New Compounds with Possible Pharmacological Activity

Robert Bruce Moffett*

Research Laboratories, The Upjohn Company, Kalamazoo, Michigan 49001

Sixty-two new organic compounds are reported. These were prepared for testing in a variety of pharmacological screens or as chemical intermediates. None was found to be more active or less toxic than known medicinals.

In our search for new and useful pharmaceutical agents we have prepared a considerable number of new organic compounds to be screened in a variety of pharmacological tests. Many of these were more or less close analogues of known active agents, but some were novel types. These new compounds are listed in Table I and their preparations are described in the Experimental Section. None was found to be more active or less toxic than known medicinals.

Experimental Section

N,N-Dimethyl-N'-(p-nitrophenyl)-N'-phenylethylenediamine Hydrochloride (1). To a solution of 5.36 g (0.025 mol) of 4-nitrodiphenylamine in 100 mL of DMF, under N_2, was added 1.25 g (0.035 mol) of 56% NaH in mineral oil. After stirring of the mixture for 2 h, a benzene solution of 0.045 mol of 2-dimethylaminoethyl chloride was slowly added, and stirring was continued at room temperature for 2 h more. After removal of the solvent in vacuo, the residue was dissolved in CH_2Cl_2 and extracted with dilute HCl and the acid solution was basified with NaOH. The free base was extracted with CH_2Cl_2, washed with water, evaporated, and converted to the hydrochloride in ether with ethereal HCl. Recrystallization from 2-propanol yielded 4.6 g (57%) of solid, mp 246–248 °C.

2-[N-[(2-Dimethylamino)ethyl]anilino]-5-nitropyridine Hydrochloride (2). This was prepared as for **1** from 5.38 g (0.025 mol) of 2-anilino-5-nitropyridine, 1.25 g (0.035 mol) of 46% NaH, 100 mL of DMF, and a benzene solution of 0.045 mol of dimethylaminoethyl chloride. The hydrochloride was recrystallized from 2-propanol, yielding 4.4 g (55%) of tan needles, mp 255–258 °C.

5-Amino-2-[N-[2-(dimethylamino)ethyl]anilino]pyridine Hydrochloride (3). A solution of 3.22 g (0.01 mol) of **2** in 40 mL of ethanol was hydrogenated with 0.3 g of PtO_2 at 3.5 kg/cm^2 and room temperature for 2 h. After filtration, evaporation in vacuo, and recrystallization from 2-propanol, 1.1 g (37%) of tan needles was obtained, mp 165.5–168 °C.

2-Methoxy-N,α-dimethyl-α-(phenylmethyl)benzeneethanamine Hydrochloride (4). A solution of Schiff's base was prepared by thoroughly drying over K_2CO_3 a solution of 123 g (0.75 mol) of (*o*-methoxyphenyl)propanone and 31 g (1 mol) of methylamine in 320 mL of absolute ether. This solution was filtered and slowly added with stirring to benzylmagnesium chloride, prepared from 75 g (3.09 mol) of Mg, 345 mL (6 mol) of benzyl chloride, and 2 L of absolute ether. After refluxing for 2.5 h, the mixture was cooled and poured into ice water containing 350 mL of concentrated HCl. The resulting solid was collected, washed with a little water and ether, and dried. This was dissolved in methanol, filtered, diluted with ethyl acetate, concentrated, and cooled, giving 54.2 g of white solid, mp 138–143 °C. This was recrystallized by again dissolving in methanol, diluting with EtCOMe, boiling to remove most of the methanol, and cooling. There was thus obtained 47 g (24.5%) of white crystals, mp 147–149 °C.

4-(p-Chlorophenyl)-4-hydroxycyclohexanone Oxime (5). A mixture of 6.25 g (0.028 mol) of 4-(*p*-chlorophenyl)-4-hydroxycyclohexanone (*1*), 6.4 g (0.092 mol) of hydroxylamine hydrochloride, 15 mL of 50% NaOH, and 80 mL of THF was refluxed for 17 h. After evaporation in vacuo the residue was mixed with water and extracted with ether. The ether solution was washed with water and dried over Na_2SO_4. Evaporation gave 4.5 g (67%) of white solid, mp 134–135 °C. Recrystallization from acetone–hexane raised the melting point to 136–137 °C.

4-(p-Chlorophenyl)-4-hydroxycyclohexanone O-Methyloxime (6). A mixture of 12.5 g (0.055 mol) of 4-(*p*-chlorophenyl)-4-hydroxycyclohexanone (*1*), 12.8 g (0.15 mol) of methoxyamine hydrochloride, 50 mL of 45% NaOH, and 160 mL of MeOH was refluxed for 17 h. After evaporation in vacuo the residue was well saturated with ether, and the extract was washed with water and dried over Na_2SO_4. Evaporation of the ether gave 12.5 g (95%) of white crystals, mp 107–108.5 °C. Recrystallization from MeOH–H_2O yielded 12 g of white crystals, mp 108–109 °C.

4-Amino-1-(p-chlorophenyl)cyclohexanol Hydrochloride (7). To a solution of 5.06 g (0.02 mol) of **6** in 80 mL of THF, at 0 °C under N_2, was slowly added with stirring 80 mL (0.08 mol) of a 1 M solution of B_2H_6 in THF. After 18 h at 0 °C, 1 mL of water was cautiously added followed by 120 mL of 0.65 N HCl. After 10 min at room temperature the solution was washed with ether and basified with NaOH, and the free base was extracted with ether. After the extract was washed with water and dried over Na_2SO_4, the solution was evaporated in vacuo giving a colorless oil. This was converted to the hydrochloride in ether with ethanolic HCl, giving 3.1 g of white solid. Recrystallization from MeOH–EtOAc yielded 3 g (60%) of white crystals, mp 285–287 °C dec.

3-[[4-(p-Chlorophenyl)-3-cyclohexen-1-yl]amino]-4'-fluoropropiophenone Hydrochloride (8). A mixture of 1 g (0.004 mol) of 4-(*p*-chlorophenyl)-3-cyclohexen-1-ylamine hydrochloride (*1*) and 0.78 g (0.005 mol) of 3-chloro-*p*-fluoropropiophenone in 60 mL of pyridine was stirred at 90 °C for 18 h. The mixture was evaporated in vacuo, acidified with dilute HCl, washed with ether, and basified with NaOH. The free base was extracted with ether, washed with water, and dried over Na_2SO_4. After filtration the solution was treated with ethanolic HCl, giving 0.7 g of nearly white hydrochloride. Recrystallization from 2-propanol yielded 0.5 g (51%) of white crystals, mp 208–210 °C.

N-[3-[2-(p-Fluorophenyl)-5,5-dimethyl-m-dioxan-2-yl]-propyl]phthalimide (9). A solution of 25.6 g (0.1 mol) of 2-(3-chloropropyl)-2-(*p*-fluorophenyl)-5,5-dimethyl-*m*-dioxane and 28 g (0.15 mol) of potassium phthalimide in 200 mL of DMF was heated at 90 °C for 5 h, cooled, and diluted with 400 mL of ice water. The product was extracted with $CHCl_3$, washed with water, dilute NaOH, and again with water, and dried over Na_2SO_4. Filtration and evaporation in vacuo gave 40 g of solid. This was boiled with 1.2 L of cyclohexane, filtered hot, and cooled, yielding 36 g (91%) of white crystals, mp 156–158 °C.

2-(p-Fluorophenyl)-5,5-dimethyl-m-dioxane-2-propylamine and Oxalate (Salt) (10). A mixture of 15 g (0.037 mol) of **9** and 7.5 g (0.15 mol) of hydrazine hydrate in 250 mL of EtOH was stirred for 30 min and allowed to stand overnight. The solution was filtered from the resulting phthalhydrazide and

* Retired. Address requests for reprints to The Upjohn Co., Unit 7251-209-7, Kalamazoo, MI 49001. All other inquiries should be addressed to the author, 2895 Bronson Blvd., Kalamazoo, MI 49008.

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evaporated in vacuo. The residue was diluted with 50 mL of ether, filtered, washed with water, dried over Na_2SO_4, and again evaporated. The free base was obtained as 7 g (70%) of colorless oil. The IR and NMR data support the structure.

A solution of 0.8 g (0.003 mol) of this free base in 40 mL of EtOH was acidified with 0.3 g (0.003 mol) of oxalic acid, warmed to effect solution, and cooled, giving 0.8 g (75%) of white oxalate salt, mp 183–185 °C.

4-(1-Adamantylamino)-4′-fluorobutyrophenone Hydrochloride (11). A mixture of 4.5 g (0.03 mol) of 1-adamantylamine, 1 g of 56% NaH in mineral oil, and 70 mL of DMF was stirred at room temperature, under N_2, for 15 min. Then 4.5 g of K_2CO_3, 2.4 g of KI, and 7.5 g (0.03 mol) of 2-(3-chlorophenyl)-2-(*p*-chlorophenyl)-5,5-dimethyl-*m*-dioxane were added. After being stirred at 90 °C for 24 h, the mixture was diluted with water and extracted with benzene. The extract was washed with water, dried over Na_2SO_4, filtered, and evaporated in vacuo, giving a yellow oil. This free base was dissolved in ethanol, acidified with ethanolic HCl, and diluted with ether. On allowing the solution to stand, 5 g of crystalline hydrochloride was obtained. This was recrystallized from ethanol; yield 4.5 g (50%) of white crystals, mp 261–263 °C dec.

1-Benzyl-1,2,3,6-tetrahydro-4-(p-chlorophenyl)pyridine Hydrochloride (12) (2). A solution of 190 g (1 mol) of 1-benzyl-4-piperidone in 200 mL of ether was added to (*p*-chlorophenyl)magnesium bromide, prepared from 36.5 g (1.5 g-atom) of Mg, 290 g (1.52 mol) of *p*-bromochlorobenzene, and 800 mL of ether. After stirring of the mixture under reflux for 2 h and at room temperature overnight, 300 mL of saturated aqueous NH_4Cl was slowly added. The ether was decanted and the solid was extracted with more ether. The combined ether solutions were dried over $MgSO_4$, filtered, and evaporated in vacuo giving an oil. This crude carbinol was dissolved in 800 mL of pyridine, treated with 150 mL of $POCl_3$, stirred for 0.5 h, and refluxed for 1 h. After the solution was cooled, 2.5 L of water was cautiously added. The solution was basified with NaOH and extracted with ether. The extract was washed with dilute NaOH and saturated NaCl solution and dried over K_2CO_3. Filtration and evaporation in vacuo gave dark oily free base which crystallized on standing. This was recrystallized from pentane and converted to the hydrochloride with ethanolic HCl. Recrystallization from ethanol yielded 81.2 g (25%) of nearly white solid, mp 216–221 °C.

4-(p-Chlorophenyl)-1-[(3,4,5-trimethoxybenzylidene)amino]piperidine (13) (2). To a solution of 2.1 g (0.01 mol) of 1-amino-4-(4-chlorophenyl)piperidine (*3*) in 80 mL of MeOH was added 2.4 g (0.012 mol) of 3,4,5-trimethoxybenzaldehyde in 40 mL of MeOH. Ten drops of AcOH was added, and the mixture was stirred under reflux for 0.5 h. Cooling gave white solid which was collected and recrystallized from EtOH, yielding 2.3 g (59%) of white needles, mp 160.5–161 °C.

2-(2,3,4,5-Tetramethyl-1-pyrrolidyl)ethanol (14). A solution of 16.7 g (0.1 mol) of 2-(2,3,4,5-tetramethyl-1-pyrrol)ethanol in 300 mL of EtOH was hydrogenated with Raney nickel at 150 °C and 900 lb/in.^{2} for 36 h. After filtration and concentration, the product was dissolved in ether and extracted with dilute HCl. The acid solution was washed with ether and basified 50% aqueous NaOH. The free base was repeatedly extracted with ether, washed with saturated NaCl solution, and dried over K_2CO_3. After filtration and removal of the solvent the product was distilled, yielding 9.68 g (56%) of light yellow liquid: bp 91 °C (0.8 mm), n^{25}_D 1.4608. No attempt was made to separate stereoisomers.

α-(3-Dimethylaminopropyl)-3,4,5-trimethoxybenzyl Alcohol Hydrochloride (15). (3-Dimethylaminopropyl)magnesium chloride was prepared from 7.8 g (0.32 g-atom) of Mg, 36.7 g (0.3 mol) of 3-dimethylaminopropyl chloride, and 150 mL of THF. To this was slowly added a solution of 36.7 g (0.16 mol) of 3,4,5-trimethoxybenzaldehyde in 200 mL of THF. After the mixture was stirred under reflux and allowed to stand overnight, a solution of 50 g of NH_4Cl in 150 mL of water was slowly added. The mixture was extracted with ether, basified with NH_4OH, and again extracted. The combined ether extracts were extracted with dilute HCl, and the acid solution was rebasified with NaOH. The free base was extracted with ether, washed with water, and dried over Na_2SO_4. Filtration and evaporation gave 23.9 g of light yellow oil. This was dissolved in acetone and acidified with ethanolic HCl. Heating to boiling and cooling yielded 23 g (45%) of white crystals, mp 127.5–129 °C. A sample recrystallized from 2-butanone had the same melting point.

3′,4′-Dimethoxy-2-[2-(1-pyrrolidinyl)ethylamino]propiophenone Dihydrochloride (16). To a solution of 122.9 g (0.45 mol) of 2-bromo-3′,4′-dimethoxypropiophenone in 200 mL of benzene was slowly added, with stirring, 103.3 g (0.9 mol) of 2-(1-pyrrolidinyl)ethylamine. After standing at room temperature for 22 h, the solution was filtered, washed with water, and extracted with dilute HCl. The acid solution was washed with ether and basified with NaOH. The product was extracted with benzene, dried over K_2CO_3, filtered, and evaporated. The oily free base was converted to the hydrochloride in ethyl acetate with an excess of ethanolic HCl. The dihydrochloride was recrystallized three times from 95% ethanol, yielding 36.5 g (21.4%) of white crystals, mp 221–223 °C.

α-[1-[2-(1-Pyrrolidinyl)ethylamino]ethyl]veratryl Alcohol Dihydrochloride (17). A solution of 32.5 g (0.086 mol) of **16** in 100 mL of water was hydrogenated with 3 g of 10% Pd on charcoal at room temperature and 3.5 kg/cm^2 for 20 h. After filtration and evaporation in vacuo the product was recrystallized from 97% ethanol, yielding 18 g (56%) of white crystals, mp 223–224 °C.

2-Methyl-1-pyrrolidinepropyl p-Hydroxybenzoate Hydrochloride (18). Crude 2-methyl-1-pyrrolidinepropyl *p*-(2-cyclohexen-1-yloxy)benzoate (*4*) was prepared from 58 g (0.24 mol of *p*-Δ^2-cyclohexenyloxybenzoic acid hydrate, 53.2 g (0.27 mol) of 3-(2-methyl-1-pyrrolidyl)propyl chloride hydrochloride, 81 g of K_2CO_3, and 500 mL of 2-butanone. This was converted to the hydrochloride but failure to use rigorously dried reagents caused cleavage of the cyclohexenyloxy group, yielding 43.3 g (59%) of **18**, recrystallized twice from ethanol-2-butanol; mp 105–107 °C.

Methyl 3,3-Dimethyl-2-(1-pyrrolidinyl)cyclobutanecarboxylate (19). A mixture of 75 g (0.6 mol) of 1-(2-methyl-1-propenyl)pyrrolidine and 51.6 g (0.6 mol) of methyl acrylate was refluxed for 3.5 h from an oil bath up to 170 °C. The resulting light yellow liquid was distilled through a short, helices packed column, yielding 93.5 g (74%) of colorless liquid: bp 74 °C (1.0 mm), n^{25}_D 1.4648, neutral equivalent, calcd 211.3, found 213. A sample was converted to the hydrochloride, mp 179.5–181 °C, which proved to be hygroscopic.

2-Bromoethyl Cyclopentylphenylacetate (20). To a solution of 53.7 g (0.24 mol) of cyclopentylphenylacetyl chloride and 33 g (0.264 mol) of 2-bromoethanol in 100 mL of benzene was slowly added with stirring 19.3 mL (0.24 mol) of dry pyridine. The mixture was refluxed for 2 h, cooled, diluted with ice water, and acidified with HCl. The product was extracted with ether and benzene, washed with water, cold dilute Na_2CO_3, and water, and dried over Na_2SO_4. After filtration and removal of the solvent in vacuo the ester was distilled through a short, helices packed column, yielding 68.3 g (91.6%) of liquid: bp 102 °C (0.005 mm), n^{24}_D 1.4307.

1-[(Cyclopentylphenylacetoxy)ethyl]quinuclidinium Bromide (21). Free base was liberated from 2.43 g (0.165 mol) of quinuclidine hydrochloride with NaOH, extracted with ether, and dried over CaH_2. After filtration and concentration this was dissolved in 10 mL of ethyl methyl ketone and 5.15 g (0.0165 mol) of **20** was added. After the mixture was allowed to stand

Table I. New Compounds Prepared

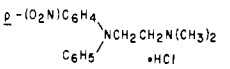
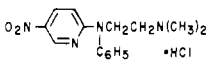
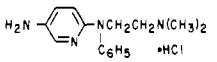
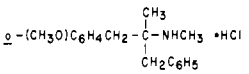
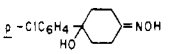
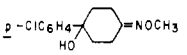
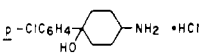
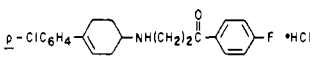
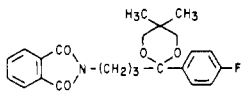
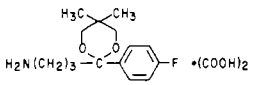
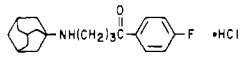
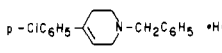
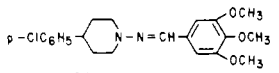
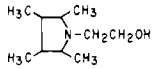
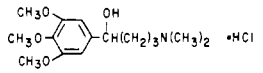
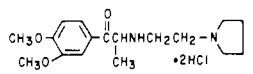
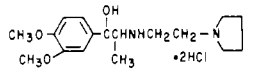
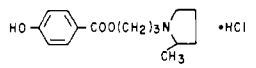
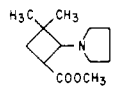
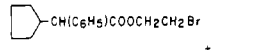
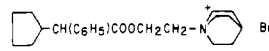
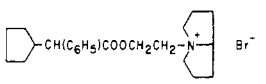
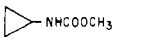
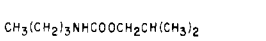
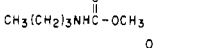
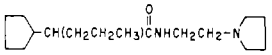
no.	structure	molecular formula	mp[a] (or bp), °C	anal.[b]
1		$C_{16}H_{20}ClN_3O_2$	246–248	C, H, N, Cl
2		$C_{15}H_{19}ClN_4O_2$	255–258	C, H, N, Cl
3		$C_{15}H_{21}ClN_4$	165.5–168	C, H, N, Cl
4		$C_{18}H_{24}ClNO$	147–149	N, Cl
5		$C_{12}H_{14}ClNO_2$	136–137	C, H, N, Cl
6		$C_{13}H_{16}ClNO_2$	108–109	C, H, N, Cl
7		$C_{12}H_{17}Cl_2NO$	285–287 dec	C, H, N, Cl
8		$C_{21}H_{22}Cl_2FNO$	208–210	C, H, N, F, Cl
9		$C_{23}H_{24}FNO_4$	156–158	C, H, N, F
10		$C_{17}H_{24}FNO_6$	183–185 dec	C, H, N, F
11		$C_{20}H_{27}ClFNO$	261–263 dec	C, H, N, F, Cl
12		$C_{18}H_{19}Cl_2N$	216–221	C, H, N, Cl
13		$C_{21}H_{25}ClN_2O_3$	160.5–161	C, H, N, Cl
14		$C_{10}H_{21}NO$	bp 91 (0.8 mm)	C, H, N
15		$C_{15}H_{26}ClNO_4$	127.5–129	C,[c] H, N, Cl, O
16		$C_{17}H_{28}Cl_2N_2O_3$	221–223	C, H, N, Cl
17		$C_{17}H_{30}Cl_2N_2O_3$	223–224	C, H, N, Cl
18		$C_{15}H_{22}ClN_3$	105–107	C, H, N, Cl
19		$C_{12}H_{21}NO_2$	bp 74 (1.0 mm)	C, H, N
20		$C_{15}H_{19}BrO_2$	bp 102 (0.005 mm)	C, H, Br
21		$C_{22}H_{32}BrNO_2$	122–125	C, H, Br
22		$C_{22}H_{32}BrNO_2$	131.5–133.5	C, H, N, Br
23		$C_5H_9NO_2$	bp 98 (24 mm)	N
24		$C_9H_{19}NO_2$	bp 115 (15 mm)	C, H, N
25		$C_6H_{13}NOS$	bp 117 (11 mm)	C, H, N, O, S
26		$C_{16}H_{20}N_2O$	111–112	N

Table I. (*Continued*)

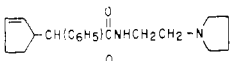
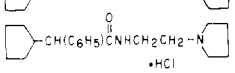
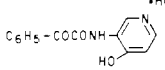
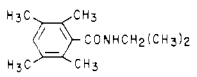
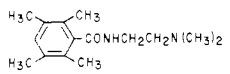
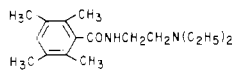
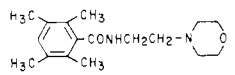
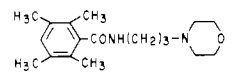
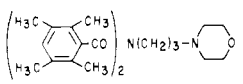
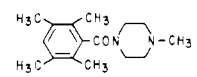
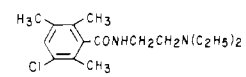
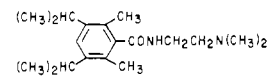
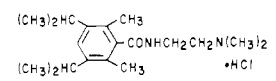
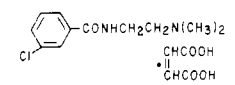
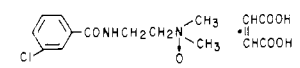
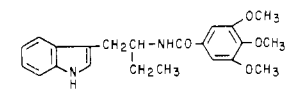
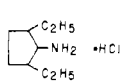
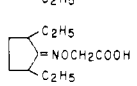
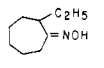
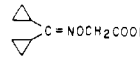
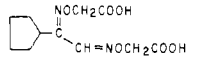
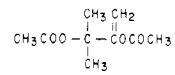
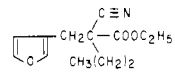
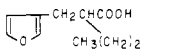
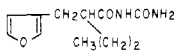
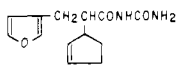
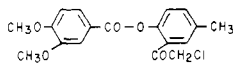
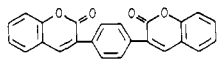
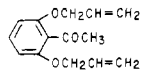
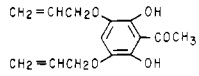
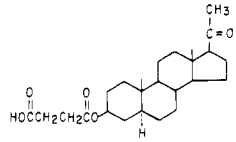
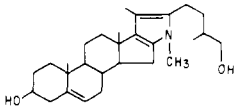
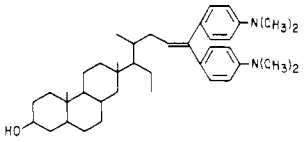
no.	structure	molecular formula	mp[a] (or bp), °C	anal.[b]
27		$C_{19}H_{26}N_2O$	bp 150 (0.015 mm)	N
28		$C_{19}H_{27}ClN_2O$	133–135.5	Cl
29		$C_{13}H_{10}N_2O_2$	245–249	C, H, N
30		$C_{14}H_{21}NO$	192.5–194	C, H, N
31		$C_{15}H_{24}N_2O$	133–134	C, H, N
32		$C_{17}H_{28}N_2O$	97–98.5	C, H, N
33		$C_{17}H_{26}N_2O_2$	130.5–132	C, H, N
34		$C_{18}H_{28}N_2O_2$	114–116	C, H, N
35		$C_{29}H_{40}N_2O_3$	137.5–139	C, H, N
36		$C_{16}H_{24}N_2O$	133–134.5	C, H, N
37		$C_{16}H_{25}ClN_2O$	107.5–109	C, H, N, Cl
38		$C_{19}H_{32}N_2O$	99.5–101.5	C, H, N
39		$C_{19}H_{33}ClN_2O$	162–164.5 dec	C, H, N, Cl
40		$C_{15}H_{19}ClN_2O_5$	106.5–107.5	C, H, N, Cl
41		$C_{15}H_{19}ClN_2O_6$	111–112	C, H, N, Cl
42		$C_{22}H_{26}N_2O_4$	179.5–180.5	C, H, N
43		$C_{17}H_{17}N_2O_4$	122.5–124	C, H, N
44		$C_9H_{17}NO$	bp 119 (1 mm)	C, H, N
45		$C_9H_{19}N$	bp 70 (1.5 mm)	C, H, N
46		$C_9H_{20}ClN$	233–234	C, H, N, Cl
47		$C_{11}H_{19}NO_3$	51–53.5	C, H, N
48		$C_9H_{17}NO$	bp 124 (1 mm)	C, H, N
49		$C_9H_{13}NO_3$	94–96	C, H, N
50		$C_{11}H_{16}N_2O_6$	171 dec	C, H, N

Table I. (*Continued*)

no.	structure	molecular formula	mp[a] (or bp), °C	anal.[b]
51		$C_9H_{14}O_4$	bp 90 (11.5 mm)	C, H
52		$C_{13}H_{17}NO_3$	bp 127 (3 mm)	C, H, N
53		$C_{10}H_{14}O_3$	bp 123 (2.5 mm)	C, H
54		$C_{11}H_{16}N_2O_3$	182.5-184	C, H, N
55		$C_{13}H_{16}N_2O_3$	181-183	C, H, N
56		$C_{18}H_{17}ClO_5$	172-174	C, H, Cl
57		$C_{24}H_{14}O_4$	>350	C, H, O
58		$C_{14}H_{16}O_3$	bp <65 (0.07 mm)	C, H
59		$C_{14}H_{16}O_3$	57.5-58.5	C, H
60		$C_{25}H_{38}O_5$	198-200	C, H
61		$C_{28}H_{43}NO_2$	219-221.5 dec	C, H, N, O
62		$C_{40}H_{56}N_2O$	166-168	C, H, N, O

[a] Melting points were taken in capillary tubes with a partial immersion thermometer. Calibration of the apparatus against standard compounds showed no need for correction. [b] Satisfactory analyses were obtained for the elements indicated. In most cases IR, NMR, and sometimes mass spectral data were obtained, and all support the structures. [c] Repeated attempts failed to give a satisfactory carbon analysis. However, all other elements, including direct oxygen, were satisfactory.

at room temperature for 6 days, the addition of ether caused precipitation of gummy quaternary salt which crystallized on long standing. Recrystallization from acetone–ethyl acetate yielded 4.8 g (69%) of white solid, mp 122–125 °C.

1-(2-Hydroxyethyl)pyrrolizidinium Bromide α-Phenylcyclopentaneacetate (22). A solution of 15.5 g (0.05 mol) of **20** in 35 mL of ether was added to 5.25 g (0.047 mol) of pyrrolizidine (*5*) in 30 mL of ether. The quaternary salt crystallized on standing, yielding 8 g (40%) of white crystals; mp 131.5–133.5 °C.

Methyl N-Cyclopropylcarbamate (23). To a solution of 17.1 g (0.3 mol) of cyclopropylamine and 30.3 g (0.3 mol) of Et_3N in 300 mL of ether was slowly added with stirring at reflux 28.2 g (0.3 mol) of methyl chloroformate. After the mixture was allowed to stand for 20 h, ice water was added. The aqueous layer was extracted with more ether, and the ether solutions were washed with saturated NaCl solution and dried over Na_2SO_4. After filtration and removal of the solvent the product was distilled, yielding 33.8 g (98%) of colorless liquid which immediately solidified: bp 98 °C (24 mm), freezing point 29 °C.

Isobutyl N-n-Butylcarbamate (24). A solution of 100 g (1.01 mol) of *n*-butyl isocyanate in 148 g (2 mol) of isobutyl alcohol was refluxed for 2.5 h, allowed to stand overnight, and distilled twice through a short helices packed column, yielding 162 g (95%) of colorless liquid: bp 115 °C (15 mm), n^{25}_D 1.4310.

Methyl N-n-Butylthiocarbamate (25). To a solution of 44.3 g (0.82 mol) of NaOMe in 350 mL of MeOH was slowly added 94.5 g (0.82 mole) of *n*-butyl isothiocyanate. The solution was refluxed for 16 h, cooled, neutralized with methanolic HCl, and distilled, yielding 51.5 g (42.6%) of colorless liquid: bp 117 °C (11 mm), n^{25}_D 1.5070.

N-[2-(1-Pyrrolidinyl)ethyl]cyclopentyl-n-propylacetamide (26). A solution of 6.85 g (0.06 mol) of 2-(1-pyrrolidinyl)-ethylamine in 15 mL of benzene was slowly added to a solution of 9.45 g (0.5 mol) of cyclopentyl-*n*-propylacetyl chloride (*6*) in 10 mL of benzene. After refluxing for 15 min, the solution was acidified with HCl and ice water. The aqueous layer was washed with ether and basified with NaOH giving crystalline free

base. This was collected, dried, and recrystallized from acetone, yielding 9 g (68%) of light tan crystals, mp 111–112 °C.

***N*-[2-(1-Pyrrolidinyl)ethyl]-Δ^2-cyclopentenylphenylacetamide (27).** This was prepared as described for **26** from 6.85 g (0.06 mol) of 2-(1-pyrrolidinyl)ethylamine, 11.1 g (0.05 mol) of Δ^2-cyclopentenylphenylacetyl chloride (*7*) and 25 mL of benzene. The free base was distilled, yielding 15 g (100%) of viscous liquid: bp 150 °C (0.015 mm), n^{25}_D 1.5472.

Hydrochloride (28). This free base was dissolved in ether and converted to the hydrochloride with HCl gas. The gummy product was boiled with EtOAc and cooled, giving 11.5 g (69%) of light tan crystals, mp 133–135.5 °C.

***N*-(4-Hydroxy-3-pyridyl)-2-phenylglyoxylamide (29).** A solution of 0.1 mol of 3-amino-4-hydroxypyridine in ethanol was prepared by hydrogenation of 14 g (0.1 mol) of 4-hydroxy-3-nitropyridine in ethanol with 1 g of 10% Pd/C catalyst at 3.5 kg/cm^2 and room temperature. After filtration 35.6 g (0.2 mol) of ethyl phenylglyoxylate was added, and the solution was allowed to stand at room temperature overnight. Evaporation in vacuo and crystallization of the residue from ethanol gave 9.6 g of crystals. Recrystallization from 2-methoxyethanol yielded 7 g of yellow crystals, mp 245–249 °C.

***N*-Isopropyl-2,3,4,6-tetramethylbenzamide (30).** A solution of 2,3,4,6-tetramethylbenzoyl chloride was prepared by refluxing for 3.5 h a solution of 17.8 g (0.1 mol) of 2,3,4,6-tetramethylbenzoic acid, 70 mL of $SOCl_2$, and 100 mL of benzene. The solvent was evaporated in vacuo and the acid chloride was dissolved in 150 mL of benzene. To this was slowly added a solution of 5.91 g (0.1 mol) of isopropylamine in 50 mL of benzene. After refluxing overnight the mixture was cooled, diluted with ether, and washed with dilute HCl. Concentration of the ether solution gave 14.12 g of crystals which was recrystallized from ethyl acetate, yielding 10.95 g (50.5%) of white crystals, mp 192.5–194 °C.

***N*-[2-(Dimethylamino)ethyl]-2,3,5,6-tetramethylbenzamide (31).** This was prepared as for **30** from 17.8 g (0.1 mol) of 2,3,5,6-tetramethylbenzoic acid, 70 mL of $SOCl_2$, 8.81 g (0.1 mol) of *N*,*N*-dimethylethylenediamine, and 150 mL of benzene. After refluxing for 5 h the reaction mixture was diluted with ether and extracted with dilute HCl. The acid solution was basified with NaOH giving 16.46 g of tan solid. This was recrystallized from methylcyclohexane, yielding 13.5 g (54.5%) of tan crystals, mp 133–134 °C.

***N*-[2-(Diethylamino)ethyl]-2,3,5,6-tetramethylbenzamide (32).** This was prepared as for **31** from 17.8 g (0.1 mol) of 2,3,5,6-tetramethylbenzoic acid, 70 mL of $SOCl_2$, 11.6 g (0.1 mol) of *N*,*N*-dimethylethylenediamine, and 300 mL of benzene. Basification of the acid solution gave 19.89 g of tan crystals, mp 91–94.5 °C. This was recrystallized from hexane, yielding 16.2 g (58.5%) of white crystals, mp 97–98.5 °C.

***N*-(Morpholinoethyl)-2,3,5,6-tetramethylbenzamide (33).** This was prepared as for **31** from 17.8 g (0.1 mol) of 2,3,5,6-tetramethylbenzoic acid, 70 mL of $SOCl_2$, 13.0 g (0.1 mol) of *N*-aminoethylmorpholine, and 150 mL of benzene. The free base was extracted with ether, washed with water, and dried over $MgSO_4$. Evaporation in vacuo gave an oil which was crystallized from methylcyclohexane and recrystallized from ethyl acetate, yielding 6.92 g (24%) of white crystals, mp 130.5–132 °C.

***N*-[3-(1-Morpholino)propyl]-2,3,5,6-tetramethylbenzamide (34) and *N*-[3-(1-Morpholino)propyl]-2,2′,3,3′,5,5′,6,6′-octamethyldibenzamide (35).** This reaction was run as described for **30** by using 17.8 g (0.1 mol) of 2,3,5,6-tetramethylbenzoic acid, 70 mL of $SOCl_2$, 14.42 g (0.1 mol) of *N*-(3-aminopropyl)-1-morpholine, and 150 mL of benzene. The reaction mixture was diluted with ether and mixed with dilute aqueous HCl. Solid hydrochloride separated in the aqueous layer and was collected giving 5.9 g of white crystals, mp 252 °C dec. The aqueous acid filtrate was basified and cooled, giving 7.49 g of white solid, mp 113.5–115 °C. Recrystallization from EtOAc yielded 5.47 g (18.2%) of white crystals: mp 114–116 °C; found by IR and NMR data to be the expected **34**.

The above hydrochloride (mp 252 °C dec) was converted to its free base with cold dilute NaOH and extracted with ether. Washing with water, drying over Na_2SO_4, filtering, and evaporating gave solid which was recrystallized from ethyl acetate, yielding 3.75 g (16.3%) of white crystals, mp 137.5–139 °C. IR, NMR, and mass spectral data (M^+ 464) showed this to be **35**.

***1*-Methyl-4-(2,3,5,6-tetramethylbenzoyl)piperazine (36).** This was prepared as for **30** from 17.8 g (0.1 mol) of 2,3,5,6-tetramethylbenzoic acid, 70 mL of $SOCl_2$, 10.01 g (0.1 mol) of *N*-methylpiperazine, and 175 mL of benzene. Basification of the HCl extract gave 21.48 g of white solid which was recrystallized from ethyl acetate, yielding 15.9 g (61%) of white crystals, mp 133–134.5 °C.

***3*-Chloro-*N*-[2-(diethylamino)ethyl]-2,5,6-trimethylbenzamide (37).** This was prepared as for **31** from 5.0 g (0.0252 mol) of 3-chloro-2,5,6-trimethylbenzoic acid (*8*), 25 mL of $SOCl_2$, 2.17 g (0.0252 mol) of *N*,*N*-diethylethylenediamine, and 70 mL of benzene. Basification of the HCl extract gave 5.87 g of tan crystals, mp 105–108 °C. Recrystallization from hexane yielded 5.0 g (67%) of tan crystals, mp 107.5–109 °C.

***N*-[2-(Dimethylamino)ethyl]-3,5-diisopropyl-2,6-dimethylbenzamide (38).** This was prepared as for **33** from 10.1 g (0.043 mol) of 3,5-diisopropyl-2,6-dimethylbenzoic acid (*8*), 50 mL of $SOCl_2$, 8.8 g (0.1 mol) of *N*,*N*-dimethylethylenediamine, and 30 mL of benzene. The free base was obtained as an oil which crystallized on standing. It was recrystallized from pentane, yielding 10.8 g (83%) of colorless crystals, mp 99.5–101.5 °C.

Hydrochloride (39). A solution of 10.6 g (0.035 mol) of **38** in 250 mL of ether was acidified with ethanolic HCl giving crystalline solid which was recrystallized from EtOAc, yielding 11.7 g (100%) of white crystals, mp 162–164.5 °C dec.

***m*-Chloro-*N*-[2-(dimethylamino)ethyl]benzamide Maleate (1:1) (40).** A solution of 43.8 g (0.25 mol) of *m*-chlorobenzoyl chloride in 200 mL of benzene was slowly added, with stirring, to a solution of 44 g (0.5 mol) of *N*,*N*-dimethylethylenediamine in 150 mL of benzene. After refluxing for 0.5 h the solution was cooled, diluted with ether, and extracted with dilute HCl. The aqueous solution was washed with ether and basified with NaOH. The free base was extracted with ether, washed with water, and dried over $MgSO_4$. Filtration and evaporation of the solvent gave oily free base which was dissolved in 500 mL of 2-propanol and acidified with an excess of maleic acid. Dilution with ether gave 59.8 g (70%) of white crystals, mp 105–107 °C. Recrystallization from ethyl methyl ketone yielded 52.4 g (61%) of white crystalline maleate salt, mp 106.5–107.5 °C.

***m*-Chloro-*N*-[2-(dimethylamino)ethyl]benzamide *N*-Oxide Maleate (1:1) (41).** A solution of 17.6 g (0.078 mol) of **40** and 18.7 mL of 30% H_2O_2 in 155 mL of ethanol was allowed to stand at room temperature for 3 days. The excess H_2O_2 was decomposed by carefully adding an aqueous slurry of 0.2 g of 30% Pd/C and vigorously stirring for 2.5 h. Filtration and evaporation in vacuo below 30 °C gave colorless syrup. This was dissolved in 2-propanol, acidified with a slight excess of maleic acid, and diluted with ether, giving 18.24 g (65.5%) of white crystals, mp 111–112 °C.

***N*-(1-Ethyl-2-indol-3-ylethyl)-3,4,5-trimethoxybenzamide (42).** An aqueous solution of 10 g (0.25 mol) of NaOH was added dropwise during 0.5 h to a stirred mixture of 37.2 g (0.15 mol) of 3-(2-aminobutyl)indole acetate, 23 g (0.1 mol) of 3,4,5-trimethoxybenzoyl chloride, and 250 mL of benzene. After stirring of the mixture for 3 h more, the solid was collected, washed with dilute Na_2CO_2 solution, water, and ether, and dried,

giving 40.15 g of solid, mp 167–176 °C. Recrystallization from ethanol–water yielded 33.2 g (87%) of white crystals, mp 179.5–180.5 °C.

2,5-Diphenylcyclopentanone Oxime (43). A mixture of 15 g (0.0635 mol) of 2,5-diphenylcyclopentanone, 10 g (0.144 mol) of hydroxylamine hydrochloride, and 30 mL (0.382 mol) of pyridine in 100 mL of ethanol was stirred under reflux for 2 h. After evaporation of the solvent the residue was dissolved in benzene, washed with water, dilute HCl, $NaHCO_3$ solution, and water, and dried over Na_2SO_4. Filtration and evaporation in vacuo gave a residue which crystallized from ethanol, yielding 3.77 g (23.6%) of white crystals, mp 122.5–124 °C.

2,5-Diethylcyclopentanone Oxime (44). A mixture of 60 g (0.43 mol) of 2,5-diethylcyclopentanone, 73.0 g (1.05 mol) of hydroxylamine hydrochloride, 100 g of $NaHCO_3$, and 400 mL of MeOH was stirred under reflux for 3 h. This was diluted with water and extracted with ether. The extract was washed with water, dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was distilled through a short helices packed column, yielding 56 g (84%) of colorless liquid: bp 119 °C (1 mm), n^{25}_D 1.4766.

2,5-Diethylcyclopentylamine (45). A solution of 45 g (0.291 mol) of **44** in 300 mL of ethanolic ammonia was hydrogenated with Raney nickel at 1000 lb/in.^{2} and room temperature. After filtration and evaporation of the solution in vacuo, the residue was dissolved in dilute HCl, washed with ether, and basified with NaOH. The free base was extracted with ether, washed with saturated NaCl solution, and dried over K_2CO_3. After filtration and removal of the solvent the product was distilled twice through a short, helices packed column, yielding 27.75 g (68.5%) of colorless liquid, bp 70 °C (11.5 mm).

Hydrochloride (46). This free base (**45**) in ether was converted to the hydrochloride with ethanolic HCl giving 30.43 g (90%) of white crystals, mp 233–234 °C.

2,5-Diethylcyclopentanone O-Carboxymethyl Oxime (47). A mixture of 21 g (0.15 mol) of 2,5-diethylcyclopentanone, 22 g (0.2 mol) of carboxymethoxyamine hemihydrochloride, 41 g (0.3 mol) of $NaOAc{\cdot}3H_2O$, and 1 L of 90% ethanol was stirred under reflux for 6 h. After removal of most of the solvent, the residue was mixed with 5% K_2CO_3 and washed with ether. The basic aqueous solution was acidified with dilute HCl, and the product was extracted with pentane. The pentane solution was dried over Na_2SO_4, filtered, concentrated, and cooled, yielding 9.49 g (29.6%) of white crystals, mp 51–53.5 °C.

2-Ethylcycloheptanone Oxime (48). This was prepared as described for **44** from 20.0 g (0.143 mol) of 2-ethylcycloheptanone, 24 g (0.347 mol) of $H_2NOH{\cdot}HCl$, 33 g (0.392 mol) of $NaHCO_3$, and 133 mL of MeOH. After the mixture was diluted with water and extracted with ether, the extract was washed with water, dried over Na_2SO_4, evaporated, and distilled, yielding 14.6 g (66%) of colorless liquid: bp 124 °C (1 mm), n^{25}_D 1.4927.

Dicyclopropyl Ketone O-(Carboxymethyl)oxime (49). A mixture of 20 g (0.182 mol) of dicyclopropyl ketone, 26.6 g (0.242 mol) of carboxymethoxyamine hemihydrochloride, 49.8 g (0.364 mol) of $NaOAc{\cdot}3H_2O$, and 850 mL of 90% ethanol was stirred under reflux for 2 h. After evaporation of the solvent in vacuo, the residue was mixed with ether, neutralized with dilute HCl, and extracted with cold 5% K_2CO_3. The basic solution was washed with ether and acidified with dilute HCl. The resulting solid was collected, dried, and recrystallized from methylcyclohexane, yielding 12.48 g (37.4%) of white crystals, mp 94–96 °C.

Cyclopentaneglyoxaldehyde Bis[O-(carboxymethyl)oxime] (50). A mixture of 20 g (0.2 mol) of cyclopentylglyoxal diethylacetal (*9*), 29.4 g (0.268 mol) of carboxymethoxyamine hemihydrochloride, 54.6 g (0.4 mol) of $NaOAc{\cdot}3H_2O$, and 1.1 L of 90% ethanol was stirred under reflux for 6 h. Most of the solvent was evaporated in vacuo, the residue was diluted with ether and washed with dilute HOAc. The ether solution was extracted with cold 5% K_2CO_3 and the basic solution was acidified with AcOH. The product was continuously extracted with ether for 20 h, and the extract was dried over Na_2SO_4. Filtration and evaporation in vacuo gave an oily solid which was crystallized from benzene–hexane, yielding 1.17 g (3.2%) of white crystals, mp 171 °C dec.

3-Methyl-1-butene-2,3-diol Diacetate (51). A solution of 51.2 g (0.5 mol) of 3-hydroxy-3-methyl-2-butanone and 3 g of *p*-toluenesulfonic acid monohydrate in 200 mL of isopropenyl acetate was allowed to stand at room temperature for 2 h and slowly distilled through a 12 in. packed column for 20 h to remove acetone. The residue was diluted with ether, washed with cold aqueous $NaHCO_3$, saturated NaCl solution, and dried over Na_2SO_4. After filtration and removal of the solvent, the product was distilled twice through a short helices packed column, yielding two fractions. The lower boiling fraction (37.3 g (40%), bp 94 °C (50 mm), n^{20}_D 1.4181) was found to be 3-acetoxy-3-methyl-2-butanone. The higher boiling fraction (14.17 g (22%), bp 90 °C (11.5 mm), n^{20}_D 1.4344) was found to be **51**. Calcd for CH_3CO: 46.23. Found: 46.19.

Ethyl α-Cyano-α-propyl-2-furanpropanoate (52). To a stirred mixture of 8.7 g (0.38 mol) of melted sodium under 105 mL of toluene was slowly added at reflux 58.3 g (0.375 mol) of ethyl α-cyanovalerate. When essentially all of the sodium had reacted, the solution was cooled, under N_2, and 40 g (0.34 mol) of furfuryl chloride in 50 mL of toluene was slowly added. After being stirred for 3 h, the mixture was washed with water. The toluene solution was concentrated and the product was carefully distilled through a short helices packed column, yielding 59.5 g (68.6%) of colorless liquid: bp 127 °C (3 mm, n^{25}_D 1.4618).

α-Propyl-2-furanpropanoic Acid (53). A mixture of 59 g (0.25 mol) of **52**, 120 mL of 50% aqueous NaOH, 100 mL of water, and 75 mL of ethanol was heated under reflux for 22 h and concentrated by distillation through a 12 in. column during 20 h while 100 mL of water was added. After cooling the mixture was diluted with water, washed with ether, and acidified with HCl. The acid was extracted with ether, washed with water, evaporated, and heated to 180 °C. The product was distilled through a 6 in. (helices packed) column, yielding 27 g (59%) of colorless liquid: bp 123 °C (2.5 mm), n^{25}_D 1.4643.

α-Propyl-2-furanpropanoyl Urea (54). α-Propyl-2-furanpropanoyl chloride was prepared from 24.13 g (0.133 mol) of **53**, 15 mL of $SOCl_2$, and 4 drops of pyridine in 40 mL of ether at room temperature for 3.5 h. After removal of the solvent the acid chloride was distilled through a 6 in. (helices packed) column, giving 23.9 g of liquid, bp 73 °C (1 mm).

This acid chloride was added to 24 g (0.4 mol) of urea and 70 mL of benzene. After shaking in a closed flask for 16 h and stirring under reflux for 0.5 h the mixture was treated with dilute Na_2CO_3. The benzene layer was evaporated in vacuo giving an oil. This crystallized on the addition of ether, yielding 2.3 g (7.7%) of solid, mp 180–183 °C. Recrystallization from 95% ethanol gave 2.15 g of crystals, mp 182.5–184 °C.

α-(Δ^2-Cyclopentenyl)-2-furanpropanoyl Urea (55). α-(Δ^2-Cyclopentenyl)-2-furanpropanoyl chloride was prepared from 12.4 g (0.06 mol) of α-(Δ^2-cyclopentenyl)-2-furanpropanoic acid (*10*), 15 mL of $SOCl_2$, 25 mL of ether, and 3 drops of pyridine. After standing at room temperature for 2 h and at the boiling point for a few minutes, the mixture was distilled, yielding 7.7 g of light yellow liquid, bp 100 °C (1 mm).

This acid chloride was added to 10 g (0.17 mol) of urea and 35 mL of benzene. After being shaken in a closed flask for 17 h and stirred under reflux for 2.5 h, the mixture was treated with cold dilute Na_2CO_3. The resulting insoluble solid was collected, washed with water and ether, dried, and recrystallized from

ethanol, yielding 1.6 g (11%) of nearly white crystals, mp 181–183 °C.

2-Chloro-2′-hydroxy-6′-methylacetophenone Veratric Acid Ester (56). Veratryl chloride was prepared from 30.3 g (0.166 mol) of veratric acid, 15.5 mL (0.2 mol) of $SOCl_2$, and 50 mL of benzene by refluxing for 2.5 h and evaporating the solvent in vacuo. To this was added 30.7 g (0.166 mol) of 2-chloro-2′-hydroxy-6′-methylacetophenone (*11*) in 100 mL of CH_2Cl_2 and 13.3 g (0.166 mol) of pyridine. After stirring of the mixture at room temperature for 24 h, ice water was added giving a solid which was collected, washed with water and CH_2Cl_2, and dried, giving 37.4 g of white solid, mp 169–172 °C. An additional 11.6 g was obtained from the CH_2Cl_2 layer. The total yield was 84.6%. A sample for analysis was recrystallized from DMF, mp 172–174 °C.

3,3′-(p-Phenylene)bis(coumarin) (57). A solution of 9.7 g (0.05 mol) of *p*-phenylenediacetic acid and 18.3 g (0.15 mol) of salicylaldehyde in 28.2 mL (0.3 mol) of Ac_2O and 14 mL (0.1 mol) of Et_3N was stirred under reflux for 11 h, diluted with water, and basified with NH_4OH. The solid was collected, washed with NH_4OH and water, and dried, giving 20 g of yellow-brown solid, mp >350 °C. Recrystallization from Me_2SO yielded 10.25 g (56%) of nearly white solid, mp >350 °C.

2′,6′-Bis(allyloxy)acetophenone (58). A mixture of 15.2 g (0.1 mol) of 2′,6′-dihydroxyacetophenone, 55.3 g (0.4 mol) of K_2CO_3, and 25.9 mL (0.3 mol) of allyl bromide in 250 mL of acetone was stirred under reflux for 6.5 h. An additional 17.3 mL (0.2 mol) of allyl bromide was added and the refluxing was continued for 16 h. The mixture was filtered and the solid was extracted with acetone. Evaporation of the acetone solutions gave 24.2 g of light tan oil. This was dissolved in hexane and extracted twice with Claisen's alkali (700 g of 45% aqueous KOH and 1 L of MeOH). The hexane solution was washed with water, dried over Na_2SO_4, filtered, and evaporated in vacuo, yielding 21.9 g of nearly colorless oil. A small sample distilled from a short path apparatus below 65 °C (0.07 mm) gave a colorless liquid whose IR data supported the structure (strong CO at 1705 cm^{-1} but no OH) and was the same as undistilled material.

3′,5′-Diallyl-2′,6′-dihydroxyacetophenone (59). A solution of 2.32 g (0.01 mol) of **58** in 10 mL of *N,N*-dimethylaniline was refluxed for 1 h and poured into ice and dilute HCl. The mixture was extracted with ether and the extract was washed with dilute HCl, water, and 2% $NaHCO_3$. The ether solution was then well extracted with 10% aqueous NaOH, and the basic extracts were washed with ether and acidified with dilute HCl. The resulting oil was extracted with ether, washed with water and dried over Na_2SO_4. Filtration and evaporation gave 1.75 g of brown oil which soon solidified. This was distilled from a short path apparatus below 150 °C (0.03 mm), giving 1.56 g of yellow solid. Recrystallization from pentane yielded 1.04 g (45%) of yellow crystals, mp 57.5–58.5 °C.

3β-Hydroxy-5α-pregnan-20-one Hydrogen Succinate (60). To a solution of 19 g (0.06 mol) of 3β-hydroxy-5α-pregnan-20-one in 200 mL of pyridine was added 20 g of succinic anhydride. After warming to 55 °C the solution was allowed to stand at room temperature for 4 days. The solution was poured into ice and 210 mL of concentrated HCl giving solid which was collected, washed with water, and dried. Recrystallization from ethanol yielded 18 g (72%) of white leaflets, mp 198–200 °C.

2,3,4,4a,4b,5,6,6a,10,10a,10b,10b,11-Dodecahydro-2-hydroxy-β,4a,6a,7,9-pentamethyl-1H-naphth-[2′,1′:4,5]indeno[2,1-b]pyrrole-8-butanol (61). A solution of 20 g (0.0465 mol) of kryptogenin in 300 mL of MeOH was cooled to 5 °C, and 20 g of methylamine gas was passed in. The solution was sealed in a pressure tube and heated in a steam bath for 2.5 h. After cooling the resulting crystalline solid was collected, washed with MeOH, and dried, giving 18.2 g of white leaflets, mp 216–221 °C dec. A sample for analysis was recrystallized from MeOH, mp 219–221.5 °C dec.

24,24-Bis(p-dimethylaminophenyl)-5,23-choladien-3β-ol (62). *p*-Dimethylaminophenyl lithium was prepared under N_2, from 15.3 g (2.25 g-atoms) of Li, 200.8 g (1 mol) of *p*-bromo-*N,N*-dimethylaniline, and 1.1 L of ether. A solution of 38.8 g (0.1 mol) of methyl 3β-hydroxy-5-cholenate in 500 mL of benzene was slowly added, and the mixture was refluxed for 3 h. After cooling the mixture was poured into ice water containing 100 g of NH_4Cl and made strongly acid with HCl. The mixture containing much solid was washed with ether and basified with NaOH. The resulting mixture was washed with pentane, the remaining solid was collected and dried, giving 51 g of solid, mp 160–165 °C. This was recrystallized from ethyl methyl ketone with the aid of decolorizing charcoal, yielding 34.6 g (60%) of nearly white crystals, mp 166–168 °C. IR, UV, and elemental analyses showed that the intermediate carbinol had dehydrated and the product was **62**.

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