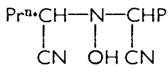
792. NN-*Di-(1-cyanoalkyl)hydroxylamines. Part I. The Preparation of* NN-*Di-(1-cyanoalkyl)hydroxylamines.*

By Masaichiro Masui, Yoshisuke Tsuda, and Chino Yijima.

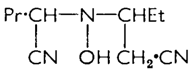
NN-Di-(1-cyanoalkyl)hydroxylamines were obtained as by-products in the reaction between aliphatic oximes and hydrogen cyanide. The mechanism of the reaction proceeding by way of an aliphatic nitrone (which is only recognised by physicochemical methods) was disclosed chemically by preparing the compounds from various starting materials and by various methods. The generality of the synthetic methods was shown by preparing several symmetrical and unsymmetrical compounds.

Oximes (II) of aldehydes and ketones (I) in general react with hydrogen cyanide to produce α-hydroxyamino-nitriles (III).[1] When this reaction was carried out with butyraldoxime (I; $R^1 = Pr^n$, $R^2 = H$) a small amount of a colourless substance, $C_{10}H_{17}N_3O$, m. p. 150—151°, was obtained as well as the hydroxyamino-nitrile (III; $R^1 = Pr^n$, $R^2 = H$). The infrared spectrum of the by-product showed bands at 2247 cm.$^{-1}$ (C≡N; in Nujol) and 3594 (OH; in CCl_4) or 3328 cm.$^{-1}$ (OH; in Nujol); the acetate did not show the latter band and developed the absorption peak at 1789 cm.$^{-1}$, assigned to OAc,[2] but had no absorption due to NAc.[2] Since the $\nu_{C=O}$ of the acetate is shifted to higher frequency than usual for enol acetates,[2] the absorption band is most likely to be attributable to N·OAc. The absorption band for δ_{NH} (1497 cm.$^{-1}$; in Nujol) [3] observed in the spectrum of the product (III), is also absent for these two compounds. The spectral evidence, combined with the existence of the absorption 1071, 829, and 816 cm.$^{-1}$ assigned to C–N–C,[3] and the polarographic behaviour which is markedly different from that of α-hydroxyaminovaleronitrile having a –CH(CN)·NH·OH grouping, present a decisive argument in favour of the structure $\begin{matrix}C\\C\end{matrix}\!\!>$N·OH (A) and (B), and exclude (C).



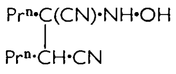
$\underset{CN}{Pr^n\cdot CH}-\underset{OH}{N}-\underset{CN}{CHPr^n}$

(A)



$\underset{CN}{Pr\cdot CH}-\underset{OH}{N}-\underset{CH_2\cdot CN}{CHEt}$

(B)



$\underset{Pr^n\cdot CH\cdot CN}{Pr^n\cdot C(CN)\cdot NH\cdot OH}$

(C)

The relatively simple infrared spectrum of the compound and the fact that iminodinitriles are obtained as by-products in the Strecker reaction [4] strongly favour the structure *NN*-di-(1-cyanobutyl)hydroxylamine (A).

Similar products having the formula of [2 × (III) — NH_3O] were also obtained on reaction of hydrogen cyanide with other aldoximes, and the production of such compounds appears to be general.

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[1] Miller and Plöch, *Ber.*, 1893, **26**, 1545; Münch, *Ber.*, 1896, **29**, 62; Hurd and Longfellow, *J. Org. Chem.*, 1951, **16**, 761.

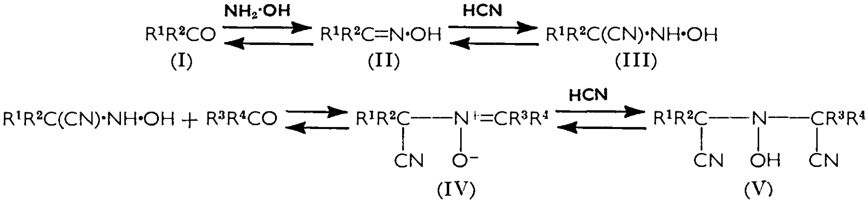
[2] Bellamy, " Infra-red Spectra of Complex Molecules," Methuen, London, 1958.

[3] Unpublished work.

[4] Erlenmeyer and Sigel, *Annalen*, 1875, **176**, 341; Stadnikoff, *Ber.*, 1908, **41**, 4364; 1911, **44**, 38.

Though the formation of these compounds might be considered as elimination of hydroxylamine from two molecules of α-hydroxyamino-nitrile (III), the annexed process seems more plausible. In this, part of the oxime (II) or/and the α-hydroxyamino-nitrile (III) is decomposed to give original carbonyl compound (I), which reacts with the hydroxyamino-nitrile to produce the nitrone (IV); then hydrogen cyanide adds to the nitrone, yielding the *NN*-di-(1-cyanoalkyl)hydroxylamine (V). In confirmation, α-hydroxyamino-nitriles decompose slowly in air at room temperature; when heated with water they decompose faster and completely, liberating hydrogen cyanide; when the decomposition is not allowed to proceed to completion and the solution is then cooled, the *NN*-di-(1-cyanoalkyl)hydroxylamine (V) is obtained. Further, if our mechanism is correct, addition of hydrogen cyanide to the nitrone (IV) should afford the same product (V), and any symmetrical and unsymmetrical compound (V) could be prepared by carrying out the reaction step by step.

Aliphatic nitrones, in contrast to alicyclic nitrones,[5b,6] considered only as intermediates of some reactions,[5] have been very little studied and their physical properties have not previously been described. When α-hydroxyaminovaleronitrile was mixed with butyraldehyde alone or in an organic solvent such as ethanol or chloroform an exothermic reaction occurred, with development of a new ultraviolet absorption peak ($\lambda_{max.}$ at 240 mμ in ethanol) and a new infrared absorption band ($\nu_{max.}$ at 1590 cm.$^{-1}$ in chloroform) very similar to those of alicyclic nitrones.[6] The intensities of absorption peaks are stable in acidic media. The mixture gives two fairly well-defined polarographic waves ($E_{\frac{1}{2}}$ *ca.* −0·76 and −1·04 v *vs.* S.C.E. at pH 2) which are constant for several days at room temperature. These findings are strongly in favour of the existence of a nitrone (IV) which is stable in acidic medium.[7] *NN*-Di-(1-cyanobutyl)hydroxylamine (V; $R^1 = R^3 = Pr^n$, $R^2 = R^4 = H$) was produced in good yield on addition of hydrogen cyanide to the reaction mixture, as expected.



$$\underset{\text{(I)}}{R^1R^2CO} \xrightleftharpoons{NH_2\cdot OH} \underset{\text{(II)}}{R^1R^2C{=}N\cdot OH} \xrightleftharpoons{HCN} \underset{\text{(III)}}{R^1R^2C(CN)\cdot NH\cdot OH}$$

$$R^1R^2C(CN)\cdot NH\cdot OH + R^3R^4CO \rightleftarrows \underset{\text{(IV)}}{R^1R^2\underset{CN}{C}-\underset{O^-}{N^+}{=}CR^3R^4} \xrightleftharpoons{HCN} \underset{\text{(V)}}{R^1R^2\underset{CN}{C}-\underset{OH}{N}-\underset{CN}{C}R^3R^4}$$

When potassium cyanide was added to the aqueous acidic reaction mixtures containing a nitrone (IV), the *NN*-di-(1-cyanoalkyl)hydroxylamine was obtained, as in the above procedure. According to the scheme proposed, reactions of COR^1R^2 with $NC{\cdot}CR^3R^4{\cdot}NH{\cdot}OH$ and of COR^3R^4 with $NC{\cdot}CR^1R^2{\cdot}NH{\cdot}OH$ might give different nitrones but should give identical final products (V), and this also was found experimentally (see Experimental section). Thus our reaction mechanism has been confirmed chemically.

Formation of the nitrone was not indicated for a mixture of acetoxime and α-hydroxylaminovaleronitrile by spectrophotometric or polarographic methods, but production of similar compounds by the above procedure and the fact that the physical methods are not sensitive within a few percent, led us to conclude that mixtures of ketones and α-hydroxyamino-nitriles can be employed as generators of aliphatic nitrones.

These methods have been applied to various α-hydroxyamino-nitriles and carbonyl compounds to afford various symmetrical and unsymmetrical *NN*-di-(1-cyanoalkyl)-hydroxylamines (V) and thus confirm the method as a general one.

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[5] (*a*) Johnson, Rogers, and Trappe, *J.*, 1956, 1093; (*b*) Brown, Marsden, Rogers, Tylor, and Wright, *Proc. Chem. Soc.*, 1960, 254; (*c*) LeBel and Whang, *J. Amer. Chem. Soc.*, 1959, **81**, 6334.

[6] Todd *et al.*, *J.*, 1959, 2094, 2102, 2105, 2109, 2117, 2123; *Proc. Chem. Soc.*, 1957, 97; Thesing and Mayer, *Ber.*, 1956, **89**, 2159; *Annalen*, 1957, **609**, 46; Delpierre and Lamchen, *Proc. Chem. Soc.*, 1960, 386.

[7] Details will be reported later.

EXPERIMENTAL

Infrared Absorption Spectra.—A Hitachi EPI-2 double-beam prism spectrophotometer with a sodium chloride cell was used for Nujol and $CHCl_3$ solutions; for the latter a cell with a 0·01 mm. light path was used with saturated solutions. A Koke DS-301 prism s.p.m. was used for CCl_4 solutions, with a light path of 20·0 mm. and concentrations $<10^{-3}$ mole/l.

Ultraviolet Absorption Spectra.—A Beckman DU type and a Hitachi automatic recording EPS-2 spectrophotometer were used.

Polarography.—Yanagimoto type PEL-3 apparatus with a GR-3 galvarecorder was used. Measurements were carried out at 25° ± 0·1°. Buffer solutions used were Britton and Robinson's containing 0·1M-potassium chloride. The pH's of the solutions were measured by a Toadempa model HM-5 pH meter with glass-saturated calomel electrodes.

Light petroleum had b. p. 62—80°. α-Hydroxyamino-nitriles were prepared from the oximes and hydrogen cyanide.[1]

Occurrence of NN-*Di*-(1-*cyanopropyl*)*hydroxylamine.*—When the filtrate from the reaction mixture of propionaldoxime and hydrogen cyanide after filtration from α-hydroxyaminobutyronitrile, or the coloured filtrate from the recrystallisation of crude α-hydroxyaminobutyronitrile, was left at room temperature for several days in air, needles were precipitated. Recrystallisation of these from water gave colourless NN-*di*-(1-*cyanopropyl*)*hydroxylamine*, m. p. 138·5—139° (Found: C, 57·4; H, 7·7; N, 25·1%; *M*, 167. $C_8H_{13}N_3O$ requires C, 57·5; H, 7·8; N, 25·1%; *M*, 167). Sometimes the compound was precipitated as a heavy powder fractionally when crude α-hydroxyaminobutyronitrile was recrystallised from ether.

Similarly obtained were NN-*di*-(1-*cyanobutyl*)*hydroxylamine*, m. p. 150—151° (from aqueous ethanol) (Found: C, 61·5; H, 8·8; N, 21·5. $C_{10}H_{17}N_3O$ requires C, 61·5; H, 8·8; N, 21·5%), and NN-*di*-(1-*cyanoheptyl*)*hydroxylamine*, m. p. 132—133·5° (from aqueous ethanol) (Found: C, 68·8; H, 10·6; N, 15·0%; *M* 277. $C_{16}H_{29}N_3O$ requires C, 68·8; H, 10·5; N, 15·0%; *M*, 279). These products are soluble in ethanol and ether, but not soluble in light petroleum or water, except the first one which is slightly soluble in water.

Preparative Method.—(*A*) α-Hydroxyaminovaleronitrile (0·3—0·5 g.) was dissolved in ethanol (several ml.), then water was added so that the ethanol content became 10—30%. The mixture was gently heated but as soon as it reached the b. p. it was cooled at once. Needles were precipitated from the solution; these were *NN*-di-(1-cyanobutyl)hydroxylamine, m. p. 150—151° (from aqueous ethanol) (see above). With too long heating, decomposition was complete and crystals were not obtained. *NN*-Di-(1-cyanopropyl)- and *NN*-di-(1-cyanoheptyl)-hydroxylamine were prepared similarly.

(*B*) To an approximately equimolar mixture of butyraldehyde and butyraldoxime a slight excess of hydrogen cyanide was added and the whole was kept at room temperature for a few days. Removal of excess of hydrogen cyanide in a stream of air and removal of the resulting crystals gave impure *NN*-di-(1-cyanobutyl)hydroxylamine; recrystallisation from aqueous ethanol gave the pure product, m. p. 150—151°.

(*C*) α-Hydroxyaminovaleronitrile (0·5 g.) and butyraldehyde (0·4 g.) were warmed in ethanol (5 ml.) to ~40°, though this was not always necessary, for about 1 hr. and then cooled and treated with hydrogen cyanide (1 ml.). After 12—48 hr. evaporation under reduced pressure left the hydroxylamine, m. p. 150—151° (from aqueous ethanol) (*ca.* 50%). From the mixture, without ethanol, treated as above, the same crystals were obtained. The other two hydroxylamines described above were prepared similarly, and also the following:

(i) NN-*Di*-(1-*cyanoethyl*)*hydroxylamine* was prepared from 1 mol. each of α-hydroxyaminopropionitrile and acetaldehyde, as prisms, m. p. 133—134° (from $CHCl_3$) (Found: C, 51·8; H, 6·6; N, 30·5. $C_6H_9N_3O$ requires C, 51·8; H, 6·5; N, 30·2%), very soluble in ethanol and water, but hardly soluble in ether.

(ii) N-(1-*Cyanobutyl*)-N-(1-*cyanopropyl*)*hydroxylamine* was prepared from (*a*) α-hydroxyaminovaleronitrile and propionaldehyde and (*b*) α-hydroxyaminobutyronitrile and butyraldehyde, as needles, m. p. 132—133° (from aqueous ethanol) (Found: C, 59·5; H, 8·3; N, 23·2. $C_9H_{15}N_3O$ requires C, 59·6; H, 8·3; N, 23·2%), soluble in ether and ethanol, but insoluble in light petroleum or water (identity was shown by mixed m. p.s and infrared absorption spectra).

(iii) N-(1-*Cyanobutyl*)-N-(1-*cyano-octyl*)*hydroxylamine*, from α-hydroxyaminovaleronitrile and octanal, formed needles, m. p. 120—121° (from hexane) (Found: C, 67·0; H, 10·1. $C_{14}H_{25}N_3O$ requires C, 66·9; H, 10·0%), soluble in ether and ethanol, but not in light petroleum or water.

(iv) N-(1-*Cyanobutyl*)-N-(1-*cyanodecyl*)*hydroxylamine* was prepared from 1-hydroxyaminovaleronitrile and decanal. Evaporation of the excess of hydrogen cyanide and ethanol left a wax that crystallised from hexane as needles, m. p. 117—118° (Found: C, 69·1; H, 10·5; N, 15·0. $C_{16}H_{29}N_3O$ requires C, 68·8; H, 10·5; N, 15·0%), soluble in ethanol, ether, and hot light petroleum, but not in water.

(v) Ethyl methyl ketone (*ca.* 2·5 ml.) was warmed with α-hydroxyaminovaleronitrile (0·5 g.) at 40—50°, then hydrogen cyanide (*ca.* 0·5 ml.) was added and the whole set aside for about a week at room temperature. Evaporation in a vacuum-desiccator left a solid, which was washed with light petroleum. This was very soluble in ether, so that it was dissolved in a very little ether and light petroleum was added to recrystallise it. N-(1-*Cyanobutyl*)-N-(1-*cyano*-1-*methylpropyl*)*hydroxylamine* formed rhombs, m. p. 55—56° (Found: C, 61·3; H, 8·7; N, 21·2. $C_{10}H_{17}N_3O$ requires C, 61·5; H, 8·8; N, 21·5%), very soluble in ether and ethanol, soluble in hot light petroleum, and hardly soluble in water.

(*D*) An ethanolic solution of butyraldehyde (0·4 g.) was added to α-hydroxyaminovaleronitrile (0·5 g.) in 50% aqueous ethanol (10—20 ml.) and warmed at about 40° for several minutes. 10% Sulphuric acid (5—6 ml.) and then an aqueous solution of potassium cyanide (0·4 g.) were added and the whole was set aside but was maintained acidic. If the solution became cloudy when the cyanide was added (precipitation of potassium sulphate), water was added to homogeneity. Colourless needles of the hydroxylamine appeared, usually in several hours, but as completion of the reaction was rather slow, it was better to filter them off only after several days and after addition of much water. From the filtrate more crystals appeared in another 2 or 3 weeks. The hydroxylamine crystals, washed with light petroleum, had m. p. 150—151° (from aqueous ethanol) (*ca.* 65%).

Similarly prepared were:

(i) N-(1-*Cyanobutyl*)-N-(1-*cyanoisobutyl*)*hydroxylamine* [from α-hydroxyaminovaleronitrile (0·5 g.), isobutyraldehyde (0·34 g.), 10% sulphuric acid (6 ml.), and potassium cyanide (0·4 g.) in aqueous ethanol], m. p. 129—130° (from aqueous ethanol) (Found: C, 61·3; H, 8·8; N, 21·3. $C_{10}H_{17}N_3O$ requires C, 61·5; H, 8·8; N, 21·5%), soluble in ethanol and ether but not in light petroleum or water.

(ii) N-(1-*Cyanodecyl*)-N-(1-*cyanoethyl*)*hydroxylamine* [from 1-hydroxyaminopropionitrile (0·76 g.), decanal (1·38 g.), etc.], m. p. 107—108° (from ether–light petroleum, then aqueous ethanol) (Found: C, 67·0; H, 9·9; N, 16·6. $C_{14}H_{25}ON_3$ requires C, 66·9; H, 10·0; N, 16·7%), soluble in ethanol and ether, hardly soluble in light petroleum or water. (This reaction was carried out in the presence of precipitated potassium sulphate; addition of water at this stage led to only the hydroxyamino-derivative.)

(iii) *N*-(1-Cyanobutyl)-*N*-(1-cyanodecyl)hydroxylamine, obtained from (*a*) α-hydroxyaminovaleronitrile (1 g.) and decanal (1·38 g.), or (*b*) 1-*hydroxyaminoundecanonitrile* [m. p. 89° (from ether–light petroleum) (Found: C, 66·6; H, 11·1; N, 14·1. $C_{11}H_{22}N_2O$ requires C, 66·6; H, 11·2; N, 14·1%)] (1·7 g.) and butyraldehyde (0·64 g.), with acid and cyanide, had m. p. and mixed m. p. 117—118° (from ether–light petroleum) and identical infrared spectra.

(iv) α-Hydroxyaminopropionitrile (0·76 g.), butyraldehyde (0·64 g.), 10% sulphuric acid (12 ml.) and potassium cyanide (0·8 g.) were set aside for several days then extracted with ether. The extract was dried (Na_2SO_4) and evaporated to give needles of N-(1-*cyanobutyl*)-N-(1-*cyanoethyl*)*hydroxylamine*, m. p. 122—123° (from aqueous ethanol) (Found: C, 57·9; H, 7·9; N, 25·1. $C_8H_{13}N_3O$ requires C, 57·5; H, 7·8; N, 25·1%).

(v) After reaction of (*a*) α-hydroxyaminovaleronitrile (0·5 g.), acetone (0·26 g.), 10% sulphuric acid (6 ml.), and potassium cyanide (0·4 g.), or (*b*) α-hydroxyaminoisobutyronitrile (0·44 g.), butyraldehyde (0·32 g.), 10% sulphuric acid (8 ml.), and potassium cyanide (0·6 g.), the ethanol and water were removed under reduced pressure until a white precipitate appeared, and then the mixture was extracted with ether. The ethereal solution gave N-(1-*cyanobutyl*)-N-(1-*cyano*-1-*methylethyl*)*hydroxylamine*, m. p. 88—89° (from ether–light petroleum) (Found: C, 60·0; H, 8·4; N, 23·4. $C_9H_{15}N_3O$ requires C, 59·6; H, 8·3; N, 23·2%), soluble in ethanol, ether, and hot water, but hardly soluble in cold water or light petroleum.

(vi) N-(1-*Cyanobutyl*)-*N*-(1-*cyanocyclohexyl*)*hydroxylamine* crystallised from the reaction mixture [α-hydroxyaminovaleronitrile (0·5 g.), cyclohexanone (0·46 g.), etc.] as needles, m. p. 132—132·5° (from aqueous ethanol) (Found: C, 65·0; H, 8·7; N, 18·8. $C_{12}H_{19}N_3O$ requires C, 65·1; H, 8·7; N, 19·0%).

O-*Acetyl*-NN-*di*-(1-*cyanobutyl*)*hydroxylamine*.—*NN*-Di-(1-cyanobutyl)hydroxylamine (0·5 g.)

was left in pyridine (5 ml.) and acetic anhydride (2 ml.) overnight, then poured into ice-water, and the precipitate was filtered off (0·5 g.); the O-*acetate* crystallised in needles, m. p. 50—51°, from ether–hexane (Found: C, 60·6; H, 7·9; N, 17·9. $C_{12}H_{19}N_3O_2$ requires C, 60·7; H, 8·1; N, 17·7%).

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SCHOOL OF PHARMACY, UNIVERSITY OF OSAKA,
OSAKA-FU, JAPAN.

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