8·HCl, 85236-52-8; **9**, 85236-53-9; **10**, 85236-54-0; **11**, 85236-55-1; **12**·HCl, 85236-56-2; **13**·3HCl, 85236-57-3; **14**, 85236-58-4; **15**, 85236-59-5; **16**·4HCl, 85236-60-8; **17**·4HCl, 85236-61-9; **18**·HCl, 85236-62-0; **19**·4HCl, 85236-63-1; **20**·4HCl, 85236-64-2; **21**·3HCl, 85236-65-3; **22**, 85236-66-4; **23**·3HCl, 85236-67-5; **24**, 85236-68-6; **25**, 85236-69-7; 3,5-bis[(*N*-pyrrolidinyl)carbonyl]benzenamine, 85236-70-0; 3,5-bis[(*N*-pyrrolidinyl)methyl]benzenamine, 85236-71-1; 1-chlorophthalazine, 5784-45-2; *p*-aminophenol, 123-30-8; pyrrolidine, 123-75-1; 4-chloroquinoazoline, 5190-68-1; *o*-aminophenol, 95-55-6; *m*-aminophenol, 591-27-5; 4-acetamidophenol, 103-90-2; 1,4-dichlorophthalazine, 4752-10-7; 1-chloroisoquinoline, 19493-44-8; 3,6-dichloropyridazine, 141-30-0; 4-chloro-6,7,8-trimethoxyquinazoline, 33371-00-5; 4-chloro-7-(trifluoromethyl)-quinoline, 346-55-4; 2-ethyl-4-chloroquinoline, 7176-10-5; 4,7-dichloroquinoline, 86-98-6; 4-chloroquinoline, 611-35-8; 2-chloroquinoline, 612-62-4; 4-chloropyridine, 626-61-9; *p*-hydroxybenzylamine, 696-60-6; *p*-methoxybenzylamine, 2393-23-9; 5-aminoisophathalic acid, 99-31-0; changrolin, 72063-47-9.

1-(Aminomethyl)-6,7-dihydroxytetralin Derivatives: Synthesis and Assessment of Dopamine-Like Effects

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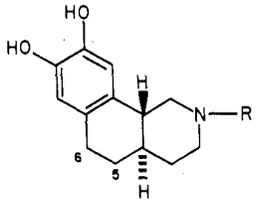
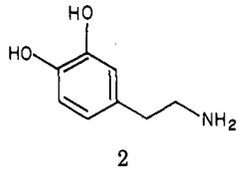
The title compounds were designed as flexible congeners of *trans*-octahydrobenz[*h*]isoquinoline, in which the dopamine moiety can exist in the α conformation. Extremely low dopamine-like effects in the title series in the cat cardioaccelerator nerve assay paralleled low activity in the *trans*-octahydrobenz[*h*]isoquinoline compounds and was consistent with a prior proposal of the presence of a bulky region on the dopamine receptor(s).

In a prior paper,[1] rigid congeners of the α conformer of dopamine derived from a *trans*-octahydrobenz[*h*]isoquinoline system, **1**, were reported to exhibit an extremely



1, R = H, Me, Et, *n*-Pr

low order of potency in inhibition of transmission in the cat cardioaccelerator nerve, an assessment of peripheral presynaptic dopaminergic effect. The compounds lowered blood pressure and heart rate in anesthetized cats, effects that were prevented by haloperidol. It was speculated[1] that carbons 5 and 6 of **1** represent a region of molecular bulk not present in molecules of other systems that are potent dopaminergic agonists and that also represent α conformations of dopamine: dopamine itself (**2**), 2-aminotetralins (**3**), apomorphine homologues (**4**), and octahydrobenzo[*f*]quinolines (**5**). This region of bulk in **1** may prevent optimal interaction of the molecule with dopamine receptors, and it was inferred[1] that the complementary region of the dopamine receptor includes some degree of physical bulk.



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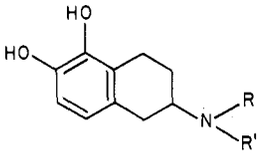

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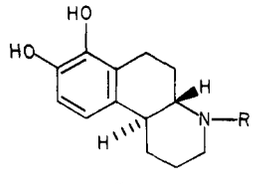
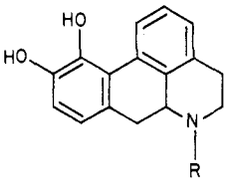


5



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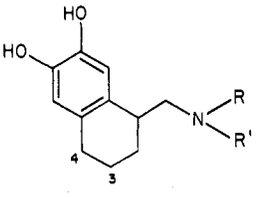
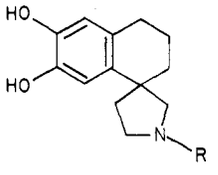
Further, to assess the low biological activity of series **1**, we designed a simpler system, the 6,7-dihydroxy-1-(aminomethyl)tetralin (**6**). Reasonable conformations exist for



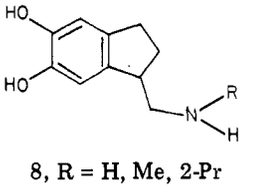
6, R, R′ = combinations of H, Me, Et, *n*-Pr, and 2-Pr

6 in which the dopamine moiety assumes an α conformation, with appropriate torsion angles very similar to those observed in **1**. Carbons 3 and 4 in the target system **6** are analogous to carbons 5 and 6 in **1**.

Crooks et al.[2] reported that the spirotetralin system **7**



7, R = H, Me



8, R = H, Me, 2-Pr

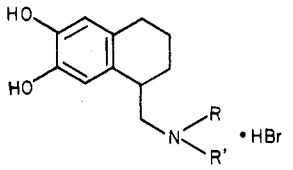
showed only extremely weak dopamine-like effects. Dreiding models reveal that the dopamine moiety in **7** cannot attain the catechol ring-amino nitrogen antiperiplanar disposition characteristic of the biologically significant α conformer of dopamine. Gaino et al.[3] claimed adrenergic β_2 activity for the 1-(aminomethyl)indan derivatives **8**. However, no pharmacological data for these could be found in the literature. Nichols et al.[4] have re-

[†] College of Pharmacy.
[‡] College of Medicine.

(1) Cannon, J. G.; Lee, T.; Hsu, F.-L.; Long, J. P.; Flynn; J. R. *J. Med. Chem.* **1980**, *23*, 502.
(2) Crooks, P. A.; Szyndler, R.; Cox, B. *Pharm. Acta Helv.* **1980**, *55*, 134.
(3) Gaino, M.; Yamamura, S.; Saito, J.; Ohashi, M. Japanese Patent 7 805 146 (Cl.CO7C87/06), 1978; *Chem. Abstr.* **1978**, *88*, 169822.

0022-2623/83/1826-0813$01.50/0

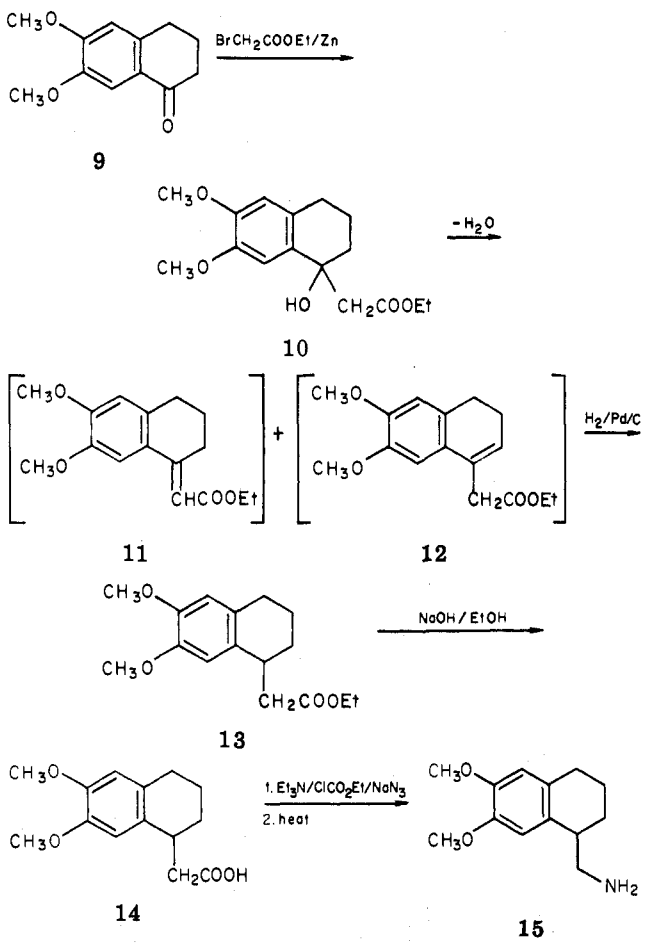
Table I. 6,7-Dihydroxy-1-(aminomethyl)tetralin Hydrobromides



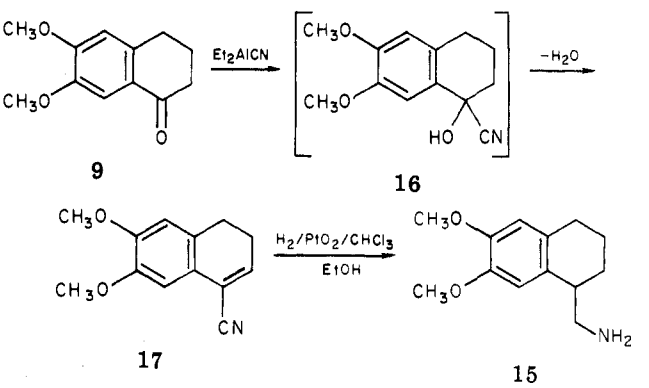
no.	R	R'	mp, °C	yield, %	formula	anal.
6a	CH_3	H	198-201[a]	57	$C_{12}H_{18}BrNO_2$	C, H, N
6b	C_2H_5	H	195-198[a]	96	$C_{13}H_{20}BrNO_2$	C, H, N
6c	2-C_3H_7	H	198-202[b]	46	$C_{14}H_{22}BrNO_2$	C, H, N
6d	n-C_3H_7	H	138-140[a]	99	$C_{14}H_{22}BrNO_2$	C, H, N
6e	CH_3	CH_3	207 dec[b]	57	$C_{13}H_{20}BrNO_2$	C, H, N
6f	C_2H_5	C_2H_5	129 dec[b]	53	$C_{15}H_{24}BrNO_2$	C, H, N
6g	CH_3	2-C_3H_7	164-169[b]	83	$C_{15}H_{24}BrNO_2$	C, H, N

[a] From EtOH-Et_2O. [b] From 2-PrOH-Et_2O.

Scheme I. Preparation of 1-(Aminomethyl)-6,7-dimethoxytetralin via the Reformatsky Reaction



Scheme II. Preparation of 1-(Aminomethyl)-6,7-dimethoxytetralin via Cyanohydrin



ported that the primary amine homologue 6 (R = R' = H) is devoid of dopamine-like effects in the canine renal artery assay.

Chemistry. The target compounds 6 were initially prepared by a sequence involving a Reformatsky reaction on 6,7-dimethoxy-1-tetralone, as shown in Scheme I. The NMR spectrum of the distilled dehydration product indicated an approximately 3:1 mixture of the dihydronaphthalene system 12 and the exocyclic double bond system 11. This mixture was subjected to catalytic hydrogenation, to give the saturated ester 13. Attempts to effect ammonolysis of 13 were unsuccessful, and alternately, the free acid 14 was converted into the primary amine 15 by a Curtius reaction. Nagata et al.[5] prepared the cyanohydrin of 6-methoxy-1-tetralone using diethylaluminum cyanide, and this reagent was utilized in an alternate sequence, illustrated in Scheme II, which is two steps shorter than the sequence in Scheme I and provides better overall yields. The primary amine 15 was appropriately N-alkylated by literature methods, and the ether links were cleaved with hydrobromic acid (see Table I). Spectral (IR, NMR) data on all intermediates and final products were consistent with the proposed structures.

Pharmacological Results and Discussion

All compounds listed in Table I were inactive at doses up to 1 mg (approximately 3.0–3.5 μmol)/kg iv as inhibitors of the positive chronotropic response induced by stimulation of the cardioaccelerator nerve of the cat. The ED_{50} for apomorphine in this assay is 0.022 μmol/kg.

Only the *N,N*-dimethyl homologue 6e (Table I) lowered arterial blood pressure in the cat, by 31.5 ± 8.0 mmHg (SEM) at 1.7 μmol/kg and by 34.5 ±4.6 mmHg (SEM) at 3.4 μmol/kg. This effect was reversed by propranolol (200 μg/kg) but not by haloperidol (100 μg/kg). Apomorphine produces hypotensive effects in the cat at a dose level of 0.008–0.032 μmol/kg. The compounds in Table I produced no significant change in heart rate in either of the dose levels used.

These data are consistent with the proposal that dopamine congeners bearing bulk in the region of the 5,6-carbons of 1 are not accommodated at dopamine receptor(s).

(4) Nichols, D. E.; Jadhar, K. P.; Buzdor, R. A. *Acta Pharm. Suec.*, in press. We express our thanks to Prof. Nichols for providing a prepublication copy of this manuscript.

(5) Nagata, W.; Yoshioka, M.; Murakame, M. *Org. Synth.* 1972, *52*, 96.

Experimental Section

Melting points were determined in open glass capillaries with a Thomas-Hoover Uni-Melt apparatus and are uncorrected. Boiling points are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Where analyses are indicated by the symbols of the elements, analytical results were within ±0.4% of the theoretical values. IR spectra were recorded on Perkin-Elmer 267 and Beckman 4240 spectrometers. NMR spectra were recorded on Varian Associates T-60 and EM360A spectrometers with tetramethylsilane as the internal standard.

Ethyl 6,7-Dimethoxy-1,2,3,4-tetrahydro-1-naphthaleneacetate (13). Five milliliters of a solution of 4.55 g (0.0272 mol) of ethyl bromoacetate and 3.75 g (0.0175 mol) of 6,7-dimethoxy-3,4-dihydro-1 (2*H*)-naphthalenone (**9**)[6] in 57 mL of benzene and 15 mL of Et_2O was added to a catalytic amount of I_2 and 3.56 g (0.0545 g-atom) of Zn. The mixture was warmed until a reaction started and then it was stirred. The remainder of the solution was added over 1 h, and the reaction mixture was heated under reflux for an additional 30 min. The cooled reaction mixture was treated with 18 mL of 10% H_2SO_4 with vigorous stirring. The acid layer was drawn off, and the organic phase was extracted twice with 8-mL portions of 5% H_2SO_4 and washed once with 4 mL of 10% Na_2CO_3. The acid solutions were combined and extracted with two 20-mL portions of Et_2O. The combined organic solutions were dried ($MgSO_4$) and filtered, the filtrate was concentrated under reduced pressure, and the residue was distilled, bp 192 °C (0.23 mm), to give 4.56 g (91%) of a clear, heavy, yellowish oil: IR (film) 1726 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.21 (t, 3 H, J = 7 Hz, CH_3), 2.18–2.88 (m, 4 H, ArCH_2CH_2), 3.36 (s, 1.5 H, CH_2COO), 3.85 (s, 6 H, OCH_3), 4.11 (q, 2 H, $COOCH_2CH_3$), 5.85 (t, 0.75 H, olefinic H), 6.15 (s, 0.25 H, olefinic H), 6.63 (s, 1 H, Ar*H*), 6.78 (s, 1 H, Ar*H*). This mixture of unsaturated esters (11.19 g, 0.0405 mol) was hydrogenated over 1.34 g of 10% Pd/C at room temperature at an initial pressure of 52 psig. The total H_2 uptake was 87% of the calculated amount. The reduction mixure was filtered, and volatiles were removed from the filtrate under reduced pressure to leave an oil, which was distilled, bp 170 °C (0.07 mm), to give 5.05 g (45%) of a clear, yellowish oil. Anal. ($C_{16}H_{22}O_4$) C, H.

6,7-Dimethoxy-1,2,3,4-tetrahydro-1-naphthaleneacetic Acid (14). Compound **13** (5.0 g, 0.017 mol) was heated under reflux in a mixture of 45 mL of 20% NaOH and 15 mL of EtOH for 24 h. The volatiles were removed under reduced pressure, and the residue was evaporated to dryness. It was taken up in a small volume of H_2O with gentle heating, and the solution was cooled and treated with excess 10% H_2SO_4. The resulting solution was extracted with Et_2O. The extract was dried ($MgSO_4$) and concentrated under reduced pressure to give 4.45 g (99%) of a yellowish oil, which solidified on standing at room temperature. Recrystallization from Et_2O–hexane gave 4.0 g (89%) of a white solid, mp 62–66 °C. Storage of this material overnight under reduced pressure at 40 °C gave mp 78–81 °C. Anal. ($C_{14}H_{18}O_4$) C, H.

1-Cyano-6,7-dimethoxy-3,4-dihydronaphthalene (17). A solution of 1.2 g (0.0058 mol) of **9** in 5 mL of anhydrous toluene, under N_2, was cooled to −25 °C and then Et_2AlCN (1.69 M in toluene; 1.28 g, 0.0116 mol) was added dropwise with stirring. The reaction mixture was kept at −15 °C for 80 min under N_2; then, under positive N_2 pressure, it was poured into a flask containing 42 mL of MeOH and 25 mL of concentrated HCl, cooled in a dry ice–EtOH bath, and the resulting mixture was stirred vigorously for 1 h. The yellowish suspension was poured into a separatory funnel containing 35 mL of concentrated HCl and 160 mL of ice, and then the resulting mixture was extracted with three 90-mL portions of CH_2Cl_2. The pooled extracts were evaporated under reduced pressure at a temperature below 40 °C from a flask containing 0.009 g of *p*-toluenesulfonic acid monohydrate. The pink residue was transferred to a distilling flask with a small amount of CH_2Cl_2–Et_2O, and it was distilled from 0.05 g of $KHSO_4$ to afford 5.82 g (78%) of an oil that solidified almost at once, bp 173–178 °C (0.15 mm). Recrystallization from MeOH gave yellowish needles, mp 107–111 °C. Anal. ($C_{13}H_{13}NO_2$) C, H, N.

(6) Thrift, R. I. *J. Chem. Soc. C* **1967**, 288.

1-(Aminomethyl)-6,7-dimethoxytetralin Hydrochloride (15). Method A. Et_3N (0.95 g, 0.009 mol) in 20 mL of Me_2CO was added dropwise to 2.35 g (0.009 mol) of **14** in 20 mL of Me_2CO and 4.4 mL of H_2O cooled to 0 °C; then a solution of 1.32 g (0.012 mol) of ethyl chloroformate in 20 mL of Me_2CO was added during 35 min. NaN_3 (0.923 g, 0.014 mol) in 3.2 mL of H_2O was added, and the reaction mixture was stirred at 0 °C for 2 h. The mixture was then poured over 50 g of crushed ice contained in a separatory funnel, and the resulting mixture was extracted with benzene. The benzene extract was dried ($MgSO_4$) and evaporated to yield 2.2 g of a yellow oil: IR (film) 2250 (N=C=O) cm^{-1}; A solution of this oil in 20 mL of THF and 4.8 mL of concentrated HCl was heated under reflux for 3 h. The volatiles were removed under reduced pressure; the residue was diluted with a small volume of H_2O, and the resulting mixture was extracted with Et_2O. The aqueous layer was evaporated to dryness, and the residue was recrystallized from 2-PrOH–Et_2O to yield 1.82 g (75%) of white crystals, mp 195–198 °C.

Method B. Compound **17** (4.3 g, 0.019 mol) in 160 mL of EtOH and 10 mL of $CHCl_3$ was hydrogenated over 0.5 g of PtO_2 at room temperature at an initial pressure of 35 psig. The reaction was complete in 6 h; the catalyst was removed, and volatiles were removed under reduced pressure. The residual solid was recrystallized from EtOH–Et_2O to give 5.0 g (97%) of white crystals, mp 204–209 °C. Anal. ($C_{13}H_{20}ClNO_2$) C, H, N. IR and NMR spectra of the product of method B were identical with corresponding spectra of the product of method A. The HCl salt was treated with excess KOH solution and extracted with CH_2Cl_2 to afford the free base as a colorless oil, bp 163 °C (0.1 mm).

1-[(Dimethylamino)methyl]-6,7-dimethoxytetralin Hydrochloride (18). The free base of **15** (1.5 g, 0.006 mol) was hydrogenated over 0.075 g of PtO_2 with 1.34 mL of 37% aqueous CH_2O (0.0168 mol) and 0.4 g of AcOH in 75 mL of EtOH at room temperature at an initial pressure of 30 psig. After the calculated amount of H_2 was absorbed, the reduction mixture was filtered, and volatiles were removed from the filtrate under reduced pressure. The residual oil was treated with ethereal HCl, and the resulting solid was recrystallized from EtOH–Et_2O to afford 1.36 g (63%) of crystals, mp 198–203.5 °C. Anal. ($C_{15}H_{24}ClNO_2$) C, H, N.

1-[(Diethylamino)methyl]-6,7-dimethoxytetralin Hydrochloride (19). The free base of **15** (1.2 g, 0.0054 mol) in 10 mL of benzene was added dropwise to a complex formed from 3.07 g (0.08 mol) of $NaBH_4$ and 16.21 g (0.27 mol) of AcOH in 50 mL of benzene, generated according to a procedure of Marchini et al.[7] The reaction mixture was heated overnight under reflux. After cooling, the mixture was treated with excess 2 N NaOH, and then it was extracted repeatedly with Et_2O. The pooled extracts were dried ($MgSO_4$) and the volatiles were removed under reduced pressure to leave a yellow oil. This was treated with 3 mL of phenyl isocyanate and permitted to stand at room temperature overnight. MeOH (25 mL) was added, and the resulting mixture was heated on a steam bath for 20 min. The MeOH was removed under reduced pressure, and the residue was treated with excess concentrated NaOH solution. The resulting mixture was extracted repeatedly with $CHCl_3$, and the pooled extracts were dried ($MgSO_4$) and evaporated to give 1.2 g (80%) of an oil; 1.15 g of this material was treated with ethereal HCl and the resulting solid was recrystallized from EtOH–Et_2O to give 1.48 g (87%) of yellowish prisms, mp 152–154 °C. Anal. ($C_{17}H_{28}ClNO_2$) C, H, N.

1-[[(Trifluoroacetyl)amino]methyl]-6,7-dimethoxytetralin (20). A mixture of 2.0 g (0.009 mol) of the free base of **15** and 50 g (0.238 mol) of trifluoroacetic anhydride was stirred at room temperature for 1 h. Volatiles were removed under reduced pressure, and the residual solid was recrystallized from Et_2O–hexane to give 2.8 g (98%) of tiny needles, mp 125–129 °C. Anal. ($C_{15}H_{18}F_3NO_3$) C, H, N.

1-[[[(Trifluoroacetyl)methyl]amino]methyl]-6,7-dimethoxytetralin (21). A mixture of 1.2 g (0.0037 mol) of **20**, 2.64 g (0.0185 mol) of MeI, and 50 mL of dry Me_2CO was warmed to the boiling point, and 1.06 g (0.0185 mol) of KOH was added. The

(7) Marchini, P.; Liso, G.; Reho, A.; Liberatore, F.; Moracci, F. M. *J. Org. Chem.* **1975**, *40*, 3453.

mixture was heated under reflux for 30 min, and then volatiles were removed under reduced pressure. The residual semisolid was extracted with three 25-mL portions of $CHCl_3$. The pooled extracts were dried ($MgSO_4$) and evaporated to leave 1.24 g (99%) of a heavy yellowish oil, which solidified on standing overnight at room temperature. Recrystallization from EtOH gave tiny needles, mp 85–88 °C. Anal. ($C_{16}H_{20}F_3NO_3$) C, H, N.

1-[(Methylamino)methyl]-6,7-dimethoxytetralin Hydrochloride (22). A mixture of 0.5 g (0.0015 mol) of **21** and 25 mL of 5% NaOH was heated under reflux for 2 h. The cooled reaction mixture was extracted with four 25-mL portions of CH_2Cl_2. The combined extracts were dried ($MgSO_4$), and the volatiles were removed under reduced pressure to give an oil, which was diluted with 25 mL of Et_2O and then treated with excess ethereal HCl. Recrystallization of the resulting solid from EtOH–Et_2O gave 0.37 g (80%) of a white powder, mp 242–245 °C. Anal. ($C_{14}H_{22}ClNO_2$) C, H, N.

1-[[[(Trifluoroacetyl)ethyl]amino]methyl]-6,7-dimethoxytetralin (23). This was prepared from 1.2 g (0.0037 mol) of **20**, 2.94 g (0.018 mol) of EtI, 1.06 g (0.018 mol) of KOH, and 50 mL of dry Me_2CO as described for **21**: yield 1.28 g (98%) of rhomboid crystals; mp 75–78 °C (EtOH). Anal. ($C_{17}H_{22}F_3NO_3$) C, H, N.

1-[(Ethylamino)methyl]-6,7-dimethoxytetralin Hydrobormide (24). This was prepared from 0.5 g (0.0014 mol) of **23** and 30 mL of 5% NaOH as described for **22**: yield 0.227 g (55%) of grayish crystals, mp 203–206 °C (EtOH–Et_2O). Anal. ($C_{15}H_{24}BrNO_2$) C, H, N.

1-[(2-Propylamino)methyl]-6,7-dimethoxytetralin Hydrochloride (25). The free base of **15** (1.2 g, 0.005 mol), 1.25 g (0.021 mol) of Me_2CO, and 0.178 g of PtO_2 in 80 mL of EtOH were hydrogenated at an initial pressure of 40 psig at room temperature. When the uptake of H_2 ceased, the reduction mixture was filtered, and volatiles were removed from the filtrate under reduced pressure. The residue was distilled, bp 145 °C (0.07 mm), to yield 1.40 g (98%) of a yellowish oil. This was treated with ethereal HCl, and the resulting soild was recrystallized from EtOH to give well-shaped crystals, mp 186–188 °C. Anal. ($C_{16}H_{26}ClNO_2$) C, H, N.

1-[(1-Propylamino)methyl]-6,7-dimethoxytetralin Hydrochloride (26). To 2.0 g (0.027 mol) of propionic acid in 15 mL of benzene maintained at 10–15 °C under N_2 was added, in small portions, 0.34 g (0.009 mol) of $NaBH_4$. When the evolution of H_2 ceased (approximately 1 h), 1.0 g (0.0045 mol) of the free amine of **15** in 5 mL of benzene was added in one portion, and the resulting mixture was heated under reflux for 3 h. The reaction mixture that contained a voluminous, gelatinous white precipitate was shaken with excess 2 N NaOH, and this mixture was extracted several times with Et_2O. The pooled extracts were dried ($MgSO_4$), and the volatiles were removed under reduced pressure to give 1.21 g of a light yellow oil. This was dissolved in Et_2O and treated with ethereal HCl. Two recrystallizations of the resulting solid (EtOH–Et_2O) gave 0.675 g (50%) of tiny needles, mp 186–188 °C. Anal. ($C_{16}H_{26}ClNO_2$) C, H, N.

1-[(Methyl-2-propylamino)methyl]-6,7-dimethoxytetralin Picrate (27). The free base of **25** (1.02 g, 0.0038 mol) and 2 mL of 37% aqueous formaldehyde (0.024 mol) were hydrogenated in the presence of 0.15 g of 10% Pd/C in 80 mL of anhydrous EtOH at an initial pressure of 40 psig. After the calculated amount of H_2 was absorbed, the reduction mixture was filtered, and volatiles were removed from the filtrate under reduced pressure. The oily residue was treated with excess 5% KOH, and this mixture was extracted with Et_2O. The volatiles were removed from this extract; the oily residue was taken up in 10% HCl, and this solution was extracted with Et_2O, which was then discarded. The aqueous phase was treated with excess KOH and then extracted with Et_2O. The extract was dried ($MgSO_4$), and the Et_2O was removed under reduced pressure to give 0.75 g (70%) of a light-colored oil. This was characterized as its picrate salt, mp 185–189 °C (Et_2O). Anal. ($C_{23}H_{30}N_4O_9$) C, H, N.

Ether Cleavage Reactions. A solution of 0.007 mol of the appropriate amine salt or free base in 6 mL of 48% HBr was heated under N_2 at 120 °C for 3 h. The volatiles were removed under reduced pressure, and the last traces of H_2O were azeotroped with EtOH. The residual solid was recrystallized. See Table I.

Pharmacology. Methods. Cat Blood Pressure and Heart Rate. Cats of either sex weighing 4–6 kg were anesthetized with an intraperitoneal injection of pentobarbital sodium (30 mg/kg). The trachea was intubated with an endotracheal tube, and respiration was supported by a Harvard respirator. The left femoral artery and right femoral vein were cannulated with polyethylene tubing for measurement of blood pressure and adminsitration of drugs, respectively. The arterial pressure cannulas were connected to a P23AA Statham arterial pressure transducer. Heart rate was monitored with a Beckman cardiotachometer. Doses of tested compound ranged from 0.5 to 1.0 mg/kg.

Cat Cardioaccelerator Nerve Stimulation. Animals were prepared as described above for monitoring heart rate and blood pressure. Cats were pretreated with atropine sulfate (200 μg/kg) and hexamethonium bromide (10 mg/kg). After endotracheal intubation, animals were artificially ventilated with a Harvard respirator. The chest was opened by a midline incision, and bipolar platinum electrodes were placed on the right postganglionic cardioaccelerator nerves. The following parameters of nerve stimulation were used: 2 Hz for 30 s, 2-ms duration, and supramaximal voltage (20–25 V). Doses of the compounds up to 1 mg/kg were administered intravenously.

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Registry No. **2**, 51-61-6; **6a**, 84854-62-6; **6b**, 85221-72-3; **6c**, 84854-56-8; **6d**, 85221-73-4; **6e**, 84854-60-4; **6f**, 85221-74-5; **6g**, 85221-75-6; **9**, 13575-75-2; **11**, 85221-77-8; **12**, 85221-78-9; **13**, 85221-76-7; **14**, 85221-57-4; **15**, 84854-45-5; **15** (base), 85221-59-6; **17**, 85221-58-5; **18**, 84854-47-7; **18** (base), 85221-60-9; **19**, 85221-61-0; **19** (base), 85221-62-1; **20**, 85221-63-2; **21**, 85221-64-3; **22**, 84854-49-9; **22** (base), 85221-65-4; **23**, 85221-66-5; **24**, 85221-67-6; **25** (base), 84854-46-6; **25**, 85221-68-7; **26**, 84854-53-5; **26** (base), 85221-69-8; **27**, 85221-71-2; **27** (base), 85221-70-1; ethyl bromoacetate, 105-36-2.