Mono-*N*-alkylation of α-Aminoacetonitriles. A Novel Route to Unsymmetrical Secondary Amines

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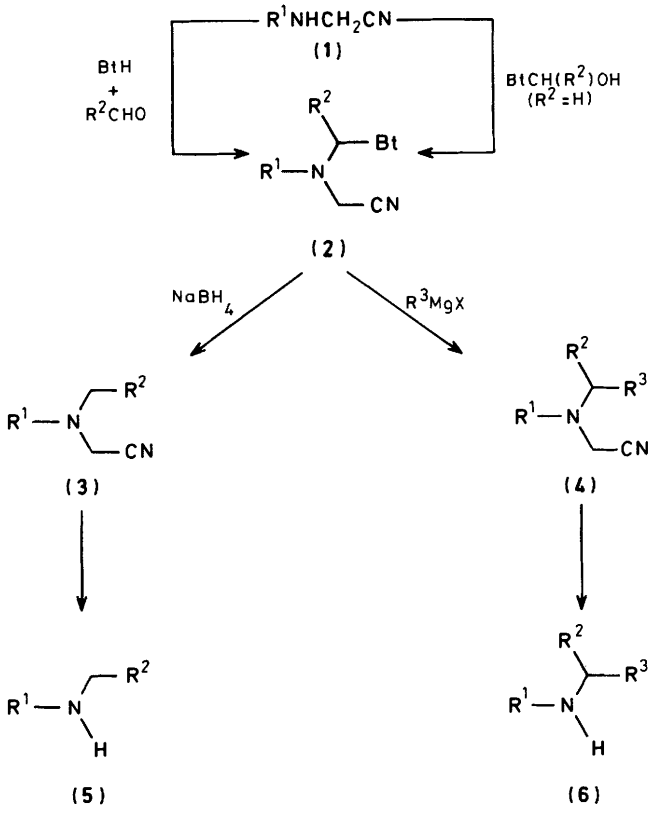
Mannich-type condensation products of an aldehyde with an α-aminoacetonitrile and benzotriazole are treated with sodium borohydride or with a Grignard reagent to give unsymmetrical *N,N*-dialkylaminoacetonitriles, which, on decyanomethylation, provide unsymmetrical secondary amines.

α-Aminonitriles are easily accessible and versatile compounds; they can be prepared from a great many primary or secondary amines.[1] Recently, benzotriazole-assisted cyanomethylation has been found to be advantageous for some more problematic amino compounds.[2] α-Aminonitriles also exhibit versatile chemical reactivity and have been used as starting compounds for various syntheses. The classical transformations usually retain the amino and cyanide structural elements; many involve additions at the cyanide group, *e.g.* of hydrogen,[3] water,[4] hydrogen sulphide,[5] carbon disulphide[6] *etc.* Application of α-dialkylaminonitriles as acyl anion equivalents was first suggested by Stork[7] and remains an attractive synthetic method.[8,9a] In these reactions, both the dialkylamino and the nitrile group serve as activating-protecting groups and are usually removed at the end of the synthesis. Elimination only of the nitrile group may give enamines[9] or, *e.g.* when a β-hydroxy group is present, α-amino ketones.[10] Substitution of CN by organometallic reagents[11] or by a hydrogen atom[12] affords a potentially versatile route to secondary or tertiary amines. Such substitutions of CN by carbanions are applicable both to *N,N*-disubstituted (Bruylants reaction)[11a,b] and to *N*-monosubstituted aminonitriles.[11c] However, side reactions, such as hydride transfer,[13c,d] additions at the nitrile function,[13a,e,f] or dimerization,[13b] frequently cause difficulties. Generally, dialkylaminoacetonitriles (*i.e.* $R^1R^2NCH_2CN$) react mainly *via* addition, while the α-substituted derivatives [$R^1R^2NCH(R^3)CN$] give displacement products.[13f]

Recently benzotriazole has been found in our laboratory to be a highly effective auxiliary group in various *N*-alkylations,[14] including selective *N*-monoalkylations of secondary amines.[14a] We now report that these benzotriazole-assisted alkylation techniques can be applied to the selective *N*-monoalkylation of α-alkylaminoacetonitriles, providing a convenient method for preparation of unsymmetrical *N,N*-dialkylaminoacetonitriles (**3**) and (**4**). We have also found that the cyanomethyl group in (**3**) or (**4**) can be cleaved easily with copper(II) sulphate[15] to provide a novel approach for the preparation of unsymmetrical secondary amines (**5**) and (**6**) (Scheme).

Condensations of *N*-alkylaminoacetonitriles with aldehydes and benzotriazole were carried out in benzene solution at 20 °C or at reflux, depending on the aldehyde component used (see Experimental). The water formed was removed by azeotropic distillation. The crude products were isolated in each case in quantitative yields and gave clean ^1H and ^{13}C NMR spectra. In the case of *N*-(primary alkyl) substituted aminoacetonitriles (exemplified by *N*-octylaminoacetonitrile), virtually any aldehyde component can be used in the reaction [Table 1, adducts (**2a–f**)]. However, with the α-branched substituent cyclohexyl, only formaldehyde could be successfully applied, obviously owing to steric hindrance. The R^1 = aryl cases have not been investigated since secondary amines of type ArNHR can easily be prepared by other methods.[14b]



Scheme. Bt = benzotriazolyl.

Adducts (**2a**) and (**2f**) are solid and were fully characterized. The $R^2 \neq H$ derivatives (**2b–e**) are oils, which were characterized by their ^1H and ^{13}C NMR spectra and were used without further purification because they are unstable on attempted chromatographic purification and did not give a molecular ion peak in the electron impact (EI) mass spectra. In the ^1H and ^{13}C NMR spectra of adducts (**2**) (Tables 2 and 3) the known[16] 1- to 2-aminoalkylbenzotriazole isomerization is apparent. In their ^1H NMR spectra, the benzotriazole adducts with R^2 = H each show for CH_2Bt and for CH_2CN two singlets at δ 5.50–6.00 and at δ 3.60–3.64, respectively, together with a triplet for the α-CH_2 of R^1 (R^1 = octyl) at δ 2.77. However, for the adducts with $R^2 \neq H$, both the CH_2CN and the α-CH_2 of the octyl group appear as multiplets, owing to the chirality of each of the benzotriazol-1-yl and -2-yl isomers.

Displacement of the benzotriazole moiety in adducts (**2**) with hydride ($NaBH_4$) or a carbanion (R^3MgHal), performed in a manner similar to that previously reported for the analogous secondary amine adducts,[14a] resulted in the formation of unsymmetrical dialkylaminoacetonitriles (**3**) and (**4**), respectively. As discussed above, α-dialkylaminonitriles react with hydride[12] or Grignard reagents[11] usually by a mixture of displacement of, and addition to, the nitrile group. Under our conditions, no, or only minor, formation of side product tertiary amines was observed. Thus, treatment of (**2a**) and (**2f**) with sodium borohydride in refluxing tetrahydrofuran gave small amounts (6–8%) of the respective *N*,*N*-dimethylalkylamines as side products. However, when the same reactions were carried out at room temperature (20 °C) no side products were detected with either of the adducts (**2a**) or (**2f**), and the respective monomethylated alkylaminoacetonitriles were obtained in good yields.

Further, treatment of either of the above adducts with Grignard reagents provided mainly the desired dialkylaminoacetonitriles (**4**). However, owing to the known two-fold reactivity of the dialkylaminonitriles, both the substitution and the addition type of side products was observed in a few cases. Thus, reaction of adduct (**2a**) with the highly reactive benzylmagnesium chloride under the conditions generally employed, gave, in addition to the major product (**4b**), 15% of the tertiary amine [*i.e.* *N*,*N*-bis-(β-phenylethyl)octylamine] as a side product by nucleophilic displacement of the cyanide. In contrast, the reaction of (**2a**) with a large excess of phenylmagnesium bromide gave the addition product, α-(*N*-octyl-*N*-benzylamino)acetophenone, in 70% yield.

Unsymmetrical dialkylaminoacetonitriles of types (**3**) and (**4**) are relatively rare in the literature[17] because of the inaccessibility of the parent secondary amines; most of the synthesized derivatives are new compounds (Table 4). The NMR spectra are listed in Tables 5 and 6.

Cleavage of both the N–C_α and the C_α–CN bonds in α-

Table 1. Preparation of *N*-alkyl-*N*-(1-benzotriazolylalkyl)aminoacetonitriles (**2**).

No.	R^1	R^2	Method[a] of prep.	M.p., *t*/°C
(**2a**)	n-Octyl	H	A	47[b]
(**2b**)	n-Octyl	Me	B	Oil[c]
(**2c**)	n-Octyl	Pr^n	B	Oil[c]
(**2d**)	n-Octyl	Pr^i	B	Oil[c]
(**2e**)	n-Octyl	Ph	B	Oil[c]
(**2f**)	Cyclohexyl	H	A	85[d]

[a] Crude products were isolated in each case in 100% yields. [b] Crystallized from light petroleum–Pr^iOH (4:1) (Found: C, 68.0; H, 8.5; N, 23.6. $C_{17}H_{25}N_5$ requires C, 68.2; H, 8.4; N, 23.4%). [c] The oils were characterized by their ^1H and ^{13}C NMR spectra only, and were used for further transformations without purification. [d] Crystallized from light petroleum–Pr^iOH (4:1) (Found: C, 66.9; H, 7.1; N, 26.4. $C_{15}H_{19}N_5$ requires C, 66.9; H, 7.1; N, 26.1%).

Table 2. ^1H NMR chemical shifts of benzotriazole adducts (**2**) (δ, $CDCl_3$).

	R^1						
No.	α-CH_2 (2 H)	Chain CH_2 (m)	ω-CH_3 (3 H, t[a])	R^2	R^2–C*H*–Bt[c]	CH_2(CN) (2 H)	Bt[c] (m, 4 H)
(**2a**)	2.77 (t)[a]	1.2–1.7 (12 H)	0.88	—	5.50 (2 H, s)	3.61 (s)	7.3–8.2
(**2b**)	2.49–2.81 (m)	1.2–1.65 (12 H)	0.87	1.96 (3 H, m)	5.75–5.93 (1 H, m)	3.55–3.97 (m)	7.29–8.15
(**2c**)	2.59–2.99 (m)	1.15–1.85 (12 H)	0.89	0.91 (3 H, t[a]), 2.15–2.57 (4 H, m)	5.65–5.82 (1 H, m)	3.59–4.12 (m)	7.35–8.23
(**2d**)	2.44–2.65 (m)	1.15–1.72 (12 H)	0.88	1.19 and 1.21, (2 × 6 H, d), 2.65–2.92 (1 H, m)	5.05–5.25 (1 H, m)	3.40–3.71 (m)	7.24–8.12
(**2e**)	2.61–2.94 (m)[a]	1.14–1.65 (12 H)	0.86	7.15–7.32 (5 H, m)	6.94–7.02 (1 H, br s)	3.52–4.12 (m)	7.35–8.12
(**2f**)	2.81–2.92 (m)[b]	1.29–1.91 (10 H)	—	—	5.59 (2 H, s)	3.64 (s)	7.34–8.07

[a] *J* 6 Hz. [b] 1 H. [c] Bt = Benzotriazolyl.

Table 3. ^{13}C NMR chemical shifts of benzotriazole adducts[a] (**2**) (δ in $CDCl_3$).

No.	R^1	R^2	CH_2(CN)	CN	R^2–C*H*–Bt[b]	Bt[b]
(**2a**)	14.01, 22.53, 26.72, 27.04, 29.09, 29.12, 31.66, 39.88		51.93	115.14	65.79	109.38, 120.12, 124.18, 127.88, 133.45, 146.00
(**2b**)	13.71, 22.49, 26.12, 27.06, 28.88, 29.04, 31.33, 36.95	17.47	49.59	115.88	72.71 (78.88)	109.86, 119.54, 123.83, 127.17, 132.39, 145.89, (117.92, 126.14, 143.78)
(**2c**)	13.21, 22.47, 26.53, 27.19, 29.10, 29.16, 34.06, 37.89	18.13, 18.51, 34.01	51.12	116.05	83.22 (76.49)	109.45, 119.79, 124.01, 127.49, 133.11, 144.74, (118.02, 126.23, 143.82)
(**2d**)	13.76, 22.29, 26.51, 26.92, 28.86, 28.96, 31.44, 37.59	18.80, 29.97	50.01	115.88	83.35 (89.08)	108.87, 119.75, 123.71, 127.45, 134.28, 144.95, (118.01, 126.25, 143.89)
(**2e**)	13.70, 22.19, 26.39, 26.89, 28.71, 29.86, 31.35, 37.01	126.45, 126.67, 127.02, 128.41	51.76	116.68	78.88 (84.52)	109.87, 118.06, 124.07, 128.41, 133.12, 145.67, (118.06, 126.45, 143.95)
(**2f**)	25.20, 25.35, 30.13, 36.86		60.05	116.56	63.54	109.56, 119.82, 124.09, 127.66, 132.79, 145.89

[a] = Signals for the benzotriazol-2-yl isomers given in parentheses when observed (see Discussion). [b] Bt = Benzotriazolyl.

Table 4. Preparation of *N,N*-dialkylaminoacetonitriles (3) and (4).

No.	R^1	R^2	R^3	%Yield[a]	Formula	M^+ Calc.	M^+ Found
(3a)	n-Octyl	H	—	66	$C_{11}H_{22}N_2$	182.1783	182.1785
(3b)	n-Octyl	Me	—	77	$C_{12}H_{24}N_2$	196.1939	196.1936
(3c)	n-Octyl	Pr^n	—	70	$C_{14}H_{28}N_2$	224.2252	224.2246
(3d)	n-Octyl	Pr^i	—	73	$C_{14}H_{28}N_2$	224.2252	224.2250
(3e)	n-Octyl	Ph	—	77	$C_{17}H_{26}N_2$	258.2095	258.2096
(3f)[1c]	Cyclohexyl	H	—	67	$C_9H_{16}N_2$	152.1313	152.1307
(4a)	n-Octyl	H	Ph	53	$C_{17}H_{26}N_2$	258.2095	258.2096
(4b)	n-Octyl	H	$PhCH_2$	65	$C_{18}H_{28}N_2$	246.2221[b]	246.2227
(4c)	n-Octyl	Ph	Ph	55	$C_{23}H_{30}N_2$	334.2409	334.2410
(4d)	Cyclohexyl	H	$PhCH_2$	63	$C_{16}H_{22}N_2$	242.1782	242.1774
(4e)	n-Octyl	Pr^n	$PhCH_2$	25	$C_{21}H_{34}N_2$	314.5236	314.5231

[a] Yields were calculated after purification of the products by column chromatography. [b] $M-26$ (Found: C, 79.4; H, 10.4. $C_{18}H_{28}N_2$ requires C, 79.4; H, 10.4%).

Table 5. ^1H NMR chemical shifts of *N,N*-dialkylaminoacetonitriles (3) and (4) (δ, in $CDCl_3$).

No.	R^1 α-CH_2 (2 H, t[a])	R^1 Chain CH_2 (m)	R^1 ω-CH_3 (3 H, t[a])	R^2	R^3	R^2–C*H*–R^3	CH_2(CN) (2 H, s)
(3a)	2.43	1.17–1.47 (12 H)	0.88	—		2.34 (3 H, s)	3.53
(3b)	2.48	1.14–1.75 (12 H)	0.88	1.81 (3 H, t)		2.51–2.62 (2 H, q)	3.57
(3c)	2.47	1.15–1.55 (12 H)	0.89	0.92 (3 H, t), 1.30–1.55 (4 H, m)		2.47 (2 H, t)	3.54
(3d)	2.46	1.13–1.55 (12 H)	0.88	0.91 (6 H, d), 1.55–1.79 (1 H, m)		2.23–2.25 (2 H, d)	3.53
(3e)	2.55	1.11–1.73 (12 H)	0.89	7.21–7.65 (5 H, m, Ph)		3.42 (2 H, s)	3.63
(3f)	2.33[b]	1.11–1.92 (10 H)				2.4 (3 H, s)	3.59
(4a)	2.61	1.15–1.63 (12 H)	0.89		7.20–7.65 (5 H, m, Ph)	3.42 (2 H, s)	3.64
(4b)	2.52	1.19–1.59 (12 H)	0.89		2.75 (2 H, t, CH_2Ph)	2.73 (2 H, t)	3.55
(4c)	2.53	1.05–1.57 (12 H)	0.87	7.08–7.52 (5 H, m, Ph)	7.08–7.52 (5 H, m, Ph)	4.57 (1 H, s)	3.46
(4d)	2.38–2.58[b]	0.95–1.89 (10 H)			2.82 (2 H, t, CH_2Ph) 7.04–7.35 (5 H, m, Ph)	2.71 (2 H, t)	3.52
(4e)	2.45–2.61 (m)	1.15–1.82 (12 H)	0.88	0.96 (3 H, t), 1.61–1.82 (2 H, m),	2.91 (2 H, s) 7.05–7.42 (5 H, m) 2.62–2.81 (2 H, m)	3.40–3.70 (1 H, m)	3.40–3.70 (m)

[a] *J* 6 Hz. [b] (m, 1 H).

dialkylaminoacetonitrile has been used as the final 'deprotection' step to regenerate the carbonyl function on the α-carbon, usually after substitution (acylanion chemistry).[8a] Acidic hydrolysis is often the method of choice for such transformations. As early as 1955, Larramona[18] successfully used cyanide-complexing methods to facilitate the aminonitrile→iminium cation dissociation; twenty years later Büchi and co-workers[15a] combined this technique with solvolysis of the highly reactive iminium cations to result in effective and mild hydrolysis of α-dialkylaminonitriles. In further studies[15c] $CuSO_4$ was the most effective reagent found, and the necessity for a slightly acidic pH of the reaction mixture was emphasized.[15b] In all these cases, regeneration of the ketone (or aldehyde) component was the aim, and the methods have apparently not previously been used for the hydrolysis of cyanomethylamines (aminoacetonitriles). We now find that the $CuSO_4$ method gives excellent results in our transformations of this type, while treatment with NaOH[19] or with $AgNO_3$[20] did not give the desired results. The reactions with $CuSO_4$ are fast and clean, and the product secondary amines (5) and (6) can easily be isolated in a pure state and high yield. The representative examples of the unsymmetrical secondary amines synthesized are listed in Table 7. Their ^1H and ^{13}C NMR spectra are given in Tables 8 and 9, respectively.

Conclusions

By using a four-step sequence consisting of (i) cyanomethylation (*i.e.* protection), (ii) benzotriazole adduct formation, (iii) displacement of the benzotriazole moiety, and (iv) de-cyanomethylation (*i.e.* deprotection), selective *N*-monoalkylation of primary amines has been accomplished. The new *N*-substituent (R^2R^3CH) introduced may be α-branched and may have a highly versatile structure. Furthermore, the new aminonitriles synthesized also provide possible access to several other types of compounds, such as tertiary amines by Bruylants[11a] displacement of the CN group in aminonitriles (3) and (4), or unsymmetrical imino-bis-acetonitriles *via* displacement of the benzotriazole moiety by cyanide[2] in adducts (2), *etc.* We are planning to continue our work in these directions.

Experimental

M.p.s were determined on a Kofler hot-stage microscope and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. ^1H and ^{13}C NMR spectra were obtained on a Varian XL 200 (200 or 50 MHz) or VXR 300 (300 or 75 MHz) instrument for solutions in deuteriated chloroform using $SiMe_4$ as internal standard for ^1H, and the solvent signal as

Table 6. ^{13}C NMR chemical shifts of *N,N*-dialkylaminoacetonitriles (**3**) and (**4**) (δ, in $CDCl_3$).

No.	R^1	R^2	R^3	R^2–*C*H–R^3	*C*H_2(CN)	CN
(**3a**)	13.81, 22.39, 26.86, 27.16, 28.99, 24.16, 31.56, 41.72	—	—	44.82	55.56	114.41
(**3b**)	12.87, 22.38, 26.93, 27.10, 28.98, 29.15, 31.56, 40.86	13.84	—	47.92	53.63	117.75
(**3c**)	13.87, 22.37, 26.89, 27.09, 28.98, 29.12, 31.55, 41.35	13.59, 20.02, 29.20	—	53.56	53.87	117.75
(**3d**)	13.99, 22.55, 26.98, 27.30	20.42, 25.99	—	54.27	62.28	115.09
(**3e**)	14.04, 22.58, 26.98, 27.26, 29.18, 29.30, 31.75, 41.07	127.57, 128.49, 128.86, 137.31	—	54.07	58.26	114.48
(**3f**)	24.65, 25.41, 28.46, 38.57	—	—	41.99	60.73	115.59
(**4a**)	14.04, 22.58, 26.98, 27.26, 29.18, 29.30, 31.75, 41.07	—	127.57, 128.49, 128.86, 137.76	54.07	58.26	114.48
(**4b**)	13.99, 22.53, 26.97, 27.04, 29.11, 29.25, 31.68, 41.75	—	33.96, 126.12, 128.29, 128.52, 139.33	54.02	55.66	114.93
(**4c**)	13.93, 22.47, 26.71, 27.07, 29.02, 29.19, 31.64, 39.22	127.29, 127.51, 128.61, 141.60	127.29, 127.51, 128.61, 141.60	72.96	51.01	114.69
(**4d**)	25.19, 25.60, 29.58, 38.27	—	34.27, 125.84, 128.04, 128.38, 139.45	51.93	61.16	116.91
(**4e**)	13.06, 22.41, 26.59, 26.93, 28.96, 29.02, 31.55, 39.17	13.87, 18.82, 33.17	37.72, 125.66, 128.07, 128.20, 140.09	51.42	54.40	116.56

Table 7. Preparation of unsymmetrical secondary amines (**5**) and (**6**).

								M^+	
No.	R^1	R^2	R^3	%Yield[a]	Ref.	M.p., (*t*/°C)	Formula	Calc.	Found
(**5a**)	n-Octyl	H	—	90	21	Oil	$C_9H_{21}N$	143.1674	143.1669
(**5b**)	n-Octyl	Pr^n	—	87	21	Oil	$C_{12}H_{27}N$	185.2143	185.2153
(**5c**)	n-Octyl	Ph	—	95	22	199[b] (decomp.)	$C_{15}H_{25}N$	*c*	
(**5d**)	n-Octyl	Pr^i	—	97	—	Oil	$C_{12}H_{27}N$	185.2143	185.2137
(**6a**)	n-Octyl	H	$PhCH_2$	99	—	190[b] (decomp.)	$C_{16}H_{27}N$	*d*	
(**6b**)	n-Octyl	Ph	Ph	60[e]	—	Oil	$C_{21}H_{29}N$	295.2299	295.2289
(**6c**)	Cyclohexyl	H	$PhCH_2$	93	23	Oil	$C_{14}H_{21}N$	202.1595[f]	202.1594

[a] Yield of crude amines; the compounds gave clean ^1H and ^{13}C NMR spectra. [b] Hydrochloride salt, obtained with conc. HCl in ether. [c] Hydrochloride: Found: C, 70.1; H, 10.4; N, 5.4. $C_{15}H_{26}NCl$ requires C, 70.45; H, 10.2 N, 5.5%. [d] Hydrochloride: Found: C, 71.2; H, 10.5; N, 5.2. $C_{16}H_{28}NCl$ requires C, 71.1; H, 10.6; N, 5.1%. [e] Yield after purification by column chromatography. [f] $M^+ - 1$.

Table 8. ^1H NMR chemical shifts of amines (**5**) and (**6**) (δ, in $CDCl_3$).

	R^1						
No.	α-CH_2 (2 H, t)	Chain CH_2 (m)	ω-CH_3 (3 H, t)	R^2	R^3	R^2–*CH*–R^3	>NH (br, 1 H)
(**5a**)	2.40	1.16–1.57 (12 H)	0.82	—	—	2.28 (3 H, s)	1.52–1.67
(**5b**)	2.62	1.18–1.42 (10 H), 1.54 (2 H, m)[b]	0.87	0.92 (3 H, t), 1.18–1.42 (2 H, m),[b] 1.54 (2 H, m)[b]	—	2.64 (2 H, m)[b]	3.55–3.72
(**5c**)	2.60	1.14–1.65 (12 H)	0.87	7.10–7.40 (5 H, m)	—	3.76 (2 H, s)	*a*
(**5d**)	2.58	1.13–1.59 (12 H)	0.89	0.89, 0.91 (6 H, d), 1.68–1.98 (1 H, m)	—	2.41 (2 H, d)	*a*
(**6a**)	2.53	1.13–1.51 (12 H)	0.88	—	2.89 (2 H, t), 7.12–7.39 (5 H, m)	2.57 (2 H, t)	1.51–1.62
(**6b**)	2.55	1.16–1.60 (12 H)	0.87	7.11–7.50 (5 H, m)	7.11–7.50 (5 H, m)	4.79 (1 H, s)	*a*
(**6c**)	2.26[c]	0.80–1.90 (10 H)		—	2.85 (2 H, t), 7.02–7.40 (5 H, m)	2.77 (2 H, t)	*a*

[a] Overlapping with the aliphatic proton signals. [b] Overlapping signals. [c] m, 1 H.

reference for ^{13}C spectra. Mass spectra were recorded at 70 eV on an AEI MS-30 mass spectrometer. Microanalyses were carried out using a Carlo Erba 1106 elemental analyser or by the Atlantic Microlab. Tetrahydrofuran or diethyl ether used as reaction medium was distilled under nitrogen from sodium–benzophenone immediately before use. M.C.B. silica gel (230–400

Table 9. ^{13}C NMR chemical shifts of amines (**5**) and (**6**) (δ, in $CDCl_3$).

	R^1					
No.	α-C	Chain C	ω-C	R^2	R^3	R^2–*C*H–R^3
(**5a**)	43.13	22.59, 27.19, 27.53, 29.22, 29.42, 31.77	14.04	—	—	58.19
(**5b**)	49.20	22.46, 27.15, 29.07, 29.22, 29.29, 31.32	13.73	13.87, 20.27, 31.64	—	49.55
(**5c**)	49.36	22.52, 27.22, 29.14, 29.39, 29.96, 31.69	13.94	126.65, 127.92, 128.16, 140.37	126.65, 127.92	53.93
(**5d**)	50.02	22.52, 27.28, 28.06, 29.15, 29.42, 31.71	13.93	20.54, 29.95	—	57.96
(**6a**)	41.93	22.61, 27.09, 27.34, 29.20, 29.36, 31.78	14.93		54.21, 126.24, 128.04, 128.76, 140.00	55.79
(**6b**)	48.28	22.62, 27.32, 29.24, 29.50, 30.23, 31.81	14.07	126.81, 127.20, 128.35, 144.33	126.81, 127.20, 128.35, 144.33	67.62
(**6c**)	36.49	24.89, 26.01, 33.39			56.54, 125.89, 128.49, 139.99	48.08

mesh) was employed for column chromatography using ethyl acetate and hexanes (5:95, 10:90, 20:80 mixtures, consecutively) as eluants to separate or purify the reaction products.

α-Aminoacetonitriles.—n-Octylaminoacetonitrile was prepared by the known procedure,[1b] b.p. 113 °C at 0.4 mmHg, 68%; lit.[1b] b.p. 120–125 °C at 2 mmHg; ^1H NMR: δ 0.88 (t, 3 H, CH_3), 1.2–1.6 (m, 12 H, CH_2), 2.71 (t, 2 H, NCH_2), and 3.59 (s, 2 H, CH_2CN); ^{13}C NMR: δ 13.80, 22.38, 26.84, 28.96, 29.14, 29.21, 31.53, 37.08 (octyl), 48.62 (*C*H_2CN), and 117.73 (CN).

Cyclohexylaminoacetonitrile was also prepared by the known procedure.[2] The crude product obtained after evaporation of the solvent was distilled *in vacuo*, b.p. 88 °C at 0.4 mmHg, 11.6 g (84%); lit.[2] b.p. 77–88 °C at 1 mmHg; ^1H NMR: δ 1.07–1.87 (m, 10 H, C_5H_{10}), 2.67 (m, 1 H, CH), and 3.62 (s, 2 H, CH_2CN); ^{13}C NMR: δ 24.04, 25.49, 32.14, 33.90 (cyclohexyl), 54.71 (*C*H_2CN), and 117.89 (CN).

N-*Alkyl*-N-(1-*benzotriazolylalkyl*)*aminoacetonitriles* (**2**).—*General procedure* (*A*). The *N*-Alkylaminoacetonitrile (0.05 mol) and 1-hydroxymethylbenzotriazole (0.05 mol) were heated together in refluxing benzene (100 ml) in a Dean–Stark apparatus for 4 h. The completion of the reaction was indicated by formation of an equivalent amount of water. The solvent was evaporated off, and the product was kept under high vacuum until completely dried.

General procedure (*B*). A mixture of the alkylaminoacetonitrile (0.02 mol), an aldehyde (0.02 mol), and benzotriazole (0.02 mol) was stirred in benzene (50 ml) at room temperature, for 4 h. At this stage the contents dissolved, and the solution became turbid. Anhydrous sodium sulphate was added, and the solution was stirred at room temperature for another 20 h and filtered, and the solvent evaporated off *in vacuo* below 50 °C. The residue was mixed with further aldehyde (0.01 mol), benzotriazole (0.02 mol), and benzene (50 ml) and stirred at room temperature for 20 h, and then refluxed for 1 h in a Dean–Stark apparatus. Solvent and the excess of aldehyde were completely removed by evaporation *in vacuo* above 70 °C. An ethereal solution (60 ml) of the residue was washed with 20% sodium carbonate (3 × 50 ml). The ethereal solution was dried over anhydrous sodium sulphate, the ether evaporated off, and the residue stored under high vacuum.

Reaction of N-*Alkyl*-N-(1-*benzotriazolylalkyl*)*aminoacetonitrile* (**2**) *with Sodium Borohydride* (*General Procedure*).—The adduct (**2**) (0.02 mol) and sodium borohydride (0.03 mol) were stirred in tetrahydrofuran (40 ml) at room temperature for 12 h, and the reaction mixture was quenched with saturated aqueous ammonium chloride (20 ml). The oily layer was removed, and the aqueous layer was extracted with ether (30 ml). The oily layer was combined with the ether extract, and the solvent was evaporated off. The residue was dissolved in ether (60 ml), and washed with 10% aqueous sodium hydroxide and then with water. The ethereal solution was dried (Na_2SO_4), the solvent evaporated off, and the residue chromatographed.

Reaction of N-*Alkyl*-N-(1-*benzotriazolylalkyl*)*aminoacetonitrile* (**2**) *with Grignard Reagent* (*General Procedure*).—The adduct (**2**) (0.02 mol) and Grignard reagent (0.022 mol) were stirred together in tetrahydrofuran for 1 h at 0 °C. The temperature was then gradually allowed to rise to 25 °C, and the stirring was continued for another 6 h. The reaction mixture was quenched with saturated aqueous ammonium chloride (20 ml). The oily layer thus separated was removed, and the aqueous layer was extracted with ether (40 ml). The ether extract was combined with the oily layer, the solvent was evaporated off, and the residue was dissolved in ether (60 ml). The solution was washed with 10% aqueous sodium hydroxide and then with water and finally dried (Na_2SO_4). The solvent was evaporated off, and the product was separated by column chromatography.

Decyanomethylation of N,N-*Dialkylaminoacetonitriles.*—Compound (**3**) or (**4**) (1 g) and copper(II) sulphate pentahydrate (1 g) were refluxed in 80% methanol (10 ml) for 1.5 h. The reaction mixture was then cooled and filtered. The solid residue was dissolved in aqueous ammonia (28%; 20 ml), diluted with water, and extracted with ether (30 ml). The ether extract was combined with the filtrate obtained above, washed with water, and dried over anhydrous potassium carbonate, and the solvent evaporated off. The product thus obtained was pure as characterized by the NMR and mass spectra.

Preparation of α-(N-*Benzyl*-N-*octylamino*)*acetophenone.*—A solution of (**2a**) (0.01 mol) in tetrahydrofuran (15 ml) was added dropwise to freshly prepared phenylmagnesium bromide (0.04 mol) in tetrahydrofuran (20 ml) at room temperature; the temperature rose to 40 °C because the reaction was exothermic. The jelly-like reaction mixture was stirred at room temperature overnight, quenched with ammonium chloride (saturated; 20

ml), and the organic layer thus formed was separated. The solvent was evaporated off, the residue dissolved in ether (20 ml), and the product extracted with 4M hydrochloric acid (20 ml). The product was liberated again with aqueous ammonia, extracted with ether (20 ml) and dried (anhydrous potassium carbonate). The solvent was evaporated off and the pure product was separated by column chromatography on silica gel, with methanol–ethyl acetate–hexanes (1:9:90) as eluant, to give a dark brown oil (2.3 g, 70%); δ_H (300 MHz, $CDCl_3$), 0.86 (3 H, t, CH_3), 1.10–1.60 (12 H, m, CH_2), 2.62 (2 H, t, $-CH_2CH_2N$), 3.74 (2 H, s, $PhCH_2$), 3.83 (2 H, s, $PhCOCH_2$), and 7.15–7.96 (10 H, m, Ph); δ_C (75 MHz, $CDCl_3$) 14.06, 22.69, 27.12, 27.19, 29.22, 29.38, 31.76, 54.34 (octyl); 58.57 (CH_2Ph); 60.18 (CH_2COPh); 127.02, 128.04, 128.15, 128.267, 129.14, 132.89, 136.15 and 138.83 (2 Ph); and 198.89 (COPh); *m/z* 337 (M^+), 232 ($M^+ - 105$), 210 ($M^+ - 127$), 105 ($M^+ - 232$), 91 ($M^+ - 246$), and 77 ($M^+ - 260$).

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