

TABLE I
 NITROGEN MUSTARDS, R-N(CH₂CH(X)Y)₂HX

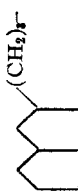
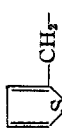
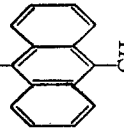
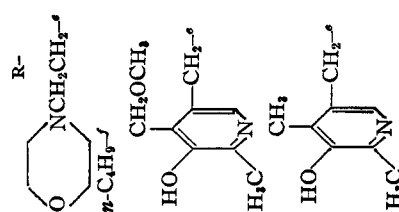
I	R-	Method	X	Y	M.p., °C. ^a	Yield, %	Crystn.-solvent	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Chlorine, %	
									Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
	(ClCH ₂ CH ₂) ₂ NCH ₂ CH ₂ CH ₂ CH ₂ - ^d	D-2	Cl	H	138-139	42 ^b	CH ₂ OH-CHCl ₃	C ₁₁ H ₂₄ Cl ₄ N ₂	33.27	33.39	6.09	5.88	7.06	6.64	53.58	53.50
II	<i>n</i> -C ₄ H ₉ - ^d	D	Cl	H	120-121	28 ^c	C ₆ H ₆ -CHCl ₃	C ₇ H ₁₆ Cl ₃ N	38.11	38.39	7.31	6.50			48.22	48.20
III	C ₆ H ₅ CH ₂ CH ₂ -	D	Cl	H	110-111	50 ^c	C ₆ H ₅ -CHCl ₃	C ₁₂ H ₁₈ Cl ₃ N	51.00	50.83	6.42	6.65			37.64	37.79
IV	(Br-CH ₂ CH ₂) ₂ NCH ₂ CH ₂ CH ₂ - ^d	D	Br	H	170-173 dec.	19 ^c	CH ₃ OH	C ₁₁ H ₂₄ Br ₂ N ₂					Br	72.24	72.20	
V	<i>n</i> -C ₁₂ H ₂₅ -	D-2	Cl	H	67.6-69	72 ^b	CHCl ₃ -pet. ether	C ₁₈ H ₃₄ Cl ₃ N	55.41	55.32	9.88	9.79			30.67	30.62
VI	(CH ₂ CHClCH ₂) ₂ N(CH ₂) ₃ - ^d	D-2	Cl	CH ₃	177-178 dec.	38 ^b	CHCl ₃ -CH ₂ OH	C ₁₃ H ₂₂ Cl ₃ N ₂ ·1/2H ₂ O	38.98	39.01	7.20	7.29			46.02	46.00
VII	<i>n</i> -C ₈ H ₁₇ -	D	Cl	H	79.8-80.6	17 ^c	C ₆ H ₅ -pet. ether	C ₉ H ₂₀ Cl ₃ N	43.48	43.28	8.11	8.18			42.79	42.50
VIII	<i>n</i> -C ₄ H ₉ -	D	Cl	H	82.2-82.8	54 ^b	CHCl ₃ -diethyl cel- losolve	C ₁₀ H ₂₂ Cl ₃ N							40.49	40.40
IX	<i>n</i> -C ₁₄ H ₂₉ -	D-2	Cl	H	73-74.4	64 ^b	CHCl ₃ -pet. ether	C ₁₈ H ₃₃ Cl ₃ N	57.68	57.75	10.22	10.59				
X	<i>n</i> -C ₁₆ H ₃₃ -	D-2	Cl	H	76.4-77.2	40 ^b	CHCl ₃ -pet. ether	C ₂₀ H ₄₂ Cl ₃ N	59.62	59.78	10.50	10.59				
XI	C ₆ H ₅ CH ₂ CH ₂ CH ₂ -	D	Cl	H	99.2-100	52 ^c	Acetone-diethyl cellosolve	C ₁₃ H ₂₆ Cl ₃ N								
XII	(CH ₃) ₂ CCH ₂ C(CH ₃) ₂ -C ₆ H ₅ - OCH ₂ CH ₂ OCH ₂ CH ₂ -	D	Cl	H	109-112	25 ^b	Acetone-ether	C ₂₂ H ₃₈ Cl ₃ N ₂ O ₂	58.08	58.19	8.42	8.45				
XIII	ClCH ₂ CH ₂ -	D-1	Cl	H	131-132.2	47 ^b	Acetone-EtOH	C ₈ H ₁₃ Cl ₃ N	29.90	30.23	5.44	5.21	5.81	5.98	58.85	58.70
XIV	CH ₃ CHClCH ₂ - ^d	D-2	Cl	H	78-79.4	22 ^b	CHCl ₃ -EtOH	C ₇ H ₁₃ Cl ₃ N							55.62	55.60
XV	-CH ₂ -C ₄ H ₉ - <i>o</i> -Cl	D-2	Cl	H	140-141	41 ^b	Acetone	C ₁₁ H ₁₉ Cl ₃ N							46.79	46.80
XVI	NO ₂ -C ₄ H ₉ - <i>p</i> -CH ₂ -	D	Cl	H	144-146	16 ^c	CHCl ₃	C ₁₁ H ₁₉ Cl ₃ N ₂ O							33.92	33.81
XVII	(ClCH ₂ CH ₂) ₂ N(CH ₂) ₇ - ^{d, i}	D	Cl	H	109.6-110.8	27 ^b	Acetone-CH ₂ OH	C ₁₆ H ₂₈ Cl ₃ N ₂	31.35	31.90	5.79	5.92	7.32	7.43	55.54	55.48
XVIII	CH ₂ CHClCH ₂ -	D	Cl	H	112-113	10 ^b	CHCl ₃ -pet. ether	C ₈ H ₁₅ Cl ₃ N ₂ ·1/2H ₂ O	37.00	37.00	6.90	6.97			48.56	48.40
XIX	CH ₂ -	D	Br	CH ₃	135-138	17.5 ^b	Acetone	C ₇ H ₁₀ Br ₂ N					Br	67.73	67.58	
XX	C ₆ H ₁₁ -	D	Cl	H	178-179	88 ^b	Acetone-CH ₂ OH	C ₁₀ H ₂₀ Cl ₃ N							40.82	40.64
XXI		D	Cl	H	128-130	52 ^c	C ₄ H ₉ -pet. ether	C ₁₇ H ₃₂ Cl ₃ N	57.22	57.40	9.04	9.30				
XXII	<i>n</i> -C ₁₆ H ₃₃ -	D-2	Cl	H	73.6-75.8	73 ^b	CHCl ₃ -pet. ether	C ₁₉ H ₃₆ Cl ₃ N	58.66	58.80	10.37	10.20				
XXIII	<i>o</i> -C ₁₀ H ₇ CH ₂ -	D	Cl	H	188-189	68 ^b	EtOH	C ₁₅ H ₁₈ Cl ₃ N	56.53	56.04	5.69	5.51			Ionic Cl	10.04
XXIV		D	Cl	H	102-104	12 ^b	C ₃ H ₆ -CHCl ₃	C ₉ H ₁₄ Cl ₃ NS	39.36	39.61	5.14	5.07			Ionic Cl	13.40
XXV	ClCH ₂ CH ₂ CH ₂ - ^d	D	Cl	H	84-86	64 ^b	Acetone-diethyl cellosolve	C ₁₇ H ₁₉ Cl ₃ N	32.97	33.25	5.93	5.78				
XXVI	Cl(CH ₂) ₁₀ -	E	Cl	H	61-63		Acetone-ether	C ₁₄ H ₂₆ Cl ₃ N								
XXVII	(ClCH ₂ CH ₂) ₂ N(CH ₂) ₁₀ - ^d	D	Cl	H	145-148	26 ^b	Acetone-EtOH	C ₁₈ H ₃₀ Cl ₃ N ₂	43.66	43.96	7.73	7.76			42.96	42.74
XXVIII	C ₂ H ₅ OCH ₂ CH ₂ CH ₂ -	D	Cl	H	75-78	62 ^b	Acetone-ether	C ₉ H ₂₀ Cl ₃ NO	40.85	40.18	7.62	7.38			Ionic Cl	13.40
XXIX	CH ₂ N(CH ₂ CH ₂ Cl) ₂ - 	E	Cl	H	200-205 dec.		EtOH	C ₂₄ H ₃₀ Cl ₆ N ₂							38.04	37.86

TABLE I (Continued)

	Method	X	Y	M.p., °C. ^e	Yield, %	Crystn.-solvent	Formula	Carbon, % Calcd. Found	Hydrogen, % Calcd. Found	Nitrogen, % Calcd. Found	Chlorine, % Calcd. Found
XXX	E	Cl	H	179-182 dec.	51 ^b	CH ₃ OH	C ₁₀ H ₁₂ Cl ₄ N ₂ O			Ionic Cl	21.61 21.43
XXXI	F	F	H	66-68	6 ^c	Acetone-ether	C ₄ H ₁₈ ClF ₂ N				17.57 17.80
XXXII	E	Cl	H	173-176 dec.	47 ^b	EtOH-acetone	C ₁₃ H ₂₂ N ₂ O ₃ Cl ₄ ·2H ₂ O	37.51 37.69	6.30 5.85	Ionic Cl	17.04 16.90
XXXIII	E	Cl	H	201-240 dec.	41 ^b	CH ₃ OH	C ₁₂ H ₂₀ N ₂ OCl ₄	41.17 41.50	5.76 5.90	Ionic Cl	20.20 20.12



^a All melting points are uncorrected. ^b Yield in halogenation reaction. ^c Over-all yield. ^d Free base described by Hanby and Rydon, *J. Chem. Soc.*, 513 (1947). ^e Dihydrohalide. ^f Hydrochloride salt. ^g Free base described by Jones and Wilson, *J. Chem. Soc.*, 547 (1949). ^h Free base described by Ford, Moore, Lidstone and Waters, *ibid.*, 820 (1946). ⁱ Free base described by Childs, *et al.*, *ibid.*, 2174 (1948).



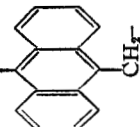
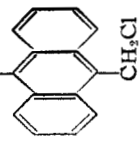
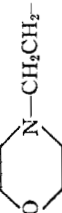
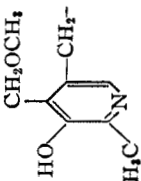
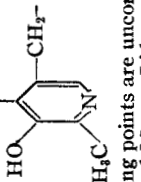
TABLE Ia

INTERMEDIATES FOR NITROGEN MUSTARDS IN TABLE I, R-N-(CH₂CHOHY)^h

c.b. = crude base used in halogenation step; D.E.A. denotes diethanolamine; d.b. isolated as distilled free base.

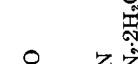
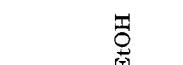
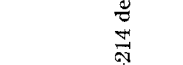


	Used as Y	X	Z	M.p., °C. ^e	Yield, %	B.p. Mm.	Prepared	Crystn.-solvent	Method
Ia	2 HCl	H	H	92, -93, 2	50		1. Br(CH ₂) ₂ Br + 2D.E.A. 2. EtOH-HCl	CH ₃ OH	A-2,3
IIa	c.b.	H	H				RBr + D.E.A.		A
IIIa	c.b.	H	H				Br(CH ₂) ₂ Br + 2D.E.A.		A-2,3
IVa	c.b.	H	H						
Va	HCl	H	H	75-76	68			Acetone	
VIa	2HCl	CH ₃	CH ₃	232-234 dec.	60		1. Br(CH ₂) ₂ Br + 2NH(CH ₂ CHOHCH ₃) ₂ 2. CHCl ₃ -HCl	CH ₃ OH-acetone	A-2,3
VIIa	c.b.	H	H				RBr + D.E.A.		A
VIIIa	d.b.	H	H		87	126-130	RBr + D.E.A.		A
IXa	HCl	H	H		50		1. RBr + D.E.A. 2. Acetone-concd. HCl	Aqueous acetone	B
Xa	HCl	H	H		62		1. RBr + D.E.A. 2. Ether-HCl		B
XIa	c.b.	H	H		85	200-210	RBr + D.E.A.		A
XIIa	d.b.	H	H			0.5	RCI ^e + D.E.A. ^d		
XIIIa	d.b.	H	H			1.0			
XIVa	HCl	H	H	132-135	75				A
XVa	HCl	H	H	100-107	87		1. RCl + D.E.A. 2. EtOH-HCl	EtOH-ether	A
XVIa	c.b.	H	H				RBr + D.E.A.		B-2
XVIIa	c.b.	H	H						

TABLE Ia (Continued)

	Used as V	M.p., °C. ^a	B.P. Mm.	Prepared ^b	Yield, %	Crystn.-solvent	Method
XVIIIa	CH ₂ CHOHCH ₂ ^{R-}						
XIXa	CH ₂ ^{R-}	88-96	0.8	CH ₃ I + NH(CH ₂ CHOHCH ₂) ₂ ^k	60		C
XXa	C ₆ H ₁₁ ^{R-}	170-175	10	RNH ₂ + 2CH ₂ -CH ₂ in CH ₂ OH; 57°	80		
XXIa				RBr ^g + D.E.A.			B-1
XXIIa	n-C ₁₆ H ₃₁ ^{R-}	73-77		1. RBr ^h + D.E.A. 2. HCl-ether	53	CHCl ₃ -ether	B-1
XXIIIa	α-C ₁₀ H ₇ CH ₂ ^{R-}	198	1.0	RCl + D.E.A.	54		B-2
XXIVa		156-158	1.0	RCl + D.E.A.	38		B-2
XXVa	HOCH ₂ CH ₂ CH ₂ ^{R-}	160-161	0.8	^p	70		A-1
XXVIa	HO(CH ₂) ₁₀ ^{R-}	75-77		1. RCl + D.E.A. 2. Acetone-HCl	60	Acetone-EtOH	A-1
XXVIIa	(HOCH ₂ CH ₂) ₂ N-(CH ₂) ₁₀ ^{R-}			Br(CH ₂) ₁₀ Br + 2D.E.A.	52	Acetone	A-5
XXVIIIa	C ₂ H ₅ OCH ₂ CH ₂ CH ₂ ^{R-}	124-130	2.5	RCl ⁱ + D.E.A.	42		A
XXIXa				1.  2. EtOH-HCl	57.5	Aqueous EtOH	A-1
XXXa		125-130 dec.	170-184	2.2 ^m 1. RNH ₂ + 2CH ₂ -CH ₂ ; EtOH; 0-15° 2. EtOH-HCl		CH ₂ OH-EtOH	
XXXIIa		175-181 dec.		RCl ⁿ + D.E.A.; EtOH-HCl	49	EtOH-CH ₂ OH	A
XXXIIIa		183-187		RCl ⁿ + D.E.A.; EtOH-HCl	46	EtOH-CH ₂ OH	A

^a All melting points are uncorrected. ^b Purchased from Carbide & Carbon Chem. Corp. ^c U. S. Patent 2,170,111. ^d Purchased from Paragon Chem. ^e Ford-Moore, Lidstone and Waters, *J. Chem. Soc.*, 820 (1946). ^f Prepared from bromine and silver salt of γ -decalylbutyric acid, b.p. 100-106° (0.2 mm.); *cf.*, *Ber.*, 74, 1567 (1941). ^g Prepared from bromine and silver palmitate, b.p. 152-156° (2.5 mm.); *cf.* ref. *g.* ^h Prepared from decamethylene glycol and phosphorus tribromide, b.p. 128-132° (0.25 mm.), m.p. 24-26° (65%). ⁱ Prepared from trimethylene chlorobromide and sodium ethoxide in alcohol, b.p. 128-131° (38%). ^k This compound has been prepared by a different method by Hanby and Rydon, *J. Chem. Soc.*, 513 (1947). ^l Badger and Cook, *ibid.*, 805 (1939). ^m Boiling point of free base. ⁿ Preparation of this halide described in Table II (XXLIX, L). ^o Padgett and Degering, *J. Ind. Eng. Chem.*, 32, 486 (1940). ^p Jones and Wilson, *J. Chem. Soc.*, 547 (1948).

TABLE II
NITROGEN MUSTARD ANALOGS

	Structure	M-p., °C. ^e	Yield, %	Crystn.-solvent	Formula	Carbon, % Calcd. Found	Hydrogen, % Calcd. Found	N or Cl (I, ionic), % Calcd. Found	Method
XXXIV	$C_6H_5N(CH_2CH_2CH_2CH_2Cl)HCl^d$	131-132.2	25 ^b	Acetone	$C_{10}H_{13}Cl_2N$	54.57 54.66	6.87 6.77		D
XXXV	$CH_2N(CH_2CH_2OCONHC_4H_9)_2 \cdot HCl$	192-194 dec.		EtOH-acetone	$C_{10}H_{24}ClN_2O_4$	57.93 57.67	6.14 6.16		G
XXXVI	$ClCH_2CH_2-N(CH_2CH_2Cl)HCl$	250 dec.	69 ^b	CH ₃ OH	$C_8H_{13}Cl_4N$	33.92 33.73	6.39 6.25		D-1 ^e
XXXVII	$C_2H_5N-CH_2CH_2NC_2H_5 \cdot 2HCl$	159-160	71 ^b	EtOH	$C_{10}H_{24}Cl_4N_2$	38.24 38.27	7.70 7.40		D
XXXVIII	$CH_2N(CH_2COCl)CH_2CH_2Cl$	145-148	8 ^c	Acetone-EtOH	$C_7H_{12}Cl_2N$	38.83 38.99	5.59 5.43	N 6.47 6.91	E
XXXIX	$ClCH_2CH_2NHCH_2CH_2NH_2 \cdot 2HCl$	163-167	68 ^b	CH ₃ OH	$C_4H_{13}Cl_2N_2$	24.57 25.31	6.90 6.70	N 14.33 14.49	E
XL	$n-C_4H_9N(CH_2CH_2CH_2Cl)_2 \cdot HCl$	78-80		C ₆ H ₆	$C_{10}H_{22}Cl_2N$	45.73 45.68	8.44 8.36	N 5.33 5.30	D
XLI	$n-C_4H_9NH(CH_2)_4Cl \cdot HCl$	226-229 dec.	65 ^b	EtOH-acetone	$C_8H_{19}Cl_2N$	48.02 48.10	9.57 9.48	Cl I 17.72 18.06	D
XLII	$n-C_4H_9NH(CH_2)_6Cl \cdot HCl$	200-205 dec.	60 ^b	Acetone	$C_{14}H_{31}Cl_2N$	59.14 59.34	11.00 11.09	Cl I 12.47 12.61	D
XLIII	$n-C_4H_9N(CH_2CH_2CH_2Cl)CH_2CH_2Cl \cdot HCl$	67-70		Acetone-diethyl cellosolve	$C_9H_{20}Cl_4N$			Cl I 14.26 13.96	E
XLIV		154-157	45 ^b	EtOH	$C_7H_9Cl_2NO$			Cl I 18.26 18.14	
XLV	$n-C_4H_9NHCH_2CH_2F \cdot HCl$	195-200			$C_6H_{13}ClFN$			Cl I 22.79 22.54	F
XLVI	$ClCH_2CH_2N-(CH_2)_6-NCH_2CH_2Cl \cdot 2HCl$	100-101	10 ^c	Acetone	$C_{18}H_{40}Cl_4N_2 \cdot 2H_2O$			Cl I 15.33 15.15	D
XLVII		138-140	94		$C_9H_{12}Cl_2O_2N$				E
XLVIII		220-225 dec.	53	EtOH	$C_8H_{11}Cl_2NO$			Cl I 17.04 17.19	E
XLIX		177-178 dec.	77 ^b	Acetone-CH ₃ OH	$C_{13}H_{23}Cl_2N_2O_2$			Cl I 30.77 30.45 Cl I 20.51 20.28	E
L		211-214 dec.	60 ^b	EtOH	$C_{12}H_{21}Cl_3N_2O \cdot H_2O$			Cl I 21.25 21.58	E

^a All melting points are uncorrected. ^b Yield on halogenation reaction. ^c Over-all yield. ^d Picrate prepared by Ross, *J. Chem. Soc.*, 183 (1949). ^e Alternate synthesis described by Childs, *et al.*, *ibid.*, 2174 (1948). ^f For preparation of free base, m.p. 88-91°, see Procedure E. ^g For preparation of free base, m.p. 133-137° dec., see Procedure E.

TABLE IIa
INTERMEDIATES FOR NITROGEN MUSTARD ANALOGS IN TABLE II
c.b. is crude base; d.b. denotes distilled base; p.b. is crystallized free base.

Structure	M.p., °C. ^a	B.p., °C.	Mm.	Prepared	Yield, %	Crystm.-solvent	Method	Used as
XXXIVa 	74-76	118-122	1.5	$\text{CH}_3\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2^b + 2\text{C}_6\text{H}_5\text{NCO} (65^\circ)$		CHCl_3 -pet. ether		d.b.
XXXVa 								p.b.
XXXVIa 								c.b.
XXXVIIa 	100-106		1.0	$\text{Br}(\text{CH}_2)_3\text{Br} + 2\text{C}_2\text{H}_5\text{NHCH}_2\text{CH}_2\text{OH}$	40		A	d.b.
XXXVIIIa 	78-80		40	$\text{CH}_3\text{NH}_2 + 2\text{CH}_2=\text{C}(\text{Cl})\text{CH}_2$			d	d.b.
XXXIXa 	114-116			$\text{HOCH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2 + \text{EtOH-HCl}$			e	2HCl
XLa 	122-128		1.0	$n\text{-C}_4\text{H}_9\text{NH}_2 + 2\text{ClCH}_2\text{CH}_2\text{OH}$	66		A	d.b.
XLIa 	84-90		1.0	$n\text{-C}_4\text{H}_9\text{NH}_2 + \text{Cl}(\text{CH}_2)_2\text{OH}^f$	35		A	d.b.
XLIIa 	85-94			$n\text{-C}_4\text{H}_9\text{NH}_2 + \text{Cl}(\text{CH}_2)_2\text{OH}$	52	Acetone	A-1	b.p.
XLIIIa 	112-118		14	1. $n\text{-C}_4\text{H}_9\text{NH}_2 + \text{Cl}(\text{CH}_2)_2\text{OH}$ -ether, 25°	18		A	d.b.
	122-128		1.0	2. $n\text{-C}_4\text{H}_9\text{NH}(\text{CH}_2)_2\text{OH} + \text{ClCH}_2\text{CH}_2\text{OH}$	42		A	d.b.
XLIVa 								p.b.
XLVIa 				$\text{Br}(\text{CH}_2)_{10}\text{Br} + 2\text{C}_2\text{H}_5\text{NHCH}_2\text{CH}_2\text{OH}$			A-4	c.b.
XLIXa 	185-190 dec.			CH_2OCH_3 HO H_3C CH_2Cl^a $+ \text{C}_2\text{H}_5\text{NHCH}_2\text{CH}_2\text{OH};$ $i\text{-C}_3\text{H}_7\text{OH-HCl}$	16	$\text{CH}_3\text{OH}-i\text{-C}_3\text{H}_7\text{OH}$	A	2HCl
LA 	220-223 dec.			CH_3 HO H_3C CH_2Cl^a $+ \text{C}_2\text{H}_5\text{NHCH}_2\text{CH}_2\text{OH};$ $i\text{-C}_3\text{H}_7\text{OH-HCl}$	20	$\text{EtOH-CH}_3\text{OH}$	A	2HCl

^a All melting points are uncorrected. ^b Purchased from Carbide & Carbon Corp. ^c Wichterle and Hudlicky, *Coll. Czech. Comm.*, **12**, 101 (1947); *C. A.*, **41**, 4148 (1947). ^d Kitchen and Pollard, *J. Org. Chem.*, **8**, 342 (1943). ^e From tetrahydrofuran and hydrogen chloride, "Org. Syntheses," Coll. Vol. II, p. 571 (1943). ^f Knunjan, *Ber.*, **68**, 397 (1935). ^g For preparation of alkylating halide, see Table II, XLVII, XLVIII.

respectively. Tables Ia and IIa also indicate whether these intermediates were used crude, as distilled free bases, or as salts.

The presence of thionyl chloride or thionyl bromide in the reaction product enhances the solubility of the nitrogen mustard. All halogenating agent should therefore be removed before an attempt is made to crystallize the nitrogen mustard product. (It is particularly necessary to do this when thionyl bromide⁹ is the halogenating agent.) Since water accelerates the cyclization of β, β' -dichlorodiethylamines, only anhydrous solvents should be used.

Alkylation. A. γ -Phenylpropyl Diethanolamine (XIA).—A mixture of 100 g. (0.5 mole) of γ -phenylpropyl bromide, 52.5 g. (0.5 mole) of diethanolamine and 35 g. (0.25 mole) of anhydrous potassium carbonate in 200 cc. of absolute ethanol was stirred and heated at reflux temperature for 48 hours. The mixture was cooled, and 200 cc. of chloroform was added. After several hours at room temperature the mixture was filtered; the solid was washed thoroughly with chloroform, and the combined filtrates were concentrated *in vacuo*. The residue was a colorless oil. (1) In the alkylation of diethanolamine with decamethylene chlorohydrin the solvent used for the reaction was xylene-ethanol (4:1); and the reaction time was extended to 72 hours. (2) For alkylation with dihalides two moles of the alkanolamine and one mole of potassium carbonate per mole of dihalide were used. (3) The alkylation with trimethylene bromide was carried out for 64 hours. (4) The reaction time used for the alkylation with decamethylene bromide of ethyl ethanolamine was 72 hours. After filtration and concentration of the reaction mixture water was added to the residue; and the undissolved oil was extracted with chloroform, which was washed with water and dried with anhydrous potassium carbonate. (5) The filtered and concentrated reaction product from the alkylation with decamethylene bromide of diethanolamine was dissolved in water. Solid sodium chloride was added until an oily layer appeared. The oil was separated, dissolved in isopropyl alcohol, and sodium hydroxide pellets were added. The solution was filtered, dried with anhydrous magnesium sulfate and again filtered. Removal of the solvent *in vacuo* left an oil that was dissolved in hot acetone. The acetone solution after being chilled deposited a hygroscopic solid, which was filtered and dried *in vacuo*.

B. *n*-Tetradecyl Diethanolamine Hydrochloride (IXa).—A solution of 138.5 g. (0.5 mole) of tetradecyl bromide, 105 g. (1 mole) of diethanolamine in 400 cc. of diethylcarbinol was heated at reflux temperature overnight. The solution was poured into ice-water, and the oily layer was extracted with ether. The ether layer was washed with water and then extracted three times with dilute hydrochloric acid. The combined acidic extracts were made alkaline with 30% sodium hydroxide solution. The oily layer was extracted with ether; and the ethereal solution was washed with water, brine and then dried with anhydrous potassium carbonate. The ether was evaporated from the filtered solution, and the residue was dissolved in a small amount of acetone. Concentrated hydrochloric acid was added, and the solution was chilled. The white solid was filtered and dried. (1) The alkylation with γ -(β' -decalyl)-propyl bromide was carried out similarly. The solvent used in the alkylation was *n*-butanol, and the reaction mixture was concentrated dry *in vacuo* before the water was added. The material was obtained as the crude free base. (2) The alkylation with *p*-nitrobenzyl bromide was carried out using absolute alcohol as the solvent. The reaction mixture, after removal of the solvent, was dissolved in dilute hydrochloric acid; and the acidic solution was extracted with ether. The acid layer was then treated as in example B. The material was used as the crude free base.

C. Methyl-diisopropanolamine (XIXa).—A solution of 284 g. of methyl iodide, 296 g. of diisopropanolamine in 600 cc. of absolute ethanol was heated at reflux temperature for 48 hours. The solvent was removed *in vacuo*, and the residue was made alkaline with 30% sodium hydroxide solution.

The mixture was extracted four times with chloroform, and the combined chloroform extracts were dried with anhydrous potassium carbonate. The solution was filtered; the filtrate was concentrated *in vacuo*, and the residual oil was distilled.

Halogenation. D. *N*- γ -Phenylpropyl- β, β' -dichlorodiethylamine Hydrochloride (XI).—A solution of 90 cc. of thionyl chloride in 100 cc. of chloroform was chilled to 0° in a four-necked, round-bottomed flask equipped with a mercury-sealed stirrer, thermometer, dropping funnel and a very efficient condenser. (The condenser and dropping funnel were fitted with calcium chloride tubes.) A solution of the aminoalcohol (from A) in 100 cc. of chloroform was added slowly to the stirred, chilled thionyl chloride solution at a rate that maintained the temperature of the reaction mixture at 0–10°. The mixture was kept overnight at room temperature and was then heated at reflux temperature a few hours. The mixture was concentrated *in vacuo*. The residue was dissolved in benzene and was again concentrated *in vacuo*. The residue was dissolved in chloroform, treated with Darco and filtered. Benzene was added to the filtrate until crystallization began. The mixture was chilled, filtered, and the solid was recrystallized from acetone-diethyl cellosolve. (1) In a few cases the thionyl chloride in chloroform was added to a chilled chloroform solution of the aminoalcohol. (2) When the alkylated product was isolated as the hydrochloride the halogenation reaction was carried out by adding the solid hydrochloride portionwise at room temperature to a stirred solution of thionyl chloride in chloroform. The reaction mixture was kept overnight at room temperature, heated at reflux temperature for two hours and worked up as in example D.

E. 3-Chloromethyl-4-methoxymethyl-5-hydroxy-6-methylpyridine Hydrochloride (XLVII).—A suspension of 127 g. (0.58 mole) of 3-hydroxymethyl-4-methoxymethyl-5-hydroxy-6-methylpyridine hydrochloride in 250 cc. of chloroform was stirred while 95 cc. of thionyl chloride was slowly added at room temperature. The mixture after remaining at room temperature overnight was heated at reflux temperature for two hours. The mixture was concentrated *in vacuo*, acetone-ether was added to the residue. A crystalline solid was deposited from the chilled solution. The solid was filtered and washed well with ether.

Free Base.—The salt was dissolved in a minimum quantity of water and treated with a saturated solution of sodium bicarbonate until the mixture was alkaline to litmus paper. The solid was filtered, washed well with water and then air-dried.

F. *N*-*n*-Butyl- β, β' -difluorodiethylamine Hydrochloride (XXXI) and *N*-*n*-Butyl- β -fluoroethylamine Hydrochloride (XLV).—A mixture of 30 g. (0.4 mole) of *n*-butylamine, 128 g. (1 mole) of β -fluoroethyl bromide, 55.2 g. of anhydrous potassium carbonate in 250 cc. of dry benzene was stirred and heated at reflux temperature 36 hours. The mixture was cooled, filtered, and hydrogen chloride gas was passed into the chilled filtrate. A small amount of ether was added, and the crystalline white solid was filtered and washed with benzene. (This material is *n*-butyl- β -fluoroethylamine hydrochloride, m.p. 185–190°.) The filtrate and benzene washes are combined, concentrated free of solvent *in vacuo*, and the residue was slurried with ether. The oily residue readily solidified to a white fluffy solid, which is *N*-*n*-butyl- β, β' -difluorodiethylamine hydrochloride, m.p. 66–68°.

Miscellaneous. G. Methyl Diethanolamine-bis-phenylcarbamate Hydrochloride (XXXV, XXXVA).—Phenyl isocyanate (131 g.) was added slowly to 59.5 g. (0.5 mole) of distilled methyl diethanolamine so that the temperature of the reaction mixture did not exceed 65° (an ice-bath was required). The mixture was warmed at 65° a few hours. The glassy mixture was dissolved in hot chloroform, and a small amount of petroleum ether was added. The precipitated white solid, m.p. 74–76° (XXXVA), was dissolved in ether-acetone and chilled while hydrogen chloride gas was bubbled into the solution. The white granular solid was filtered and washed with ether (XXXV).

(9) Elderfield, *et al.*, THIS JOURNAL, 68, 1581 (1946).