Dehydrogenation of Cyanamides. An Approach to Cyanimides and Carbonyl Compounds

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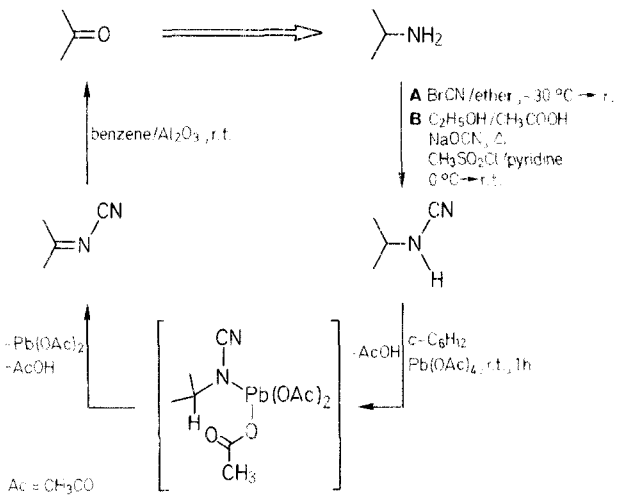
Treatment of cyanamides with lead tetraacetate afforded the corresponding cyanimides in high yields. As these compounds can be readily and efficiently hydrolysed to carbonyl compounds; this sequence of reactions allows the synthesis of aldehydes and ketones from primary amines.

Cyanimides, although relatively unknown compounds, seem to be attractive intermediates in organic synthesis. To our knowledge, these compounds have only been obtained by addition of cyanogen azide to olefins[1].

We describe here a convenient synthesis of several cyanimides from the corresponding amines[2,3]. This method involves preparation of cyanamide derivatives[4,5] (see Table 1) followed by dehydrogenation with lead tetraacetate (see Table 2). Although the cyanimides are easily hydrolysed to the corresponding carbonyl compounds in high yields (see Table 3), in general, in the examples described here it was possible to isolate them by quick rotative chromatography, except for the cyanimide corresponding to **1b**, which was hydrolysed to **1c** under the reaction conditions and could not be isolated. The application of this sequence of reactions allows the synthesis of aldehydes and ketones from primary amines (see Scheme).



Various synthetically useful procedures are available for the conversion of primary amines into aldehydes and ketones[6] although, in general, poor yields are obtained for aliphatic amines. Although three steps are involved in our method, the yields are high, affording the cyanimides and the carbonyl compounds in a high state of purity.

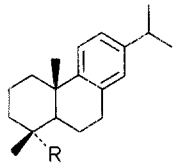
Dehydroabietylamine (**1a**) was purchased (Aldrich). The steroidal amines **2a** (3α- and 3β-), **3a**, and **5a** were prepared by reduction of the corresponding oximes with lithium aluminum hydride[2] and **6a** (20*R*- and 20*S*-) with sodium-*n*-propanol[3] and were used without purification in the syntheses of the cyanamides **2b**, **2c**, **3b**, **5b**, and **6b** and **6c**, respectively. The cyanamide **4a** was obtained by pyrolysis of 3β-acetoxy-5α,5α-*N*-cyanoepiminocholestane[7].

TLC analyses were conducted on silica gel plates (Merck 60). Column chromatography on Merck silica gel (0.063–0.2 mm) and circular layers of 1 mm of silica gel (Merck 60 PF 254) on a Harrison

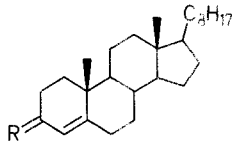
Table 1. Conversion of Amines to Cyanamides.

Substrate	Method: Yield [%]	Products	m.p. [°C] (solvent)	$[\alpha]_D$ (conc.)	IR ($CHCl_3$) $\nu_{NH,CN}$ cm^{-1}	MS (70 eV) *m/e* (rel.int. %)	^{1}H-NMR ($CDCl_3$/TMS) δ [ppm]
1a	A: 64 B: 95	**1b**	137–138 (ethyl acetate/*n*-hexane)	+39 (0.208)	3400, 2220	310 (M^+, 14) 295 ($M^+ - CH_3$, 100)	0.94 (s, 3H, 4-CH_3); 1.21 (s, 3H, 10-CH_3); 1.22 (d, 6H, J = 7 Hz, 15-2CH_3); 6.90 (br s, 1H, 14-H); 6.99 (dd, 1H, J = 8.1 and 2.0 Hz, 12-H); 7.01 (d, 1H, J = 8.1 Hz, 11-H)
2a	B: 8	**2b** and	137–139 (*n*-pentane)	+84 (0.114)	3390, 2210	410.3672 ($C_{28}H_{46}N_2$ = 410.3661, 14) 368.3436 ($C_{27}H_{44}$ = 368.3443, 100)	0.65 (s, 3H, 13-CH_3); 0.83 (d, 6H, J = 6.7 Hz, 25-2CH_3); 0.86 (d, 3H, J = 7.2 Hz, 20-CH_3); 0.96 (s, 3H, 10-CH_3); 3.33 (m, 1H, N–H); 3.66 (m, 1H, 3β-H); 5.29 (d, 1H, J = 5 Hz, 4-H)
	34	**2c**	153–155 (acetone/*n*-pentane)	+28 (0.224)	3380, 2210	410.3672 ($C_{28}H_{46}N_2$ = 410.3661, 100) 368.3463 ($C_{27}H_{44}$ = 368.3443, 85)	0.63 (s, 3H, 13-CH_3); 0.82 (d, 6H, J = 6.7 Hz, 25-2CH_3); 0.86 (d, 3H, J = 7.0 Hz, 20-CH_3); 1.00 (s, 3H, 10-CH_3); 3.64 (m, 1H, 3α-H); 5.17 (s, 1H, 4-H)
3a	A: 55 B: 50	**3b**	130–132 (methanol)	−25 (0.300)	3390, 2200	472.5958 ($C_{30}H_{52}N_2O_2$ = 472.4029, 48) 410.3700 ($C_{28}H_{46}N_2$ = 410.3547, 100)	0.68 (s, 3H, 10-CH_3); 0.85 (d, 6H, J = 6.7 Hz, 25-2CH_3); 0.89 (d, 3H, J = 7.0 Hz, 20-CH_3); 0.96 (s, 3H, 13-CH_3); 3.36 (s, 3H, OCH_3); 3.53 (m, 1H, 3-α-H); 4.65 (s, 2H, OCH_2O)
		4a	176–177 (acetone/*n*-hexane)	−157 (0.146)	3390, 2205	408 ($M^+ - CH_3COOH$, 45) 366 ($M^+ - CH_3COOH - NH_2CN$, 100)	0.68 (s, 3H, 13-CH_3); 0.86 (d, 6H, J = 7.0 Hz, 25-2CH_3); 0.93 (d, 3H, J = 7.0 Hz, 20-CH_3); 1.02 (s, 3H, 10-CH_3); 2.03 (s, 3H, CH_3CO_2); 3.47 (m, 1H, 7β-H); 4.65 (m, 1H, 3α-H); 5.58 (m, 1H, 6-H)
5a	B: 96	**5b**	168–172 (methanol)	−77 (0.312)	3390, 2220	343.2377 ($C_{21}H_{31}N_2O_2$ = 343.2386, 1) 296.2228 ($C_{20}H_{28}N_2$ = 296.2253, 100)	0.77 (s, 3H, 13-CH_3); 1.02 (s, 3H, 10-CH_3); 3.03 (m, 1H, 17-H); 3.37 (s, 3H, O–CH_3); 3.45 (m, 1H, 3α-H); 4.69 (s, 2H, OCH_2O); 5.34 (m, 1H, 6-H)
6a	B: 33	**6b** and	167–169 (methanol)	−40 (0.196)	3390, 2220	371 ($M^+ - CH_3$, 1) 324 ($M^+ - CH_3OCH_2OH$, 100)	0.68 (s, 3H, 13-CH_3); 1.00 (s, 3H, 10-CH_3); 1.33 (d, 3H, J = 6.5 Hz, 20-CH_3); 3.09 (m, 1H, 20-H); 3.37 (s, 3H, OCH_3); 3.40 (m, 1H, 3α-H); 4.66 (s, 2H, OCH_2O); 5.33 (m 1H, 6-H)
	32	**6c**	153–155 (methanol)	−58 (0.268)	3400, 2215	386 (M^+, 1) 324 ($M^+ - CH_3OCH_2OH$, 100)	0.75 (s, 3H, 13-CH_3); 1.01 (s, 3H 10-CH_3); 1.25 (d, 3H, J = 6.4 Hz 20-CH_3); 3.16 (m, 1H, 20-H); 3.37 (s, 3H, OCH_3); 3.42 (m, 1H, 3α H); 4.68 (s, 2H, OCH_2O); 5.34 (m 1H, 6-H)

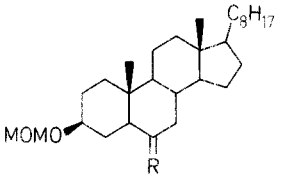
chromatotron were used for quick chromatography. Physical constants and spectra were determined using the following instrumentation. Melting points (uncorrected): Kofler hot-stage. Optical rotations: Perkin Elmer 141 polarimeter ($CHCl_3$). IR spectra: Perkin Elmer 257 or 681 spectrophotometer. UV spectra: Perkin Elmer 550 SE spectrophotometer. MS spectra: Hewlett Packard 5930 A or VG Micromass ZAB-2F spectrometer. ^{1}H-NMR spectra: Perkin Elmer R-32 (90 MHz) or Bruker WP 200 SY (200 MHz) spectrometer.



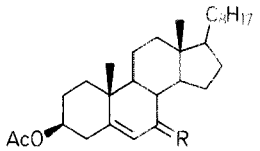
1a R = CH_2NH_2
1b R = CH_2NHCN
1c R = CHO



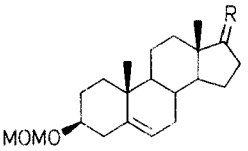
2a R = 3β-NH_2, H
2b R = 3α-NHCN, 3β-H
2c R = 3β-NHCN, 3α-H
2d R = N—CN
2e R = O



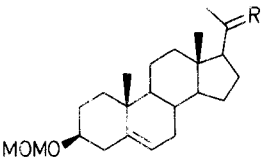
3a R = 6β-NH_2, 6α-H
3b R = 6β-NHCN, 6α-H
3c R = N—CN
3d R = O



4a R = 7α-NHCN, 7β-H
4b R = N—CN
4c R = O



5a R = 17β-NH_2, 17α-H
5b R = 17β-NHCN, 17α-H
5c R = N—CN
5d R = O



6a R = 20(S)-NH_2, H
6b R = 20-(S)-NHCN, H
6c R = 20-(R)-NHCN, H
6d R = N—CN
6e R = O

Synthesis of the Cyanamides; General Procedure:

Method A[4]: To a stirred solution of the amine (1 mmol) in dry ether (15 ml), at −30 °C, cyanogen bromide (1.1 mmol) is added and the stirring continued at −30 °C for 30 min. The mixture is then allowed to warm to room temperature and stirred for 2 h. The solution is poured into hydrochloric acid (5%) and extracted with chloroform (3 × 25 ml). The combined organic extracts are washed with aqueous sodium hydrogencarbonate and water and concentrated under reduced pressure. The residue is purified by column chromatography on silica gel (eluants: *n*-hexane/ethyl acetate).

Table 2. Conversion of Cyanamides to Cyanimides.

Substrate	Product	Yield [%]	m.p. [°C] (solvent)	$[\alpha]_D$ (conc.)	IR ($CHCl_3$) $\nu_{CN,C=N}$ cm^{-1}	UV (EtOH) λ_{max} nm (ε)	MS (70 eV) *m/e* (rel. int. %)	^{1}H-NMR ($CDCl_3$/TMS) δ [ppm]
2c	**2d**[a]	87	156–158 (*n*-pentane)	+157 (0.150)	2180 1600, 1560	281 (24956)	408.3559 ($C_{28}H_{44}N_2$ = 408.3502, 89) 295.2151 ($C_{20}H_{27}N_2$ = 295.2173, 100)	0.71 (s, 3H, 13-CH_3); 0.87 (d, 6H, *J* = 6.9 Hz, 25-2CH_3); 0.91 (d, 3H, *J* = 6.5 Hz, 20-CH_3); 1.15, 1.19 (s, s, 3H, 10-CH_3); 6.02, 6.47 (s, s, 1H, 4-H)
3b	**3c**	80	100–102 (methanol)		2195 1610	222 (Sh.)	470.3822 ($C_{30}H_{50}N_2O_2$ = 470.3869, 23) 410.3678 ($C_{28}H_{46}N_2$ = 410.3659, 100)	0.66 (s, 3H, 13-CH_3); 0.75 (s, 3H, 10-CH_3); 0.86 (d, 6H, *J* = 6.9 Hz, 25-2CH_3); 0.91 (d, 3H, *J* = 6.4 Hz, 20-CH_3); 3.36 (s, 3H, OCH_3); 3.48 (m, 1H, 3α-H); 4.67 (s, 2H, OCH_2O)
4a	**4b**	90	140–142 (*n*-hexane)	−200 (0.220)	2180 1620, 1560	275 (19357)	466.3575 ($C_{30}H_{46}N_2O_2$ = 466.3559, 1) 406.3313 ($C_{28}H_{42}N_2$ = 406.3348, 100)	0.69 (s, 3H, 13-CH_3); 0.85 (d, 6H, *J* = 6.5 Hz, 25-2CH_3); 0.92 (d, 3H, *J* = 6.4 Hz, 20-CH_3); 1.19 (s, 3H, 10-CH_3); 2.05 (s, 3H, CH_3CO_2); 4.71 (m, 1H, 3α-H); 6.46 (m, 1H, 6-H)
5b	**5c**	94	152–153 (*n*-hexane)	−40 (0.204)	2195 1630	220 (Sh.)	341.2213 ($C_{21}H_{29}N_2O_2$ = 341.2229, 1) 294.2058 ($C_{20}H_{26}N_2$ = 294.2096, 100)	0.98 (s, 3H, 13-CH_3); 1.04 (s, 3H, 10-CH_3); 3.37 (s, 3H, OCH_3); 3.43 (m, 1H, 3α-H); 4.69 (s, 2H, OCH_2O); 5.36 (m, 1H, 6-H)
6b	**6d**	94	118–120 (*n*-pentane)	+14 (0.142)	2190 1600	223 (8533)	384.2903 ($C_{24}H_{36}N_2O_2$ = 384.2775, 1) 322.2355 ($C_{22}H_{30}N_2$ = 322.2406, 100)	0.65 (s, 3H, 13-CH_3); 1.04 (s, 3H, 10-CH_3); 2.40 (s, 3H, 20-CH_3); 3.37 (s, 3H, OCH_3); 3.40 (m, 1H, 3α-H); 4.69 (s, 2H, OCH_2O); 5.35 (m, 1H, 6-H)

[a] Mixture of *E* and *Z* cyanimide isomers as established by ^{1}H-NMR.

Table 3. Conversion of Cyanimides to Ketones.

Substrate	Product	Yield [%]	m.p. [°C] (solvent)	Lit. m.p. [°C]	$[\alpha]_D$ (conc.)	Lit. $[\alpha]_D$	IR ($CHCl_3$) $\nu_{C=O}$ cm^{-1}	MS (70 eV) *m/e* (rel. int. %)	^{1}H-NMR ($CDCl_3$/TMS) δ [ppm]
1b	**1c**	90	85–87[a] (sublimated)	53-5[8]	+69[a] (0.196)	+52[8]	1715	284.2126 ($C_{20}H_{28}O$ = 284.2140, 42) 241.1924 ($C_{18}H_{25}$ = 241.1956, 100)	1.16 (s, 3H, 4-CH_3); 1.22 (d, 6H, *J* = 6.7 Hz, 15-2CH_3); 1.23 (s, 3H, 10-CH_3); 6.89 (bs, 1H, 14-H); 7.01 (dd, 1H, *J* = 8.1 Hz and 1.9 Hz, 12-H); 7.18 (d, 1H, *J* = 8.1 Hz, 11-H); 9.26 (s, 1H, CHO)
2d	**2e**	88	79–81 (methanol)	82[9]	+88 (0.210)	+92[9]			
3c	**3d**	95	105–107 (methanol)		−12 (0.260)		1695	446 (M^+, 17) 386 ($M^+ - CH_3OCH_2OH$, 100)	0.66 (s, 3H, 13-CH_3); 0.75 (s, 3H, 10-CH_3); 0.86 (d, 6H, *J* = 6.5 Hz, 25-2CH_3); 0.91 (d, 3H, *J* = 6.4 Hz, 20-CH_3); 3.36 (s, 3H, OCH_3); 3.48 (m, 1H, 3α-H); 4.68 (s, 2H, OCH_2O)
4b	**4c**	89	158–160 (methanol)	157-9[10]	−101 (0.218)	−103[10]			
5c	**5d**	97	133–134 (methanol)		−5 (0.206)		1725	270 ($M^+ - CH_3OCH_2OH$, 100)	0.89 (s, 3H, 13-CH_3); 1.04 (s, 3H, 10-CH_3); 3.38 (s, 3H, OCH_3); 3.43 (m, 1H, 3α-H); 4.69 (s, 2H, OCH_2O); 5.39 (m, 1H, 6-H)
6d	**6e**	96	109–111 (methanol)		+13 (0.254)		1690	298 ($M^+ - CH_3OCH_2OH$, 100)	0.63 (s, 3H, 13-CH_3); 1.01 (s, 3H, 10-CH_3); 2.12 (s, 3H, 20-CH_3); 3.37 (s, 3H, OCH_3); 3.43 (m, 1H, 3α-H); 4.69 (s, 2H, OCH_2O); 5.35 (m, 1H, 6-H)

[a] The previously reported[7] physical constants are erroneous.

Method B[5]: To a stirred solution of the amine (1 mmol) in ethanol (45 ml), water (1.35 ml) and acetic acid (0.12 ml), sodium cyanate (1.5 mmol) is added and the mixture refluxed for 1.5 h, then poured into brine and extracted with ethyl acetate (3 × 25 ml). The organic phase is washed with sodium hydrogencarbonate and water and concentrated under reduced pressure. To the crude residue in pyridine (5 ml) at 0 °C, methanesulfonyl chloride (0.24 ml) is added. After stirring an additional 30 min at 0 °C, the mixture is allowed to warm up to room temperature and stirred for 1 h. The mixture is then quenched by the addition of water (100 ml) and extracted with chloroform (3 × 25 ml). The organic extracts are treated and purified as described previously for Method A.

Dehydrogenation of the Cyanamides; General Procedure:
To a stirred solution of the cyanamide (1 mmol) in cyclohexane (50 ml) or in cyclohexane/dichloromethane, lead tetraacetate (dried on sodium hydroxide, 2 mmol) is added, and the mixture stirred at room temperature for 1 h and then poured into water and extracted with chloroform (3 × 25 ml). Rotative chromatography (Harrison-chromatotron) of the residue gives the corresponding cyanimide. Alternatively, the crude material could be used in the next reaction without purification.

Hydrolysis of the Cyanimides; General Procedure:
A solution of the cyanimide in benzene is absorbed on neutral alumina (grade III) overnight. Ethyl acetate is then added, the mixture filtered, and the organic extracts evaporated under vacuum. The resulting aldehyde or ketone is purified by column chromatography on silica gel (results in Table 3).

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