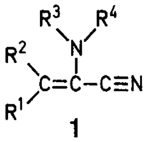
Synthesis of α-Iminonitriles (Imidoyl Cyanides)

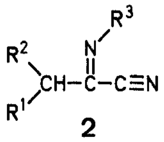
Norbert De Kimpe*, Roland Verhé, Laurent De Buyck, Jan Chys, Niceas Schamp

Laboratory of Organic Chemistry, Faculty of Agricultural Sciences, State University of Gent, Coupure 533, B-9000 Gent, Belgium

α-Cyanoenamines (2-amino-2-alkenenitriles, **1**) have been shown to be versatile synthons in organic chemistry. Thus, secondary α-cyanoenamines (**1**, $R^4 = H$) have been used as precursors of ketenimines[1] and their role as intermediates in the conversion of aldehydes into *N*-monosubstituted carboxamides has been investigated[2]. Tertiary α-cyanoenamines[3,4] (**1**, R^3 and $R^4 \neq H$) are converted into *vic*-diketones on treatment with organolithium compounds[4].



1



2

Secondary α-cyanoenamines (**1**, $R^4 = H$) may be synthesized from α-chloroaldimines and potassium cyanide in methanol; they were shown to undergo tautomeric transformation into α-iminonitriles (imidoyl cyanides, **2**) and the two isomers **1** and **2** could be isolated by preparative G.L.C.[5]. A prerequisite for the formation of **1** ($R^4 = H$) is the presence of two groups at C-3 (R^1 and $R^2 \neq H$). We have now developed

0039-7881/78/1232-0895 $ 03.00

a facile synthesis of aliphatic α-iminonitriles (**2**, R^1 = alkyl, R^2 = H, alkyl) which, although simple compounds, represent a new compound class. The only example mentioned in the literature is the unstable 2-cyano-5,5-dimethyl-1-pyrroline, obtained in low yield (9%) by dehydrogenation of 2-cyano-5,5-dimethylpyrrolidine with manganese dioxide in benzene[6].

Our method for the synthesis of aliphatic α-iminonitriles (2-alkyliminoalkanenitriles, **2**) consists of the conversion of aldehydes (**3**) into 2-alkylaminoalkanenitriles (**4**) via the hydrogen sulfite adducts[7], *N*-chlorination of **4** with *t*-butyl hypochlorite[8] in benzene at room temperature, and dehydrochlorination of the *N*-chloro compounds **5** with triethylamine or 1,4-diazabicyclo[2.2.2]octane (DABCO) in benzene at 50° without previous isolation.

Table 1. 2-Aminoalkanenitriles (**4**)

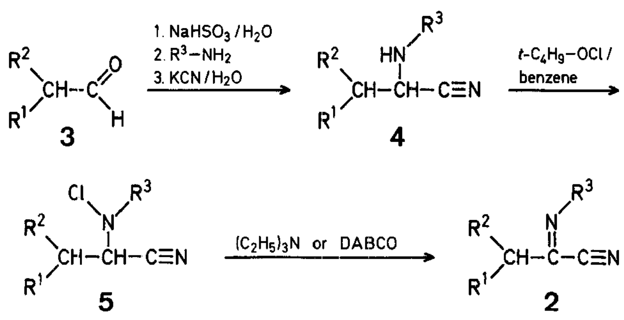
4	R^1	R^2	R^3	Yield[a] [%]	b.p./torr	Lit. b.p./torr
a	C_2H_5	H	i-C_3H_7	94	75–76°/12	86°/20[10]
b	n-C_3H_7	H	i-C_3H_7	85	68–72°/0.04	$C_9H_{18}N_2$ (154.3)[c]
c	CH_3	CH_3	i-C_3H_7	72	75–76°/14	74°/14[11]
d	CH_3	CH_3	c-C_6H_{11}	69[b]	95°/0.01	—[d]

[a] Yield of pure distilled product.

[b] Product **4d** contained 10% *N*-cyclohexyl-2-methylpropanimine, formed from **4d** by elimination of HCN. Compound **4d** solidified on standing; m.p. 42°.

[c] Compound **4b** gave satisfactory microanalyses (see footnote c in Table 2).

[d] No analytical data obtained (see footnote b).



The α-iminonitriles **2** are stable liquid compounds which do not undergo hydrogen shift to the corresponding α-cyanoenamines[9]. Even prolonged standing of compounds **2** in pyridine or triethylamine does not lead to the formation of detectable amounts of the isomeric α-cyanoenamines **1**.

By the available methods and by the method reported here it is now possible to prepare either one of the isomeric compounds **1** (R^4 = H) and **2** exclusively.

2-Isopropylimino-3-methylbutanenitrile (2c); Typical Procedure:

2-Isopropylamino-3-methylbutanenitrile (**4c**): A solution of sodium hydrogen sulfite (10.92 g, 0.105 mol) in water (50 ml) is added dropwise, with stirring, to isobutyraldehyde (7.2 g, 0.1 mol). Stirring is continued for 2 h at ambient temperature. Then, a solution of potassium cyanide (14.3 g, 0.22 mol) in water (25 ml) is added dropwise and stirring is continued for 5 h. The upper, organic layer is taken up in ether and the aqueous layer is extracted with ether (2 × 100 ml). The combined extracts are dried with potassium carbonate, the solution is filtered and evaporated, and the oily residue is distilled in vacuo; yield: 10.0 g (72%); b.p. 75–76°/13 torr.

Table 2. Synthesis of 2-Alkyliminoalkanenitriles (**2**)

2	R^1	R^2	R^3	Base used[a]	Yield[b] [%]	b.p./torr	Molecular formula[c]
a	C_2H_5	H	i-C_3H_7	triethylamine	72	49–53°/12	$C_8H_{14}N_2$ (138.2)
b	n-C_3H_7	H	i-C_3H_7	triethylamine	72	34–38°/12	$C_9H_{16}N_2$ (152.2)
c	CH_3	CH_3	i-C_3H_7	triethylamine	61	47°/12	$C_8H_{14}N_2$ (138.2)
				DABCO	73		
d	CH_3	CH_3	c-C_6H_{11}	triethylamine	73	67°/0.04[d]	$C_{11}H_{18}N_2$ (178.3)

[a] Reagents: 1.15 equiv *t*-butyl hypochlorite, 1.2 equiv base.

[b] Yield of pure distilled product.

[c] All compounds **2** gave satisfactory microanalyses: C, ±0.15; H, ±0.08; N, ±0.07.

[d] Known compound; Ref. [5].

Table 3. Spectral Data of 2-Alkyliminoalkanenitriles (**2**)

2	Mass Spectrum *m/e* (relative intensity)	I.R. (NaCl) [cm^{-1}] $\nu_{C=N}$	$\nu_{C\equiv N}$	^{1}H-N.M.R. (CCl_4/TMS) δ [ppm]
a	138 (M^+, 4), 123 (99), 110 (21), 96 (26), 95 (100), 81 (27), 70 (16), 69 (23), 68 (23), 54 (14), 43 (73), 42 (27), 41 (5), 40 (28), 39 (14)	1632	2220	0.98 (t, 3H, J = 6.5 Hz, $\underline{H}_3C-C-C-C{\equiv}N$); 1.20 [d, 6H, J = 6 Hz, $CH(C\underline{H}_3)_2$]; 1.74 (sextet, 2H, J = 6.5 Hz, $C\underline{H}_2-C-C{\equiv}N$); 2.46 (t, 2H, J = 6.5 Hz, $C\underline{H}_2-C{\equiv}N$); 3.94 (septet, 1H, J = 6 Hz, $NC\underline{H}$)
b	152 (M^+, 0.5), 151 (2), 137 (32), 123 (8), 110 (37), 109 (14), 95 (100), 82 (6), 81 (18), 70 (6), 69 (11), 68 (19), 55 (8), 54 (12), 44 (10), 43 (49), 42 (17), 41 (35), 40 (10), 39 (10)	1633	2220	0.96 (t, 3H, $C\underline{H}_3$); 1.2–1.9 [m, 4H, $CH(C\underline{H}_2)_2$]; 1.19 [d, 6H, J = 6 Hz, $CH(C\underline{H}_3)_2$]; 2.46 (t, 2H, J = 7 Hz, $C\underline{H}_2-C{\equiv}N$); 3.90 (septet, 1H, J = 6 Hz, $NC\underline{H}$)
c	138 (M^+, 9), 137 (5), 123 (100), 109 (11), 96 (15), 95 (14), 91 (12), 81 (11), 70 (12), 43 (66), 42 (17), 41 (20), 40 (46), 39 (8)	1634	2220	1.20 [d, 6H, J = 6 Hz, $N-CH(C\underline{H}_3)_2$]; 1.22 [d, 6H, J = 7.5 Hz, $(C\underline{H}_3)_2C-C{\equiv}N$]; 2.66 (septet, 1H, J = 7.5 Hz, $C\underline{H}-C{\equiv}N$); 3.93 (septet, 1H, J = 6 Hz, $N-C\underline{H}$)
d	Ref. [4]	Ref. [4]		Ref. [4]

2-Isopropylimino-3-methylbutanenitrile (**2c**): A solution of *t*-butyl hypochlorite[8] (8.7 g, 0.080 mol) in dry benzene (15 ml) is added dropwise to a stirred solution of 2-isopropylamino-3-methylbutanenitrile (**4c**; 10.0 g, 0.070 mol) in dry benzene (100 ml) at 0°. Stirring is continued for 1 h at 0°. Then, triethylamine (8.4 g, 0.084 mol; or the same amount of DABCO) is added, stirring is continued for 1 h at room temperature, and the mixture is then heated at 50° overnight with stirring. The precipitated triethylamine hydrochloride is filtered off, the solvent evaporated, and the residue distilled in vacuo; yield: 5.9 g (61 %); b.p. 47°/12 torr.

Received: June 7, 1978

---

* N. De Kimpe: „Aangesteld Navorser" of the Belgian „Nationaal Fonds voor Wetenschappelijk Onderzoek".

[1] N. De Kimpe, R. Verhé, L. De Buyck, J. Chys, N. Schamp, *J. Org. Chem.* **43**, 2670 (1978).

[2] N. De Kimpe, R. Verhé, L. De Buyck, J. Chys, N. Schamp, *Org. Prep. Proced. Int.* **10**, 149 (1978).

[3] J. Toye, L. Ghosez, *J. Am. Chem. Soc.* **97**, 2276 (1975).

[4] H. Ahlbrecht, D. Liesching, *Synthesis* **1977**, 495.

[5] N. De Kimpe, R. Verhé, L. De Buyck, H. Hasma, N. Schamp, *Tetrahedron* **32**, 3063 (1976).

[6] G. Dannhardt, W. Wiegrebe, *Arch. Pharm. (Weinheim)* **310**, 802 (1977).

[7] D. B. Luten, *J. Org. Chem.* **3**, 588 (1939).

[8] M. J. Mintz, C. Walling, *Org. Synth. Coll. Vol.* V, 184 (1973).

[9] G.L.C. analysis (SE 30 5%; 3 m; H_2) of the pure α-cyanoenamines **1** ($R^4 = H$) showed two compounds, i.e. **1** ($R^4 = H$) and **2**. As both isomers could be isolated by preparative G.L.C., the isomerism should in this case be referred to as desmotropism.

[10] A. H. Cook, S. F. Cox, *J. Chem. Soc.* **1949**, 2334.

[11] R. Tiollais, *Bull. Soc. Chim. Fr.* **1947**, 959.