacuo* and the residue in ethanol added to hot 2,4-dinitrophenylhydrazine solution. After cooling, the hydrazone was collected by filtration, washed with ethanol, and dried to constant weight; yield 2.21 g (67 %) of the 2,4-dinitrophenylhydrazone of *p*-nitrobenzaldehyde, m.p. 326–327° (decomp); mixed m.p. with an authentic sample 325–326°.

Since the reaction employing *p*-nitrobenzyl chloride proceeded for 20 hr (*vide infra*), a 20 hr run at –18° was carried out with *p*-nitrobenzyl iodide. An aliquot of the product on treatment with 2,4-dinitrophenylhydrazine, without the prior base treatment, gave a 38 % yield of the 2,4-dinitrophenylhydrazone of *p*-nitrobenzaldehyde. Chromatography on basic alumina of another aliquot of the product gave a 7 % yield of the C-alkylate (IV). Thus a longer

¹⁶ F. Goss, W. Hanhart and C. K. Ingold, *J. Chem. Soc.* 261 (1927).

¹⁷ H. B. Hass, E. J. Berry and M. L. Bender, *J. Amer. Chem. Soc.* 71, 2290 (1949).

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reaction time does not increase the amount of C-alkylate and the 95 % yield of C-alkylate obtained from *p*-nitrobenzyl chloride cannot be attributed to rearrangement of initially produced nitronic ester.

Vapor phase chromatography at 200° using a GE-SF96 silicone oil on Chromasorb W column showed, by comparison with standard solutions of IV and *p*-nitrobenzaldehyde, that the yield of IV is 7 % and that of *p*-nitrobenzaldehyde is 81 %.

Reaction of p-nitrobenzyl bromide with the lithium salt of 2-nitropropane in DMF at -19°

To a solution of 21.60 g (0.10 mole) *p*-nitrobenzyl bromide in 200 ml DMF at -19°, 19.00 g (0.20 mole) lithium salt of 2-nitropropane dissolved in 200 ml DMF at -19° was added with development of a red solution. After 4 hr at -19°, the reaction mixture was poured into ca. 1400 ml cold water, acidified with acetic acid, and then extracted with benzene. The extracts were washed with water, dried over sodium sulfate and the benzene removed by fractionation at atm press through a glass-packed column under nitrogen. The residue, after removing most of the benzene, was made up to a volume of 100 ml with benzene.

As in the preceding experiments with *p*-nitrobenzyl iodide, the yields were determined by isolation and by gas chromatography. Isolation gave 16 % of the C-alkylate (IV) and 50 % of the 2,4-dinitrophenylhydrazone of *p*-nitrobenzaldehyde whereas gas chromatography gave a 17 % yield of IV and a 65 % yield of the aldehyde.

Reaction of p-nitrobenzyl tosylate with the lithium salt of 2-nitropropane in DMF at -16°

To a solution of 15.35 g (0.05 mole) of *p*-nitrobenzyl tosylate in 100 ml DMF at -16°, 9.5 g (0.10 mole) lithium salt of 2-nitropropane dissolved in 100 ml DMF at -16° was added, the tosylate solution turning red. After 12 hr at -16°, the product was poured into ca. 700 ml cold water, acidified with acetic acid, and extracted with benzene. The extracts were washed with water, dried over sodium sulfate, the benzene removed *in vacuo* and the residue diluted to 100 ml with benzene. Analysis by gas phase chromatography showed that 32 % of the product was *p*-nitrobenzaldehyde and 40 % the carbon alkylate (IV).

Reaction of p-nitrobenzyl chloride with the lithium salt of 2-nitropropane in DMF at -16°

To 17.16 g (0.10 mole) *p*-nitrobenzyl chloride dissolved in 200 ml DMF at -16°, 19.00 g (0.20 mole) lithium salt of 2-nitropropane in 200 ml DMF at -16° was added, the reaction mixture turning red. After 20 hr at -16°, the mixture was poured into ca. 1400 ml cold water, acidified with acetic acid, and extracted with benzene. The extracts were washed with water, dried over sodium sulfate and the benzene removed, under red press, to constant weight. The crude residue, 22.29 g; m.p. 61-63.5° was dried on a clay plate (theoretical yield of C-alkylate, 22.5 g), then dissolved in 100 ml benzene and 20 ml aliquot portions chromatographed on basic alumina yielding 4.22 g (95 %) of the pure carbon alkylate (IV); m.p. 65-66°. From a 25 ml aliquot portion 0.08 g (1 %) of 2,4-dinitrophenylhydrazone of *p*-nitrobenzaldehyde, m.p. 321-322° (decomp) was obtained; mixed m.p. with an authentic sample, 325-326°.

Reaction of p-nitrobenzyl trimethyl ammonium bromide with the lithium salt of 2-nitropropane in DMF at 25°

To 11.00 g (0.04 mole) of *p*-nitrobenzyltrimethylammonium bromide dissolved in 120 ml DMF at 25°, a solution of 7.60 g (0.08 mole) lithium salt of 2-nitropropane in 40 ml DMF was added at 25°, the reaction mixture turning red. After 35 hr, when the reaction was 72 % complete as shown by titration of the lithium salt of 2-nitropropane, $\frac{2}{3}$ of the mixture was poured into cold water, acidified with hydrochloric acid, and extracted with benzene. The

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extracts were washed with water, dried over sodium sulfate and the benzene removed *in vacuo* leaving a residue (A) of 4.82 g. The theoretical yield of C-alkylate (IV) is 4.85 g, based on 72 % completion and $\frac{3}{4}$ of the mixture. From a 2 g portion of (A) chromatographed on basic alumina, 1.85 g (93 %) of IV, m.p. 64.5–66.5°, was obtained. When the remaining 2.82 g of (A) was treated in the usual way no *p*-nitrobenzaldehyde was detected.¹⁸

1-p-Nitrophenyl-2-nitro-2-methyl-1-propanol. *p*-Nitrobenzaldehyde, 3.00 g (0.02 mole), 2-nitropropane, 2.5 g (0.028 mole), and 0.3 g (0.0031 mole) lithium salt of 2-nitropropane were reacted for 1 day in 100 ml DMF. The reaction mixture was poured into 600 ml water and chilled. The crystals which precipitated were collected by filtration, washed with water and sucked dry. On recrystallization from ethanol–water and drying *in vacuo* crystals m.p. 149–150° were obtained. (Found: C, 50.3; H, 4.9; N, 11.5. $C_{10}H_{12}N_2O_5$ requires: C, 50.0; H, 5.0; N, 11.7 %).

¹⁸ H. Shechter and R. Kaplan [*J. Amer. Chem. Soc.* **73**, 1883 (1951)], on refluxing an ethanolic solution of the sodium salt of 2-nitropropane and *p*-nitrobenzyltrimethylammonium iodide for 30 hr obtained the carbon alkylate (IV) in 72 % yield.