1,2-Ethanedithiol, 1,3-propanedithiol, 1,4-butanedithiol, and 1,5-pentanedithiol distearates. To 17 g. (0.06 mol.) of stearic acid and 100 ml. of petroleum ether in a 200-ml. round bottomed flask, fitted with a reflux condenser, was added 12 g. of PCl_5. The mixture was boiled under gentle reflux for 2 hr., cooled, and washed rapidly with four 25-ml. portions of ice water, and then dried over anhydrous Na_2SO_4.[7] To the dried solution of the acid chloride in petroleum ether was added a mixture of 0.03 mol. of the appropriate mercaptan and 0.06 mol. of pyridine in 100 ml. of petroleum ether. The rest of the procedure is identical to that used above.

2-Mercaptoethanol distearate. Stearoyl chloride was prepared by the method of Youngs *et al.* as described above. After the water wash and drying, the petroleum ether was removed by distillation and equivalent amounts of 2-mercaptoethanol and pyridine were added. The rest of the procedure is identical to that used above.

Chromatography. Analytical samples of the dithiol and monothiol diesters were chromatographed, using 20 g. of Florisil per gram of ester. The column was eluted with a total of 400 ml. of a solution containing 30% benzene–70% petroleum ether. The 1,2-ethanedithiol diesters were eluted with a total of 400 ml. of a solution containing 50% benzene–50% petroleum ether. After the solvent was removed by distillation, the product was crystallized from acetone-alcohol or acetone-benzene.

Reaction of methanol with 1,2-ethanedithiol and 1,5-pentanedithiol dioctadecanoate. To 0.005 mol. of 1,2-ethanedithiol or 1,5-pentanedithiol dioctadecanoate in a 200-ml. round bottomed flask, fitted with a reflux condenser, was added 0.05 g. of sodium methoxide and 70 ml. of methanol and the mixture was heated on a steam bath for 12 hr. At the end of the heating period, the methanol was removed by distillation and the product was dissolved in 100 ml. of ether. After the ether solution was washed with three 50-ml. portions of water, it was dried over anhydrous sodium sulfate. The ether then was removed by distillation and the methyl stearate was crystallized from methanol. The yield of product was 60–65% of the theoretical amount. Admixture of the products with an authentic sample of methyl stearate showed no depression of melting point.

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Benzilates and Related Esters of Aminophenylethanols

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In continuation of our exploration of derivatives of the aminophenylethanols,[1] a series of basic esters (Table I) of the formula $R_1COOCH(C_6H_5)$-$CH_2NR_2R_3.R_4X$ (I) has been synthesized and examined for pharmacological activity.

Esters evaluated included benzilates[2] as well as variants of R_1CO— of lesser molecular bulk.[3] Structural relationships with proven active drugs suggested examination of the basic esters I as central nervous system depressants,[4] anti-tremorine agents,[5] and local anesthetics.[3d]

Treatment of the aminophenylethanol[1] with the acid chloride R_1COCl gave the basic ester I, either isolated directly as the hydrochloride, or converted to its free base which was distilled. The corresponding benzilates were prepared from the α-chloro-α,α-diphenylacetates by hydrolysis.[6]

Selected compounds showed activity as anesthetic agents,[7] reversed the neurotoxicity of tremorine,[8] depressed motor activity,[9] and were active as hypotensive agents.[10]

EXPERIMENTAL[11]

The acid chlorides were available commercially, or were processed as described in the literature in the instance of ω-cyclohexylbutyryl chloride,[12] and α-chloro-α,α-diphenylacetyl chloride.[13]

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(8) Following the procedure outlined in ref. 3d, the compound No. of Table I/LD_{min} mg./kg./TED_{50} mg./kg. was noted: 34/750/75; 35/100/18; 36/450/89; 40/750/100; 49/250/56; 54/200/52.

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TABLE I

$R_1COOCH(C_6H_5)CH_2NR_2R_3.R_4X$

No.	R_2	R_3	R_4X	M.P.[a] or B.P. (Mm.)	RS[b]	Yield,[c] %	Formula	Analyses,[d] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
	$R_1 = C_3F_7$—												
1	C_2H_5—	C_2H_5—	HCl	117–118	A	17	$C_{16}H_{19}ClF_7NO_2$	45 1	45.3	4.5	5.1	3.3	3.1
	$R_1 = C_6H_5CH_2$—												
2	C_2H_5—	C_2H_5—	HCl	146–148	B	43	$C_{20}H_{26}ClNO_2$	69.0	69.2	7.5	7.3		
3	C_2H_5—	C_2H_5—	C_2H_5I	132–134	A	40	$C_{22}H_{30}INO_2$	56.5	56.6	6.5	6.5	3.0	2.8
4	C_2H_5—	C_2H_5—	EBA[e]	162–163	C	49	$C_{24}H_{32}BrNO_4$	60.2	60.1	6.7	6.8	2.9	2.8
	$R_1 = C_6H_{11}CH_2$—[f]												
5	C_2H_5—	C_2H_5—		155–157 (0.6)		56							
6	C_2H_5—	C_2H_5—	Pic[g]	76–78	D		$C_{26}H_{34}N_4O_9$	57.1	57.4	6.2	6.2		
7	C_2H_5—	C_2H_5—	EBA[e]	163–165	B	68	$C_{24}H_{38}BrNO_4$	59.5	59.7	7.9	7.8	2.9	3.3
8		—$(CH_2)_4$—	HCl	195–197	E	66	$C_{20}H_{30}ClNO_2$	68.3	68.1	8.6	8.4	4.0	4.0
9		—$(CH_2)_4$—	CH_3Br	189–191	C	52	$C_{21}H_{32}BrNO_2$	61.3	61.4	8.1	7.6		
10		—$(CH_2)_4$—	C_2H_5Br	157–158	A	67	$C_{22}H_{34}BrNO_2$	62.3	62.3	8.1	7.9		
11		—$(CH_2)_4$—	EBA[e]	150–151	A	57	$C_{24}H_{36}BrNO_4$	59.7	60.2	7.5	7.3	2.9	2.8
	$R_1 = C_6H_5CH_2CH_2$—												
12	C_2H_5—	C_2H_5—	HCl	114–116	F	69	$C_{21}H_{28}ClNO_2$	69.7	70.0	7.8	7.6		
13	C_2H_5—	C_2H_5—	CH_3Br	127–129	A	38	$C_{22}H_{30}BrNO_2$	62.9	63.0	7.2	7.3	3.3	3.3
14	C_2H_5—	C_2H_5—	EBA[e]	129–132	A	47	$C_{25}H_{34}BrNO_4$	61.0	61.3	7.0	6.9	2.8	2.7
	$R_1 = C_6H_5CH_2CH_2CH_2$—												
15	C_2H_5—	C_2H_5—		146–150 (0.1)		31	$C_{22}H_{29}NO_2$	77.8	77.9	8.6	8.4	4.1	3.8
16	C_2H_5—	C_2H_5—	CH_3Br	132–133	A	39	$C_{23}H_{32}BrNO_2$	63.6	63.2	7.4	7.5	3.2	3.5
17		—$(CH_2)_4$—	HCl	197–198	D	69	$C_{22}H_{28}ClNO_2$					3.8	3.6
18		—$(CH_2)_4$—	CH_3Br	184–185	C	65	$C_{23}H_{30}BrNO_2$					3.2	3.1
19		—$(CH_2)_4$—	C_2H_5Br	125–127	A	55	$C_{24}H_{32}BrNO_2$	64.6	64.9	7.2	7.2	3.1	3.3
	$R_1 = C_6H_5CH(C_2H_5)$—												
20	C_2H_5—	C_2H_5—		142–146 (0.03)		92	$C_{22}H_{29}NO_2$	77.8	77.9	8.6	8.7	4.1	3.9
21		—$(CH_2)_4$—	HCl	188–190	C	49	$C_{22}H_{28}ClNO_2$	70.7	71.1	7.6	7.3	3.8	4.0
22		—$(CH_2)_4$—	CH_3Br	153–155	A	67	$C_{23}H_{30}BrNO_2$	63.9	63.6	7.0	6.5	3.2	2.9
23		—$(CH_2)_4$—	C_2H_5Br	173–174	D	54	$C_{24}H_{32}BrNO_2$	64.6	64.5	7.2	7.2	3.1	3.1
	$R_1 = C_6H_{11}CH_2CH_2CH_2$—[f]												
24	CH_3—	CH_3—	HCl	175–178	B	61	$C_{14}H_{28}ClNO_2$	60.5	60.0	10.2	10.0		
25	CH_3—	CH_3—	CH_3I	143–145	G	60	$C_{21}H_{34}INO_2$	47.0	47.2	7.9	8.0		
27		—$(CH_2)_4$—	HCl	182–184	B	75	$C_{22}H_{34}ClNO_3$	69.5	69.8	9.0	9.3		
28		—$(CH_2)_4$—	CH_3I	118–121	G	72	$C_{23}H_{36}INO_2$	56.9	57.0	7.5	7.4		
29		—$(CH_2)_4$—	C_2H_5Br	157–159	H	13	$C_{24}H_{38}BrNO_2$	63.7	63.5	8.5	8.4	3.0	2.7
30		—$(CH_2)_5$—	HCl	128–131	B	66	$C_{23}H_{36}ClNO_2$[h]	65.1	64.6	10.3	10.4		
	$R_1 = (C_6H_5)_2CH$—												
31	C_2H_5—	C_2H_5—		194–195 (0.2)		74	$C_{26}H_{29}NO_2$	80.6	80.3	7.5	7.3	3.6	3.8
32	C_2H_5—	C_2H_5—	CH_3I	161–163	D	63	$C_{27}H_{32}INO_2$					2.7	2.8
33	C_2H_5—	C_2H_5—	C_2H_5I	152–157	C	48	$C_{28}H_{34}INO_2$	61.9	61.9	6.3	6.4	2.6	2.6
	$R_1 = (C_6H_5)_2CCl$—												
34	CH_3—	CH_3—	HCl	141–143	I	25	$C_{24}H_{25}Cl_2NO_2$					3.3	3.3
35	CH_3—	i-C_3H_7—	CH_3I	151	I	25	$C_{17}H_{31}ClINO_2$	57.5	57.3	5.5	5.6	2.5	2.0
36	CH_3—	C_6H_{11}—[f]	HCl	185–187	D	59	$C_{29}H_{33}Cl_2NO_2$	69.9	70.4	6.7	6.7		
37	C_2H_5—	C_2H_5—	HCl	138–139	C	32	$C_{26}H_{29}Cl_2NO_2$	68.1	68.3	6.4	6.2	3.1	2.7
38		—$(CH_2)_4$—	HCl	178–181	C	31	$C_{26}H_{27}Cl_2NO_2$	68.4	68.2	6.0	5.9	3.1	3.0
39		—$(CH_2)_4$—[i]	HCl	182–184	C	25	$C_{26}H_{27}Cl_2NO_2$	68.4	67.9	6.0	5.8		
40		—$(CH_2)_5$	HCl	169–171	A	66	$C_{27}H_{29}Cl_2NO_2$	68.9	68.2	6.2	6.8	3.0	3.3
41	—$(CH_2)_2O(CH_2)_2$—		HCl	184–186	D	36	$C_{26}H_{27}Cl_2NO_3$	66.1	66.1	5.8	6.0	3.0	3.1
42	i-C_3H_7—	$C_6H_5CH_2$—	HCl	153–155	C	21	$C_{32}H_{33}Cl_2NO_2$	71.9	72.1	6.2	6.2		

TABLE I (*Continued*)

No.	R_2	R_3	R_4X	M.P.[a] or B.P. (Mm.)	RS[b]	Yield,[c] %	Formula	Analyses,[d] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
	$R_1 = (C_6H_5)_2C(OH)$—												
43	CH_3—	CH_3—	HCl	183–185	C	71	$C_{24}H_{26}ClNO_3$	70.0	70.2	6.4	6.1	3.4	3.1
44	CH_3—	CH_3—	CH_3I	176–178	C	69	$C_{25}H_{28}INO_3$	58.0	58.0	5.5	5.5	2.7	2.5
45	CH_3—	*i*-C_3H_7—	HCl	170–172	C	39	$C_{26}H_{30}ClNO_3$	71.0	70.5	6.9	7.0	3.2	2.8
46	C_2H_5—	C_2H_5—	HCl	164–165	C	80	$C_{26}H_{30}ClNO_3$	71.0	70.9	6.9	6.9	3.2	3.4
47	C_2H_5—	C_2H_5—	CH_3I	178–179	C	58	$C_{27}H_{32}INO_3$	59.5	59.3	5.9	6.1	2.6	2.6
48	CH_3—	C_6H_{11}—[f]	HCl	193–196	D	23	$C_{29}H_{34}ClNO_3$	72.6	72.7	7.1	7.2	2.9	3.1
49	CH_3—	C_6H_{11}—[f]	CH_3I	125–127	C	24	$C_{30}H_{36}INO_3$	61.5	61.9	6.2	6.6	2 4	2.8
50	—$(CH_2)_4$—		HCl	193–195	E	46	$C_{26}H_{28}ClNO_3$	71.3	71.2	6.4	6.6	3.2	2.8
51	—$(CH_2)_4$—		CH_3I	141–143	C	64	$C_{27}H_{30}INO_3$					2.6	2.7
52	—$(CH_2)_4$—		EBA[e]	168–169	D	49	$C_{30}H_{34}BrNO_5$	63.4	63.3	6.0	6.2	2.5	2.4
53	—$(CH_2)_5$—		HCl	203–205	D	49	$C_{27}H_{30}ClNO_3$	71.7	71.4	6.7	6.9	3.1	3.0
54	—$(CH_2)_5$—		CH_3I	178–181	C	43	$C_{28}H_{32}INO_3$	60.3	60.0	5.8	5.6	2.5	2.9
55	—$(CH_2)_2O(CH_2)_2$—		HCl	198–200	D	65	$C_{26}H_{28}ClNO_4$	68.8	69.1	6.2	6.2	3.1	2.8
56	*i*-C_3H_7	$C_6H_5CH_2$—	HCl	161–163	D	29	$C_{32}H_{36}ClNO_4$[j]	72.1	71.6	6.8	6.6	2.6	2.8

[a] Melting points are not corrected. [b] RS = recrystallizing solvent: A = methyl ethyl ketone; B = isopropyl alcohol–isopropyl ether; C = isopropyl alcohol; D = ethanol; E = acetonitrile; F = benzene; G = not recrystallized; H = chloroform-ether; I = *n*-propanol. [c] Yields are expressed as % of recrystallized or distilled product. [d] Analyses by Weiler and Strauss, Oxford, England. [e] EBA = ethyl bromoacetate quaternary salt. [f] C_6H_{11} = cyclohexyl. [g] Pic = picric acid. [h] Chlorine, Calcd.: 10.7. Found: 10.9. [i] The compound is derived from the isomeric 2-(1-pyrrolidino)-2-phenylethanol (described in ref. 1). [j] The formula represents a monohydrate.

2-Diethylamino-1-phenylethyl diphenylacetate (Compound 31). To a stirred solution of 23.1 g. (0.1 mol.) of diphenylacetyl chloride in 100 ml. of benzene was added 19.3 g. (0.1 mol.) of 2-diethylamino-1-phenylethanol in 100 ml. of benzene at a rate sufficient to maintain reflux. After heating under reflux for 3 hr., the benzene was removed and the residue treated with 250 ml. of water, cautiously basified with 40% aqueous sodium hydroxide and the separated free base extracted with five 60-ml. portions of ether. The combined extracts were dried (anhydrous magnesium sulfate), filtered, and distilled to give 74% of product, b.p. 194–195° (0.2 mm.).

2-Diethylamino-1-phenylethyl diphenylacetate methiodide (Compound 32). To a cooled solution of 3.9 g. (0.01 mol.) of 2-diethylamino-1-phenylethyl diphenylacetate in 20 ml. of acetonitrile was added 1 ml. (0.016 mol.) of methyl iodide. The solution was allowed to stand 20 hr. at room temperature and then poured into 150 ml. of dry ether. Trituration of the precipitated gum with several additional portions of dry ether gave 4.9 g. (93%) of product, m.p. 154–159°.

2-Piperidino-1-phenylethyl α-chloro-α,α-diphenylacetate hydrochloride (Compound 40). A solution of 19.9 g. (0.075 mol.) of α-chlorodiphenylacetyl chloride in 70 ml. of acetonitrile was added to a suspension of 14.3 g. (0.07 mol.) of 2-piperidino-1-phenylethanol in 30 ml. of acetonitrile. After storage at 20° for 24 hr. there was obtained 30.2 g. of product.

2-Diethylamino-1-phenylethyl benzilate hydrochloride (Compound 46). A suspension of 18 g. (0.039 mol.) of 2-diethylamino-1-phenylethyl α-chloro-α,α-diphenylacetate hydrochloride in 900 ml. of water upon warming on a steam bath for 20 min., yielded a clear solution. Sodium chloride (180 g.) was then added and the precipitate and solution extracted with a total of 2 l. of chloroform. The chloroform was removed and the residue recrystallized (isopropyl alcohol) to give 13.8 g. (80%) of product; m.p. 164–165°.

2-Diethylamino-1-phenylethyl benzilate methiodide (Compound 47). Methyl iodide (2.9 g., 0.02 mol.) was added to a cooled solution of 5.4 g. (0.013 mol.) of 2-diethylamino-1-phenylethyl benzilate in 26 ml. of acetonitrile. Upon storage for 20 hr. at 20°, and scratching, the product crystallized, and was separated and recrystallized (isopropyl alcohol) to give 4.1 g. (58%) of product; m.p. 178–179°.

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Bicarbonate-catalyzed Displacement of a Nitro Group of 1,3,5-Trinitrobenzene

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During an investigation of methods for the selective reduction of one of the nitro groups of *sym*-trinitrobenzene, reduction by means of sodium sulfide and sodium bicarbonate in aqueous methanol was tried.[1] Among the reaction products none of the desired 3,5-dinitroaniline could be detected, but 3-amino-5-nitroanisole was isolated in 20% yield. Since the displacement of aromatic nitro groups by alcohols has previously been reported to occur only in strongly alkaline media,[2,3] this result was unexpected. The conditions for this displacement were then investigated and at the same

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