282. *Aliphatic Nitro-compounds. Part III. Preparation of Alkyl 2-Nitroalkyl Ethers.**

By A. Lambert, C. W. Scaife, and A. E. Wilder-Smith.

Alcohols add to α-nitro-olefins giving alkyl 2-nitroalkyl ethers, which on reduction yield amines, and on reaction with formaldehyde afford α-hydroxymethyl derivatives. 1 : 2-Dinitroethane (or 2-nitroethyl nitrate), 1 : 2-dinitropropane, and 1 : 2-dinitro-2-methyl-

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* Cf. E.PP. 573,872, 581,134.

propane may be used as convenient substitutes for nitroethylene, 1-nitroprop-1-ene, and 1-nitro-2-methylprop-1-ene respectively.

THE addition of alcohols to some substituted nitro-olefins has been reported previously; thus, β-nitrostyrene (Rosenmund, *Ber.*, 1913, **46**, 1034; Meisenheimer and Heim, *ibid.*, 1905, **38**, 467), β-bromo-β-nitrostyrene (Thiele and Haeckel, *Annalen*, 1902, **325**, 1), 2-nitro-1-(*p*-methoxyphenyl)prop-1-ene (Meisenheimer and Jochelson, *ibid.*, 1907, **355**, 293), 1-bromo-1-nitrobut-1-ene and 1-bromo-1-nitropent-1-ene (Loevenich, Koch, and Pucknat, *Ber.*, 1930, **63**, 636) all add alcohols in the presence of a basic catalyst to give 2-nitroalkyl ethers; benzylidene-ω-nitroacetophenone behaves similarly with boiling alcohol in the absence of a base (Wieland, *Annalen*, 1903, **328**, 189; cf. Friedlander, Mahly, and Lazarus, *ibid.*, 1885, **229**, 210, 234; Flürscheim, *J. pr. Chem.*, 1902, **66**, 16). Since the present work was completed, the preparation of 2-nitroalkyl ethers by reaction of 1-nitrobut-1-ene and some higher nitro-olefins with sodium alkoxides has also been reported (U.S.P. 2,391,815).

The reaction of alcohols with 1 : 2-dinitro-paraffins and 2-nitroalkyl nitrates, obtained from the addition of nitrogen tetroxide to olefins (see Levy *et al.*, *J.*, 1946, 1096, 1100), and with α-nitro-olefins, was undertaken as part of a general investigation of the chemistry of these compounds and as a route to a wide variety of nitro- and amino-ethers. With boiling alcohols, 1 : 2-dinitroethane (or 2-nitroethyl nitrate) and 1 : 2-dinitropropane gave nitro-ethers as follows :

$$\left.\begin{array}{l}\mathrm{NO_2\cdot CH_2\cdot CH_2\cdot NO_2 + ROH \longrightarrow NO_2\cdot CH{:}CH_2 + R\cdot O\cdot NO + H_2O}\\ \mathrm{NO_2\cdot CH_2\cdot CH_2\cdot O\cdot NO_2 + ROH \longrightarrow NO_2\cdot CH{:}CH_2 + R\cdot O\cdot NO_2 + H_2O}\end{array}\right\}\ \mathrm{NO_2\cdot CH{:}CH_2 + R\cdot OH \longrightarrow NO_2\cdot CH_2\cdot CH_2\cdot OR}$$

The reaction was found to be a general one, but yields diminished with increasing molecular weight of the alcohol and were lower with 2-nitroethyl nitrate than with 1 : 2-dinitroethane. Treatment of 1 : 2-dinitro-2-methylpropane with boiling alcohols gives 1-nitro-2-methylprop-1-ene which adds alcohols only in the presence of a basic catalyst. 2-Nitroprop-1-ene, 2-nitrobut-2-ene, and β-nitro-β-methylstyrene also require a basic catalyst, the highest yields being obtained by the use of an equivalent of the appropriate sodium alkoxide. In the reaction of 2-nitroprop-1-ene with sodium methoxide, in addition to *methyl 2-nitro-*n*-propyl ether*, some methyl 2 : 4-dinitro-2-methylamyl ether was obtained as a by-product, formed by addition of the mononitro-ether to 2-nitropropene (cf. Part VIII in this series) :

$$\begin{tikzcd} \mathrm{CH_3\cdot C(NO_2){:}CH_2 + CH_3\cdot OH} \arrow[r] & \mathrm{CH_3\cdot CH(NO_2)\cdot CH_2\cdot O\cdot CH_3} \arrow[d, "\mathrm{CH_3\cdot C(NO_2){:}CH_2}"] \\ & \mathrm{CH_3\cdot CH(NO_2)\cdot CH_2\cdot C(CH_3)(NO_2)\cdot CH_2\cdot O\cdot CH_3} \end{tikzcd}$$

β-Nitrostyrene and sodium methoxide have been reported to give a small yield of methyl 2 : 4-dinitro-1 : 3-diphenylbutyl ether by a similar mechanism (Meisenheimer and Heim, *loc. cit.*). Nitroethylene was very reactive; even when stabilised with a small amount of phosphoric acid it added 2-methoxyethyl alcohol at ordinary temperature.

The nitro-ethers were readily hydrogenated to amines, and reaction with formaldehyde in the presence of a base gave α-hydroxymethyl derivatives.

The *2-nitrobut-2-ene* used in this work was obtained from 2-nitro-3-acetoxybutane (Vanderbilt and Hass, *Ind. Eng. Chem.*, 1940, **32**, 34) by heating it with sodium acetate (cf. Gen. Aniline and Film Corp., U.S.P. 2,257,980). Its structure was established by reduction with zinc and acetic acid (cf. Bouveault and Wahl, *Bull. Soc. chim.*, 1903, **29**, 643) to methyl ethyl ketoxime. It is interesting that a product from the decomposition of the silver salt of nitroethane was described by Angeli and Alessandri (*Atti R. Accad. Lincei*, 1910, **19**, 784; *Chem. Zentr.*, 1910, II, 731) as being probably 2-nitrobut-2-ene, but its structure was not proved.

EXPERIMENTAL.

Analyses are by Mr. E. S. Morton and Mr. A. E. Heron. All m. ps. are uncorrected.

Alkyl 2-Nitroalkyl Ethers.

(a) *From 1 : 2-Dinitro-paraffins.—Alkyl 2-nitroethyl ethers.* Methyl and ethyl 2-nitroethyl ethers were prepared by refluxing a 15% solution of 1 : 2-dinitroethane (Levy, Scaife, and Wilder-Smith, *J.*, 1946, 1096) in the appropriate alcohol for 36 hours. The excess of alcohol was distilled, and the residual crude nitro-ether distilled first in steam at 60 mm. (to avoid the unstable residue formed on distillation) and then in high vacuum. For the higher alkyl 2-nitroethyl ethers, molten 1 : 2-dinitroethane was added to the boiling alcohol, the temperature of the bath being adjusted to distil off the alkyl nitrite as formed. The nitro-ether was then isolated by fractional distillation. The compounds prepared by this method are ***methyl*** (60% yield), b. p. 38°/1 mm., 67°/12 mm.; $d_{4^\circ}^{20^\circ}$ 1·128; n^{20° 1·417 (Found : C, 34·7; H, 6·9; N, 13·4. $C_3H_7O_3N$ requires C, 34·3; H, 6·7; N, 13·3%); ethyl (50% yield), b. p. 46°/1 mm.;

72°/12 mm.; $d_{4°}^{16°}$ 1·069 (Henry, *Rec. Trav. chim.*, 1899, **18**, 259, records b. p. 178°/760 mm.; $d_{D}^{16°}$ 1·148) (Found: C, 40·5; H, 7·5; N, 12·0. Calc. for $C_4H_9O_3N$: C, 40·3; H, 7·6; N, 11·8%); n-*propyl* (45% yield), b. p. 48°/0·5 mm. (Found: N, 10·3. $C_5H_{11}O_3N$ requires N, 10·5%); iso*propyl*, b. p. 43°/0·5 mm. (Found: N, 10·6. $C_5H_{11}O_3N$ requires N, 10·5%); n-*butyl* (27% yield), b. p. 70—72°/2 mm. (Found: N, 9·7. $C_6H_{13}O_3N$ requires N, 9·5%); and n-*amyl 2-nitroethyl ether* (39% yield), b. p. 80—82°/1·5 mm. (Found: N, 8·4. $C_7H_{15}O_3N$ requires N, 8·7%).

Methyl nitro-tert.-*butyl ether*. 1 : 2-Dinitro-2-methylpropane (29·6 g.) (Levy and Scaife, in the press) in methyl alcohol (50 c.c.) was added dropwise with stirring during 30 minutes to a solution of sodium methoxide [from sodium (9·2 g.) in methyl alcohol (200 c.c.)]. The product after dilution with water and neutralisation (acetic acid) was extracted with ether and fractionated, giving *methyl nitro*-tert.-*butyl ether* (5·7 g.), b. p. 75°/15 mm. (Found: C, 45·1; H, 8·3; N, 10·8. $C_5H_{11}O_3N$ requires C, 45·1; H, 8·3; N, 10·5%).

Ethyl nitro-tert.-*butyl ether*. 1 : 2-Dinitro-2-methylpropane (29·6 g.), urea (6·0 g.), and alcohol (300 c.c.) were refluxed for 15 hours. Fractionation gave *ethyl nitro*-tert.-*butyl ether* (4·9 g.), b. p. 75°/15 mm. (Found: C, 48·7; H, 8·7; N, 9·3. $C_6H_{13}O_3N$ requires C, 49·0; H, 8·8; N, 9·5%). Some 1-nitro-2-methylprop-1-ene, b. p. 54—58°/11 mm., was also formed, and the alcohol recovered contained acetone, formed by hydrolysis of the dinitro-paraffin.

*Methyl 2-nitro*iso*propyl ether*. 1 : 2-Dinitropropane (30 g.) (Levy and Scaife, *J.*, 1946, 1100) was refluxed with methyl alcohol (70 g.) for 17 hours, and the mixture fractionated, giving *methyl 2-nitro*iso*propyl ether* (8 g.), b. p. 36—41°/1 mm., 62°/12 mm. (Found: C, 40·9; H, 7·7; N, 11·5. $C_4H_9O_3N$ requires C, 40·3; H, 7·6; N, 11·8%).

(b) *From Nitro-olefins.*—*2-Nitro-2′-methoxydiethyl ether*. A mixture of nitroethylene (19·7 g.), 2-methoxyethyl alcohol (100 c.c.), and orthophosphoric acid (1 c.c.), after being kept for 1 month at ordinary temperature, was distilled to give *2-nitro-2′-methoxydiethyl ether* (12·5 g.), b. p. 81—84°/0·5 mm. (Found: C, 40·3; H, 7·3; N, 9·6. $C_5H_{11}O_4N$ requires C, 40·3; H, 7·4; N, 9·4%).

Methyl nitro-tert.-*butyl ether*. 1-Nitro-2-methylprop-1-ene (20·2 g.) was added dropwise with stirring during 30 minutes to a solution of an equivalent of sodium methoxide [from sodium (4·6 g.) in methyl alcohol (100 c.c.)] at ordinary temperature. The product, after dilution with water and neutralisation (acetic acid), was extracted with ether and distilled, giving methyl nitro-*tert.*-butyl ether (17·3 g.), b. p. 75°/15 mm.

2-Nitro-3-methoxybutane. This was prepared as described above from 2-nitrobut-2-ene (101 g.) and sodium methoxide in methyl alcohol. *2-Nitro-3-methoxybutane* was obtained as a colourless liquid, b. p. 61—63°/15 mm. (Found: C, 45·1; H, 8·3. $C_5H_{11}O_3N$ requires C, 45·1; H, 8·3%). The 2-p-*nitrophenylazo*-derivative, from the sodium salt of the nitro-ether and *p*-nitrobenzenediazonium chloride, separated in two forms; *α-form*, fine yellow needles from light petroleum, m. p. 91° (Found: C, 46·6; H, 5·3; N, 19·7. $C_{11}H_{14}O_5N_4$ requires C, 46·8; H, 5·0; N, 19·8%), and *β-form*, red prisms from light petroleum, m. p. 84° (Found: C, 46·8; H, 5·1; N, 19·3%).

Methyl 2-nitropropyl ether. This was prepared from 2-nitroprop-1-ene (27 g.; see Part I of this series) and sodium methoxide in methyl alcohol as described above. Distillation gave *methyl 2-nitropropyl ether* (15·2 g.) as a colourless oil, b. p. 61—64°/14 mm. (Found: C, 40·6; H, 7·3. $C_4H_9O_3N$ requires C, 40·3; H, 7·6%). Some methyl 2 : 4-dinitro-2-methylamyl ether (4·8 g.), b. p. 92·5°/0·2 mm. (see Part VIII of this series), was also obtained.

*Methyl 2-nitro*iso*propyl ether*. Interaction of 1-nitroprop-1-ene (50 g.; see Part I of this series) with sodium methoxide in methyl alcohol as described above afforded methyl 2-nitro*iso*propyl ether (29 g.), b. p. 62°/12 mm., identical with that obtained from 1 : 2-dinitropropane.

*2-Nitro*iso*propyl* n-*butyl ether*. 1-Nitroprop-1-ene (25 g.) and a solution of sodium butoxide [from sodium (6·6 g.) in *n*-butyl alcohol (120 c.c.)], brought into reaction at 0—10° and worked up in the usual way, afforded *2-nitro*iso*propyl* n-*butyl ether* (28 g.) as a colourless oil, b. p. 98—101°/14 mm. (Found: C, 52·7; H, 9·1; N, 8·6. $C_7H_{15}O_3N$ requires C, 52·2; H, 9·3; N, 8·7%).

Nitro-tert.-*butyl* n-*amyl ether*. 1-Nitro-2-methylprop-1-ene (50 g.) interacted with sodium *n*-amyloxide as described above to afford *nitro*-tert.-*butyl* n-*amyl ether* (26 g.), b. p. 75°/1 mm. (Found: C, 57·7; H, 9·9; N, 7·2. $C_9H_{19}O_3N$ requires C, 57·2; H, 10·0; N, 7·4%).

Methyl 2-nitro-1-phenyl-n-*propyl ether*. A solution of *β*-nitro-*β*-methylstyrene (489 g.; cf. Alles, *J. Amer. Chem. Soc.*, 1932, **54**, 271) in dioxan (150 c.c.) was added to a solution of sodium methoxide [from sodium (10·35 g.) in methyl alcohol (150 c.c.)] at 10° during ½ hour. After being stirred for 2 hours at room temperature, the mixture was diluted with water, acidified (acetic acid), extracted with ether, and distilled. Fractionation gave *methyl 2-nitro-1-phenyl*-n-*propyl ether* (51·3 g.) as a colourless oil, b. p. 138—141°/16 mm. (Found: C, 61·6; H, 6·5; N, 7·5. $C_{10}H_{13}O_3N$ requires C, 61·5; H, 6·6; N, 7·2%).

(c) *From 2-Nitroethyl Nitrate.*—2-Nitroethyl nitrate (30 g.) was refluxed with alcohol (150 c.c.) for 8 hours. Fractionation gave ethyl 2-nitroethyl ether (15 g.), b. p. 46°/1 mm.

Interaction of Nitroalkyl Ethers with Formaldehyde.

2-Nitro-3-methoxy-n-*propyl Alcohol.*—A solution of methyl 2-nitroethyl ether (26·25 g.) in alcohol (25 c.c.) was added to a solution of sodium hydroxide (10 g.) in alcohol (150 c.c.). Paraformaldehyde (7·5 g.) was added and the mixture stirred until a homogeneous solution was obtained. The sodium salt which separated was collected, dissolved in water, acidified (acetic acid), and extracted with ether. Distillation afforded *2-nitro-3-methoxy*-n-*propyl alcohol* (13·5 g.), b. p. 99—104°/0·5 mm. (Found: C, 35·2; H, 6·8; N, 10·5. $C_4H_9O_4N$ requires C, 35·6; H, 6·7; N, 10·4%). Reduction of the nitro-alcohol with Adams's platinum catalyst in alcohol at 20°/100 atms. afforded methyl 2-aminoethyl ether, isolated as the *picrate*, m. p. 148—150° (Found: C, 35·9; H, 4·1. $C_3H_9ON,C_6H_3O_7N_3$ requires C, 35·6; H, 4·0%).

2-Nitro-2-methoxymethylpropane-1 : 3-diol.—Methyl 2-nitroethyl ether (9·32 g.) in methyl acetate (20 c.c.) was treated with paraformaldehyde (5·32 g.) and a trace of alcoholic potassium hydroxide.

After neutralisation the product was collected and crystallised from methyl acetate–light petroleum (b. p. 40—60°), giving 2-*nitro*-2-*methoxymethylpropane*-1 : 3-*diol*, m. p. 82·5—83·5° (Found : C, 36·2; H, 6·8; N, 8·4. $C_5H_{11}O_5N$ requires C, 36·4; H, 6·7; N, 8·5%). Reduction of the nitro-diol with Adams's platinum catalyst in alcohol gave 2-amino-2-methoxymethylpropane-1 : 3-diol, isolated as the *picrolonate*, m. p. 219—220° (Found : N, 17·6. $C_5H_{13}O_3N,C_{10}H_8O_5N_4$ requires N, 17·6%).

2-*Nitro*-2-*ethoxymethylpropane*-1 : 3-*diol*.—This was prepared from ethyl 2-nitroethyl ether as described above for the lower homologue. The diol was obtained as an undistillable oil, identified as the *di*-p-*nitrobenzoyl* derivative, m. p. 240—241° (Found : C, 50·7; H, 3·7; N, 8·3. $C_{20}H_{19}O_{11}N_3$ requires C, 50·4; H, 4·0; N, 8·8%).

2-*Nitro*-3-*methoxy*-2-*methyl*-n-*butyl Alcohol*.—A mixture of 2-nitro-3-methoxybutane (40 g.), paraformaldehyde (9·1 g.), aqueous sodium hydroxide (1·5 c.c. of 40%), and methyl alcohol (80 c.c.) was stirred overnight at ordinary temperature. After neutralisation with 2N-hydrochloric acid, distillation gave 2-*nitro*-3-*methoxy*-2-*methyl*-n-*butyl alcohol* (42 g.) as a colourless oil, b. p. 110°/15 mm., 82°/0·5 mm. (Found : C, 43·5; H, 7·7; N, 8·3. $C_6H_{13}O_4N$ requires C, 44·2; H, 7·9; N, 8·6%).

2-*Nitro*-3-n-*butoxy*-n-*butyl Alcohol*.—2-Nitro*iso*propyl *n*-butyl ether (53 g.) was dissolved in a solution of sodium hydroxide (13·5 g.) in water (100 c.c.) at 10°, and paraformaldehyde (10 g.) was added portionwise with stirring, the temperature being allowed to rise to 32°. After 20 minutes the solution was acidified (2N-hydrochloric acid), concentrated at 40—50° under reduced pressure, filtered, and distilled, giving 2-*nitro*-3-n-*butoxy*-n-*butyl alcohol* (53 g.) as a pale yellow oil, b. p. 98°/0·2 mm. (Found : C, 49·9; H, 9·2; N, 7·5. $C_8H_{17}O_4N$ requires C, 50·3; H, 8·9; N, 7·3%). Reduction of the nitro-alcohol (42 g.) in methyl alcohol (700 c.c.) with Raney nickel and hydrogen at 20°/68 atms. (initial pressure) gave 2-*amino*-3-n-*butoxy*-n-*butyl alcohol* (27 g.) as a colourless oil, b. p. 90—92°/0·1 mm. (Found : N, 9·1 $C_8H_{19}O_2N$ requires N, 8·7%).

Alkylaminoethyl Ethers.

Methyl 2-*Aminoethyl Ether*.—Methyl 2-nitroethyl ether (2·0 g.) in alcohol (22 c.c.) was hydrogenated with Adams's platinum catalyst at 20°/100 atms. to give methyl 2-aminoethyl ether, isolated as the *picrate*, m. p. 148—150° (Found : C, 35·9; H, 4·1. $C_3H_9ON,C_6H_3O_7N_3$ requires C, 35·6; H, 4·0%).

Ethyl 2-aminoethyl ether, obtained in 52% yield by similar reduction of ethyl 2-nitroethyl ether, had b. p. 105°; picrolonate, m. p. 208—209° (decomp.) (Found: C, 47·7; H, 5·5; N, 19·6. Calc. for $C_4H_{11}ON,C_{10}H_8O_5N_4$: C, 47·6; H, 5·4; N, 19·8%); picrate, m. p. 121—123° (Found: C, 37·2; H, 4·6; N, 17·8. Calc. for $C_4H_{11}ON,C_6H_3O_7N_3$: C, 37·6; H, 4·4; N, 17·6%). (Meyer, *Ber.*, 1905, **38**, 3130, records m. p. 204° and 122° respectively for these derivatives.)

2-*Amino*-3-*methoxybutane*.—2-Nitro-3-methoxybutane (20 g.) was added slowly with stirring to a mixture of iron powder (3·5 g.), ferric chloride (1 g.), concentrated hydrochloric acid (10 c.c.), and water (75 c.c.) at 100°. After being stirred at 100° for 15 hours, the mixture was basified strongly with aqueous sodium hydroxide and distilled in steam. The distillate was neutralised with hydrochloric acid, evaporated to dryness, basified with excess of 50% aqueous potassium hydroxide, and extracted with ether. The dried extract was fractionated, giving 2-*amino*-3-*methoxybutane* (5 g.) as colourless oil, b. p. 114—116° (Found : N, 13·3. $C_5H_{13}ON$ requires N, 13·6%). The *platinichloride* formed orange prisms from methyl alcohol–ether, m. p. 189—190° (decomp.) [Found : Pt, 31·1. $(C_5H_{13}ON)_2,H_2PtCl_6$ requires Pt, 31·6%]; the 2 : 4-*dinitrophenylurea* (cf. McVeigh and Rose, *J.*, 1945, 621) formed yellow prisms from alcohol, m. p. 152—154° (Found : C, 45·9; H, 4·7; N, 17·6. $C_{12}H_{16}O_6N_4$ requires C, 46·1; H, 5·1; N, 17·9%). The same amine was formed in 50% yield by catalytic reduction of the nitro-ether with Raney nickel–methyl alcohol at 50°/120 atms.

2-*Nitrobut*-2-*ene*.—2-Nitro-3-acetoxybutane (161 g.; Vanderbilt and Hass, *loc. cit.*) was stirred with anhydrous sodium acetate (0·6 g.) at 100° for 1 hour and then distilled. The acidic distillate was washed successively with brine, aqueous sodium hydrogen carbonate, and brine, and the product fractionated, giving 2-*nitrobut*-2-*ene* (86 g.) as a pale yellow liquid, b. p. 55·5°/15 mm., $n_D^{22°}$ 1·4600 (Found : C, 46·9; H, 6·8; N, 13·8. $C_4H_7O_2N$ requires C, 47·5; H, 6·9; N, 13·8%). Reduction of the nitro-olefin (30 g.) with zinc and acetic acid (cf. Bouveault and Wahl, *loc. cit.*) gave methyl ethyl ketoxime (17 g.), b. p. 140—150°, which with 2 : 4-dinitrophenylhydrazine in hydrochloric acid gave methyl ethyl ketone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. with an authentic specimen, 115°.

The authors wish to thank Mr. R. H. Stanley and Mr. H. Baldock for assistance with the preparative work, and Dr. N. Levy and Dr. H. A. Piggott for their interest and advice.

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[*Received, January 23rd,* 1947.]