

293. *Aliphatic Nitro-compounds. Part XIV. Preparation of 3-Nitroalkyl Cyanides by Reaction of Nitro-paraffins with Unsaturated Cyanides.**

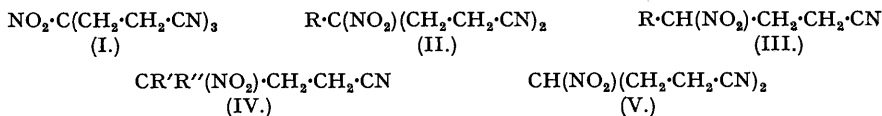
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A series of 3-nitroalkyl cyanides is prepared by the interaction of vinyl cyanide with primary and secondary nitro-paraffins in the presence of alkali. Both propenyl and allyl cyanide react with 1-nitropropane to give 3-nitro-2-methyl-n-amyl cyanide and with 2-nitropropane to give 3-nitro-2 : 3-dimethyl-n-butyl cyanide. α -Cyanostilbenes react with primary nitro-compounds in presence of secondary aliphatic amines to give 3-nitro-1 : 2-diarylalkyl cyanides, e.g., α -cyanostilbene and nitromethane give 3-nitro-1 : 2-diphenylpropyl cyanide (VIII; R = H).

WHEN this work was carried out only two 3-nitroalkyl cyanides had been reported : 3-nitropropyl cyanide, prepared by Henry (*Bull. Acad. Sci. Belg.*, 1895, **36**, 152) by the action of silver nitrite on 3-iodopropyl cyanide, and nitrotris-(2-cyanoethyl)methane (I) prepared by Bruson and Reiner (*J. Amer. Chem. Soc.*, 1943, **65**, 23) by addition of nitromethane to vinyl cyanide (acrylonitrile). As large quantities of 3-nitroalkyl cyanides were required in connection with other investigations, we decided to extend the application of Bruson's method to other olefins and nitro-paraffins.

* Patent application pending.

Since our work was completed, Bruson (U.S.P. 2,361,259) has reported the addition of nitro-paraffins to vinyl cyanide in an inert solvent (*e.g.*, dioxan or *tert.*-butyl alcohol), preferably at about 40° and in the presence of a small amount of alkali such as sodium hydroxide or a quaternary ammonium base as catalyst. In this way nitromethane gave the tris-adduct (I), other primary nitro-paraffins gave mixtures of bis- (II) and mono-adducts (III), whereas secondary nitro-paraffins gave mono-adducts (IV).

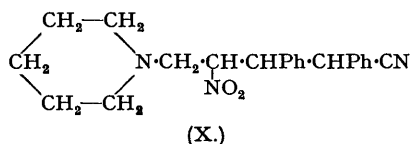
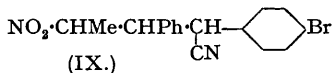


We have found it more convenient to effect the addition by refluxing an alcoholic solution of the cyanide, nitro-paraffin, and catalyst for a short time. The yields of mono-adducts (type III) from primary nitro-paraffins are improved by using a full molecular proportion of alkali as condensing agent, and with this technique, the bis-adduct to nitromethane (V) has been obtained.

The following new 4-nitro-cyanides have been made by this method: 1-nitro-1-(2-cyanoethyl)-cyclohexane, 3-nitro-4-methoxy-4-phenyl-3-methyl-n-butyl cyanide (VI), 3-nitro-5-n-butylsulphonyl-3-methyl-n-amyl cyanide, and 3-nitro-1:5-dicyanopentane. The known 3-nitro-3-methyl-n-butyl cyanide and 3-nitro-n-butyl cyanide (*cf.* Bruson, *loc. cit.*) have been prepared by the modified method: the first of these has been converted into its *iminoethyl ether* and *amidine hydrochloride*, and the second has been hydrolysed with acid to 3-keto-n-butyl cyanide (lævulonitrile).

The general method of addition has been extended by the use of substituted vinyl cyanides. Thus 2-nitropropane reacted with *isopropenyl* cyanide (methacrylonitrile) in presence of a little methyltriethylammonium hydroxide to give 3-nitro-1:3-dimethyl-n-butyl cyanide and with propenyl cyanide (crotononitrile) to give the isomeric 3-nitro-2:3-dimethyl-n-butyl cyanide, which was also formed by interaction of allyl cyanide and 2-nitropropane. Similarly, both propenyl and allyl cyanide reacted with 1-nitropropane to give 3-nitro-2-methyl-n-amyl cyanide (VII), the identity of the products being established by hydrolysis to 3-keto-2-methyl-n-amyl cyanide, which was characterised as the 2:4-dinitrophenylhydrazone. The allyl cyanide was presumably isomerised to propenyl cyanide by the alkaline catalyst before reaction with the nitro-paraffin, but a curious feature was that in both cases much higher yields of nitro-cyanide were obtained from allyl cyanide than from propenyl cyanide.

Aryl substituted vinyl cyanides behaved in an anomalous manner. Attempts to cause nitroethane to react with α -cyanostilbene in presence of strong alkalis failed, but by using a secondary aliphatic amine as catalyst 3-nitro-1:2-diphenyl-n-butyl cyanide (VIII; R = Me) was produced in 60% yield.



Similarly, nitromethane gave one of the isomerides of 3-nitro-1:2-diphenyl-n-propyl cyanide (VIII; R = H), and nitroethane reacted with 4-bromo- α -cyanostilbene to give one of the isomerides of 3-nitro-2-phenyl-1-p-bromophenyl-n-butyl cyanide (IX), but all attempts to cause secondary nitro-paraffins to react with α -cyanostilbene were unsuccessful. Methyl 2-nitroethyl ether reacted with α -cyanostilbene in the presence of piperidine, but unexpectedly the product was acid-soluble, the methoxyl group having been replaced by a piperidine residue to give 3-nitro-4-piperidino-1:2-diphenyl-n-butyl cyanide (X).

In many of the above products (IV), (VII), (VIII), (IX), and (X) there is more than one asymmetric carbon atom, so that the compounds would be expected to be formed as mixtures of stereoisomerides. In these cases, only one isomer has been identified and no attempt has been made to isolate the other stereoisomerides: the yields recorded therefore do not necessarily indicate the extent of the reaction.

EXPERIMENTAL.

Microanalyses are by Mr. E. S. Morton. M. ps. are uncorrected.

3-Nitro-3-methyl-n-butyl Cyanide.—Aqueous potassium hydroxide (10 c.c. of 33%) was added to a solution of 2-nitropropane (261 g.) in alcohol (750 c.c.), which was then heated to boiling. Vinyl cyanide

(159 g.) was run into the stirred solution at such a rate that the mixture refluxed gently. After a further 1 hour's refluxing, the solution was cooled, made just acid to Congo-red by addition of 20% sulphuric acid, stirred with barium carbonate to remove excess of acid, and filtered. The filtered solution was fractionated to give the cyanide as a colourless oil (330 g.), b. p. 70°/0.09 mm. (Bruson, *loc. cit.*, gives b. p. 105—107°/1 mm.) (Found: C, 50.55; H, 7.0; N, 19.7. Calc. for $C_6H_{10}O_2N_2$: C, 50.7; H, 7.05; N, 19.7%). The *iminoethyl ether hydrochloride*, prepared by passing dry hydrogen chloride into an alcoholic solution of the cyanide below 20°, had m. p. 108° (Found: N, 11.75; Cl, 16.2. $C_6H_{10}O_2N_2 \cdot HCl$ requires N, 12.4; Cl, 15.8%). The *amidine hydrochloride*, prepared by the action of alcoholic ammonia on the iminoethyl ether hydrochloride, had m. p. 214° (Found: Cl, 18.4. $C_6H_{10}O_2N_3 \cdot HCl$ requires Cl, 18.15%).

1-Nitro-1-(2-cyanoethyl)cyclohexane.—Nitrocyclohexane (43 g.) was brought into reaction with vinyl cyanide (18 g.) as described for 2-nitropropane. Distillation gave the *product* as a pale yellow oil (24 g.), b. p. 98—108°/0.15 mm., which from light petroleum (b. p. 40—60°) gave colourless needles, m. p. 42° (Found: C, 59.9; H, 7.45; N, 15.25. $C_8H_{14}O_2N_2$ requires C, 59.35; H, 7.7; N, 15.4%).

3-Nitro-1 : 2-dimethyl-n-butyl Cyanide.—(a) 2-Nitropropane (6.65 g.), allyl cyanide (5.0 g.), ethyl alcohol (50 c.c.), and aqueous methyltriethylammonium hydroxide (2.7 c.c. of 37%) were refluxed for 20 hours. The *product* (9.45 g.; 80%), isolated as in the previous cases, was a colourless oil, b. p. 86—87°/0.24 mm. (Found: C, 54.5; H, 7.8; N, 17.55. $C_7H_{12}O_2N_2$ requires C, 53.85; H, 7.7; N, 17.95%).

(b) The above experiment was repeated using propenyl cyanide in place of allyl cyanide. A colourless oil, b. p. 86—87°/0.24 mm., was isolated in 55% yield (Found: N, 18.25%).

3-Nitro-1 : 2-dimethyl-n-butyl Cyanide.—2-Nitropropane (8.9 g.) was brought into reaction with isopropenyl cyanide (7.0 g.) as described above for propenyl cyanide. After isolation as before, the crude *product* was distilled, giving the *cyanide* (6.3 g.), b. p. 65°/0.08 mm., m. p. 51—53° (from alcohol) (Found: C, 53.5; H, 7.35; N, 17.7. $C_7H_{12}O_2N_2$ requires C, 53.85; H, 7.7; N, 17.95%).

3-Nitro-4-methoxy-4-phenyl-3-methyl-n-butyl Cyanide.—Aqueous sodium hydroxide (5 c.c. of 32%) and vinyl cyanide (37.5 g.) were added to a solution of methyl 2-nitro-1-phenylpropyl ether (48.5 g.; this series, Part III) in dioxan (100 c.c.), and the mixture was stirred at 20° for 18 hours. The solution was poured into water, acidified with hydrochloric acid, and extracted with chloroform. Fractionation of the extract gave the *product* as a colourless oil (50 g.), b. p. 163—167°/0.5 mm. (Found: C, 62.5; H, 6.3; N, 11.3. $C_{13}H_{16}O_2N_2$ requires C, 62.9; H, 6.45; N, 11.3%).

3-Nitro-5-n-butylsulphonyl-3-methyl-n-amyl Cyanide.—Vinyl cyanide (1.05 g.) and methyltriethylammonium hydroxide (0.75 c.c. of 37%) were added to a solution of 3-nitrodibutyl sulphone (4.2 g.; this series, Part XVII) in alcohol (20 c.c.), which was then refluxed for 3 hours, cooled, and poured into water (250 c.c.). The mixture was extracted with ether and the extract was washed with dilute aqueous sodium hydroxide, dried, and the solvent removed to yield the *cyanide* as a very viscous brown oil, which could not be distilled or induced to crystallise (Found: N, 9.9; S, 11.4. $C_{11}H_{20}O_4N_2S$ requires N, 10.5; S, 11.6%).

4-Nitro-n-butyl Cyanide.—A solution of sodium methoxide [from sodium (11.5 g.) and methyl alcohol (150 c.c.)] was slowly run into a stirred solution of nitroethane (38 g.) in methyl alcohol (75 c.c.) at 0—10°. Vinyl cyanide (27 g.) was slowly added at 20—25°; during the addition the white precipitate of the sodium salt of nitroethane dissolved. The mixture was then acidified with acetic acid (32 g.), the solvent removed under reduced pressure at 40°, and the residue diluted with sufficient water to dissolve the sodium acetate and extracted with ether. The extract was dried and fractionated to give the *cyanide* as a colourless oil (19 g.), b. p. 82—84°/0.25 mm. (Bruson, *loc. cit.*, gives b. p. 107—110°/2 mm.) (Found: N, 21.65. Calc. for $C_5H_8O_2N_2$: N, 21.85%).

3-Keto-n-butyl Cyanide.—3-Nitro-n-butyl cyanide (13 g.) was dissolved in alcohol (10 c.c.) and aqueous sodium hydroxide (8 c.c. of 32%) was added at 10—15°. The resulting solution was diluted with water (30 c.c.) and run into dilute sulphuric acid (70 c.c. of 30%) at 10—15°. After being stirred for a further 15 minutes the mixture was extracted with ether. The extract was dried and fractionated to give the *ketone* as a colourless oil, b. p. 98—102°/9 mm. The 2 : 4-dinitrophenylhydrazones formed orange leaflets, m. p. 146°, from 2-ethoxyethyl alcohol (Found: C, 47.55; H, 4.05; N, 25.25. $C_{11}H_{11}O_4N_6$ requires C, 47.65; H, 4.0; N, 25.25%).

3-Nitro-2-methyl-n-amyl Cyanide.—(a) 1-Nitropropane (8.9 g.) was added dropwise to a solution of potassium hydroxide (5.6 g.) in alcohol (20 c.c.), the temperature being kept below 10°. The solution was then stirred at 50° and a solution of allyl cyanide (6.7 g.) in alcohol (30 c.c.) was added dropwise. The solution was stirred at 50° for 18 hours, cooled, and neutralised by dropwise addition of 5N-sulphuric acid, followed by treatment with barium carbonate. The filtered solution was fractionated, giving 3-nitro-2-methyl-n-amyl cyanide as a colourless oil (12.5 g.; 80% yield), b. p. 76°/0.1 mm.

The oil (1 g.), dissolved in a solution of sodium hydroxide (0.5 g.) in alcohol (5 c.c.) and water (5 c.c.), was added dropwise to ice-cold sulphuric acid (10 c.c. of 30%) and the mixture poured into excess of a saturated solution of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid. After standing overnight the precipitate was collected and crystallised from alcohol, giving 3-*keto-2-methyl-n-amyl cyanide* 2 : 4-dinitrophenylhydrazone as orange needles, m. p. 103—104° (Found: C, 51.25; H, 4.7; N, 23.25. $C_{13}H_{15}O_5N_6$ requires C, 51.15; H, 4.9; N, 22.95%).

(b) The above experiment was repeated using propenyl cyanide in place of allyl cyanide. This gave the nitro-cyanide in 35% yield as a colourless oil, b. p. 74—75°/0.09 mm. Hydrolysis and reaction with 2 : 4-dinitrophenylhydrazine as before gave a *product*, m. p. 102—103°, identical with the 2 : 4-dinitrophenylhydrazone described in (a) above (Found: N, 22.95%).

3-Nitro-1 : 5-dicyanopentane.—A solution of sodium methoxide [from sodium (7.5 g.) and methyl alcohol (150 c.c.)] was added dropwise to a stirred solution of nitromethane (20 g.) in methyl alcohol (75 c.c.) at 0—10°, and vinyl cyanide (32 g.) added during 1 hour. The mixture was treated with acetic acid (20 g.), concentrated under reduced pressure, and the residue diluted with water (300 c.c.) and shaken with ether, which caused the separation of crystals. Repeated recrystallisation from alcohol (charcoal) gave colourless needles (4 g.) of 3-nitro-1 : 5-dicyanopentane, m. p. 63° (Found: C, 50.2; H, 5.4; N, 24.95. $C_7H_8O_2N_4$ requires C, 50.3; H, 5.4; N, 25.1%).

3-Nitro-1 : 5-dicyano-3-p-bromophenylpentane.—Methyltriethylammonium hydroxide (1 c.c. of 37%) was added to a solution of *p*-bromophenylnitromethane (4.3 g.) and vinyl cyanide (1.6 g.) in *tert*-butyl alcohol (50 c.c.). Next day, the precipitate was collected (1.7 g.) and recrystallised repeatedly from alcohol, giving the dicyanide as colourless needles, m. p. 138—139° (Found : N, 13.2; Br, 24.45. Calc. for $C_{13}H_{12}O_2N_3Br$: N, 13.05; Br, 24.85%).

3-Nitro-1 : 2-diphenyl-*n*-butyl Cyanide (III; R = Me).— α -Cyanostilbene (205 g.), nitroethane (75 g.), and diethylamine (100 c.c.) were heated at 35—40° until a clear solution resulted. On being kept overnight, the mixture solidified. After crystallisation, first from alcohol and then from 2-ethoxyethyl alcohol, the cyanide was obtained as colourless crystals (160 g.), m. p. 164—165° (Found : C, 72.3; H, 5.7; N, 10.1. $C_{17}H_{16}O_2N_3$ requires C, 72.85; H, 5.7; N, 10.0%).

3-Nitro-4-piperidino-1 : 2-diphenyl-*n*-butyl Cyanide (X).— α -Cyanostilbene (2.7 g.) was brought into reaction with methyl 2-nitroethyl ether (2.4 g.) in the presence of piperidine (1.75 g.) as described above for nitroethane. The product was collected, washed with methyl alcohol, and recrystallised repeatedly from acetone, giving colourless needles (2.9 g.), m. p. 171° (Found : C, 72.1; H, 6.65; N, 11.7. $C_{22}H_{25}O_2N_3$ requires C, 72.7; H, 6.9; N, 11.6%). The product was soluble in dilute acid and was reprecipitated unchanged by addition of sodium hydroxide.

3-Nitro-1 : 2-diphenyl-*n*-propyl Cyanide (VIII; R = H).— α -Cyanostilbene (38.5 g.), nitromethane (15 g.), and diethylamine (20 c.c.) were heated at 50° until a homogeneous solution resulted. After several days at 20°, the crystalline precipitate was collected, washed with ether, and recrystallised from alcohol, giving the cyanide as colourless prisms (5.5 g.), m. p. 94—96° (Found : N, 10.55. $C_{16}H_{14}O_2N_2$ requires N, 10.55%).

3-Nitro-2-phenyl-1-p-bromophenyl-*n*-butyl Cyanide (XIV).—Nitroethane (1.65 g.), 4-bromo- α -cyanostilbene (5.7 g.; Frost, *Annalen*, 1889, 250, 161) and piperidine (1.75 g.) were mixed and kept at 20° for 3 days. The semi-solid mass was then dissolved in hot methyl alcohol (10 c.c.) and allowed to cool. The crystalline product was collected (3.35 g.) and purified by repeated recrystallisation from alcohol, giving colourless crystals of the cyanide, m. p. 187—189° (Found : C, 56.65; H, 4.2; N, 8.05; Br, 21.75. $C_{17}H_{15}O_2N_2Br$ requires C, 56.8; H, 4.2; N, 7.8; Br, 22.3%).

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