16.8 g (0.46 mole) of LAH, and treatment of the Et_2O soln of the crude free base with 5% aq HCl gave cryst hydrochloride insol in both layers. It was collected, dried, and recrystd first from a mixt of *i*-PrOH and EtOH and then from EtOH yielding 18.5 g of white crystals, mp 280–281°.

Free Base 59.—A sample of the hydrochloride was converted to the free base with NaOH and recrystd from methylcyclohexane giving white crystals, mp 178.5–179.5°.

9-(2-Amino-1-methylethyl)-10,10-dimethyl-9-anthrol maleate (61) was prepd from 22 g (0.1 mole) of 10,10-dimethyl-9-anthrone and 6.6 g (0.123 mole) of EtCN by the method used for 1 using 0.12 mole and $LiNEt_2$[16] in place of the $NaNH_2$. The crude free base was isolated as an oil, dissolved in Et_2O, and acidified with a slight excess of ethanolic maleic acid. The resulting maleate salt was recrystd from 100 ml of *i*-PrOH, yielding 18.8 g of light tan crystals, mp 154–155° dec.

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Central Nervous System Agents. 3.[1] Structure–Activity Relationship of a Series of Diphenylaminopropanols

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A series of diphenylaminopropanols was evaluated for acute toxicity, anticonvulsant, anorexigenic, and anticholinergic activity as well as effect on simple reflexes. Therapeutic ratio was maximized in 1,1-diphenyl-2-methyl-3-aminopropanol·HCl (II-2). Anticholinergic activity was minimized by the presence of a 2-Me group. In general, tertiary amines were less active as anticonvulsants and on simple reflexes, than primary or secondary amines. Also increasing the size of the substituents on the amine decreased activity. Substitution on the Ph rings decreased activity except for the *m*-F derivative which was more active than II-2 but also more toxic. The optical isomers of II-2 were resolved and the *l* isomer (II-6) was no more toxic but markedly superior in activity.

The synthesis of a series of diphenyl aminopropanols which we have studied is reported in the two preceding communications.[1] Our interest in the compounds was due to their unique dose-related spectrum of pharmacologic activity. Administration of one of the more potent analogs to a variety of species produces apparent stimulation at low doses. At slightly higher doses the effect is one of mixed stimulation and depression with marked motor incoordination. In this dose range some of the compounds appeared to be potent anticonvulsants. Still higher doses produce convulsions in rats and mice and an apparent paralysis with ocassional clonic twitching in cats and dogs. Because of this spectrum of effects, structure–activity studies had to include a broad spectrum of tests. For this reason, testing included effects of the compounds on anticonvulsant and anorexigenic end points as well as effects on several simple reflexes. Anticholinergic testing was also included since many diphenyl aminopropanols are known cholinergic blocking agents.[2] Although it is not known which, if any, of the CNS effects are mediated by a cholinergic mechanism, it was hoped useful compounds could be found by maximizing the CNS effects while minimizing the peripheral effects.

Methods.—Male albino mice of the Carworth Farms strain (18–22 g) and adult mongrel dogs were used in all studies. For studies in mice, compounds were suspended or dissolved in 0.25% aq methylcellulose and administered ip. At least 3 dose levels spaced at a 0.3 log interval were used for each end point. The effective dose (ED_{50}) was calcd by the Spearman and Karber method.[3]

Procedures for measuring acute toxicity (LD_{50}), antagonism of nicotine seizure (N_{50}), and antagonism of isolation-induced stress (FM_{50}) have been described.[4] The same source also describes methods for evaluation of compounds on simple behavioral reflexes—traction

(1) Articles 1 and 2: R. B. Moffett, R. E. Strube, and L. L. Skaletzky, *J. Med. Chem.*, **14**, 1088 (1971); and R. B. Moffett and T. L. Pickering, *ibid.*, **14**, 1100 (1971). The numbering of compounds in this article refers to that used in the preceding articles. I refers to Table I in article I. II refers to Table I in article II. Compounds designated III have been previously reported (see ref 2 and footnotes in tables).

(2) (a) J. J. Denton, H. P. Schedl, W. B. Neir, and V. A. Lawson, *J. Amer. Chem. Soc.*, **71**, 2054 (1949); (b) R. W. Cunningham, B. K. Hained, M. C. Clark, R. R. Cosgrove, N. S. Daugherty, C. H. Hine, R. E. Vessey, and N. N. Yda, *J. Pharmacol. Exp. Ther.*, **96**, 151 (1949); (c) D. W. Adamson, *J. Chem. Soc., Suppl.*, **5**, 144 (1949).

(3) D. J. Finney, "Statistical Methods in Biological Assay," Hafner Publishing Co., New York, N. Y., 1952.

(4) G. A. Youngdale, D. G. Anger, W. C. Anthony, J. P. DaVanzo, M. E. Greig, R. V. Heinzelman, H. H. Keasling, and J. Szmuszkovicz, *J. Med. Chem.*, **7**, 415 (1964).

(Tr_{50}), chimney (CH_{50}), and dish (D_{50}). Kerley, *et al.*,[5] gave the method used for evaluation central (TC_{50}) and peripheral (Tp_{50}) anticholinergic activity as indicated by antagonism of the actions of Tremorine. Other test procedures used for this series of compounds were as follows.

Thiosemicarbazide Antagonism (TSC_{50}).—Groups of 6 mice were dosed with test compound and immediately challenged with TSC, 20 mg/kg by the ip route. ED_{50}'s were calcd from the number of survivers 4 hr later.

Electroshock Antagonism (ES_{50}).—Groups of 6 mice were dosed with test compound and shocked *via* ear electrodes 30 min later with a 60-Hz current for 0.2 sec at 25 mA. Protection was indicated by failure of the mice to show a tonic extensor seizure.

Mydriatic Activity (P_{50}).—The pupil diameter was estimated visually on a scale of 0–4 30 min after compound administration. Normal pupil size was rated as 1 while a 4 indicated maximum dilation and a 0, constriction. The number of mice out of 6 with pupil diameters of 3 or 4 was used to calculate the P_{50}.

Anorexigenic Activity.—Dogs weighing 10–15 kg were housed singly and fed dog pellets (Purina Laboratory Chow) at the same time each day for a 30-min period. Compounds were given orally to groups of 4 dogs at 1 or 5 mg/kg in gelatin capsules 1 hr prior to food presentation. Per cent decrease in food consumption was calcd based on the average amount of food eaten in the previous 5 days.

Results and Discussion

Substituents on the Amine.—Effects of changes in substituents on the amine of the diphenyl aminopropanols are depicted in Table I. The effects of several known centrally acting drugs on the test procedures used is shown at the bottom of this table.

Monoalkylation of the amine N with Me (II-18) and Et (II-23) had little effect on overall activity (compare with the free amine II-2). Larger substituents such as Pr (II-25), *i*-Pr (II-28), and Bu (II-31) were more toxic but otherwise less active. Still larger substituents (II-42, II-44, II-47, II-50) were less active on all end points. Increasing the chain length of dialkyl substituents from Me (III-1), to Et (III-2), Pr (I-4), and Bu (I-8) resulted in a progressive loss of activity. The relatively high activity of the lower alkyl substituted amines may be due to bioconversion of the primary amine, the most active compound. Activity of compounds with the amino group incorporated in a heterocyclic ring was maximized in the pyrrolidine structure (I-16). Increasing (III-3) or decreasing (I-14) the ring size by 1 C decreased activity. Heterocyclic 6-membered rings containing O (III-4, I-62, I-63), S (I-64), or N (I-67) generally showed little activity or toxicity. Exceptions were I-67, which was more toxic and I-63 which was a potent TSC antagonist and moderately active against nicotine-induced convulsions.

(5) T. L. Kerley, A. B. Richards, R. W. Begley, B. E. Abrew, and L. C. Weaver, *J. Pharmacol. Exp. Ther.*, **132**, 360 (1961).

Five Schiff's bases were tested (II-26, II-34, II-41, II-45, II-48), 2 had activity of merit. The isopropylidene (II-26) and 1-cyclopropylethylidene (II-34) were as active as the primary amine (II-2) on all end points except antagonism of Tremorine and isolation-induced stress. Like other Schiff's bases they were less toxic than the primary amine. Activity of the Schiff's bases appears to correlate with their ease of hydrolysis.

Connecting Link.—Table II depicts changes in the connecting link. Removal of the β-Me group (III-5 *vs.* I-16) increased activity against Tremorine but otherwise had little effect on activity. Changing the β-Me to CH_2 decreased activity on all end points with the possible exception of Tremorine antagonism. Increasing the size of the β substituent from Me to Et (I-28 *vs.* I-16 and II-12 *vs.* II-2), *i*-Pr (I-29 *vs.* I-16), or Ph (I-31 *vs.* I-16) decreased activity on all end points but increased toxicity. Likewise, Me_2 substitution on the β-C (I-32 *vs.* I-16) decreased activity but this compound was also less toxic. Toxicity and potency as a Tremorine antagonist was increased by moving the Me group from the β to the γ-C (I-34-I-16) but other activity was decreased.

A 3-C chain length was optimum for activity. Either increasing (I-37 *vs.* I-16) or decreasing (III-6 *vs.* III-5) chain length by 1 C decreased activity on most end points, but anticholinergic activity was high with the unbranched pyrrolidinobutanol (I-35).

Phenyl Ring Substitution.—Table III shows that regardless of the nature of the group, ortho substitution of the Ph rings decreased activity but not toxicity (I-80, I-72, I-86 *vs.* I-16). Activity was further reduced by para substitution and again the kind of substituent was of little consequence (I-79, I-82, I-71 *vs.* III-2 and II-14 *vs.* II-2). Meta substitution resulted in compounds of more interest since some were more active than their unsubstituted congeners. *m*-F derivatives were 3- to 10-fold more active than their unsubstituted congeners in the primary amine (II-15 *vs.* II-2), ethylamine (I-74 *vs.* III-2), and pyrrolidine (I-77 *vs.* I-16) series. *m*-Cl derivatives, however, had no consistent effect on biologic activity (I-78 *vs.* III-2 and II-16 *vs.* II-2). These compounds were more active on some and less active on other end points. Meta substitution of Br (I-81 *vs.* III-2), MeO (I-87 *vs.* I-16), or CF_3 (I-83 *vs.* I-16) resulted in less active compounds.

An interesting dichotomy was found when the optical isomer of the most active compounds in the pyrrolidine and primary amine series which were resolved and tested. The *l* isomer in the pyrrolidine series (I-23) was more toxic but only slightly more active than the *d* isomer (I-21). In contrast, toxicity of the primary amine stereoisomers was equivalent but the *l* isomer (II-6) was markedly more active than the *d* isomer (II-9).

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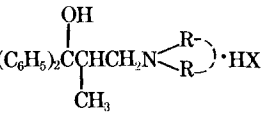
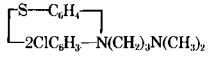
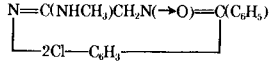
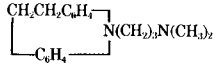
TABLE I: SUBSTITUENTS ON THE AMINE 

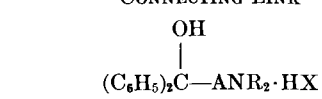
No.[b]	N(R)(R)	HX	Mouse ED50, mg/kg ip[a]											
				Simple reflexes			Anticonvulsant			Anticholingeric				
			Lethal	Traction	Chimney	Dish	TSC	Electroshock	Nicotine	Tremorine: Tremor	Tremorine: Antichol	Pupil	Fighting	Dog anorexigenic[c]
II-2	NH_2	HCl	133	10	>25[d]	4	>25	12	4	10	>20	>25	4	28†
II-18	$NHCH_3$	HCl	178	20	12.5	7	8	20	4	30	<20	>25	9	84
II-23	$NHCH_2CH_3$	HCl	133	23	10	8	25	20	7	>40	>40	>25	12	100
II-25	$NHCH_2CH_2CH_3$	Maleate	56	25	>25	12	9	>25	4	>40	>40	>25	20	16
II-28	$NHCH(CH_3)_2$	HBr	75	36	25	16	25	18	6	>40	>40	>50	6	0
II-31	$NH(CH_2)_3CH_3$	Maleate	56	36	25	4	>25	25	18	24	>40	>50	9	0
II-33	$NHCHCH_2CH_2$	Base	100	36	>50	16	>50	>50	12	>40	>40	>50	15	0
II-38	$NHCHCH_2CH_2CH_2$	HCl	100	28	25	12	10	14	3.5	>40	>40	>50	23	23
II-40	$NHCH(CH_2)_3CH_2$	HCl	75	36		13	15	32	13	>40	>40	>50	50	0
II-36	$NHCH(CH_3)CHCH_2CH_2$	HCl	56	25	23	20	9	20	4	>40	>40		8	0
II-42	$NHCH_2C_6H_5$	Base	1000	>200	>200	200	>200	>200	200	>40	>40	>200		76
II-44	$NHCH_2[3,4,5](OCH_3)_3C_6H_2$	HCl	100	>100	89	32	50	100	25	>40	>40	>100	27	0
II-47	$NHCH_2C{=}CHCH{=}CHO$	Maleate	178	>100	>100	63	56	89	50	>40	>40	>100		0
II-50	$NHCH_2C{=}CHCH{=}CHS$	Maleate	178	159	>100	71	50	>100	40	>40	>40	>100	>50	0
II-51	$NHCH_2C(CH_3)_2COOH$		1000	>200	>200	71	>200	>200	100	>40	>40	>200		0
II-53	$NHCHCH_2CH_2N(CH_3)CH_2CH_2$	2HCl	316	45	25	9	20	25	3	>40	>40	>50		0
II-26	$N{=}C(CH_3)_2$	Base	237	14	18	11	8	9	1.4	>40	>40		>50	75
II-34	$N{=}C(CH_3)CHCH_2CH_2$	Base	316	13		4	3.1	12	2.5	40	>40		12	9
II-41	$N{=}CHC_6H_5$	Base	562	>200	>200	100	178	>200	159	>40	>40	>200		0†
II-45	$N{=}CHC{=}CHCH{=}CHO$	Base	562	>200	>200	126	14	>200	57	>40	>40	>200	27	0
II-48	$N{=}CHC{=}CHCH{=}CHS$	Base	237	>200	>200	100	100	>200	126	>40	>40	>200		0
III-1[e]	$N(CH_3)_2$	HCl	56	36	>25	18	8	20	3	30	40	>50	>20	78
I-1	$N(CH_3)CH_2CH_3$	HBr	178	>100	63	16	10	50	3	20	>40	>100	15	10
III-2[e]	$N(CH_2CH_3)_2$	HCl	133	32	>25	23	10	25	3	27	47	>50	>20	46
I-2	$N(CH_3)(CH_2)_2CH_3$	HBr	133	36	>50	9	>50	25	3.6	>40	>40	>50	6	83
I-3	$N(CH_3)CH(CH_3)_2$	HBr	178	56	>100	18	12.5	45	7	19	26	>100	14	0†
I-4	$N(CH_2CH_2CH_3)_3$	HCl	100	36	>50	18	25	>50	13	>40	>40	>50	15	0
I-7	$N[CH(CH_3)_2]_2$	HCl	133	32	>50	10	8	23	8	>40	>40	>50	20	0
I-8	$N[(CH_2)_3CH_3]_2$	HBr	178	142	63	45	>200	>200	40	>40	>40	>200	20	0
I-9	$N[CH_2CH(CH_3)_2]_2$	Base	1000	>200	>200	112	89	>200	>200	>40	>40	>200		0
I-11	$N(CH_3)CH_2CH{=}CH_2$	HCl	178	23	>25	8	25	>25	5	>40	>40		18	56†
I-12	$N(CH_2CH{=}CH_2)_2$	HCl	178	18	>25	6	>25	>25	6.2	>40	>40		20	34
I-53	$N(CH_3)CH_2C_6H_5$	HCl	316	78	>100	40	12	50	16	>40	>40		40	18†
I-56	$N(C_2H_5)CH_2C_6H_5$	HCl	316	142	>25	23	>25	>25	70	>40	>40			0
I-57	$N(CH_2C_6H_5)_2$	HCl	1000	>25	29	45	>25	>25	50	>40	>40		7	0

I-60	$N(CH_2CH_2OCH_3)_2$	HCl	178	71	>100	45	50	>100	10	32	>40			0
I-13	$N(CH_3)CH(CH_2)_3CH_2$	Maleate	133	36	>50	20	15	50	9	40	>40	9	9	39
I-14	$NCH_2CH_2CH_2$	HBr	178	63	>100	25	>100	>100	10	40	>40		30	12
I-16	$N(CH_2)_3CH_2$	HCl	200	36	>25	20	10	32	7	77	22	32	>20	0
III-3[e]	$N(CH_2)_4CH_2$	HCl	178	71	50	36	36	>50	12	25	25	>100	>20	46
I-39	$N(CH_2)_3CHCH_3$	HCl	178	>100	18	79	45	100	23	21	3	17		0†
I-41	$NCH(CH_3)(CH_2)_2CHCH_3$	HBr	133	79	>100	>100	>100	>100	20	36	25	<20		0†
I-43	$N(CH_2)_3C(CH_3)_2$	HCl	237	>100	63	89	>100	>100	14	14	4	63		0†
I-46	$N(CH_2)_3C(CH_2)_4CH_2$	HBr	1000								>40			0
I-49	$CH_2NCHCH_2CH_2CHCH_2CH_2$	HCl	178	>50	>50	>50	45	>50	100	40	<40		35	0
I-51	$CH_2NCH_2CHCH_2CHCH_2CH_2$	HCl	1000			100								
III-4[e]	$NCH_2CH_2OCH_2CH_2$	HCl	316	71	>50	>50	36	>50	20	30	50	>100	39	
I-62	$NCH_2CH(CH_3)OCH(CH_3)CH_2$	HCl	422			45			36		47	45		39
I-63	$NCH(CH_3)CH_2OCH_2CHCH_3$	CH_3SO_3H	422	142	>100	50	4	100	14	>40	>40			0
I-64	$NCH_2CH_2SCH_2CH_2$	HBr	1000	>200	>200	142	>200	>200	126	>40	>40			0
I-67	$NCH_2CH_2N(CH_3)CH_2CH_2$	2HCl	75	>100	89	79	>100	>100	36	18	4	32		12†
I-65	$N(CH_3)CH_2CH_2N(CH_3)_2$	2HCl	178	142	100	63	57	142	25	>40	>40	142		42
I-25	$N(\rightarrow O)(CH_2)_3CH_2$	HCl	178	>200	>200	>200	18	200	32	40	>30			0†
Methylphenidate	$NH(CH_2)_4CHCH(C_6H_5)COOCH_3$	HCl	167	50	50	50	50	50	28	40	40	50	25	100
Amphetamine	$C_6H_5CH_2CH(CH_3)NH_2$	$0.5H_2SO_4$	65	40	25	25	25	25	25	20	10	5	5	100
Chlorpromazine		HCl	165	6	3	2	6.2	6.2	2.3	1.9	40	6.2	2	11†
Chlordiazepoxide		HCl	200	13	6.2	6.2	7	6.2	1.5	7.3	40	6.2	23	8†
Imipramine		HCl	200	36	20	8	25	25	13	37	40	25	21	0†
Scopolamine	$C_6H_5CH(CH_2OH)COOC_7H_9NO$	HBr	650	200	0.6	159	200	200	200	2.8	1.3	0.15	0.2	87†

[a] Several of the biological endpoints in this and subsequent tables are related and can be grouped together. For example, the ED_{50}'s for traction, chimney, and dish all measure effects on simple behavioral reflexes. Likewise, anticonvulsant action can be inferred from thiosemicarbazide, electroshock, and nicotine endpoints and anticholinergic activity from the pupil and the Tremorine antagonism data. [b] See ref 1. [c] Per cent inhibition of food consumption. Values marked with a dagger represent inhibition after a 5 mg/kg dose. All other values are for a 1 mg/kg dose. [d] > indicates lack of activity at the listed dose which was the highest dose tested. [e] A. W. Ruddy and J. S. Buckley, *J. Amer. Chem. Soc.*, **72**, 718 (1950).

Table II

Connecting Link

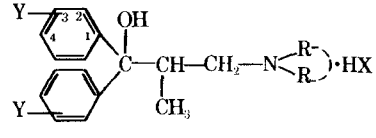


No.[b]	AN< R R'	HX	Mouse ED50, mg/kg ip[a]											
				Simple reflexes			Anticonvulsant			Anticholinergic				
								Electro-		Tremorine				Dog
			Lethal	Traction	Chimney	Dish	TSC	shock	Nicotine	Tremor	Antichol	Pupil	Fighting	anorexigenic[c]
I-16	CH(CH3)CH2N(CH2)3CH2	HCl	200	36	>25[d]	20	10	32	7	77	22	32	20	0
II-5[e]	CH2CH2N(CH2)3CH2	HCl	133	23	25	20	20	20	4.5	9	13	38	16	14
I-6	C(=CH2)CH2N[CH(CH3)2]2	HCl	100	200	100	50	40	126	16	40	40	100	41	0
I-7	CH(CH3)CH2N[CH(CH3)2]2	HCl	133	32	50	10	8	23	8	40	40	50	20	0
I-27	C(C=CH2)CH2N(CH2)3CH2	HCl	56	50	50	50	50	50	16	22	20	63	12	19
I-28	CH(CH2CH3)CH2N(CH2)3CH2	HCl	178	89	50	50	50	50	8	40	40	50	50	0†
I-29	CH[CH(CH3)2]CH2N(CH2)3CH2	HCl	56	71	36	36	50	50	32	10	40	50	8	10
I-31	CH(C6H5)CH2N(CH2)3CH2	HCl	56	142	100	100	100	100	100	40	40	100	40	0†
II-2	CH(CH3)CH2NH2	HCl	133	10	25	4	25	12	4	10	20	25	4	28†
II-12	CH(C2H5)CH2NH2	HCl	56	25	25	12	25	25	18			25	2.2	0
II-13	CH[CH(CH3)2]CH2NH2	HCl	56	40	25	12.5	25	25	25	20	20	25	12	19
I-32	C(CH3)2CH2N(CH2)3CH2	HBr	562	200	200	142	89	200	142	40	40	200	50	0†
I-34	CH2CH(CH3)N(CH2)3CH2	HCl	56	71	36	40	50	50	20	7	11	21	14	0†
II-20	CH2CH(CH3)NHCH3	HCl	133	56	50	15	50	50	28	40	40	50	27	0
I-35	CH2CH2CH2N(CH2)3CH2	HCl	100	72	45	50	50	36	20	2.5	2	15	50	0†
I-37	CH(CH3)CH2CH2N(CH2)3CH2	HCl		56	40	50	50	50	28			50	50	0
III-6[f]	CH(CH2)3N(CH2)3CH2	HCl	75	50	36	40	50	50	12	40	40	50	20	
I-36	CH2CH(CH3)CH2N(CH2)3CH2	HCl	133	100	72	79	100	79	23	20	14	80	50	0†
I-54	CH2CH(CH3)N(CH3)CH2C6H5	HBr	562	200	200	126	200	200	89	40	40	200	50	0†
I-69	CHCH2N(CH3)CH2CH2	HBr	75	50	50	28	50	50	10	18	19	50	50	40†
I-70	CHCH2NCH2CH2CHCH2CH2	HCl	56	50	45	40	50	50	63	40	40	60	50	

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*. [c] See Table I, footnote *c*. [d] See Table I, footnote *d*. [e] 1,1-Diphenyl-3-pyrrolidinopropanol·HCl (ref 2c). [f] 1,1-Diphenyl-2-pyrrolidinopropanol·HCl [L. Stein and E. Linder, U. S. Patent 2,827,460 (1958); *Chem. Abstr.*, **53**, 415*f* (1959)].

Table III

Substituents on the Phenyl Ring



No.[b]	Y	N(R)(R)	HX	Lethal	Mouse ED50, mg/kg ip[a]: Simple reflexes: Traction	Simple reflexes: Chimney	Simple reflexes: Dish	Anticonvulsant: TSC	Anticonvulsant: Electroshock	Anticonvulsant: Nicotine	Anticholinergic: Tremorine: Tremor	Anticholinergic: Tremorine: Antichol	Anticholinergic: Pupil	Fighting	Dog anorexigenic[c]
II-2	H	NH_2	HCl	133	10	25[d]	4	25	12	4	10	20	25	4	28†
III-2	H	$N(CH_2CH_3)_2$	HCl	133	32	25	23	10	25	3	27	47	50	20	46
I-16	H	$N(CH_2)_3CH_2$	HCl	200	36	25	20	10	32	**7**	77	22	32	20	0
I-80	2-Cl	$N(CH_2)_3CH_2$	HCl	133	112	72	45	29	56	28	40	40	100	18	0
I-72	2-CH_3	$N(CH_2)_3CH_2$	HBr	178	71	50	50	50	50	10	40	40	50	50	0
I-86	2-OCH_3	$N(CH_2)_3CH_2$	HBr	56	71	32	50	50	50	23	22	21	50	14	0
I-79	4-Cl	$N(CH_2CH_3)_2$	HCl	178	200	200	79	200	200	79	40	40	200	11	0†
II-14	4-CH_3	NH_2	Base	75	100	56	36	100	100	63	40	40	100	41	0
I-82	4-Br	$N(CH_2CH_3)_2$	HCl	1000	200	178	126	200	200	200	40	40	200	27	0
I-71	4-CH_3	$N(CH_2CH_3)_2$	HCl	178	50	50	50	50	50	20	28	40	50	50	24
II-15	3-F	NH_2	Maleate	100	3.9	3.1	1.6	2.2	3.2	1.1	5	5	3.2	7	0
I-74	3-F	$N(CH_2CH_3)_2$	HBr	56	8	6.2	3.5	3.5	3.5	5	6.2	40	40	13	
I-77	3-F	$N(CH_2)_3CH_2$	HBr	178	16	12.5	8	5	12.5	9	4	14	20	12.5	0
I-78	3-Cl	$N(CH_2CH_3)_2$	HCl	56	18	12.5	12.5	5	36	12	40	40	50	18	26
II-16	3-Cl	NH_2	HCl	56	25	23	16	3.5	25	14	40	40	25	5	0
I-81	3-Br	$N(CH_2CH_3)_2$	HCl	237	71	50	50	20	50	10	40	40	50	50	
I-87	3-OCH_3	$N(CH_2)_3CH_2$	HBr	178	142	79	71	100	100	40	40	40	100	50	0
I-83	3-CF_3	$N(CH_2)_3CH_2$	HCl	562	200	200	200	200	200	200	14	14	200	50	
I-93	2-C_4H_3S[e]	$N(CH_2)_3CH_2$	Base	133	50	50	50	50	50	23	40	40	100	50	30†
I-88	3,4-$(OCH_3)_2$	$N(CH_2CH_3)_2$	Base	42	71	50	36	36	50	32	50	40	40	50	0
I-85	3,5-$(CF_3)_2$	$N(CH_2)_3CH_2$	HCl	1000	200	200	112	200	200	200	40	40	200	50	0
I-89	3,4-OCH_2O	$N(CH_2CH_3)_2$	Base	316	100	89	63	100	100	40	15	40	100	50	0
II-57	2,2′-bond[f]	NH_2	HCl	178	71	50	50	50	50	23	50	40	40	27	0
I-100	2,2′-bond[f]	$N(CH_2)_3CH_2$	HCl	133	79	50	50	50	45	32	40	40	40	50	50
I-106	2,2′-CH=CH[g]	$N(CH_2CH_3)_2$	HCl	75	36	25	25	25	25	25	40	40	25	30	29
II-60	2,2′-CH=CH[g]	NH_2	HCl	56	32	25	16	25	25	8	20	20	25	15	0
I-109	2,2′-CH_2CH_2[h]	$N(CH_2CH_3)_2$	HCl	75	40	25	25	25	25	2	40	40	25	18	20
I-113	2,2′-CH_2CH_2[h]	$N(CH_2)_3CH_2$	HBr	178	100	100	**71**	100	100	71	40	40	100	50	0
I-116	2,2′-O[i]	$N(CH_2CH_3)_2$	Maleate	133	40	25	25	25	25	13	40	40	25	46	11
II-61	2,2′-$C(CH_3)_2$[j]	NH_2	Maleate	562	63	50	36	50	50	3.5	20	20	50	50	0
I-119	2,2′-S[k]	$N(CH_2CH_3)_2$	HCl	75	71	45	40	50	50	13	40	40	50	18	29
I-121	2,2′-S[k]	$N(CH_2)_3CH_2$	HBr	178	100	100	72	63	79	18	10	40	100	50	0
I-21	H	$N(CH_2)_3CH_2$	HCl[l]	178	28	50	20	45	25	7	37	26	50	40	25†
I-23	H	$N(CH_2)_3CH_2$	HCl[m]	100	36	50	14	12	28	6	15	15	72	40	
II-6	H	NH_2	HCl[n]	178	4	5.6	2	1.4	5	1.6	3.8	10	25	2.6	78
II-9	H	NH_2	HCl[o]	178	14	25	5	25	25	8	20	20	25	5	0

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*. [c] See Table I, footnote *c*. [d] See Table I, footnote *d*. [e] 2-Thienyl in place of the phenyl rings. [f] Fluoren-9-ol-9-yl in place of benzhydrol-α-yl. [g] 5*H*-Dibenzo[*a*,*d*]cyclohepten-5-ol-5-yl in place of benzhydrol-α-yl. [h] 10,11-Dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol-5-yl in place of benzhydrol-α-yl. [i] Xanthen-10-ol-10-yl in place of benzhydrol-α-yl. [j] 10,10-Dimethylanthr-9-ol-9-yl in place of benzhydrol-α-yl. [k] Thioxanthen-10-ol-10-yl in place of benzhydrol-α-yl. [l] *d* (dextro) rotating hydrochloride (from levo rotating base). [m] *l* (levo) rotating hydrochloride (from dextro rotating base). [n] *l* (levo) rotating hydrochloride. [o] *d* (dextro) rotating hydrochloride.