(1.3 g.) was recrystallized from a methanol–acetone mixture and finally from 2-propanol, m.p. 169–170°.

Anal. Calcd. for $C_{25}H_{33}N_3O_5$: C, 65.85; H, 7.3; N, 9.22. Found: C, 65.74; H, 7.32; N, 9.16.

5-(3-Bis[2-hydroxyethyl]aminopropyl)-6,7,8,9,10,11-5H-cyclooct[*b*]indole (IX, *n* = 6).—5-(3-Aminopropyl)-6,7,8,9,10,11-5H-cyclooct[*b*]indole (11.5 g., 0.045 mole) was dissolved in methanol (50 ml.), and ethylene oxide (4.4 g., 0.1 mole) was added slowly. The solution was allowed to stand for 2 days and the solvent then distilled. The residue was transferred to a small (25 ml.) pear-shaped flask and distilled *in vacuo*. The product (12 g., 77.5%) was an extremely viscous liquid, b.p. 245–250° (0.01 mm.), and it was necessary to apply heat to the condenser to maintain a flow.

Acknowledgments.—The authors wish to thank Drs. Melvin Gluckman and Larry Stein for the pharmacologic data supplied and Dr. Gordon Ellis and his staff for microanalyses.

Central Nervous System Depressants. VI. Polymethoxyphenyl Esters and Amides

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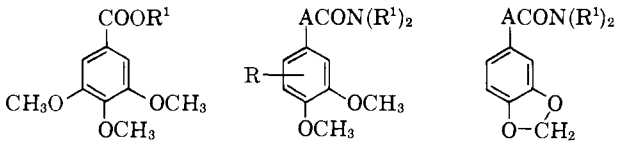
A large number of esters and amides were prepared from 3,4,5-trimethoxy-, 3,4-dimethoxy-, and 3,4-methylenedioxybenzoic, -phenylacetic, -cinnamic, and -hydrocinnamic acids (I, II, and III). Most of these were made by reaction of the acid chlorides with the appropriate alcohol or amine, but some involved the rearrangements shown in Chart I. The compounds generally produced central nervous system (CNS) depressant effects as shown by gross observation of intact animals and confirmed by avoidance behavior and motor activity studies.

The interesting central nervous system depressant activity found for certain di- and trimethoxyacetophenones, described in paper V of this series,[1] encouraged us to continue the study. In previous, somewhat related work,[2] acids, esters, and especially amides were found to be active depressants. Therefore a considerable number of compounds of the types I, II, and III were prepared.



I II III

A = single bond, $-CH_2-$, $-CH_2CH_2-$, or $-CH{=}CH-$; R = H or 5-OCH_3

In general the esters and amides were prepared from the corresponding acid chlorides by treatment with the appropriate alcohol or amine in the presence of a proton acceptor. In the preparation of the amides an excess of the amine usually served for this purpose.

The preparation of several compounds involved rearrangement of oxazoline hydrohalides to N-(β-haloethyl)amides. These in turn rearranged during hydrolysis to β-aminoethyl esters as is shown in Chart I.

These findings confirm and extend the work of Fry[3] who carried out some similar rearrangements from N-benzoylethanolamine. It is interesting to note that whereas the oxazoline hydrochloride **18** rearranged essentially completely to the β-chloroethylamide **16** on heating, either the corresponding oxazoline hydrobromide **19** or the β-bromoethylamide **17** went to an equilibrium mixture when heated under the same conditions. This doubtless reflects the difference between the C–Cl and C–Br bond energies.

Pharmacology.—Table I lists the compounds prepared in this work with some of their central nervous system activities in mice and rats. A number of old compounds are included for comparison. Methodology details may be found in paper V of this series.[1] It may be noted that most of these compounds are depressants. This was observed in intact mice and rats during toxicity studies and confirmed by avoidance behavior studies[4] and in some cases by motor activity tests.[2]

In general, the amides are more depressive than the esters and the 3,4,5-trimethoxyphenyl compounds are more active than the corresponding dimethoxy compounds. The methoxybenzamides and cinnamides are better than the phenylacetamides or hydrocinnamides. It seems that small substituents, for example hydrogen, methyl or allyl, on the amide nitrogen are desirable. Larger radicals, especially those containing functional groups, decrease the depressant activity.

Experimental[5]

1-Methyl-4-piperidyl 3,4,5-Trimethoxybenzoate[6] [2 (base)].—A solution of 23.0 g. (0.1 mole) of 3,4,5-trimethoxybenzoyl chloride and 23.0 g. (0.2 mole) of N-methyl-4-hydroxypiperidine in 300 ml. of benzene was heated under reflux for 2 hr. A white solid separated and after cooling the mixture was extracted with cold dilute hydrochloric acid. The free base was liberated with sodium hydroxide and extracted with ether. After washing with water and saturated sodium chloride, the ether solution was dried over sodium sulfate, filtered, and evaporated. The

(1) R. B. Moffett, A. R. Hanze, and P. H. Seay, *J. Med. Chem.*, **7**, 178 (1964).

(2) R. B. Moffett, P. H. Seay, and W. B. Reid, *ibid.*, **2**, 179 (1960).

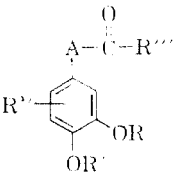
(3) E. M. Fry, *J. Org. Chem.*, **14**, 887 (1949).

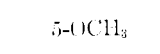
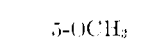
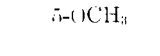
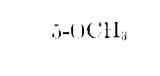
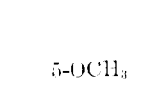
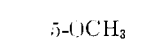
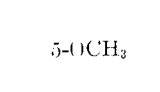
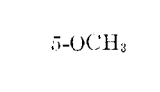
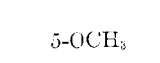
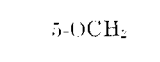
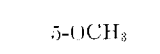
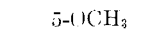
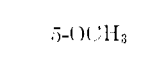
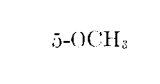
(4) To be reported by Dr. D. G. Anger, The Upjohn Co., Kalamazoo, Mich.

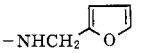
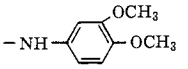
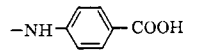
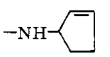
(5) Melting points were taken in capillary tubes with a partial immersion thermometer. Calibration of the apparatus against standard compounds showed no need for correction. Infrared spectra were obtained on all pure compounds and unless otherwise noted were in accordance with the proposed structures.

(6) Prepared by Dr. R. P. Holysz in these laboratories.

TABLE I: PHARMACOLOGICAL ACTIVITY

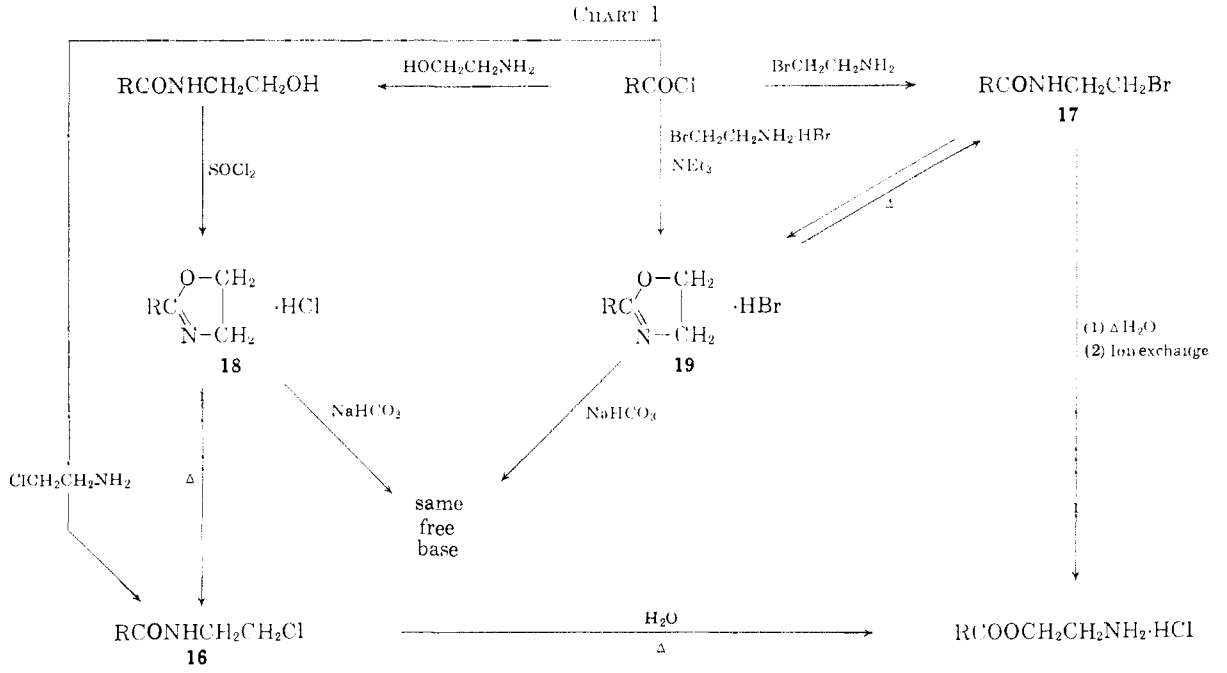


No.	R	R′	R″	A	R‴	Mouse LD_{50}[a] mg./kg.	Depression[b] mg./kg.
1	CH_3	CH_3	5-OCH_3	...	$-OCH_2CH_2NH_2 \cdot HCl$	650	–
2[c,d]	CH_3	CH_3	5-OCH_3	...		80	–
3[d]	CH_3	CH_3	5-OCH_3	...		10	–
4[d]	CH_3	CH_3	5-OCH_3	...		100	–
5[d]	CH_3	CH_3	5-OCH_3	...		50	–
6	CH_3	CH_3	5-OCH_3	...		200	–
7[e]	CH_3	CH_3	5-OCH_3	...	NH_2	>1000	300
8[f]	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH=CH_2$	650	–
9	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH=CHCH_3$	>1000	100
10	CH_3	CH_3	5-OCH_3	...	$-NHCH_2C(CH_3)=CH_2$	>1000	100
11	CH_3	CH_3	5-OCH_3	...	$-N(CH_2CH=CH_2)_2$	650	–
12	CH_3	CH_3	5-OCH_3	...		>1000	–
13	CH_3	CH_3	5-OCH_3	...		300	100
14	CH_3	CH_3	5-OCH_3	...		650	100
15[g]	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH_2OH$	>1000	–
16	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH_2Cl$	>1000	100
17	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH_2Br$	>1000	100
18	CH_3	CH_3	5-OCH_3			770	100[h]
19	CH_3	CH_3	5-OCH_3			770	200
20	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH_2N(CH_3)_2 \cdot HCl$	300	–
21	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH_2N(CH_3)_3Br^-$	80	–
22	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH(OCH_2CH_3)_2$	>1000	100
23	CH_3	CH_3	5-OCH_3	...	$-NHCH_2CH=NOH$	>1000	–
24	CH_3	CH_3	5-OCH_3	...		>1000	100
25[i]	CH_3	CH_3	5-OCH_3	...		>1000	300
26	CH_3	CH_3	5-OCH_3	...		200	–
27	CH_3	CH_3	5-OCH_3	...			

No.	R	R′	R″	A	R‴	Mouse LD_{50},[a] mg./kg.	Depression,[b] mg./kg.
28	CH_3	CH_3	5-OCH_3	...		>1000	–
29	CH_3	CH_3	5-OCH_3	...		650	–
30	CH_3	CH_3	5-OCH_3	...	$-N(C_6H_5)CH_2CH{=}CH_2$	650	–
31	CH_3	CH_3	5-OCH_3	...		>1000	–
32	CH_3	CH_3	5-OCH_3	...		1000	–
33	CH_3	CH_3	5-OCH_3		—A—$COR''' = -CSNH_2$	650	–
34	CH_3	—$CH_2CH{=}CH_2$	5-OCH_3	...	NH_2	>1000	100[j]
35[k]	CH_3	H	5-OCH_3	...	NH_2	>1000	–[l]
36	CH_3	CH_3	H	...	—$NHCH_2CH{=}CH_2$	650	100
37	—CH_2—		H	...	—$NHCH_2CH{=}CH_2$	230	100
38[m,n]	CH_3	—OR′=H	5-OCH_3	...	—$NHCH(CH_2CH_3)CH_2OH$		
39	CH_3	—OR′=CH_3	5-OCH_3	...	NH_2	>1000	300
40[n]	CH_3	CH_3	5-OCH_3	—CH_2—	NH_2	>1000	–
41	CH_3	CH_3	5-OCH_3	—CH_2—	—$NHCH_2CH{=}CH_2$	1000	200
42	CH_3	CH_3	H	—CH_2—	—$NHCH_2CH{=}CH_2$	650	100
43	CH_3	CH_3	H	—CH_2—		>1000	300
44[o,p]	CH_3	CH_3	5-OCH_3	—CH=CH—	NH_2	1000	100[q]
45[p]	CH_3	CH_3	5-OCH_3	—CH=CH—	—$NHCH_3$	650	100
46[p,r]	CH_3	CH_3	5-OCH_3	—CH=CH—	—$N(CH_3)_2$	750	100[s]
47[p]	CH_3	CH_3	5-OCH_3	—CH=CH—	—$NH(CH_2)_3CH_3$	>1000	300
48[p]	CH_3	CH_3	5-OCH_3	—CH=CH—	—$NHCH_2CH{=}CH_2$	>1000	100
49	CH_3	CH_3	5-OCH_3	—CH=CH		>1000	–
50[p]	CH_3	CH_3	5-OCH_3	—CH=CH—		650	100
51	CH_3	CH_3	5-OCH_3	—CH=CH—		560	–
52[p]	CH_3	CH_3	5-OCH_3	—CH=CH—	—NH—C_6H_5	650	100
53	CH_3	H	5-OCH_3	—CH=CH—	—NH_2	>1000	300
54[t]	CH_3	CH_3	H	—CH=CH—	NH_2	500	30
55	CH_3	CH_3	H	—CH=CH—	—$NHCH_2CH{=}CH_2$	760	300
56	O—R=H	CH_3	2-OCH_3	—CH=CH—	—NH_2	>1000	300
57[r]	CH_3	CH_3	5-OCH_3	—CH_2CH_2—	—$N(CH_3)_2$	>1000	200
58[m,n]	—CH_2—		H	—CH_2CH_2—	—$NHCH(CH_3)CH_2OH$	650	–[u]
59[m,n]	—CH_2—		H	—CH_2CH_2—	—$NHC(CH_3)_2CH_2OH$		
60[m]	—CH_2—		H	—CH_2CH_2—	—$NHCH(CH_2CH_3)CH_2OH$		
61[v]	CH_3	CH_3	H	—$CH(CH_3)CH_2$—	—OH	>1000	30[w]
62	CH_3	CH_3	H	—$CH(CH_3)CH_2$—	—OCH_2CH_3	770	100[x]
63[v]	CH_3	CH_3	H	—$CH(CH_3)CH_2$—	—NH_2	1000	100[y]
64	CH_3	CH_3	H	—$CH(CH_3)CH_2$—	—COR‴=—$CH_2NH_2\cdot HCl$	200	–
65	CH_3	CH_3	5-OCH_3	—$C(CH_3)$=CH—	—OCH_2CH_3	>1000	300

[a] Compounds were administered to mice intraperitoneally. The values (mg./kg.) are approximations with an accuracy of about +100% to −50%. [b] Mice (or rats) were observed during the toxicity tests (footnote *a*). The lowest dose at which significant depression was noted in mice is recorded in this column. Depression at doses greater than 40% of the LD_{50} is not considered significant and is indicated as negative (−). For the most part the rat toxicity studies were not carried to doses as low as 40% of the LD_{50} but in cases where depression was noted at such a dose it is recorded in footnotes. Any other significant effects on the CNS which were observed are also noted in footnotes in this column. [c] See footnote 7. [d] See footnote 6. [e] Available commercially but included for comparison. [f] R. B. Moffett, U. S. Patent 3,036,128 (1962). [g] See footnote 11. [h] Sleep in rats at 500 mg./kg. (70% of the rat LD_{50}). [i] Trioxazine, see L. Vargha, E. Kasztreiner, J. Borsy, L. Farkas, J. Kuszmann, and B. Dumbovich, *Biochem. Pharmacol.*, **11**, 639 (1962); J. Borsy, M. Feketa, and Zs. Csizmedia, *Acta. Physiol. Acad. Sci. Hung.*, **19**, 27 (1961). [j] Sleep in mice at 370 mg./kg. and in rats at 500 mg./kg. Extreme depression in rats at 250 mg./kg. (50% of the rat LD_{50}). Motor activity of mice 50% decrease at 60 mg./kg. [k] See Table II, footnote *gg*. [l] Depression in rats at 100 mg./kg (<10% of the rat LD_{50}). [m] See footnote 13. [n] This amide has been prepared by several workers by a Wolff rearrangement [for example by G. P. Schiemenz and H. Engelhard, *Chem. Ber.*, **92**, 1336 (1959)]. We prepared it *via* the acid chloride and ammonia from the commercially available (Aldrich Chem. Co.) 3,4,5-trimethoxyphenylacetic acid, m.p. 124–125°. [o] G. P. Schiemenz and H. Engelhard, *Chem. Ber.*, **93**, 1751 (1960). [p] C. M. Hofmann, Union of South Africa Patent Spec. 4314 (1960); Brit. Patent 906,319 (1962). No analysis is given. [q] Motor activity of mice 50% decrease at 30 mg./kg. [r] See footnote 14. [s] Motor activity of mice 99% decrease at 100 mg./kg. [t] K. W. Gopinath, T. R. Govindachari, K. Nagarajan, and K. K. Purushothaman, *J. Chem. Soc.*, 1144 (1957). [u] Depression in rats at 325 mg./kg. (30% of the rat LD_{50}). [v] See footnote 15. [w] Motor activity of mice 50% decrease at 50 mg./kg. [x] Motor activity of mice 50% decrease at 150 mg./kg. [y] Motor activity of mice 50% decrease at 300 mg./kg.

CHART I



R = 3,4,5-$(CH_3O)_3C_6H_2$-

resulting solid was recrystallized from 150 ml. of methylcyclohexane giving 23.8 g. of nearly white crystals, m.p. 83–85°.[7]

Hydrochloride[6] **(2).**—A solution of 23.5 g. (0.076 mole) of the free base in 300 ml. of ethyl acetate was acidified with ethanolic hydrogen chloride. The white crystals were collected and dried; weight 23.24 g., m.p. 228° dec. This was recrystallized from 225 ml. of 2-propanol containing 20 ml. of methanol giving 20.8 g. of white crystals, m.p. 233–234° dec. Palazzo, *et al.*,[7] report m.p. 230°.

Methobromide[6] **(3).**—To a cold benzene solution of crude free base (from 0.06 mole of 3,4,5-trimethoxybenzoyl chloride) was added 20 ml. of cold methyl bromide. After standing for 3 days, 100 ml. of ether was added and the crystalline quaternary salt was collected. After 3 crystallizations from methanol, 9.4 g. of white crystals was obtained, m.p. 237.5–238°.

1-Phenethyl-4-piperidyl 3,4,5-Trimethoxybenzoate Hydrochloride[6] **(4).**—A solution of 13.84 g. (0.06 mole) of 3,4,5-trimethoxybenzoyl chloride in 40 ml. of toluene was added dropwise during 3 hr. to a solution of 10.26 g. of 1-phenethyl-4-piperidinol in 40 ml. of anhydrous pyridine. The mixture was stirred for 18 hr., and diluted with 300 ml. of toluene and 10 ml. of water. The mixture was washed with dilute sodium hydroxide solution and water. The toluene solution was filtered and evaporated to dryness under reduced pressure leaving 18.5 g. of red oil. This base was dissolved in 50 ml. of absolute ethanol, decolorized with activated charcoal, and 10 ml. of concentrated hydrochloric acid and 50 ml. of ether were added. Refrigeration of the solution yielded 16.30 g. of crystals, m.p. 222–223°.

Methobromide[6] **(5).**—An ether solution of free base from 5 g. of the hydrochloride (**4**) was cooled to 0° and 20 ml. of cold methyl bromide was added. The solution was allowed to stand for several days and the resulting white solid was collected. This was recrystallized from a mixture of methanol and ether yielding 5 g. of the quaternary salt, m.p. 226–227° dec.

1-(2-Thienyl)-3-diethylamino-2-propanol.[8]—2-Thienyllithium[9] was prepared in a 22-l. flask from 200 g. of lithium, 1360 g. of butyl bromide, 840 g. of thiophene, and 8 l. of absolute ether. To this solution was added slowly, at reflux, 1040 g. of 3-diethylamino-1,2-epoxypropane.[10] After stirring under reflux for an additional hour, sufficient water was added to dissolve the inorganic salts. The ether layer was separated, dried, and the solvent was removed. The oily product was distilled under reduced pressure giving 1333 g. of product, b.p. 121° (6.0 mm.). A sample was further purified by careful redistillation, b.p. 140° (15 mm.).

Anal. Calcd. for $C_{11}H_{19}NOS$: C, 61.92; H, 8.98; N, 6.57; S, 15.03. Found: C, 62.39; H, 8.73; N, 6.22; S, 14.80.

3,4,5-Trimethoxybenzoate Ester of 1-(2-Thienyl)-3-diethylamino-2-propanol Hydrochloride (6).—A solution of 23 g. (0.1 mole) of 3,4,5-trimethoxybenzoyl chloride, and 21.3 g. (0.1 mole) of 1-(α-thienyl)-3-diethylamino-2-propanol in 100 ml. of benzene was heated under reflux for 0.5 hr. and allowed to stand for 6 days. The mixture was poured into ice–water and acidified with hydrochloric acid. The resulting crystalline solid was collected, washed with water and benzene, dried, and recrystallized from methanol, m.p. 156–158°. This was shown, by comparison of its infrared spectrum with that of an authentic sample, to be 3,4,5-trimethoxybenzoic anhydride. Dilution of the methanolic filtrate with ether gave 14.8 g. of the desired ester hydrochloride. The aqueous solution was separated, washed with benzene, and made basic with sodium hydroxide. The oily free base was extracted with ether, washed with water, and dried over sodium sulfate. After filtration the ether solution of the free base was acidified with ethanolic hydrogen chloride. The resulting hydrochloride slowly crystallized and was recrystallized from 75 ml. of 2-propanol giving an additional 9.8 g. of ester hydrochloride, m.p. 160–162.5°.

General Method for the Preparation of Amides.—To a solution of 0.2 mole of the acid chloride in a mixture of absolute ether and benzene was added slowly, with stirring, a solution of 0.4 mole of the requisite amine in the same solvents. The mixture became warm and usually reached reflux, and a solid separated. After stirring for an additional 2 hr. ice–water was added, and the mixture was acidified with hydrochloric acid. If solid amide remained insoluble in both layers it was collected, washed with cold dilute sodium carbonate solution, water, and ether, and recrystallized from the solvent indicated in Table II. If the amide was appreciably soluble, it was extracted from the aqueous solution with ether, washed with cold dilute sodium carbonate solution, water, and saturated sodium chloride. After drying over sodium sulfate, filtering, and removing the solvent, the residue was crystallized from the indicated solvent.

2-(3,4,5-Trimethoxyphenyl)-oxazoline Hydrochloride (18).—To 100 ml. of thionyl chloride was added portionwise at 5–7° during 15 min. 25.5 g. (0.1 mole) of N-(β-hydroxyethyl)-3,4,5-trimethoxybenzamide.[11] After stirring the solution for 2 hr. at

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(9) H. Gilman and D. A. Shirley, *J. Am. Chem. Soc.*, **71**, 1870 (1949).

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(11) M. E. Kuehne and B. F. Lambert, *ibid.*, **81**, 4278 (1959).

TABLE II

CHEMICAL PROPERTIES

No. from Table I	Yield,[a] %	M.p., °C.[b]	Crystallizing solvent	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
1	56[c]	166.5–168.5	*i*-PrOH	$C_{12}H_{18}ClNO_5$[d]	49.40	49.29	6.22	6.20	4.80	4.86
2[e,f] base	77[c]	83–85	MeC_6H_{11}[g]	$C_{16}H_{23}NO_5$	62.12	61.70	7.49	7.20	4.53	4.63
2[e,f]	80[c]	233–234	*i*-PrOH	$C_{16}H_{24}ClNO_5$[h]	55.57	55.43	6.99	7.11	4.05	3.95
3[f]	39[c]	237.5–238	MeOH	$C_{17}H_{26}BrNO_5$[i]	50.50	50.48	6.48	6.13	3.46	3.20
4[f]	75[c]	222–223	EtOH + Et_2O	$C_{23}H_{30}ClNO_5$[j]	63.36	63.20	6.94	6.95	3.21	3.16
5[f]	89[c]	226–227 (dec.)	MeOH + Et_2O	$C_{24}H_{32}BrNO_5$[k]	58.30	57.63	6.52	6.71	2.83	3.25
6	56[c]	160.5–162.5	*i*-PrOH	$C_{21}H_{30}ClNO_5S$[l]	56.81	56.77	6.81	6.45	3.16	3.16
8[cc]	96	123.5–126	EtOH	$C_{13}H_{17}NO_4$	62.14	62.31	6.82	6.67	5.57	5.51
9	81	134–136	*i*-PrOH	$C_{14}H_{19}NO_4$	63.38	63.43	7.22	6.83	5.28	5.16
10	83	101–102	*i*-PrOH	$C_{14}H_{19}NO_4$	63.38	63.74	7.22	7.16	5.28	5.40
11	94[t]	78–80	MeC_6H_{11}[g]	$C_{17}H_{21}NO_4$	65.95	66.00	7.27	7.33	4.81	4.92
12	68	147–149	*i*-PrOH + C_6H_{14}[v]	$C_{15}H_{19}NO_4$	64.96	65.19	6.91	7.22	5.05	4.99
13	68[dd]	67–69	C_7H_{16}[ee]	$C_{18}H_{23}NO_4$	68.12	68.10	7.31	6.98	4.41	4.47
14	58[p]	66–69	MeC_6H_{11}[g]	$C_{19}H_{27}NO_4$	68.44	68.52	8.16	8.02	4.20	4.27
16	84[c]	132–134.5	BuOH	$C_{12}H_{16}ClNO_4$[w]	52.65	52.50	5.89	5.84	5.12	5.29
17	52[c]	160–162.5	C_6H_6	$C_{12}H_{16}BrNO_4$[x]	45.30	45.75	5.07	4.99	4.40	4.28
18	82[c]	135.5–137.5	MeOH	$C_{12}H_{16}ClNO_4$[m]	52.65	52.83	5.89	5.83	5.12	5.00
19	65[c]	162.5–165	EtOH	$C_{12}H_{16}BrNO_4$[n]	45.30	45.57	5.07	5.00	4.40	4.27
20	32[c]	137–139	*i*-PrOH	$C_{14}H_{23}ClN_2O_4$[y]	52.74	53.17	7.27	7.10	8.79	8.70
21	92[c]	139–141	*i*-PrOH + Et_2O	$C_{15}H_{25}BrN_2O_4$[z]	47.75	47.47	6.68	6.63	7.43	7.32
22	86	115–117.5	EtOAc + C_6H_{12}[aa]	$C_{16}H_{26}NO_6$	58.70	58.69	7.70	7.70	4.28	4.25
23	43[c]	173–177	EtOH	$C_{12}H_{16}N_2O_5$	53.72	53.70	6.01	5.74	10.44	10.29
24	68	126–128.5	MeOH	$C_{16}H_{22}NO_5$	62.12	62.29	7.49	7.30	4.53	4.67
26	89	100–103	C_6H_{12}[aa]	$C_{16}H_{23}NO_5$	62.12	62.28	7.49	7.42	4.53	4.57
27	94[bb]	...	...	$C_{16}H_{23}NO_5$	62.12	62.28	7.49	7.79	4.53	4.58
28	40[c]	189–191	*i*-PrOH	$C_{14}H_{18}N_2O_5$	57.13	56.91	6.17	6.00	9.52	9.50
29	90	138–140	*i*-PrOH	$C_{15}H_{17}NO_6$	61.85	61.73	5.88	5.72	4.81	5.00
30	66	62.5–64.5	EtOAc + C_6H_{14}[q]	$C_{19}H_{21}NO_4$	69.70	69.70	6.47	6.54	4.28	4.31
31	68	170–171	DMF[r]	$C_{18}H_{21}NO_6$	62.24	62.49	6.10	6.22	4.03	3.75
32	74[c]	243–245.5	EtOH	$C_{17}H_{17}NO_6$	61.62	62.01	5.17	4.95	4.23	4.30
33	[c]	182.5–184	EtOH	$C_{10}H_{13}NO_3S$[hh]	52.84	53.11	5.76	5.56	6.16	6.02
34	85[c,u]	159–161	MeOH	$C_{12}H_{15}NO_4$	60.75	60.78	6.37	6.46	5.90	6.01
35		181–183.5[gg]	*i*-PrOH	$C_9H_{11}NO_4$	54.82	54.91	5.62	5.82	7.10	7.10
36	70[u]	120.5–122	MeOH	$C_{12}H_{15}NO_3$	65.14	65.13	6.83	6.56	6.33	6.62
37	74[u]	99–100	*i*-PrOH	$C_{11}H_{11}NO_3$	64.38	64.59	5.40	5.15	6.83	6.81
38[ff]	[c]	94–95.5	EtOAc	$C_{13}H_{15}NO_4$	61.64	60.67	7.56	7.43	5.53	5.39
39	82[u]	232–233	MeOH	$C_{10}H_{13}NO_3$	61.52	61.69	6.71	6.72	7.18	7.08
41	58[u]	73–75	EtOAc	$C_{14}H_{19}NO_4$	63.38	63.23	7.22	6.95	5.28	5.50
42	45	81.5–83	EtOAc	$C_{13}H_{17}NO_3$	66.36	66.24	7.28	7.21	5.95	6.03
43	82	104.5–106	*i*-PrOH	$C_{14}H_{19}NO_4$	63.38	63.13	7.22	7.09	5.28	5.09
45[s]	78[t,u]	120–123	EtOAc	$C_{13}H_{17}NO_4$	62.14	62.40	6.82	6.66	5.57	5.72
46[s,v]	65[u]	125.5–127	MeCOMe + C_6H_{14}[q]	$C_{14}H_{19}NO_4$	63.39	63.44	7.22	7.00	5.28	5.50
47[s]	84[u]	153–154.5	EtOH	$C_{16}H_{23}NO_4$	65.51	65.61	7.90	7.65	4.78	4.93
48[s]	100[u]	148–150	MeOH	$C_{16}H_{19}NO_4$	64.96	65.07	6.91	7.01	5.05	4.81
49	49[u]	162–163.5	*i*-PrOH	$C_{17}H_{21}NO_4$	67.31	67.37	6.98	6.93	4.62	4.64
50[s]	64[u]	132–133.5	*i*-PrOH	$C_{16}H_{21}NO_5$	62.52	62.84	6.88	6.74	4.56	4.64
51	56[u]	169–171	H_2O	$C_{16}H_{20}N_2O_5$	59.99	59.61	6.29	6.28	8.75	8.86
52[s]	53[u]	128–130.5	EtOH	$C_{18}H_{19}NO_4$	68.99	69.16	6.11	5.99	4.47	4.71
53	71[c,u]	183–185	*i*-PrOH	$C_{11}H_{13}NO_4$	59.18	59.43	5.87	5.99	6.28	5.99
55	92[u]	131–133	MeOH	$C_{14}H_{17}NO_3$	67.99	67.87	6.93	6.63	5.66	5.68
56	44[u]	172–174	MeOH	$C_{11}H_{13}NO_3$	63.75	64.02	6.32	6.33	6.76	6.64
57[v]	92[c]	86–87	MeCOMe + C_6H_{14}[q]	$C_{14}H_{21}NO_4$	62.90	63.10	7.92	7.75	5.24	5.36
58[ff]	50[c,u]	111–113	EtOAc	$C_{13}H_{17}NO_4$	62.13	62.19	6.82	6.83	5.58	5.46
59[ff]	28[c,u]	81–83	EtOAc	$C_{14}H_{19}NO_4$	63.38	63.37	7.22	7.60	5.28	5.38
60[ff]	38[c,u]	81–83	EtOAc	$C_{14}H_{19}NO_4$					5.28	5.03
62	63[c]	...	...	$C_{14}H_{20}O_4$	66.64	66.71	7.99	7.78	...	...
64	33[c]	197.5–199.5	*i*-PrOH	$C_{12}H_{20}ClNO_2$[o]	58.64	59.07	8.20	8.32	5.70	5.99
65	60[c]	55.5–57.5	*i*-PrOH	$C_{15}H_{20}O_5$	64.27	64.27	7.19	6.86	...	...

[a] Unless otherwise indicated the amides in this Table were prepared by the general method described in the Experimental section. Yields are based on the starting acid chloride and are calculated for material melting not less than 2° below the highest melting point obtained. [b] See footnote 5. [c] See experimental section for specific preparation of this compound. [d] *Anal.* Calcd.: Cl, 12.15; O, 27.42. Found: Cl, 12.14; O, 26.22. [e] See footnote 7. [f] See footnote 6. [g] MeC_6H_{11} = methylcyclohexane. [h] *Anal.* Calcd.: Cl 10.25. Found: Cl, 10.34. [i] *Anal.* Calcd.: Br, 19.77. Found: Br, 19.31. [j] Anal. Calcd.: Cl, 8.13. Found: Cl, 8.07. [k] *Anal.* Calcd.: Br, 16.16. Found: Br, 16.40. [l] *Anal.* Calcd.: Cl, 7.99; S, 7.22. Found: Cl, 8.10 S, 7.26. [m] *Anal.* Calcd.: Cl, 12.95; O, 23.88. Found: Cl, 13.14; O, 22.88. [n] *Anal.* Calcd.: Br, 25.12; O, 20.11. Found: Br, 25.41; O, 19.83. [o] *Anal.* Calcd.: Cl, 14.43. Found: Cl, 14.22 [p] Extracted from the aqueous solution with chloroform. The product was repeatedly fractionally crystallized from methylcyclohexane. [q] C_6H_{14} = petroleum hexane (Skellysolve B). [r] DMF = dimethylformamide. [s] See Table I, footnote *p*. [t] Extracted from the aqueous solution with chloroform and benzene. [u] The acid chloride was prepared from the corresponding acid and thionyl chloride and was used without purification. The yield is calculated from the starting acid. [v] See footnote 14. [w] *Anal.* Calcd.: Cl, 12.95; O, 23.38. Found: Cl, 12.65; O, 23.64. [x] *Anal.* Calcd.: Br, 25.12; O, 20.11. Found: Br, 25.03; O, 19.04. [y] *Anal.* Calcd.: Cl, 11.12; O, 20.08. Found: Cl, 11.22; O, 20.18. [z] *Anal.* Calcd.: Br, 21.18. Found: Br, 21.02. [aa] C_6H_{12} = cyclohexane. [bb] This product failed to crystallize and was distilled in a short path distillation apparatus at 170° (bath temp.) (0.02 mm.) giving a 94% yield of colorless gum. [cc] See Table I, footnote *f*. [dd] Extracted from the aqueous solution with ether and then with methylene chloride. After removing the solvent the residue was dissolved in benzene and passed through a column of 250 g. of acid-washed alumina which was eluted with more benzene. The solvent was removed and the product crystallized from heptane. [ee] C_7H_{16} = petroleum heptane (Skellysolve C). [ff] See footnote 13. [gg] Commerical syringamide was obtained from Aldrich Chemical Co. Inc., Milwaukee, Wis. A sample was sublimed at 170° (bath, 0.01 mm.) giving white solid which was crystallized from 2-propanol. [hh] *Anal.* Calcd.: S, 14.11. Found: S, 14.02.

0–5°, the excess thionyl chloride was removed under reduced pressure. The resulting white solid was slurried well with 150 ml. of methanol at room temperature. After filtration and washing with methanol 22.3 g. of white crystalline solid was obtained, m.p. 135.5–137.5° (after sintering at about 125°).

N-(β-Chloroethyl)-3,4,5-trimethoxybenzamide (16).—Crude oxazoline hydrochloride was prepared as described. This was dissolved in about 150 ml. of 1-butanol and boiled for a few seconds. On cooling, crystals separated which were collected, washed with butanol and ether, and dried giving 23 g. (84%) of white solid, m.p. 132–134.5°. This reaction could also be carried out by heating at 150° in the absence of solvent or with xylene at the boiling point. Boiling with methanol or toluene gave incomplete reaction.

N-(β-Bromoethyl)-3,4,5-trimethoxybenzamide (17).—A benzene solution of β-bromoethylamine was prepared by extracting with benzene a cold mixture of an excess of 2-bromoethylamine hydrobromide and 0.28 mole of strong sodium hydroxide. After drying over potassium carbonate and filtering, 23.0 g. (0.1 mole) of 3,4,5-trimethoxybenzoyl chloride in 100 ml. of benzene was added slowly with cooling. The mixture was stirred for 1 hr. at temperatures up to 22° and filtered, giving 16.5 g. of white solid, m.p. 160–162.5°. The infrared spectrum showed that no salt was present, and was very similar to that of the corresponding chloride.

2-(3,4,5-Trimethoxyphenyl)oxazoline Hydrobromide (19).—To a mixture of 40.6 g. (0.2 mole) of β-bromoethylamine hydrobromide and a solution of 23.0 g. (0.1 mole) of 3,4,5-trimethoxybenzoyl chloride in 100 ml. of benzene was added slowly at 10–20° with stirring 38.0 g. (0.25 mole) of triethylamine in 50 ml. of benzene. After stirring for 4 hr. the mixture was poured into ice–water and made weakly acidic (pH about 6) with acetic acid. The resulting solid was collected, washed with ice–water and ether, and dried giving 20.99 g. of nearly-white solid, m.p. 160–163°. This was boiled with benzene and filtered hot. The insoluble crystals were the oxazoline hydrobromide, weight 9.6 g.; m.p. 162–164°. This was recrystallized from 300 ml. of absolute ethanol giving 3.8 g. of white crystals, m.p. 162.5–165°. By concentration and cooling there was obtained from the benzene and ethanol filtrates an additional 7.7 g. of the same product.

A small sample of this oxazoline hydrobromide in water was treated with sodium bicarbonate solution. A crystalline solid (free base) soon separated which was collected and dried, m.p. 69–71°. It contained no halogen and the infrared spectrum was essentially identical with that of the base obtained similarly from 2-(3,4,5-trimethoxyphenyl)oxazoline hydrochloride (18).

Heating either the β-bromoethylamide or the oxazoline hydrobromide either in butanol or without solvent gave material which, as judged from the infrared spectrum, is a mixture of the oxazoline hydrobromide and the β-bromoethylamide. This is in contrast to the oxazoline hydrochloride which went almost completely to the β-chloroethylamide on heating.

β-Aminoethyl 3,4,5-Trimethoxybenzoate Hydrochloride (1).—Crude N-(β-chloroethyl)-3,4,5-trimethoxybenzamide was prepared from 23 g. (0.1 mole) of 3,4,5-trimethoxybenzoyl chloride as previously described for the corresponding bromo compound using β-chloroethylamine hydrochloride in place of β-bromoethylamine hydrobromide. The amide was boiled with 400 ml. of water, treated with decolorizing charcoal, and the solution concentrated under reduced pressure. Benzene was added and partly distilled to remove any remaining water. Warming and the addition of a little methanol caused crystallization of 15.2 g. of nearly-white solid, m.p. 165–168°. Recrystallization from 2-propanol gave 13.8 g. of crystals, m.p. 166–168°.

A small sample of the N-(β-bromoethyl)-3,4,5-trimethoxybenzamide (17) was boiled with water and the solution was passed through a column of quaternary ammonium chloride ion exchange resin (IRA-400). The solution was then evaporated to dryness under reduced pressure and the residue was recrystallized from 2-propanol giving white crystals, m.p. 165–167.5°, shown by infrared spectrum and mixture melting point to be identical with the above.

N-(β-Dimethylaminoethyl)-3,4,5-trimethoxybenzamide Hydrochloride (20).—The base[12] was prepared in 87% yield by the general method described. A solution of 28.22 g. (0.1 mole) of this base in 500 ml. of ethyl acetate and 40 ml. of methanol was acidified with ethanolic hydrogen chloride giving an oil which crystallized on standing. The mixture was diluted to 2 l. with absolute ether and cooled overnight. The solid was collected, washed with ether, and dried giving 31.6 g. of crystals, m.p. 94–96°. This was recrystallized first from methyl ethyl ketone and then from 2-propanol yielding 10.3 g. of white crystals, m.p. 137–139°.

N-(β-Trimethylammoniumethyl)-3,4,5-trimethoxybenzamide Bromide (21).—To a cold solution of 28.22 g. (0.1 mole) of the free base[12] in 200 ml. of methyl ethyl ketone and 30 ml. of methanol was added 28.6 g. (0.3 mole) of cold methyl bromide. The flask was stoppered, clamped, and allowed to stand at room temperature for 4 days. The solution was concentrated and diluted with ethyl acetate. On shaking, a white granular solid was obtained which was collected and dried giving 34.8 g. (92.5%) of solid, m.p. 137–141°. This was recrystallized from 2-propanol and diluted with ether yielding 32.1 g. of white solid, m.p. 139–141°.

α-(3,4,5-Trimethoxybenzoylamino)acetaldoxime (23).—A solution of 30.7 g. (0.0935 mole) of the acetal (Table II, 7) in 250 ml. of 60% ethanol at 30° was acidified with 2 ml. of concentrated hydrochloric acid and allowed to stand at room temperature for 20 hr. An aqueous solution of 10 g. of hydroxylamine hydrochloride was added and the solution was made basic to phenolphthalein (pH about 9) with about 45 ml. of 4 *N* sodium hydroxide. After standing at room temperature for 5 days a small amount of crystalline material had separated. This was collected and recrystallized from absolute ethanol giving 1.33 g. of nearly white crystals, m.p. 173–177°. By concentration of the filtrates and repeated recrystallization of the resulting solid from water and then from absolute ethanol, 9.45 g. of slightly less pure crystals, m.p. 163–171°, was obtained.

4-(3,4,5-Trimethoxybenzoyl)-2-piperazinone (28).—A solution of 46 g. (0.2 mole) of 3,4,5-trimethoxybenzoyl chloride in 100 ml. of warm benzene was added slowly with stirring at 80–100° to a solution of 45 g. (0.45 mole) of 2-ketopiperazine in 350 ml. of diethyleneglycol dimethyl ether. After heating on a steam bath for 0.5 hr., the mixture was concentrated nearly to dryness under reduced pressure on a steam bath. The residue was neutralized with acetic acid and recrystallized twice from 2-propanol, filtering the hot solution each time from insoluble salt of the starting material. The yield was 23 g. of nearly white crystals, m.p. 159–161° which was free of chloride as shown by a Beilstein test.

***p*-N-(3,4,5-Trimethoxybenzamido)benzoic Acid (32).**—To a solution of 27.4 g. (0.2 mole) of *p*-aminobenzoic acid in 200 ml. of *N* sodium hydroxide was added 23 g. (0.1 mole) of finely ground 3,4,5-trimethoxybenzoyl chloride with stirring and cooling. Then 100 ml. of *N* sodium hydroxide was added dropwise at such a rate that the mixture was kept approximately neutral to phenolphthalein. About 15 min. was required. The slightly basic mixture was stirred at 5° for an additional 2.5 hr. during which practically all the solid dissolved. After filtration, the solution was acidified giving a gummy solid. This was collected, washed with dilute hydrochloric acid, dissolved in dilute sodium hydroxide, and reprecipitated with dilute hydrochloric acid. The solid was collected, washed with water, and dried, yielding 31.8 g. of nearly-white solid, m.p. 238–243°. This was recrystallized from 700 ml. of absolute ethanol giving 24.3 g. of light tan crystals, m.p. 243–245.5°.

3,4,5-Trimethoxythiobenzamide (33).—A solution of 9.65 g. (0.05 mole) of 3,4,5-trimethoxybenzonitrile and 7.51 g. (0.1 mole) of thioacetamide in 150 ml. of dimethylformamide was saturated with hydrogen chloride gas with stirring at 25–45°. The mixture was then heated on a steam bath for 0.5 hr. giving a red solution. This was concentrated to about 25% its volume and neutralized with aqueous sodium bicarbonate. The red solid was collected and dried giving 8.31 g. of material, m.p. 168.5–177°. This was recrystallized from 75 ml. of ethanol with the aid of decolorizing charcoal (Darco) giving 6.04 g. of yellow crystals, m.p. 180.5–182.5°. A small sample was recrystallized again from ethanol, m.p. 182.5–184°.

4-Allyloxy-3,5-dimethoxybenzamide (34).—A mixture of 18.7 g. (0.083 mole) of 4-allyloxy-3,5-dimethoxybenzoic acid,[1] 10 ml. (0.14 mole) of thionyl chloride, and 100 ml. of benzene was heated under reflux for 3 hr. The solvent was distilled under reduced pressure and benzene was added and distilled, leaving crude light yellow acid chloride. This was dissolved in 100 ml. of benzene and shaken with 250 ml. of aqueous ammonium hydroxide for 3.5 hr. The resulting gummy white solid was collected, washed

(12) This base was prepared by G. P. Schiemenz and H. Engelhard, *Chem. Ber.*, **92**, 857 (1959), by a different method.

with pentane and water giving 16.7 g. of white solid, m.p. 159–161°. This was recrystallized from 150 ml. of methanol yielding 11.6 g. of solid, m.p. 159–161°.

N-[(1-Hydroxymethyl)propyl]-3,5-dimethoxybenzamide[13] (**38**).—A mixture of 3.83 g. (0.0182 mole) of ethyl 3,5-dimethoxybenzoate and 1.61 g. (0.0182 mole) of 2-aminobutanol was heated under reflux for 5 hr., cooled, and extracted with hexane. Warming the lower layer removed solvent and caused it to crystallize yielding 2.5 g. of tan solid. Four recrystallizations from ethyl acetate gave colorless needles, m.p. 94–95.5°.

4-Hydroxy-3,5-dimethoxycinnamamide (**53**).—A mixture of 20.0 g. (0.089 mole) of 3,5-dimethoxy-4-hydroxycinnamic acid, 1 g. of sodium acetate, and 150 ml. of acetic anhydride was warmed slightly to effect solution and allowed to stand overnight. The excess acetic anhydride was distilled under reduced pressure on a steam bath. The oily residue was diluted with 50 ml. of benzene and 50 ml. of thionyl chloride was added. The mixture was stirred under reflux for 2 hr. and the solvent was removed under reduced pressure. The resulting solid was suspended in absolute ether and ammonia gas was passed in with stirring for 3 hr. After standing overnight, the thick mixture was shaken with water and filtered. The solid was well washed with water and ether, and dried, giving 20.85 g. crude 4-acetoxy-3,5-dimethoxybenzamide, m.p. 154–165°. This was hydrolyzed with dilute aqueous sodium hydroxide at about 85° for 15 min. The solution was filtered, acidified, and concentrated, giving crystalline solid. After recrystallization from 2-propanol there was obtained 14 g. of light tan crystals, m.p. 183–185°.

N,N-Dimethyl-3,4,5-trimethoxyhydrocinnamamide[14] (**57**).—A solution of 10.3 g. of N,N-dimethyl-3,4,5-trimethoxycinnamamide in 100 ml. of methanol was hydrogenated with 0.5 g. of 5% palladium-on-charcoal at 3.5 kg./cm.^{2} pressure and room temperature. In 40 min. about the theoretical amount of hydrogen was taken up. After filtration and evaporation, the oily residue was crystallized from ether–hexane giving 9.53 g. of colorless prisms, m.p. 85.9–87.2°. Recrystallization from acetone–hexane gave large colorless prisms, m.p. 86.5–87.2°.

3,4-Dimethoxyphenylacetyl Chloride.—A solution of 160.8 g. (0.86 mole) of 3,4-dimethoxyphenylacetic acid, and 146 ml. (2.0 moles) of thionyl chloride, in 1 l. of benzene, was heated under reflux with stirring for 6 hr. The solvent was removed and the product was distilled giving 82.7 g. (45%) of liquid, b.p. 124° (0.05 mm.).

N-(2-Hydroxy-2-propyl)-3,4-methylenedioxyhydrocinnamamide[13] (**58**).—A solution of 20.8 g. (0.1 mole) of methyl 3,4-methylenedioxyhydrocinnamate and 7.5 g. (0.1 mole) of 2-aminopropanol was heated under reflux for 3 hr., cooled, and extracted with hexane. The lower layer was warmed to remove solvent and on cooling it crystallized. This material was recrystallized twice from ethyl acetate giving 10 g. of colorless crystals, m.p. 111–113°.

N-[(2-Hydroxy-1-(2-methyl)propyl]-3,4-methylenedioxyhydrocinnamamide[13] (**59**).—This was prepared from 20.8 g. (0.1 mole) of methyl 3,4-methylenedioxyhydrocinnamate and 8.9 g. (0.1 mole) of 2-amino-2-methylpropanol. Recrystallization from ethyl acetate yielded 7.5 g. of colorless crystals, m.p. 81–93°.

N-[(1-Hydroxymethyl)-2-propyl]-3,4-methylenedioxyhydrocinnamamide[13] (**60**).—This was prepared from 20.8 g. (0.1 mole) of methyl 3,4-methylenedioxyhydrocinnamate and 8.9 g. (0.1 mole) of 2-aminobutanol. Recrystallization from ethyl acetate gave 10 g. of product, m.p. 76–79°. After two more recrystallizations from ethyl acetate colorless material was obtained, m.p. 81–83°.

Ethyl β-(3,4-Dimethoxyphenyl)butyrate (**62**).—A mixture of 11.8 g. (0.052 mole) of β-(3,4-dimethoxyphenyl)butyric acid,[15] 73 ml. (1 mole) of thionyl chloride, and 100 ml. of benzene was heated under reflux for 5 hr. and the solvent was distilled under reduced pressure. This crude acid chloride was dissolved in 50 ml. of benzene and 100 ml. of absolute ethanol and 5.7 ml. of pyridine were added. After boiling for 15 min. the solution was evaporated under reduced pressure. The oil was mixed with ether and washed with dilute hydrochloric acid, water, dilute sodium hydroxide, water, and saturated salt solution. After drying over sodium sulfate and distilling the solvent, the product was distilled twice through a short column giving 8.27 g. of colorless liquid, b.p. 107° (0.008 mm.); n^{25}D 1.5078.

3-(3,4-Dimethoxyphenyl)butylamine Hydrochloride (**64**).—From a Soxhlet extractor, 9.9 g. (0.045 mole) of β-(3,4-dimethoxyphenyl)butyramide[15] was reduced with 3.8 g. (0.1 mole) of lithium aluminum hydride in 300 ml. of absolute ether. After extracting for 21 hr. there were carefully added in succession 10 ml. of ethyl acetate, 4 ml. of water, 3 ml. of 20% sodium hydroxide, and 14 ml. of water. After thorough mixing the solution was filtered and the solid washed with ether. The ether solution was extracted with dilute hydrochloric acid which was washed with ether and made basic with sodium hydroxide. The free base was extracted with ether, washed with saturated salt solution, and dried. After removal of the solvent an oil remained which was taken up in absolute ether, and acidified with ethanolic hydrogen chloride. The white solid hydrochloride was collected and recrystallized from 2-propanol yielding 3.04 g. of white crystals, m.p. 197.5–199.5°. An additional 0.62 g. was obtained from the filtrates.

Ethyl 3,4,5-Trimethoxy-β-methylcinnamate (**65**).—A mixture of 53.1 g. (0.253 mole) of 3,4,5-trimethoxyacetophenone, 50 g. (0.3 mole) of ethyl bromoacetate, 280 ml. of benzene, and 20 g. of zinc turnings was heated under reflux with stirring for 2 hr. The solution was decanted from unchanged zinc and shaken with 14 ml. of concentrated sulfuric acid in 100 ml. of water. The benzene layer was separated, well washed with water, and dried over sodium sulfate. After filtration and removal of the solvent, the product was distilled giving 60.8 g. of crystalline solid, b.p. 134° (0.05 mm.). This was recrystallized from 2-propanol yielding 42.5 g. of nearly white crystals, m.p. 55.5–57.5°.

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(13) Prepared by Dr. M. F. Zienty in these laboratories.

(14) Prepared by Dr. Gilbert A. Youngdale in these laboratories.

(15) E. H. Woodruff, *J. Am. Chem. Soc.*, **64**, 2859 (1942).