Biological Activity

The estrogenic and antiestrogenic activities of these compounds were assessed on the basis of stimulation of the growth of the uterus of immature female rats. The test compounds were given by gavage either alone or in combination with estradiol (0.002 mg/kg per day) administered subcutaneously. On the 4th day the uteri were excised, blotted dry, and weighed. The antifertility activity was determined by administering the compound by gavage to mature female rats for 6 days beginning the morning after a proven insemination. The rats were autopsied 9 days after the last medication and their uteri were removed and examined for implantation sites and gross abnormalities.

Synthesis and Antiarrhythmic Activity of Naphthylalkylamines

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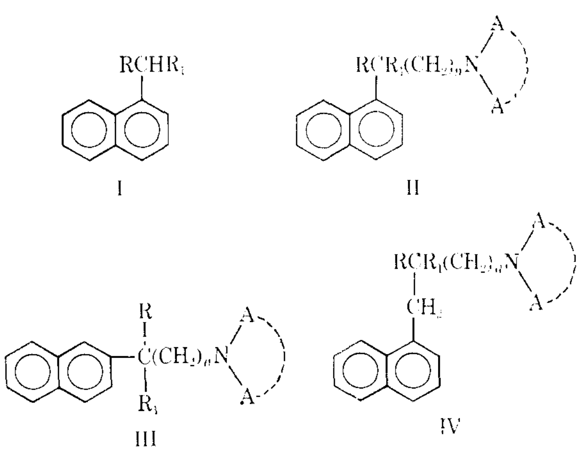
A further series of naphthylalkylamines was prepared and assayed for antiarrhythmic activity. Many of the compounds were found to be active *in vitro*, but only for five of them was activity confirmed *in vivo*. Comparative regression line analysis revealed that among the naphthylalkylamines so far investigated for antiarrhythmic activity, 1,5-dimorpholino-3-(α-naphthyl)pentane is still the most interesting one.

Our finding[1] that some α-naphthylalkylamines, especially 1,5-dimorpholino-3-(α-naphthyl)pentane, possess marked antiarrhythmic activity led us to extend this investigation to 83 chemically related compounds. The new naphthylalkylamines had the general structures I–IV, in which R was an alkyl or aminoalkyl group; R_1 was a primary amino or aminomethyl group; NAA was a tertiary amino group; n = 2–4.



Naphthylalkylamines with $R_1 = NH_2$ were prepared from the corresponding amides by the Hofmann reaction. Reduction of the related nitriles with excess LAH in Et_2O afforded naphthylalkylamines with $R_1 = CH_2NH_2$, reaction time and excess LAH depending on the steric hindrance of the nitriles.

Pharmacology.—All of the substances listed in Table II were submitted to the *in vitro* antiarrhythmic test, using quinidine and 1,5-dimorpholino-3-(α-naphthyl)pentane as reference standards. Many of them considerably reduced the maximal rate of stimulation of electrically driven isolated guinea pig auricles but did not inhibit the amplitude of contractions. These results are included in Table II in terms of relative potency, which was calculated from ED_{35} values as previously described[2] and expressed in relation to the antiarrhythmic activity of quinidine, which has been assigned the potency of 1.0.

Due to the promising results *in vitro*, all of the above compounds were tested subcutaneously in rats for the action on arrhythmias induced by $CaCl_2$. The procedure was essentially the same as previously described,[2] except that 120 mg/kg of $CaCl_2$ was infused. Reference standards and expression of results were as *in vitro*. Of all the tested substances, only **51**, **64**, **82**,

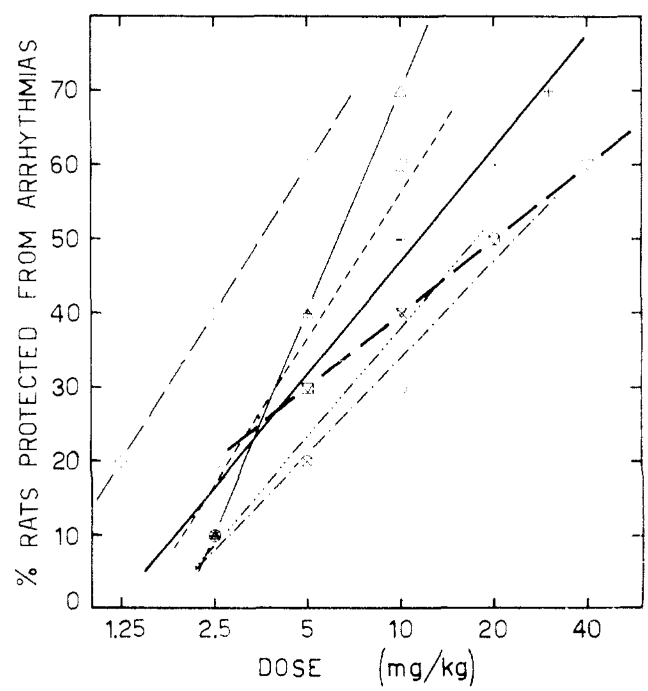


Figure 1.—$CaCl_2$-induced arrhythmias in rats. Regression lines of: **51** (△—△); **64** (○·-·-·-○); **82** (□------□); **84** (◇···◇); **120** (×·····×); 1,5-dimorpholino-3-(α-naphthylpentane) (+—+); and quinidine (▽----▽).

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(2) C. Bianchi, G. P. Sanna, and C. Turba, *Arzneim. Forsch.*, **18**, 845 (1968).

TABLE I
INTERMEDIATE NITRILES

Compd	R	R1	(A)N(CH2)n	Structure	Yield, %[a]	Bp (mm) or mp, °C	Formula[b]
1	n-C_3H_7	CN	$(CH_3)_2N(CH_2)_2$	II	53.9	145–150 (0.2)	$C_{19}H_{24}N_2$
2	n-C_4H_9	CN	$(CH_3)_2N(CH_2)_2$	II	62.8	177–180 (0.2)	$C_{20}H_{26}N_2$
3	i-C_4H_9	CN	$(CH_3)_2N(CH_2)_2$	II	82.3	147–150 (0.4)	$C_{20}H_{26}N_2$
4	sec-C_4H_9	CN	$CH_3(C_2H_5)N(CH_2)_2$	II	78	167–169 (0.2)	$C_{21}H_{28}N_2$
5	$CH_3(C_2H_5)N(CH_2)_2$	CN	$CH_3(C_2H_5)N(CH_2)_2$	II	77.6	190–195 (0.6)	$C_{22}H_{31}N_3$
6	sec-C_4H_9	CN	$(C_2H_5)_2N(CH_2)_2$	II	74	170–175 (0.5)	$C_{22}H_{30}N_2$
7	$(C_2H_5)_2N(CH_2)_2$	CN	$(C_2H_5)_2N(CH_2)_2$	II	84.6	174–178 (0.1)	$C_{24}H_{35}N_3$
8	i-C_3H_7	CN	$(i\text{-}C_3H_7)_2N(CH_2)_2$	II	68.6	167–170 (0.3)	$C_{23}H_{32}N_2$
9	sec-C_4H_9	CN	$(i\text{-}C_3H_7)_2N(CH_2)_2$	II	51.6	168–170 (0.1)	$C_{24}H_{34}N_2$
10	$(i\text{-}C_3H_7)_2N(CH_2)_2$	CN	$(i\text{-}C_3H_7)_2N(CH_2)_2$	II	70	200–205 (0.6)	$C_{28}H_{43}N_3$
11	CH_3	CN	c	II	35.3	180–182 (0.5)	$C_{19}H_{22}N_2$
12	C_2H_5	CN	c	II	77.5	185–188 (0.7)	$C_{20}H_{24}N_2$
13	n-C_3H_7	CN	c	II	74.8	190–191 (0.75)	$C_{21}H_{26}N_2$
14	i-C_3H_7	CN	c	II	77.1	85–87	$C_{21}H_{26}N_2$
15	n-C_4H_9	CN	c	II	69.5	195–200 (0.15)	$C_{22}H_{28}N_2$
16	i-C_4H_9	CN	c	II	69.3	180–183 (0.2)	$C_{22}H_{28}N_2$
17	sec-C_4H_9	CN	c	II	89	187–190 (0.5)	$C_{22}H_{28}N_2$
18	c	CN	c	II	78.8	215–220 (0.15)	$C_{24}H_{31}N_3$
19	n-C_3H_7	CN	d	II	66.2	179–182 (0.05)	$C_{22}H_{28}N_2$
20	n-C_4H_9	CN	d	II	79.2	190–195 (0.2)	$C_{23}H_{30}N_2$
21	i-C_4H_9	CN	d	II	63.5	205–209 (0.8)	$C_{23}H_{30}N_2$
22	n-C_3H_7	CN	e	II	43.7	109–111	$C_{21}H_{26}N_2O$
23	n-C_4H_9	CN	e	II	39	200–205 (0.2)	$C_{22}H_{28}N_2O$
24	i-C_4H_9	CN	e	II	52.4	190–195 (0.2)	$C_{22}H_{28}N_2O$
25	CH_3	CN	$(CH_3)_2N(CH_2)_3$	II	48.7	155–157 (0.2)	$C_{18}H_{22}N_2$
26	sec-C_4H_9	CN	$(CH_3)_2N(CH_2)_3$	II	79	164–167 (0.4)	$C_{21}H_{28}N_2$
27	sec-C_4H_9	CN	f	II	54.3	96–99	$C_{23}H_{30}N_2$
28	sec-C_4H_9	CN	g	II	44.4	123–124	$C_{24}H_{32}N_2$
29	sec-C_4H_9	CN	h	II	58	90–92	$C_{25}H_{30}N_2O$
30	sec-C_4H_9	CN	$(CH_3)_2N(CH_2)_4$	II	29	165–170 (0.25)	$C_{22}H_{30}N_2$
31	i-C_3H_7	CN	i	II	80	182–185 (0.25)	$C_{23}H_{30}N_2$
32	sec-C_4H_9	CN	i	II	75.7	187–190 (0.1)	$C_{24}H_{32}N_2$
33	i-C_3H_7	CN	j	II	71.7	207–210 (0.5)	$C_{24}H_{32}N_2$
34	sec-C_4H_9	CN	j	II	61.7	196–200 (0.2)	$C_{25}H_{34}N_2$
35	i-C_3H_7	CN	k	II	55	200–202 (0.25)	$C_{23}H_{30}N_2O$
36	sec-C_4H_9	CN	k	II	70	205–210 (0.1)	$C_{24}H_{32}N_2O$
37	sec-C_4H_9	CN	$(CH_3)_2N(CH_2)_2$	III	75.3	150–155 (0.09)	$C_{20}H_{26}N_2$
38	i-C_3H_7	CN	e	III	66	192–195 (0.15)	$C_{21}H_{26}N_2O$
39	sec-C_4H_9	CN	e	III	74.5	193–196 (0.1)	$C_{22}H_{28}N_2O$
40	sec-C_4H_9	CN	$(CH_3)_2N(CH_2)_2$	IV	41.5	62–63	$C_{21}H_{28}N_2$
41	i-C_3H_7	CN	d	IV	41	96–98	$C_{23}H_{30}N_2$
42	sec-C_4H_9	CN	d	IV	66	102–103	$C_{24}H_{32}N_2$

[a] Purified product. [b] All compounds were analyzed for C, H, N and the analytical results were within ± 0.4% of the theoretical values. [c] 2-(1-Pyrrolidinyl)ethyl. [d] 2-Piperidinoethyl. [e] 2-Morpholinoethyl. [f] 3-(1-Pyrrolidinyl)propyl. [g] 3-Piperidinopropyl. [h] 3-Morpholinopropyl. [i] 4-(1-Pyrrolidinyl)butyl. [j] 4-Piperidinobutyl. [k] 4-Morpholinobutyl.

84, and **120** had confirmed activity *in vivo;* the relative potencies (quinidine = 1.0) were 1.6, 0.7, 1.5, 3.4, and 0.8, respectively; the potency of 1,5-dimorpholino-3-(α-naphthyl)pentane was 1.2. However, an examination of the regression lines (Figure 1) revealed that the new compounds had a range of active doses narrower than both the reference standards.

On the basis of previous[1] and present results the conclusion may be drawn that, among the naphthylalkylamines so far investigated for antiarrhythmic activity, 1,5-dimorpholino-3-(α-naphthyl)pentane is still to be considered as the most interesting one.

Experimental Section[3]

Intermediates.—Many of the nitriles were prepared as previously described.[4-8] The new nitriles (Table I) were obtained similarly. Except for the following compound, all the amides were prepared as previously reported.[8-10]

α-(2-Dimethylaminoethyl)-1-naphthylacetamide.—A solution of α-(2-dimethylaminoethyl)-1-naphthylacetonitrile (10 g, 0.042 mol) and KOH (7 g, 0.125 mol) in 95% EtOH (40 ml) was refluxed for 3 hr with stirring, cooled, and poured into H_2O. The separated pasty product was extracted (Et_2O), washed (H_2O), and dried (Na_2SO_4). Evaporation of the solvent yielded a

(3) Boiling points are uncorrected. Melting points are corrected and were taken on a Büchi capillary melting point apparatus.

(4) S. Casadio, G. Pala, and T. Bruzzese, *Farmaco Ed. Sci.*, **17**, 871 (1962).
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(6) G. Pala, S. Casadio, T. Bruzzese, E. Crescenzi, and E. Marazzi-Uberti, *ibid.*, **8**, 698 (1965).
(7) G. Pala, S. Casadio, T. Bruzzese, and G. Coppi, *ibid.*, **9**, 786 (1966).
(8) S. Casadio, T. Bruzzese, G. Pala, G. Coppi, and C. Turba, *ibid.*, **9**, 707 (1966).
(9) S. Casadio, G. Pala, T. Bruzzese, E. Crescenzi, E. Marazzi-Uberti, and G. Coppi, *ibid.*, **8**, 594 (1965).
(10) M. Julia and M. Baillargé, *Bull. Soc. Chim. Fr.*, 928 (1957).

TABLE II

PHYSICAL PROPERTIES AND ANTIARRHYTHMIC ACTIVITY OF NAPHTHYLALKYLAMINES

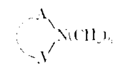
Compd	R	R_1		Structure	Method	Reaction conditions: Time, hr	Reaction conditions: LAH: nitrile, mol ratio	Yield, %[a]	Bp (mm), °C	Formula[b]	Rel potency
43	CH_3	NH_2		I	A			66	118–120 (0.1)	$C_{12}H_{13}N$	0.6
44	$(CH_3)_2N(CH_2)_2$	NH_2		I	A			62	130–133 (0.2)	$C_{17}H_{26}N_2$	0.3
45	CH_3	CH_2NH_2		I	B	20	2	81	112–113 (0.1)	$C_{13}H_{15}N$	*e*
46	*i*-C_3H_7	CH_2NH_2		I	B	20	2	83	130–132 (0.2)	$C_{15}H_{19}N$	0.9
47	*n*-C_4H_9	CH_2NH_2		I	B	10	4	82	130–132 (0.2)	$C_{16}H_{21}N$	*e*
48	$(CH_3)_2N(CH_2)_2$	CH_2NH_2		I	B	10	2	66	147–150 (0.3)	$C_{16}H_{22}N_2$	1.1
49	$CH_3(C_2H_5)N(CH_2)_2$	CH_2NH_2		I	B	10	2	67	141–142 (0.3)	$C_{17}H_{24}N_2$	*e*
50	$(C_2H_5)_2N(CH_2)_2$	CH_2NH_2		I	B	10	2	60	150–153 (0.2)	$C_{18}H_{26}N_2$	*e*
51	*d*	CH_2NH_2		I	B	20	2	76	183–184 (0.2)	$C_{19}H_{26}N_2$	1.2
52	*e*	CH_2NH_2		I	B	40	5	53	180 (0.3)	$C_{18}H_{24}N_2O$	*e*
53	$(CH_3)_2N(CH_2)_3$	CH_2NH_2		I	B	10	2	57	170–172 (0.2)	$C_{17}H_{24}N_2$	0.3
54	*i*-C_3H_7	NH_2	$(CH_3)_2N(CH_2)_2$	II	A			83	137–139 (0.2)	$C_{18}H_{26}N_2$	*e*
55	*i*-C_3H_7	NH_2	*d*	II	A			26	180–183 (0.5)	$C_{21}H_{31}N_2$	*e*
56	*i*-C_3H_7	NH_2	$(CH_3)_2N(CH_2)_3$	II	A			45	140–141 (0.1)	$C_{19}H_{28}N_2$	*e*
57	*i*-C_3H_7	NH_2	*f*	II	A			23	190–194 (0.4)	$C_{22}H_{32}N_2$	*e*
58	CH_3	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	II	B	15	4	78	145 (0.2)	$C_{17}H_{24}N_2$	0.4
59	C_2H_5	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	II	B	15	2	62	152–155 (0.2)	$C_{18}H_{26}N_2$	0.5
60	*n*-C_3H_7	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	II	B	10	2	67	157–158 (0.1)	$C_{19}H_{28}N_2$	0
61	*i*-C_3H_7	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	II	B	20	4	77	148–149 (0.1)	$C_{19}H_{28}N_2$	0.7
62	*n*-C_4H_9	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	II	B	4	2	73	167–169 (0.1)	$C_{20}H_{30}N_2$	*e*
63	*i*-C_4H_9	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	II	B	20	2	85	157–158 (0.5)	$C_{20}H_{30}N_2$	*e*
64	*sec*-C_4H_9	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	II	B	15	5	80	168–170 (0.4)	$C_{20}H_{30}N_2$	0.4
65	$(CH_3)_2N(CH_2)_2$	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	II	B	60	4	68	160–162 (0.1)	$C_{20}H_{31}N_3$	*e*
66	*i*-C_3H_7	CH_2NH_2	$CH_3(C_2H_5)N(CH_2)_2$	II	B	20	4	82	174–176 (0.8)	$C_{20}H_{30}N_2$	*e*
67	*sec*-C_4H_9	CH_2NH_2	$CH_3(C_2H_5)N(CH_2)_2$	II	B	20	4	81	176–178 (0.7)	$C_{21}H_{32}N_2$	*e*
68	$CH_3(C_2H_5)N(CH_2)_2$	CH_2NH_2	$CH_3(C_2H_5)N(CH_2)_2$	II	B	10	4	58	163–164 (0.1)	$C_{22}H_{35}N_3$	*e*
69	*i*-C_3H_7	CH_2NH_2	$(C_2H_5)_2N(CH_2)_2$	II	B	10	4	67	163–165 (0.5)	$C_{21}H_{32}N_2$	*e*
70	*sec*-C_4H_9	CH_2NH_2	$(C_2H_5)_2N(CH_2)_2$	II	B	15	6	82	168–170 (0.2)	$C_{22}H_{34}N_2$	*e*
71	$(C_2H_5)_2N(CH_2)_2$	CH_2NH_2	$(C_2H_5)_2N(CH_2)_2$	II	B	10	3	82	180–182 (0.2)	$C_{24}H_{39}N_3$	*e*
72	*i*-C_3H_7	CH_2NH_2	$CH_3(C_6H_5CH_2)N(CH_2)_2$	II	B	15	6	72	184–185 (0.1)	$C_{25}H_{32}N_2$	*e*
73	*i*-C_3H_7	CH_2NH_2	$(i\text{-}C_3H_7)_2N(CH_2)_2$	II	B	40	6	68	180–182 (0.1)	$C_{23}H_{36}N_2$	*e*
74	*sec*-C_4H_9	CH_2NH_2	$(i\text{-}C_3H_7)_2N(CH_2)_2$	II	B	30	6	60	176–178 (0.4)	$C_{24}H_{38}N_2$	*e*
75	$(i\text{-}C_3H_7)_2N(CH_2)_2$	CH_2NH_2	$(i\text{-}C_3H_7)_2N(CH_2)_2$	II	B	10	3	80	184–185 (0.5)	$C_{28}H_{47}N_3$	*e*
76	CH_3	CH_2NH_2	*g*	II	B	30	2	76	168–171 (0.1)	$C_{19}H_{26}N_2$	*e*
77	C_2H_5	CH_2NH_2	*g*	II	B	10	2	67	179–181 (0.2)	$C_{20}H_{28}N_2$	0.7
78	*n*-C_3H_7	CH_2NH_2	*g*	II	B	4	2	71	190–192 (0.2)	$C_{21}H_{30}N_2$	*e*
79	*i*-C_3H_7	CH_2NH_2	*g*	II	B	20	5	81	188–190 (0.3)	$C_{21}H_{30}N_2$	0.3
80	*n*-C_4H_9	CH_2NH_2	*g*	II	B	4	3	85	188–190 (0.4)	$C_{22}H_{32}N_2$	*e*
81	*i*-C_4H_9	CH_2NH_2	*g*	II	B	10	3	78	182–184 (0.4)	$C_{22}H_{32}N_2$	1.5
82	*sec*-C_4H_9	CH_2NH_2	*g*	II	B	40	4	75	194–196 (0.3)	$C_{22}H_{32}N_2$	0.7
83	*g*	CH_2NH_2	*g*	II	B	10	3	77	216–218 (0.3)	$C_{24}H_{35}N_3$	*e*
84	CH_3	CH_2NH_2	*d*	II	B	15	3	75	170–173 (0.1)	$C_{20}H_{28}N_2$	0.4
85	C_2H_5	CH_2NH_2	*d*	II	B	10	2	81	172–174 (0.2)	$C_{21}H_{30}N_2$	1.8
86	*n*-C_3H_7	CH_2NH_2	*d*	II	B	20	2	59	170–173 (0.1)	$C_{22}H_{32}N_2$	0.6
87	*i*-C_3H_7	CH_2NH_2	*d*	II	B	40	3	79	172–175 (0.1)	$C_{22}H_{32}N_2$	1.3
88	*n*-C_4H_9	CH_2NH_2	*d*	II	B	4	2	89	192–194 (0.5)	$C_{23}H_{34}N_2$	*e*
89	*i*-C_4H_9	CH_2NH_2	*d*	II	B	10	4	86	190–192 (0.4)	$C_{23}H_{34}N_2$	1.3
90	*sec*-C_4H_9	CH_2NH_2	*d*	II	B	30	2	68	196–199 (0.3)	$C_{23}H_{34}N_2$	1.3
91	*d*	CH_2NH_2	*d*	II	B	15	2	79	220–223 (0.1)	$C_{26}H_{39}N_3$	*e*
92	CH_3	CH_2NH_2	*e*	II	B	15	3	76	175–176 (0.1)	$C_{19}H_{26}N_2O$	*e*
93	C_2H_5	CH_2NH_2	*e*	II	B	15	3	74	195–196 (0.2)	$C_{20}H_{28}N_2O$	0.3
94	*n*-C_3H_7	CH_2NH_2	*e*	II	B	20	2	58	190–194 (0.2)	$C_{21}H_{30}N_2O$	*e*
95	*i*-C_3H_7	CH_2NH_2	*e*	II	B	105	4	71	193–195 (0.2)	$C_{21}H_{30}N_2O$	0.6
96	*n*-C_4H_9	CH_2NH_2	*e*	II	B	10	4	68	200–201 (0.4)	$C_{22}H_{32}N_2O$	*e*
97	*i*-C_4H_9	CH_2NH_2	*e*	II	B	15	3	72	198–200 (0.5)	$C_{22}H_{32}N_2O$	2.0
98	*sec*-C_4H_9	CH_2NH_2	*e*	II	B	20	6	77	203–204 (0.3)	$C_{22}H_{32}N_2O$	0.3
99	*e*	CH_2NH_2	*e*	II	B	180	4	43	230–233 (0.1)	$C_{24}H_{35}N_3O_2$	*e*
100	CH_3	CH_2NH_2	$(CH_3)_2N(CH_2)_3$	II	B	10	4	81	150–151 (0.1)	$C_{18}H_{26}N_2$	*e*
101	*i*-C_3H_7	CH_2NH_2	$(CH_3)_2N(CH_2)_3$	II	B	20	2	66	166–168 (0.2)	$C_{20}H_{30}N_2$	0.4
102	*sec*-C_4H_9	CH_2NH_2	$(CH_3)_2N(CH_2)_3$	II	B	15	4	78	167–169 (0.2)	$C_{21}H_{32}N_2$	0.4
103	$(CH_3)_2N(CH_2)_3$	CH_2NH_2	$(CH_3)_2N(CH_2)_3$	II	B	10	4	60	186–188 (0.3)	$C_{22}H_{35}N_3$	*e*
104	*i*-C_3H_7	CH_2NH_2	*h*	II	B	30	5	83	180–182 (0.2)	$C_{22}H_{32}N_2$	*e*
105	*sec*-C_4H_9	CH_2NH_2	*h*	II	B	60	4	84	195–196 (0.4)	$C_{23}H_{34}N_2$	*e*

TABLE II (*Continued*)

Compd	R	R_1	⟨A/A⟩N$(CH_2)_n$	Structure	Method	Reaction conditions: Time, hr	Reaction conditions: LAH:nitrile, mol ratio	Yield, %[a]	Bp (mm), °C	Formula[b]	Rel potency
106	i-C_3H_7	CH_2NH_2	*f*	II	B	40	3	77	186–188 (0.2)	$C_{23}H_{34}N_2$	*c*
107	*sec*-C_4H_9	CH_2NH_2	*f*	II	B	40	9	73	193–195 (0.2)	$C_{24}H_{36}N_2$	*c*
108	i-C_3H_7	CH_2NH_2	*i*	II	B	20	4	71	198–200 (0.1)	$C_{22}H_{32}N_2O$	*c*
109	*sec*-C_4H_9	CH_2NH_2	*i*	II	B	30	5	87	190–192 (0.2)	$C_{23}H_{34}N_2O$	*c*
110	i-C_3H_7	CH_2NH_2	$(CH_3)_2N(CH_2)_4$	II	B	10	2	71	156–158 (0.1)	$C_{21}H_{32}N_2$	1.0
111	*sec*-C_4H_9	CH_2NH_2	$(CH_3)_2N(CH_2)_4$	II	B	15	4	86	170–172 (0.1)	$C_{22}H_{34}N_2$	0.7
112	i-C_3H_7	CH_2NH_2	*j*	II	B	40	3	71	195–196 (0.1)	$C_{23}H_{34}N_2$	*c*
113	*sec*-C_4H_9	CH_2NH_2	*j*	II	B	40	3	75	184–186 (0.1)	$C_{24}H_{36}N_2$	*c*
114	i-C_3H_7	CH_2NH_2	*k*	II	B	40	3	80	189–191 (0.2)	$C_{24}H_{36}N_2$	*c*
115	*sec*-C_4H_9	CH_2NH_2	*k*	II	B	40	3	75	195–197 (0.2)	$C_{25}H_{38}N_2$	*c*
116	i-C_3H_7	CH_2NH_2	*l*	II	B	40	5	78	220–223 (0.4)	$C_{23}H_{34}N_2O$	*c*
117	*sec*-C_4H_9	CH_2NH_2	*l*	II	B	15	3	92	210–212 (0.3)	$C_{24}H_{36}N_2O$	*c*
118	i-C_3H_7	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	III	B	15	4	56	154–156 (0.1)	$C_{19}H_{28}N_2$	1.8
119	*sec*-C_4H_9	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	III	B	4	5	70	162–164 (0.2)	$C_{20}H_{30}N_2$	2.3
120	i-C_3H_7	CH_2NH_2	*e*	III	B	4	5	64	205–206 (0.2)	$C_{21}H_{30}N_2O$	1.6
121	*sec*-C_4H_9	CH_2NH_2	*e*	III	B	4	5	77	207–208 (0.1)	$C_{22}H_{32}N_2O$	2.0
122	i-C_3H_7	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	IV	B	3	2	69	154–156 (0.1)	$C_{20}H_{30}N_2$	0.7
123	*sec*-C_4H_9	CH_2NH_2	$(CH_3)_2N(CH_2)_2$	IV	B	15	2	83	162–164 (0.1)	$C_{21}H_{32}N_2$	*c*
124	i-C_3H_7	CH_2NH_2	*d*	IV	B	15	2	87	184–183 (0.1)	$C_{23}H_{34}N_2$	0.9
125	*sec*-C_4H_9	CH_2NH_2	*d*	IV	B	15	4	76	202–204 (0.5)	$C_{24}H_{36}N_2$	*c*
1,5-Dimorpholino-3-(α-naphthyl)pentane											1.8
Quinidine											1.0

[a] Distilled product. [b] All compounds were analyzed for C, H, N and the analytical results were within ±0.4% of the theoretical values. [c] Inactive or cardiotoxic compound. [d] 2-Piperidinoethyl. [e] 2-Morpholinoethyl. [f] 3-Piperidinopropyl. [g] 2-(1-Pyrrolidinyl)-ethyl. [h] 3-(1-Pyrrolidinyl)propyl. [i] 3-Morpholinopropyl. [j] 4-(1-Pyrrolidinyl) butyl. [k] 4-Piperidinobutyl. [l] 4-Morpholinobutyl.

residue which, on trituration with 1:1 Et_2O–petroleum ether (bp 40–70°) gave a colorless solid (6.9 g, 64%), mp 79–81°. *Anal.* ($C_{16}H_{20}N_2O$) C, H, N.

Naphthylalkylamines with R_1 = NH_2 or CH_2NH_2 are listed in Table II, and their preparation is illustrated by the following methods.

Method A. 1-Dimethylamino-3-amino-3-(α-naphthyl)-4-methylpentane (54).—α-Isopropyl-α-(2-dimethylaminoethyl)-1-naphthylacetamide (17.5 g, 0.059 mol) was added with stirring to a solution of Na (2.7 g, 1.17 g-atom) in anhydrous MeOH (100 ml), and then Br_2 (9.38 g, 0.059 mol) was rapidly dropped into the solution. After 6 hr stirring at room temperature, the mixture was allowed to stand overnight, and the solvent was removed under reduced pressure. The residue was dissolved in Et_2O, washed (H_2O), and dried (Na_2SO_4) and the solution was evaporated to dryness. The new residue was dissolved in 95% EtOH (130 ml), 50% KOH (130 ml) was added to it, and the mixture was refluxed for 6 hr, poured into cold H_2O, and extracted (Et_2O). The extract was washed (H_2O) and dried (Na_2SO_4), the solvent was evaporated, and the residue was distilled to give a viscous and colorless oil, bp 137–139° (0.2 mm).

Method B. *N*-[3-Aminomethyl-3-(α-naphthyl)heptyl]piperidine (88).—A solution of α-*n*-butyl-α-(2-piperidinoethyl)-1-naphthylacetonitrile (50 g, 0.15 mol) in dry Et_2O (100 ml) was dropped at room temperature for 2 hr into a stirred suspension of LAH (11.35 g, 0.3 mol) in dry Et_2O (900 ml). The mixture was refluxed for 4 hr with stirring, cooled, and cautiously decomposed with H_2O (100 ml). The organic layer was separated, washed (H_2O), and dried (Na_2SO_4). The solvent was evaporated and the residue was distilled to give a viscous and colorless oil, bp 192–194° (0.5 mm).

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