TABLE I

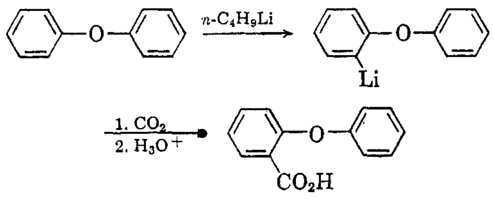
REACTION OF *n*-BUTYL BROMIDE WITH LITHIUM IN PHENYL ETHER FOLLOWED BY CARBONATION

Run	Lithium, G.-atom	*n*-Butyl Bromide, Mole	Phenyl Ether, Mole	Reaction Time, Hr.	Conditions	*o*-Phenoxybenzoic Acid, %	Valeric Acid, %
1	0.25	0.125	0.50	112	50°[a]	12.6	—
2	0.512	0.265	0.50	48	R.T.[a]	3.34	Trace[c]
3	0.690	0.125	0.50	5	R.T.[b]	3.06	7.82
4	0.275	0.0625	0.50	26	R.T.[b]	13.4	—

[a] *n*-Butyl bromide was added dropwise to a suspension of finely cut lithium wire in phenyl ether. [b] Lithium was added portionwise to a solution of *n*-butyl bromide in phenyl ether. [c] Valeric acid identified by means of its *p*-toluidide, m.p. and mixed m.p. 73–74°.

under corresponding conditions. Carbonation of the reaction mixtures led to either mixtures of valeric acid and *o*-phenoxybenzoic acid or to only *o*-phenoxybenzoic acid according to the following:

$$n\text{-}C_4H_9Br \xrightarrow{Li} n\text{-}C_4H_9Li \xrightarrow[2.\ H_3O^+]{1.\ CO_2} n\text{-}C_4H_9CO_2H$$



The extent to which *n*-butyllithium forms and the extent to which it metalates the phenyl ether present depends upon the time of reaction and upon the concentration of the reactants.

In view of the ready formation of *n*-butyllithium in phenyl ether, it appeared altogether reasonable that *n*-butylmagnesium bromide might form in the same solvent. Actually, we have found this to be the case, although the yield of this Grignard reagent is very small. It seems fair to conclude that some of the homologous *n*-amylmagnesium bromide[1] may be formed under corresponding conditions.

EXPERIMENTAL[7]

n-Butyllithium in phenyl ether (*Run 1*). To a stirred mixture of 85.1 g. (0.5 mole) of freshly distilled phenyl ether containing 1.74 g. (0.25 g.-atom) of finely cut lithium wire was added 17.3 g. (0.125 mole) of *n*-butyl bromide over a period of 20 min. Subsequent to the addition the solution became turbid and slight warming was noticed. Color Test I[8] was positive, and Color Test II[9] was negative. The reaction mixture was warmed to 50° and kept at this temperature for 112 hr. Carbonation by means of a Dry Ice–ether slurry and subsequent alkaline extraction gave 5.20 g. (19.7%) of crude *o*-phenoxybenzoic acid. Recrystallizations from ethanol-water, and from petroleum ether (b.p. 60–70°) gave 3.37 g. (12.6%) of pure acid, m.p. and mixed m.p. 111–113°.

n-Butylmagnesium bromide in phenyl ether. To 3.0 g. (0.123 g.-atom) of magnesium turnings and 81.5 g. (0.5 mole) of phenyl ether was added 8.65 g. (0.0625 mole) of *n*-butyl bromide. Inasmuch as no reaction took place, the mixture was stirred for several hours at room temperature with no indication of reaction. A crystal of iodine was added and the mixture allowed to stir overnight at 70°. Color Test I was still negative. The temperature was increased to 120–130° in which range a white precipitate began to form slowly incidental to frothing of the mixture. Color Test I became positive indicating the presence of a Grignard reagent. The mixture was allowed to stir at this temperature for 24 hr., cooled, and then carbonated by pouring into a Dry Ice–ether slurry. Subsequent to hydrolysis and work-up in a customary manner there was obtained valeric acid, which formed a derivative with *p*-toluidine to give 0.42 g. of the *p*-toluidide of valeric acid; m.p. and mixed m.p. 71–72°.

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Derivatives of Some Nitroalkanes

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Simple methods for the preparation of solid derivatives of nitroalkanes are sparse. Usually a nitroalkane is characterized by reduction of the nitro group to a primary amine followed by an acylation or benzoylation of the amine, or alternatively the sodium salt of a nitroalkane is treated with 2,4-dinitrobenzenesulfenyl chloride to form solid α-nitro sulfides.[1–3] Sodium salts of nitroalkanes can also be coupled with aryldiazonium salts to yield solid derivatives.[4]

Primary and secondary nitroalkanes have been shown to undergo the Mannich type condensation with ease and in the case of 2-nitropropane a num-

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(7) Organometallic reactions were carried out under an atmosphere of dry, oxygen free nitrogen. Melting points are uncorrected.

(8) H. Gilman and F. Schulze, *J. Am. Chem. Soc.*, 47, 2002 (1925).

(9) H. Gilman and J. Swiss, *J. Am. Chem. Soc.*, 62, 1847 (1940).

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(1) N. Kharasch and J. L. Cameron, *J. Am. Chem. Soc.*, 73, 3864 (1951).

(2) N. Kharasch, *J. Chem. Ed.*, 33, 585 (1956).

(3) R. B. Langford and O. D. Lawson, *J. Chem. Ed.*, 34, 510 (1957).

(4) O. C. Cermer and J. W. Hutcheson, *Proc. Okla. Acad. Sci.*, 23, 60 (1943).

TABLE I

Nitroalkane	M.P. of *N*-(2-Nitroalkyl)-*p*-toluidine	Yield, %	Molecular Formula	Nitrogen, % Calcd.	Nitrogen, % Found
2-Nitropropane[a]	75.5–76	72	$C_{11}H_{16}N_2O_2$	13.46	13.58
2-Nitrobutane	95.5–96.5	90	$C_{12}H_{18}N_2O_2$	12.61	12.74
2-Nitrooctane	63–64	71	$C_{16}H_{26}N_2O_2$	10.06	10.26
Nitrocyclohexane	76.5–77.5	81	$C_{14}H_{20}N_2O_2$	11.28	11.27
Nitrocyclopentane	69.3–70	66	$C_{13}H_{18}N_2O_2$	11.96	11.83
1-Chloro-1-nitropropane	67	60	$C_{11}H_{15}ClN_2O_2$	11.54	11.71

[a] Johnson[6] reported a m.p. of 74.5° for this derivative.

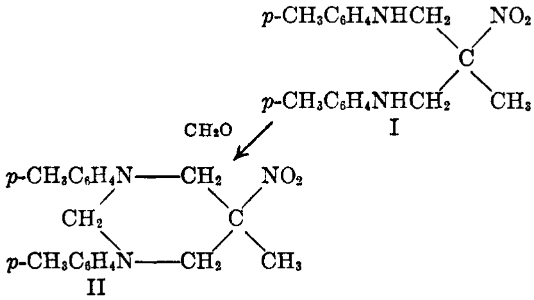
ber of solid derivatives have been prepared.[5,6] Thus, it appeared that this reaction could be easily adapted for identification and characterization of nitroalkanes. Accordingly, six secondary nitroalkanes were treated with *p*-toluidine and formaldehyde in the presence of a base. *N*-(2-*N*itroalkyl)-*p*-toluidines were produced in good yields and were easily purified by recrystallization.

$$p\text{-}CH_3C_6H_4NH_2 + CH_2O + RR'CHNO_2 \longrightarrow p\text{-}CH_3C_6H_4NHCH_2C(NO_2)RR'$$

The results are listed in Table I.

Primary nitroalkanes undergo this condensation to form either a di(*p*-tolylaminomethyl) derivative or a hexahydropyrimidine derivative. For example, nitroethane condensed with two equivalents of formaldehyde and two equivalents of *p*-toluidine to form the crystalline di-*p*-tolyl derivative (I). By employing excess formaldehyde and two equivalents of *p*-toluidine the crystalline hexahydropyrimidine (II) was isolated.

$$2p\text{-}CH_3C_6H_4NH_2 + 2\ CH_2O + CH_3CH_2NO_2 \longrightarrow$$



I

II

The hexahydropyrimidine derivative of 1-nitropropane was also prepared by this method. The condensation of primary nitroalkanes with formaldehyde and ammonia to form the corresponding hexahydropyrimidine has been reported in several instances.[7,8]

EXPERIMENTAL

The following experimental procedure was followed for the preparation of *N*-(2-nitroalkyl)arylamine derivatives from secondary nitroalkanes.

One gram of *p*-toluidine (0.0935 mole) was placed in a 50-ml. Erlenmeyer flask equipped with a reflux condenser. To this were added 5 ml. of methanol, 0.28 g. of paraformaldehyde, and 10 drops of tetramethylammonium hydroxide (Triton B) in that order. The secondary nitroalkane (0.0935 mole; approximately 1 g.) was then added and the mixture refluxed for 1 hr. Shortly after heat was applied the paraformaldehyde was completely in solution. Initially the solution was colorless, but on heating it gradually turned to a lemon yellow color. After the reflux time had elapsed the solution was cooled to room temperature and yellowish colored crystals precipitated. In case no crystals formed the solution was refrigerated overnight. The product was filtered, washed with cold methanol, and dried.

The product was recrystallized from 5 ml. (or less) of either methanol or petroleum ether (b.p. 65–110°). It was sometimes necessary to add water to the methanol solvent to instigate the formation of crystals. Recrystallization was continued until a constant melting point was obtained.

N,N'-Di-p-tolyl-2-methyl-2-nitro-1,3-propanediamine. Twenty-one and one-half grams of *p*-toluidine (0.2 mole) was dissolved in 35 ml. of boiling methanol in a round bottomed flask equipped with a reflux condenser. To this solution were added 16.2 g. of 37% formaldehyde (0.2 mole), 50 drops of tetramethylammonium hydroxide, and 7.5 g. (0.1 mole) of nitroethane. The solution was refluxed for 45 min., and the yellow product crystallized from the hot solution. The solution was cooled, the product filtered and dried, and then recrystallized from methanol-acetone mixed solvent to yield 16 g. (54%) of purified product melting at 145.5°. Infrared spectra analysis showed a NH peak at 3450 cm.$^{-1}$ Recrystallization of the product raised the m.p. to 146.5–147°.

Anal. Calcd. for $C_{18}H_{23}N_3O_2$: C, 68.98; H, 7.40; N, 13.41. Found: C, 68.93; H, 7.60; N, 13.61.

1,3-Di-p-tolyl-5-methyl-5-nitrohexahydropyrimidine. Eleven grams (0.035 mole) of *N,N'*-di-*p*-tolyl-2-methyl-2-nitro-1,3-propanediamine was dissolved in a hot mixture of 250 ml. of methanol and 75 ml. of acetone. Forty and one-half grams (0.5 mole) of 37% formaldehyde was added, and the solution refluxed for 1 hr. Upon cooling overnight the cotton-like product crystallized, was filtered and dried, and recrystallized from methanol-acetone mixed solvent to yield 5.4 g. (47%) of product melting at 112.5–113°. Infrared spectral analysis showed the absence of a NH peak at 3450 cm.$^{-1}$ Upon recrystallization twice again the product melted at 110–111.5°.

Anal. Calcd. for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 69.98; H, 7.20; N, 12.66.

1,3-Di-p-tolyl-5-ethyl-5-nitrohexahydropyrimidine. To a mixture of 8.9 g. (0.1 mole) of 1-nitropropane, 16.2 g. (0.2 mole) 37% formaldehyde, and 5 ml. of tetramethylammonium hydroxide in 10 ml. of ethanol was added 21.5 g. (0.2 mole) of *p*-toluidine dissolved in 25 ml. of hot ethanol. The mixture turned milky during the 1.5-hr. reflux period. The reaction mixture stood for 4 days during which time the product crystallized. The product was washed with a little ethanol and then was recrystallized from methanol-acetone, m.p. 103.5–104.5°.

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(5) M. Senkus, *J. Am. Chem. Soc.*, **68**, 10 (1946).

(6) H. B. Johnson, *J. Am. Chem. Soc.*, **68**, 14 (1946).

(7) T. Urbanski and H. Piotrowski, *Roczniki Chem.* **29**, 379–391 (1955); *Chem. Abstr.*, **50**, 4967b (1956).

(8) Thompson, R. B., U.S. Pat. 2,734,814, Feb. 14, 1956. *Chem. Abstr.*, **50**, 8194g (1956).

Anal. Calcd. for $C_{20}H_{25}N_3O_2$: C, 70.77; H, 7.42. Found: C, 71.02; H, 7.64.

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The Stereochemistry of Protonation of Anions of 9,10-Dihydro-9,10-(*trans*-11-nitro-12-R-ethano)anthracenes

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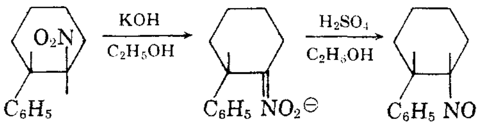
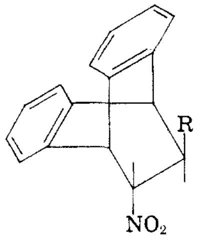
Zimmerman and Nevins[2] have shown that acidification of the potassium salt of *trans*-1-nitro-2-phenylcyclohexane (Ia) with ethanolic sulfuric acid yields 98 ± 3% *cis*-1-nitro-2-phenylcyclohexane (Ic), the product of kinetic control. It was shown that the conjugate base, the nitro compound anion (Ib), and not the *aci*-nitro compound, is the intermediate in this conversion. The *cis* isomer was isomerized to 99 ± 3% *trans* isomer, the product of thermodynamic control, by boiling with a small amount of sodium bicarbonate in ethanol solution. Similar cases of protonation of nitro compound anions



Ia Ib Ic

to yield less stable products of kinetic control, and their subsequent isomerization with very dilute alkali under equilibration conditions to more stable products of thermodynamic control, have been reported in the 6-nitro steroid series.[3,4] In contrast to the isomerization of a *trans* to a *cis* nitro compound, it had been reported earlier[5,6] from semiquantitative observations in our laboratory that the *trans* bicyclic nitro compounds, 9,10-dihydro-9,10-(*trans*-11-methyl-12-nitroethano)anthracene (IIa) and 9,10-dihydro-9,10-(*trans*-11-nitro-12-phenylethano)anthracene (IIb), were regenerated in 42–70% and 66% yields, respectively, upon acidification of their potassium salts.



IIa. R = CH_3
IIb. R = C_6H_5

The apparent difference in behavior between our bicyclic compounds (II) and the simple alicyclic case (I) caused us to reinvestigate the behavior of the bicyclic nitro compounds, with the intention of establishing the following: (a) that, prior to acidification, the nitro compounds were fully converted to anions by action of alkali; (b) the maximum yield of products; and (c) the identity of products with starting material. The quality of the nitro compound starting materials was ensured by infrared, and particularly by ultraviolet analysis, which is a sensitive indicator of traces of contaminating anthracene. In order to ensure complete conversion of the nitro compounds to their salts, the nitro compounds were boiled briefly with ethanolic aqueous alkali and the resulting solution, containing precipitated nitro compound salt, was evaporated to dryness. The dried residue was pulverized and a known aliquot was dissolved in water, in which the unchanged nitro compounds are insoluble, and extracted with ether, in which the nitro compounds are soluble, to remove any trace of unchanged nitro compound or of autoxidation[7] or decomposition products formed from the salt. Such ether-extractable organic impurities did not exceed 5% of the original nitro compound starting material. To ensure complete and irreversible protonation of the nitro compound anion and yet avoid the competing Nef reaction which occurs with stronger acid,[6] the aqueous solution of the salt was added dropwise to cold, stirred, aqueous acetic acid.

The *trans*-methyl derivative (IIa) was regenerated in 84–97% yield, the product obtained in the higher yield differing from the starting material in just one respect: the presence of a medium weak carbonyl band in the infrared spectrum, suggesting contamination by a small amount of the corresponding ketone, possibly arising from a Nef reaction.[6] The *trans*-phenyl derivative (IIb) was regenerated in 91% yield. These results indicate a clear preference for formation under conditions of kinetic control of *trans*-11-nitro-12-substituted derivatives in the 9,10-dihydro-9,10-ethanoanthracene series. The corresponding *cis*-11-nitro-12-substituted deriv-

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[1] N.S.F. undergraduate research participant, Summer 1959. It is a pleasure to acknowledge support of J.M.E. through research grant NSF-G8179 from the National Science Foundation.

[2] H. E. Zimmerman and T. E. Nevins, *J. Am. Chem. Soc.*, **79**, 6559 (1957).

[3] A. Bowers, M. B. Sánchez, and H. J. Ringold, *J. Am. Chem. Soc.*, **81**, 3702 (1959).

[4] A. Bowers, L. C. Ibáñez, and H. J. Ringold, *J. Am. Chem. Soc.*, **81**, 3707 (1959).

[5] W. E. Noland, H. I. Freeman, and M. S. Baker, *J. Am. Chem. Soc.*, **78**, 188 (1956).

[6] W. E. Noland, M. S. Baker, and H. I. Freeman, *J. Am. Chem. Soc.*, **78**, 2233 (1956).

[7] G. A. Russell, *J. Am. Chem. Soc.*, **76**, 1595 (1954).