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Reaction of N-(Dialkylaminomethyl)amides and N-(α-Dialkylaminobenzyl)amides with Sulfides and Cyanide

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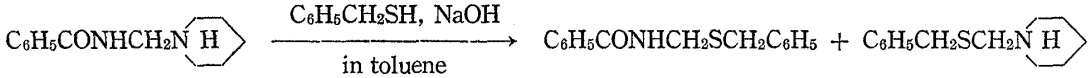
The substitution of the dialkylamine residue of N-(dialkylaminomethyl)amides with nucleophiles leading to the formation of the amidomethyl compounds, reported in several papers by Hellmann, *et al.* has been shown not to occur with sulfides and cyanide under the condition of heating in methanol preferably in the presence of sodium hydroxide, whereas the substitution of the amide residue is chiefly effected. By similar manners the substitution reactions of N-(α-dialkylaminobenzyl)amides with sulfides and cyanide have been also realized.

Hellmann, *et al.* reported in a number of papers[2–8] that the reaction of N-(dialkylaminomethyl)amides with nucleophiles such as active methylene compounds,[2,3,7] sulfides,[6] amines[4,5] and amides[4] affects the substitution of the dialkylamine residue with the nucleophiles leading to the formation of the amidomethyl compounds. Recently in our laboratory the need arose to prepare N-[(benzylthio)methyl]benzamide by nucleophilic substitution reaction of N-(piperidinomethyl)benzamide with benzyl mercaptan on heating in toluene suspending sodium hydroxide, referring to Hellmann's experiment[6] with N-(diethylaminomethyl)benzamide. Despite our expectation of the predominant formation of N-[(benzylthio)methyl]-benzamide, its yield was only 23%, unexpectedly N-[(benzylthio)methyl]piperidine being obtained as a major product in 51% yield. More satisfactory yield (76%) of the latter was



obtained by carrying out the reaction on heating a methanolic solution containing sodium hydroxide, whereas the formation of the former was not detected. Being inconsistent with Hellmann's paper,[6] the above result shows that the substitution of the benzamide residue is predominant over that of the amine residue, preferably in the methanolic sodium hydroxide reaction medium.

Further experiments were conducted with a number of N-(piperidinomethyl)amides varying amide residue by carrying out the reaction in methanol containing sodium hydroxide and, with the selected substrates, N-(piperidinomethyl)benzamide and N-(piperidinomethyl)-succinimide, not only in the above medium but also in methanol itself and in methanol containing acetic acid. Results are summarized in Table I. With the two substrates absence of sodium hydroxide and presence of acetic acid brought about marked effect on the yield of N-[(benzylthio)methyl]piperidine and did not induce the formation of N-[(benzylthio)-

1) Location: *2-2-1 Oshika, Shizuoka-shi*; *a*) Present address: *Fuji Plant, Kowa Co., Ltd., Oono-cho, Fuji-shi.*
2) H. Hellmann, I. Löschmann, and F. Lingens, *Chem. Ber.*, **87**, 1690 (1954).
3) R.O. Atkinson, *J. Chem. Soc.*, **1954**, 1329.
4) H. Hellmann and G. Haas, *Chem. Ber.*, **90**, 50 (1957).
5) H. Hellmann and G. Haas, *Chem. Ber.*, **90**, 53 (1957).
6) H. Hellmann and G. Haas, *Chem. Ber.*, **90**, 444 (1957).
7) H. Hellmann and G. Haas, *Chem. Ber.*, **90**, 1357 (1957).
8) H. Hellmann, *Angew. Chem.*, **69**, 463 (1957).

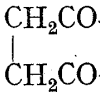
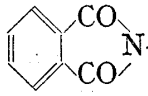
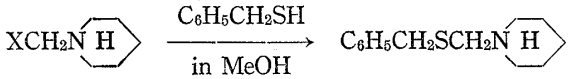
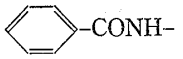
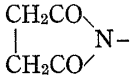
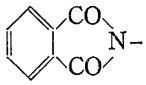
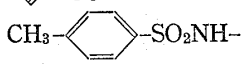
methyl]benzamide. As can be seen from the data in the use of equimolar amount of sodium hydroxide,  -,  - and *p*-$CH_3C_6H_4SO_2NH$- gave better yield of N-[(benzylthio)methyl]piperidine than C_6H_5CONH-.

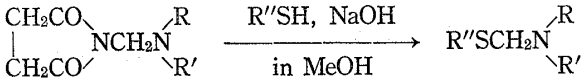
Table I. Reaction[a] of N-(Piperidinomethyl)amides with Benzyl Mercaptan

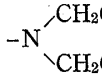
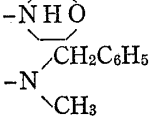
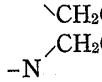
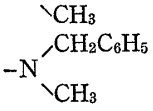
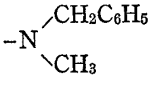


X-	Condition[b] and yield (%)			
	A	B	C	D
	32	76	84	80
	89	77	42	78
	88	—	—	—
	94	—	—	—

a) substrate (50 mmole) :benzyl mercaptan=1: 1.1, MeOH: 90 ml, refluxing time: 4 hr
b) The reaction medium used is as follows. A: MeOH containing 2.2 g (55 mmole) of NaOH; B: MeOH containing 0.22 g (5.5 mmole) of NaOH; C: MeOH itself; D: MeOH containing 3.0 g (50 mmole) of AcOH

Table II. Reaction[a] of N-(Dialkylaminomethyl)-succinimides with Sulfides



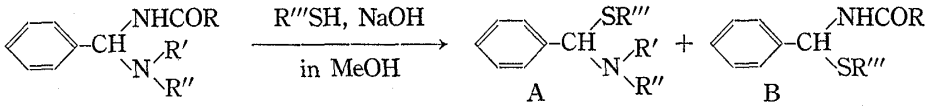
-N(R)(R′)	R″	Yield (%)	-N(R)(R′)	R″	Yield (%)
	$C_6H_5CH_2$	86		$C_6H_5CH_2$	50
	C_6H_5	66		C_6H_5	50
	C_2H_5	54		C_2H_5	55
	$C_6H_5CH_2$	83	-NHC_6H_5	$C_6H_5CH_2$	73
	C_6H_5	74	-NHC_6H_5	C_6H_5	34
	C_2H_5	53		C_6H_5	83
	$C_6H_5CH_2$	80		C_2H_5	65
	C_6H_5	82			
	C_2H_5	60			

a) substrate (50 mmole): sulfide: NaOH=1: 1.1: 1.1, MeOH: 90 ml, refluxing time: 4 hr

Selecting $\begin{matrix}CH_2CO\\ |\quad\quad N-\\ CH_2CO\end{matrix}$, the reaction in methanol containing sodium hydroxide was extensively conducted for yielding N-[(alkylthio)methyl]dialkylamines varying dialkylamine and alkylthio residues. As can be seen in Table II results are satisfactory in yielding this type of the compounds.

Synthesis of the benzylidene analogs of secondary amide type, N-(α-dialkylaminobenzyl)-amides, has already been reported[9] from this laboratory. An attempt to carry out the reaction of an available N-(α-piperidinobenzyl)benzamide with benzyl mercaptan in alkaline methanol by the manner similar to the above reaction was also successful in yielding N-[α-(benzylthio)benzyl]piperidine(65%). Additionally, in this run N-[α-(benzylthio)benzyl]-benzamide(13% yield) was obtained as a side reaction product. The above condition appears preferable, because trials in other reaction media, methanol itself and methanol containing acetic acid, did not show remarkable increase of the yield of the former product. With a number of N-(α-piperidinobenzyl)amides control experiments showed that C_6H_5CONH- was the best in yielding the product among the amide residue such as $C_6H_5CH_2CONH$-, CH_3CONH- and HCONH-, as can be seen in Table III in the runs with benzyl mercaptan. With benzyl mercaptan and thiophenol the reaction was then extended by the use of a number of N-(α-dialkylaminobenzyl)benzamides varying amine residue. Results are shown in Table III, where both the substitutions at the amine and amide sites of the substrates were effected to give N-[α-(alkylthio)benzyl]benzamide and N-[α-(alkylthio)benzyl]dialkylamine. Both types of these compounds have not been known in literature.

Table III. Reaction[a] of N-(α-Dialkylaminobenzyl)amides with Sulfides



R	$\begin{matrix}R'\\ \\ R'''\end{matrix}$N-	R'''	Yield (%) A	Yield (%) B
C_6H_5	-NH (pyrrolidino)	$C_6H_5CH_2$	65	13
$C_6H_5CH_2$	-NH (pyrrolidino)	$C_6H_5CH_2$	45	—
CH_3	-NH (pyrrolidino)	$C_6H_5CH_2$	42	—
H	-NH (pyrrolidino)	$C_6H_5CH_2$	48	—
C_6H_5	$-N(CH_3)_2$	$C_6H_5CH_2$	31	51
C_6H_5	$-N(CH_2C_6H_5)CH_3$	$C_6H_5CH_2$	28	35
C_6H_5	-NHO (morpholino)	$C_6H_5CH_2$	0	59
C_6H_5	$-N(CH_3)_2$	C_6H_5	30	26
C_6H_5	-NHO (morpholino)	C_6H_5	18	47

a) substrate (50 mmole): sulfide: NaOH=1: 1.1: 1.1, MeOH: 90 ml, refluxing time: 4 hr

9) M. Sekiya and H. Sakai, *Chem. Pharm. Bull.* (Tokyo), **17**, 32 (1969).

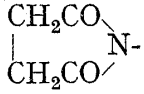
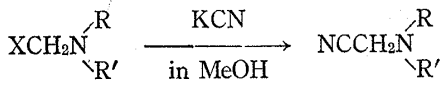
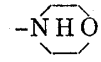
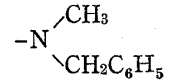
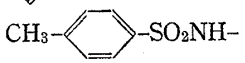
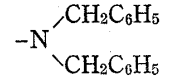
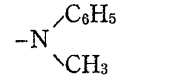
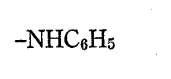
Success in the above substitution reactions with sulfides prompted us to examine the reaction of the methylene and benzylidene compounds with cyanide as a nucleophile, which had not been known. N-(Piperidinomethyl)amides possessing varied amide residue were allowed to react with potassium cyanide in methanol under refluxing. Successful formation of piperidinoacetonitrile was brought about as can be seen in Table IV, where fair yield of the product was attained with the amide residues except C_6H_5CONH-. Selecting  as an amide residue, the reaction was extensively conducted with N-(dialkylaminomethyl)-succinimides possessing varied dialkylamine residue, as shown in Table IV, resulting in the formation of the corresponding dialkylaminoacetonitriles in good yields.

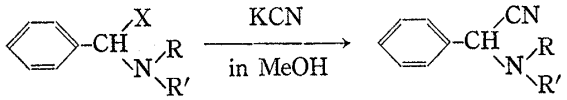
Table IV. Reaction[a] of N-(Dialkylaminomethyl)amides with Cyanide

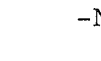
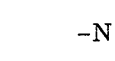
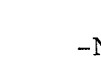
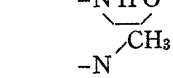


X-	-N(R)(R′)	Yield (%)	X-	-N(R)(R′)	Yield (%)
		82			92
		70			89
		63			96
		27			86
					50

a) substrate (50 mmole): KCN=1: 1, MeOH: 150 ml, refluxing time: 4 hr

Table V. Reaction[a] of N-(α-Dialkylaminobenzyl)amides with Cyanide



X-	-N(R)(R′)	Yield (%)	X-	-N(R)(R′)	Yield (%)
C_6H_5CONH-		64	C_6H_5CONH-		63
$C_6H_5CH_2CONH$-		38	C_6H_5CONH-		55
CH_3CONH-		42	C_6H_5CONH-		0
HCONH-		62	C_6H_5CONH-		23

a) substrate (25 mmole): KCN: AcOH=1: 1.2: 1, MeOH: 75 ml, reaction time: 48 hr at room temperature

Further examination was conducted by the use of N-(α-dialkylaminobenzyl)amides as substrates. On refluxing a cyanide-containing methanolic solution of N-(α-piperidinobenzyl)-benzamide α-(piperidino)phenylacetonitrile was obtained in less than 35%. In pursuit of the reaction condition 64% yield of α-(piperidino)phenylacetonitrile was obtained when a methanolic solution of the substrate, potassium cyanide and acetic acid in 1: 1.2: 1 molar proportion was allowed to stand for two days. Anyway, in the above runs a possible by-product by substitution of piperidine residue was not detected. Under the above condition among a number of N-(α-piperidinobenzyl)amides available synthetically better yields were obtained with those possessing the amide residue, C_6H_5CONH- and HCONH-, as can be seen in Table V. Extensive experiments were carried out by the use of N-(α-dialkylamino-benzyl)benzamides possessing varied dialkylamine residue, resulting in the formation of the corresponding α-(dialkylamino)phenylacetonitriles in the yields given in Table V.

Experimental[10]

Reaction of N-(Piperidinomethyl)benzamide with Benzyl Mercaptan in Toluene——To a solution of 10.9 g (50 mmole) of N-(piperidinomethyl)benzamide(mp 129—130°)[11] and 6.8 g (55 mmole) of benzyl mercaptan dissolved in 90 ml of toluene 0.22 g (5.5 mmole) of powdered NaOH was suspended, and the whole was stirred under refluxing for 4 hr. After filtration toluene was evaporated under reduced pressure and the residue was submitted to extraction with petr. ether. The petr. ether solution was dried over anhyd. $MgSO_4$. After removal of the drying agent and petr. ether, the residue was distilled under reduced pressure to give 5.6 g (51%) of N-[(benzylthio)methyl]piperidine, bp 146—148° (4 mmHg). NMR τ: 2.81 (5H, s, C_6H_5), 6.20 and 6.28 (4H, 2s, NCH_2S and $C\underline{H}_2C_6H_5$), 7.32—7.85 and 8.30—9.00 (10H, m, NC_5H_{10}). Analytical data are recorded in Table VI. The residue insoluble in petr. ether was theen extracted with dry ether. Concentration of the etheral solution gave 3.1 g (23%) of N-[(benzylthio)methyl]benzamide, needles from petr. ether-ether (1: 1), mp 74—75° (lit.[6,12] mp 82°). IR ν_{max}^{KBr} cm^{-1}: 3296 (NH), 1640 (CO). NMR τ: 2.10—2.90 (10H, m, aromatic protons), 3.16—3.66 (1H, broad, NH), 5.52 (2H, d, J=3.0 Hz, NCH_2S), 6.20 (2H, s, $C\underline{H}_2$-C_6H_5). *Anal.* Calcd. for $C_{15}H_{15}ONS$: C, 70.00; H, 5.87; N, 5.44; S, 12.45. Found: C, 70.05; H, 5.81; N, 6.04; S, 12.31. Benzamide was obtained from the residue by extraction with benzene.

Reaction of N-(Dialkylaminomethyl)amides with Mercaptans——The following N-(dialkylaminomethyl)-amides shown with their melting points were prepared and used as substrates for the reaction with mercaptans: N-(piperidinomethyl)benzamide(mp 129—130°),[11] N-(piperidinomethyl)succinimide(mp 107—108°),[13] N-(piperidinomethyl)phthalimide(mp 119—120°),[14] N-(piperidinomethyl)-*p*-toluenesulfonamide(mp 88—89°),[15] N-(morpholinomethyl)succinimide(mp 111—112°),[16] N-(N-methylbenzylaminomethyl)succinimide(mp 72—73°),[17] N-(methylanilinomethyl)succinimide(mp 87—88°),[15] N-(anilinomethyl)succinimide(mp 172—173°),[18] N-(dibenzylaminomethyl)succinimide(mp 122—123°).[17]

A solution of 55 mmole of mercaptan in 40 ml of MeOH containing NaOH (2.2 g (55 mmole) in runs in Tables I and II; 0.22 g (5.5 mmole) in two runs in Table I) was added to a solution of 50 mmole of N-(dialkyl-aminomethyl) amide in 50 ml of MeOH. The mixture was refluxed for 4 hr. The reaction solution was concentrated under reduced pressure, and the residue was submitted to extraction with petr. ether. Removal of petr. ether gave N-[(alkylthio)methyl]dialkylamine as those shown with their yields in Tables I and II. Their analytical data are recorded in Table VI. The residue insoluble in petr. ether contains the unreacted N-(dialkylaminomethyl)amide in some runs and the corresponding amide.

In addition, 50 mmole each of N-(piperidinomethyl)benzamide and N-(piperidinomethyl)succinimide was allowed to react with 6.8 g (55 mmole) of benzyl mercaptan on refluxing for 4 hr in MeOH (90 ml) and

10) All melting and boiling points were uncorrected. Infrared (IR) spectra were determined on a Hitachi EPI-G2 grating spectrophotometer. Nuclear magnetic resonance (NMR) spectra were taken at 60 MHz in $CDCl_3$ solution with a JEOL JNM-C-60H spectrometer using tetramethylsilane as the internal standard.

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in AcOH-containing MeOH(3.0 g (50 mmole) of AcOH in 90 ml of MeOH). The reaction solution was concentrated, in the latter after removal of AcOH by treatment with Amberlite IRA-411 (OH type). N-[(Benzylthio)methyl]piperidine was obtained by the same treatment of the residue as described in the foregoing.

Table VI. N-[(Alkylthio)methyl]dialkylamines

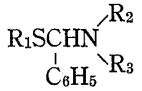
$$R_1SCH_2N\begin{matrix}R_2\\R_3\end{matrix}$$

R_1	R_2	R_3	bp[°C(mmHg)] or mp	n_D^{25}	Formula	Analysis (%) Calcd. (Found) C	H	N	S
$C_6H_5CH_2$	$-(CH_2)_5-$		146—148(4)	1.5613	$C_{13}H_{19}NS$	70.55 (70.40)	8.65 (8.48)	6.33 (5.86)	14.46 (14.23)
	$-CH_2CH_2OCH_2CH_2-$		142—143(6)[a] mp44°, needles (ether)		$C_{12}H_{17}ONS$	64.55 (64.29)	7.68 (7.18)	6.27 (5.96)	14.38 (14.33)
	$C_6H_5CH_2$	CH_3	167—169(3)	1.5850	$C_{16}H_{19}NS$	74.68 (74.11)	7.44 (7.14)	5.44 (5.19)	12.44 (12.59)
	C_6H_5	CH_3	162—168(0.02)	1.6204	$C_{15}H_{17}NS$	74.05 (73.73)	7.04 (7.21)	5.76 (5.51)	13.15 (13.64)
	C_6H_5	H	mp 47.5°, needles (ligroin)		$C_{14}H_{15}NS$	73.34 (73.77)	6.59 (6.39)	6.11 (6.09)	13.96 (13.97)
C_6H_5	$-(CH_2)_5-$		138—141(5)[b]		$C_{12}H_{17}NS$	69.53 (69.08)	8.27 (8.16)	6.76 (6.91)	
	$-CH_2CH_2OCH_2CH_2-$		141—142(5)[c]	1.5793	$C_{11}H_{15}ONS$	63.14 (62.69)	7.23 (6.95)	6.69 (6.90)	15.29 (14.55)
	$C_6H_5CH_2$	CH_3	154—155(5)	1.5942	$C_{15}H_{17}NS$	74.05 (73.67)	7.04 (7.18)	5.76 (6.11)	13.15 (13.04)
	$C_6H_5CH_2$	$C_6H_5CH_2$	141—143(0.1) mp 52°, needles (petr. ether)		$C_{21}H_{21}NS$	78.97 (78.69)	6.63 (6.42)	4.39 (4.39)	10.02 (10.12)
	C_6H_5	CH_3	167—170(3)[d]	1.5718	$C_{14}H_{15}NS$	73.34 (73.00)	6.59 (6.26)	6.11 (5.97)	13.96 (13.79)
	C_6H_5	H	93—95(1)[e]	1.6340	$C_{13}H_{13}NS$	72.54 (72.63)	6.09 (6.59)	6.51 (6.94)	
C_2H_5	$-(CH_2)_5-$		78(3)[f]	1.5015	$C_8H_{17}NS$	60.34 (60.30)	10.76 (10.77)	8.80 (8.67)	20.10 (19.74)
	$-CH_2CH_2OCH_2CH_2-$		80—81(3)	1.4988	$C_7H_{15}ONS$	52.15 (52.40)	9.38 (9.17)	8.69 (8.48)	19.87 (19.52)
	$C_6H_5CH_2$	CH_3	110(5)	1.5170	$C_{11}H_{17}NS$	67.66 (67.95)	8.78 (8.92)	7.17 (7.60)	16.39 (16.17)
	$C_6H_5CH_2$	$C_6H_5CH_2$	152—153(2)	1.5723	$C_{17}H_{21}NS$	75.24 (75.46)	7.80 (7.67)	5.16 (5.04)	11.79 (11.46)
	C_6H_5	CH_3	113—116(4)	1.5805	$C_{10}H_{15}NS$	66.27 (66.48)	8.34 (8.61)	7.73 (7.23)	17.66 (17.37)

a) lit. bp 103—105° (0.02 mmHg) [H. Boehme and H.H. Otto, *Arch. Pharm.*, **300**, 647 (1967)]
b) lit. bp 138—141° (5—6 mmHg) [G.F. Grillot, H.R. Felton, B.R. Garrett, H. Greenberg, R. Green, R. Clementi, and M. Moskowitz, *J. Am. Chem. Soc.*, **76**, 3969 (1954)]
c) lit. bp 146—149° (5—6 mmHg) [G.F. Grillot, H.R. Felton, B.R. Garrett, H. Greenberg, R. Green, R. Clementi, and M. Moskowitz, *J. Am. Chem. Soc.*, **76**, 3969 (1954)]
d) lit. mp 36.4—38° [G.F. Grillot and R.E. Schaffrath, *J. Org. Chem.*, **24**, 1035 (1959)]
e) lit. mp 52—54.5° [G.F. Grillot and R.E. Schaffrath, *J. Org. Chem.*, **24**, 1035 (1959)]
f) lit. bp 90—92° (10 mmHg) [H. Boehme and K. Hartke, *Chem. Ber.*, **96**, 604 (1963)]

Reaction of N-(α-Dialkylaminobenzyl)amides with Mercaptans——The following N-(α-dialkylaminobenzyl)amides shown with their melting points were prepared according to the previously reported method[9] and were used as substrates for the reaction with mercaptans: N-(α-piperidinobenzyl)benzamide (mp 144—145°), N-(α-piperidinobenzyl)phenylacetamide(mp 158—159°), N-(α-piperidinobenzyl)acetamide(mp 144—145°), N-(α-piperidinobenzyl)formamide (mp 109—110°), N-(α-dimethylaminobenzyl)benzamide (mp 107—108°), N-(α-N-methylbenzylaminobenzyl)benzamide (mp 112—113°), N-(α-morpholinobenzyl)benzamide (mp 166—167°).

TABLE VII. N-[α-(Alkylthio)benzyl]dialkylamines and N-[α-(Alkylthio)benzyl]benzamides



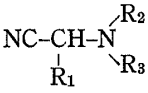
R_1	R_2	R_3	Appearance (recryst. solvt)	mp (°C) or bp [°C (mmHg)]	Formula	Analysis (%) Calcd. (Found) C	H	N	S	Ref.
$C_6H_5CH_2$	$-(CH_2)_5-$		needles (hexane)	42— 43	$C_{19}H_{23}NS$	76.73 (76.70)	7.80 (7.72)	4.71 (4.68)	10.76 (10.57)	*a*)
	CH_3	CH_3	liquid	133—134 (0.01)	$C_{16}H_{19}NS$	74.68 (74.99)	7.44 (7.87)	5.44 (5.89)		
	$C_6H_5CH_2$	CH_3	liquid	98—100 (0.02)	$C_{22}H_{23}NS$	79.25 (78.58)	6.95 (6.68)	4.20 (4.89)		
C_6H_5	$-CH_2CH_2OCH_2CH_2-$		prisms (petr. ether)	35— 36	$C_{17}H_{19}ONS$	71.56 (71.59)	6.71 (6.61)	4.91 (4.97)	11.23 (11.36)	*b*)
	CH_3	CH_3	liquid	112—120 (0.01)	$C_{15}H_{17}NS$	74.05 (73.22)	7.04 (7.39)	5.76 (5.35)	13.15 (13.29)	
$C_6H_5CH_2$	C_6H_5CO	H	needles (MeOH)	129—131	$C_{21}H_{19}ONS$	75.65 (75.85)	5.74 (5.72)	4.20 (4.12)	9.60 (9.83)	*c*)
C_6H_5	C_6H_5CO	H	needles (MeOH)	170—171	$C_{20}H_{17}ONS$	75.22 (75.19)	5.36 (5.29)	4.39 (4.18)	10.04 (9.86)	

a) NMR τ: 2.34—2.77 (10H, m, aromatic protons), 5.20 (1H, s, CH), 6.02—6.57 (2H, double d, CH_2), 7.25—7.62 and 8.16—8.75 (10H, m, piperidine protons)

b) NMR τ: 2.25—2.87 (10H, m, aromatic protons), 4.62 (1H, s, CH), 6.23—6.39 and 7.20—7.41 (8H, m, morpholine protons)

c) IR ν_{max}^{KBr} cm^{-1}: 3308 (NH), 1638 (CO); NMR τ: 2.30—2.90 (15H, m, aromatic protons), 3.28—3.71 (2H, m, CH and NH), 6.17 (2H, s, CH_2)

TABLE VIII. Dialkylaminoacetonitriles and α-(Dialkylamino)phenylacetonitriles



R_1	R_2	R_3	Appearance (recryst. solvt)	bp [°C (mmHg)] or mp (°C) [lit. bp or mp]	n_D (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N	Ref.
H	$-(CH_2)_5-$		liquid	90— 91(14) [83(9)][a]	1.4605 (27)	$C_7H_{12}N_2$	67.70 (67.66)	9.74 (9.74)	22.56 (22.82)	
	$-CH_2CH_2OCH_2CH_2-$		needles (petr. ether)	61— 62 [61—63][b]		$C_6H_{10}ON_2$	57.11 (56.78)	7.99 (8.02)	22.21 (22.39)	
	$C_6H_5CH_2$	CH_3	liquid	98— 99(3—4) [117—119(7)][c]	1.5170 (19)	$C_{10}H_{12}N_2$	74.96 (74.85)	7.55 (7.90)	17.49 (17.17)	
	$C_6H_5CH_2$	$C_6H_5CH_2$	plates (petr. ether)	47—48 [45—46][d]		$C_{16}H_{16}N_2$	81.32 (81.14)	6.83 (6.76)	11.86 (11.57)	
	C_6H_5	CH_3	liquid	113(3) [138—141(9)][a]	1.5550 (19)	$C_9H_{10}N_2$	73.94 (74.01)	6.90 (6.88)	19.16 (19.00)	
	C_6H_5	H	leaves (petr. ether)	129—130(0.4) 40[47][e]		$C_8H_8N_2$	72.70 (72.34)	6.10 (6.18)	21.20 (20.82)	
C_6H_5	$-(CH_2)_5-$		prisms (iso-PrOH)	62— 63 [62—64][f]		$C_{13}H_{16}N_2$	77.96 (78.10)	8.05 (8.08)	13.99 (13.94)	
	$-(CH_2)_4-$		liquid	101—103(0.005)	1.5370 (17)	$C_{12}H_{14}N_2$	77.38 (77.21)	7.58 (7.57)	15.04 (15.05)	
	CH_3	CH_3	liquid	96—97(0.3) [85—87(1.0)][f]	1.5175 (17)	$C_{10}H_{12}N_2$	74.96 (75.00)	7.55 (7.74)	17.49 (17.26)	
	$C_6H_5CH_2$	CH_3	prisms (petr. ether)	48— 49		$C_{16}H_{16}N_2$	81.32 (81.06)	6.83 (6.84)	11.86 (11.73)	

a) D.B. Luten, Jr., *J. Org. Chem.*, **3**, 588 (1939)

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c) M. Freifelder, *J. Am. Chem. Soc.*, **82**, 2386 (1960)

d) F. Johnson and W.A. Nasutavicus *J. Org. Chem.*, **29**, 153 (1964)

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f) L.H. Goodson and H. Christopher, *J. Am. Chem. Soc.*, **72**, 358 (1950)

To a solution of 50 mmole of N-(α-dialkylaminobenzyl)amide in 50 ml of MeOH 55 mmole of mercaptan in NaOH-containing MeOH (0.44 g (11 mmole) of NaOH in 40 ml of MeOH) was added and the mixture was stirred for 4 hr under refluxing. The reaction mixture was concentrated to remove MeOH and extraction of the residue with petr. ether followed. Evaporation of petr. ether and recrystallization or distillation of the residue gave N-[α-(alkylthio)benzyl]dialkylamine as those shown with their yields in Table III. Their physical and analytical data are recorded in Table VII.

The residue insoluble in petr. ether easily solidified in the runs with N-(α-dialkylaminobenzyl)benzamides. This was subjected to fractional recrystallization from MeOH to give N-[α-(alkylthio)benzyl]benzamide as the first crop of crystals in the yield listed in Table III. Their physical and analytical data are recorded in Table VII. Benzamide and N,N′-benzylidenebisbenzamide were obtained in some runs as the succeeding crops of crystals.

Reaction of N-(Dialkylaminomethyl)amides with Potassium Cyanide——A solution of 3.3 g (50 mmole) of potassium cyanide dissolved in 100 ml of MeOH was added to a refluxing solution of 50 mmole each of the N-(dialkylaminomethyl)amides, listed in the foregoing, in 50 ml of MeOH. After the whole was heated under refluxing for 4 hr, MeOH was removed from the reaction solution. The residue was submitted to extraction with dry ether. Evaporation of ether and recrystallization or distillation of the resultant residue gave the corresponding dialkylaminoacetonitriles in the yields as shown listed in Table IV. Their physical and analytical data are recorded in Table VIII.

Reaction of N-(α-Dialkylaminobenzyl)amides with Potassium Cyanide——In 75 ml of MeOH 25 mmole each of N-(α-dialkylaminobenzyl)amides, listed in the foregoing, 2.1 g (30 mmole) of potassium cyanide and 1.2 g (25 mmole) of AcOH were dissolved, and the whole was allowed to stand at room temperature. After 48 hr the reaction solution was neutralized by addition of 0.3 g (5 mmole) of AcOH and treated by the same manner as described for the reaction of N-(dialkylaminomethyl)amides. Yields and analytical data of the products, α-(dialkylamino)phenylacetonitriles thus obtained, are given in Tables V and VIII, respectively.

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