Cyanoethylation of Some Alkanolamines

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Compounds possessing labile hydrogen atoms may add to acrylonitrile, forming molecules containing a cyanoethyl group[1]. Hydrogen donors may be amines, alcohols, or compounds in which hydrogen atoms are activated by electron-withdrawing groups.

Most amines add to acrylonitrile without the aid of a catalyst. Primary aliphatic amines react readily with acrylonitrile at low temperatures to give the 2-cyanoethyl derivative; at higher temperatures, the N,N-bis-[2-cyanoethyl] compound may be formed from some amines in the presence of excess acrylonitrile[1,2], but reaction is slow unless an acid catalyst is present[3,4,5]. Alcohols react with acrylonitrile in the presence of alkaline catalysts to form cyanoethyl ethers[1].

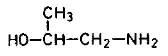
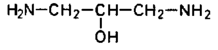
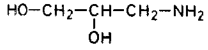
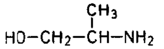
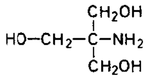
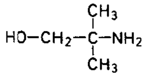
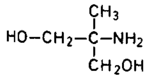
Hoffman and Jacobi[6] have prepared some N-(2-cyanoethyl)-alkanolamines by adding the parent alkanolamine to cooled acrylonitrile. The only disubstituted alkanolamine previously reported is N,N-bis-[2-cyanoethyl]-ethanolamine[2], but reaction conditions were not specifed, and no yield was quoted.

We have examined the reaction of various other alkanolamines with acrylonitrile under reflux or in an autoclave, and the mono- and bis-[2-cyanoethyl] derivatives obtained are described here (Table 1).

N,N-Bis-[2-cyanoethyl] derivatives were obtained from alkanolamines in which the amino group is attached to a methylene group. Introduction of alkyl groups onto the α-carbon atom progressively reduces the reactivity. Thus, compound **6** yields a mixture of mono- and bis-cyanoethyl derivatives, compounds **7**, **8**, and **9** give only mono-cyanoethyl derivatives. Compound **2**, which contains a methyl group on the β-carbon atom, was less reactive than ethanolamine.

The N,N-bis-cyanoethyl derivatives obtained could also be prepared by heating the reactants at 110–120° (bath temperature) in a stainless-steel autoclave (internal pressure, 1.7–2.4 atm) for 2 hr, but similar treatment did not effect

Table 1. Preparation of N-Cyanoethyl-alkanolamines

Reactants			Reaction conditions	Product Yield of cyano-ethyl compound		Appearance, m.p., and purification	Analytical data	*p*-Nitrobenzoates[b]		
Amine (0.02 mol)		Acrylo-nitrile (mol)		mono(%)	bis(%)			Appearance, m.p.	I.R. maxima cm^{-1} ν_{O-CO-}	ν_{N-CO-}
$HO-CH_2-CH_2-NH_2$	**1**	0.04	5–20°, 15 min.	94[2,6]	–	pale yellow oil	$C_5H_{10}N_2O$ calc. C 52.67 H 8.83 N 24.57 Mol. Wt. 114.2 found 52.30 9.04 24.66 Equiv. Wt. 117.8	colorless needles, m.p. 136.5–138°	1725	1635
		0.08	16 hr reflux	–	89[2]	pale yellow oil	$C_8H_{13}N_3O$ calc. C 57.48 H 7.84 N 25.13 Mol. Wt. 167.2 found 57.52 7.82 24.95 Equiv. Wt. 166.5	colorless needles, m.p. 78°	1725	–
 $HO-\overset{CH_3}{CH}-CH_2-NH_2$	**2**	0.04	5–20°, 15 min.	98	–	colorless needles, m.p. 52–53° (from ethanol/petroleum ether)	$C_6H_{12}N_2O$ calc. C 56.19 H 9.44 N 21.86 Mol. Wt. 128.2 found 56.29 9.50 21.79 Equiv. Wt. 128.6	cream needles, m.p. 92–99°	1725	1645
		0.08	16 hr reflux	mixture			calc. Mol. Wt. 181.2 found Equiv. Wt. 158.7			
		0.08	96 hr reflux	–	90	red oil	$C_9H_{15}N_3O$ calc. C 59.65 H 8.34 N 23.28 Mol. Wt. 181.2 found 59.28 8.51 22.62 Equiv. Wt. 188.1	colorless needles, m.p. 81–82°	1720	–
$HO-CH_2-CH_2-CH_2-NH_2$	**3**	0.04	5–20°, 15 min.	99	–	colorless oil	$C_6H_{12}N_2O$ calc. C 56.19 H 9.44 N 21.85 Mol. Wt. 128.2 found 55.90 9.46 21.46 Equiv. Wt. 131.5	colorless needles, m.p. 112–114°	1720	1645
		0.08	16 hr reflux	–	93	pale yellow oil	$C_9H_{15}N_3O$ calc. C 59.65 H 8.34 N 23.18 Mol. Wt. 181.2 found 59.19 8.46 22.74 Equiv. Wt. 176.7	oil	–	–
 $H_2N-CH_2-\underset{OH}{CH}-CH_2-NH_2$	**4**	0.08	5–20°, 15 min.	87	–	colorless needles, m.p. 50–50.5° (from acetone/petroleum ether)	$C_9H_{16}N_4O$ calc. C 55.05 H 8.22 N 28.54 Mol. Wt. 196.2 found 55.30 8.21 28.31 Equiv. Wt. 198.7	cream needles, m.p. 208–210°	1725	1640
		0.16	16 hr reflux	–	78	orange oil	$C_{15}H_{22}N_6O$ calc. C 59.58 H 7.34 N 27.80 Mol. Wt. 302.3 found 59.03 7.70 27.94 Equiv. Wt. 306.2	oil	–	–
 $HO-CH_2-\underset{OH}{CH}-CH_2-NH_2$	**5**	0.04	5–20°, 15 min.	98	–	pale yellow oil	$C_6H_{12}N_2O_2$ calc. C 50.0 H 8.4 N 19.4 Mol. Wt. 144.2 found 48.3 8.4 20.0 Equiv. Wt. 143.7	pale yellow plates, m.p. 191.5–192.5°	1740	1650
		0.08	16 hr reflux	–	96	pale yellow oil	$C_9H_{15}N_3O_2$ calc. C 54.8 H 7.7 N 21.3 Mol. Wt. 197.2 found 54.3 7.7 22.5 Equiv. Wt. 199.8	pale yellow needles, m.p. 109–110°	1720	–
 $HO-CH_2-\overset{CH_3}{CH}-NH_2$	**6**	0.04	5–20°, 15 min.	94	–	colorless oil	$C_6H_{12}N_2O$ calc. C 56.19 H 9.44 N 21.86 Mol. Wt. 128.2 found 55.76 9.61 21.42 Equiv. Wt. 124.8	cream needles, m.p. 159.5–160°	1730	1630
		0.08	16 hr reflux	mixture		pale yellow oil	$C_9H_{15}N_3O$ calc. Mol. Wt. 181.2 found Equiv. Wt. 166.2			
 $HO-CH_2-\underset{CH_2OH}{\overset{CH_2OH}{C}}-NH_2$	**7**	0.04[a]	16 hr reflux	94	–	colorless needles m.p. 81–84° (from ethanol/petroleum ether)	$C_7H_{14}N_2O_3$ calc. C 48.27 H 8.10 N 16.09 Mol. Wt. 174.1 found 48.36 8.05 16.10 Equiv. Wt. 175.2	colorless needles, m.p. 124–129°	1725	–
 $HO-CH_2-\underset{CH_3}{\overset{CH_3}{C}}-NH_2$	**8**	0.08	16 hr reflux	98	–	colorless needles, m.p. 62.5° (from ether)	$C_7H_{14}N_2O$ calc. C 59.13 H 9.92 N 19.71 Mol. Wt. 142.2 found 58.75 10.02 19.58 Equiv. Wt. 142.9	cream needles, m.p. 159–160°	1720	1645
 $HO-CH_2-\underset{CH_2OH}{\overset{CH_3}{C}}-NH_2$	**9**	0.08	16 hr reflux	100	–	colorless needles, m.p. 81.5° (from acetone/petroleum ether)	$C_7H_{14}N_2O_2$ calc. C 53.15 H 8.92 N 17.71 Mol. Wt. 158.2 found 53.00 8.81 17.39 Equiv. Wt. 160.2	colorless needles, m.p. 161–162°	1730	1645
$HO-CH_2-CH_2-NH-CH_2-CH_2-OH$	**10**	0.08	25°, 15 min.	95[6]	–	colorless oil	$C_7H_{14}N_2O_2$ calc. C 53.15 H 8.92 N 17.71 Mol. Wt. 158.2 found 52.88 8.77 17.61 Equiv. Wt. 164.6	cream needles, m.p. 120–121°	1725	–

[a] Refluxed with acrylonitrile (26.64 ml, 0.04 mol) in ethanol (100 ml).

[b] Combustion analyses of all 4-nitrobenzoates were satisfactory.

further cyanoethylation of compounds **6**–**9**. Attempts to obtain the bis-cyanoethyl derivatives of compounds **6**–**9** by adding acetic acid to refluxing reaction mixtures were unsuccessful.

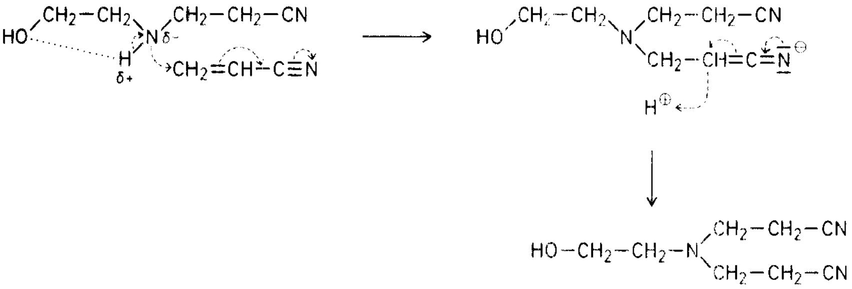
We also investigated the cyanoethylation of the isomeric butylamines in excess acrylonitrile (reflux, 16 hr). Products obtained had equivalent weights 132.9 (from *n*-), 128.6 (from *i*-), 130.3 (from *sec*-), and 128.3 (from *t*-butylamine), indicating that little if any bis-cyanoethylation had occurred (molecular weights of the mono- and bis-cyanoethyl derivatives are 126.2 and 179.3, respectively).

The greater reactivity of the unsubstituted alkanolamines is probably due to hydrogen bonding, enhancing the nucleophilicity of the tertiary nitrogen atom.

Melting points were determined using a Kofler micro hot stage and are not corrected. I.R. spectra were measured using a Perkin-model 237 spectrophotometer.

Preparation of N-(2-Cyanoethyl)-alkanolamines (Table 1):

The alkanolamine (0.02 mol) was added dropwise to redistilled acrylonitrile (0.04 or 0.08 mol), the temperature being maintained below 5° by external cooling (TCE/CO_2) as required. Subsequent reaction was conducted at 5–20° or under reflux. Reaction complete, polymerised acrylonitrile, if present, was removed by passing the mixture through a filter aid, then excess acrylonitrile was removed under reduced pressure using a rotary film evaporator to leave the crude products. Solid products were purified by recrystallisation; attempts to purify liquid products by distillation resulted in decomposition.



The lower reactivity of the substituted alkanolamines is probably due to steric hindrance of this hydrogen bonding.

Attempts to purify the cyanoethylated alkanolamines by distillation under reduced pressure were unsuccessful. All the compounds examined behaved like N,N-bis-[2-cyanoethyl]-ethanolamine[2], decomposing into acrylonitrile and the starting alkanolamine.

Structures of the products obtained were confirmed by elemental and I.R. analyses, by equivalent-weight determination involving titration with perchloric acid in acetic acid, and by preparing 4-nitrobenzoyl derivatives. The presence of residual hydroxy groups in the cyanoethylated alkanolamines was established by the presence of the O—CO-band (*ν*, 1635 cm^{-1}) in the I.R. spectra of their 4-nitrobenzoates; the presence of NH groups in the monocyanoethyl derivatives was shown by the N—CO— (*ν*, 1725 cm^{-1}) absorption of the 4-nitrobenzoate. The absence of N—CO— bands in the I.R. spectra of the 4-nitrobenzoates of the bis-[2-cyanoethyl] compounds eliminated the possibility that the OH group had been cyanoethylated. Further confirmation was obtained from the failure to cyanoethylate propane-1,2-diol in excess boiling acrylonitrile.

The proportions of mono- and bis-[2-cyanoethyl]-alkanolamine and of non-basic materials in the products can be obtained by titrating with perchloric acid before and after acetylation of the sample[7]. On acetylation the monocyanoethyl derivative, being a secondary amine, is acetylated and is insufficiently basic to titrate. A typical sample of N,N-bis-[2-cyanoethyl]-2,3-dihydroxypropylamine of apparent molecular weight 200.2 (197.2 required) was calculated to contain bis-[2-cyanoethyl] compound (97.7%), mono-cyanoethyl derivative (0.6%), and non-basic material (1.7%).

4-Nitrobenzoates were prepared conventionally, but only oils were obtained from N,N-bis-[2-cyanoethyl]-3-hydroxypropylamine and from 1,3-bis-[2-cyanoethylamino]-2-propanol; attempted preparation of 3,5-dinitrobenzoates of these compounds also gave oils. N-(2-Cyanoethyl)-N-(tris-[hydroxymethyl]-methyl)-amine afforded only a tris-[4-nitrobenzoate], which contained no N—CO-absorption but a small NH peak in the I.R. spectrum, suggesting that the amine hydrogen had not reacted.

The reaction of N-(tris-[hydroxymethyl]-methyl)-amine (**7**), which was almost insoluble in acrylonitrile, was accomplished by using ethanol as solvent. No further cyanoethylation occurred when the monocyanoethyl derivative was dissolved in boiling acrylonitrile for 16 hr.

Preparation of 4-Nitrobenzoates

4-Nitrobenzoates (Table 1) were prepared by shaking a mixture of the cyanoethyl alkanolamine (0.01 mol) with 4-nitrobenzoyl chloride (0.02 mol per replaceable hydrogen atom) in pyridine (100 ml) for 16 hr. The mixture was then added to water (500 ml) and extracted with chloroform (3 × 100 ml). The combined extracts were washed successively with water (100 ml), aqueous sodium carbonate (2 × 100 ml), dilute hydrochloric acid (3 × 100 ml), and water (100 ml), then dried ($MgSO_4$) and evaporated under reduced pressure (60°/15 mm Hg.). The crude product was crystallised from aceton (charcoal)/light petroleum (b.p. 60°–80°).

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