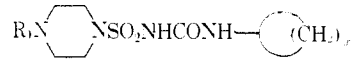
TABLE I

PIPERAZINESULFAMYLUREAS



No.	R_2	x	Mp, °C	Cryst solvent	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
1	CH_3CO	5	200–201	*a*	$C_{10}H_{21}N_5O_4S$	47.0	7.3	16.9	46.9	7.3	16.9
2	CH_3CO	6	197.5–198.5	*a*	$C_{11}H_{23}N_5O_4S$	48.5	7.6	16.2	48.7	7.6	15.9
3	CH_3CO	7	183–184	*a*	$C_{12}H_{25}N_5O_4S$	50.0	7.8	15.5	50.0	7.8	15.3
4	$(CH_3)_2CHO$	5	162.5–163.5	*a*	$C_{12}H_{25}N_5O_4S$	50.0	7.8	15.5	49.5	7.4	15.7
5	$(CH_3)_2CHCO$	6	168–169	*a*	$C_{16}H_{30}N_5O_4S$	51.3	8.1	15.0	51.2	8.0	14.8
6	$(CH_2)_5CHCO$	6	174–175	*b*	$C_{18}H_{34}N_5O_4S$	55.0	8.3	13.5	55.0	8.4	13.2
7	CH_3OC_2HCO	5	189–190	*a*	$C_{11}H_{23}N_5O_5S$	46.4	7.2	15.5	46.3	7.2	15.7
8	CH_3OCH_2CO	6	188–189	*a*	$C_{12}H_{25}N_5O_5S$	47.0	7.5	14.9	47.9	7.8	14.9
9	$(CH_3)_2CHSCH_2CO$	5	184.5–185.5	*a*	$C_{16}H_{30}N_5O_4S_2$	47.3	7.4	13.8	46.9	7.2	13.8
10	$(CH_3)_2CHSCH_2CO$	6	188.5–189.5	*a*	$C_{17}H_{32}N_5O_4S_2$	48.5	7.7	13.3	48.7	7.6	13.0
11	CH_3CH_2NHCO	5	194–195.5	*b*	$C_{11}H_{24}N_6O_4S$	46.5	7.5	19.4	46.4	7.5	19.0
12	CH_3CH_2NHCO	6	182–183	*b*	$C_{12}H_{26}N_6O_4S$	48.0	7.8	18.7	48.3	7.2	18.5
13	CH_3SO_2	5	202–203	*a*	$C_{12}H_{24}N_4O_6S_2$	39.1	6.6	15.2	38.6	6.7	15.5
14	CH_3SO_2	6	194–195	*a*	$C_{13}H_{26}N_4O_6S_2$	40.8	6.9	14.7	40.6	7.0	15.0

[a] Not recrystallized. [b] Acetonitrile.

1-Cyclohexylcarbonyl-4-sulfamylpiperazine.—By a similar procedure 16.5 g (0.1 mole) of 1-sulfamylpiperazine and 16.1 g (0.11 mole) of cyclohexanecarbonyl chloride in 150 ml of methylene chloride containing 11.0 g (0.11 mole) of triethylamine gave 8.2 g of the desired product, mp 205–206.5°.

Anal. Calcd for $C_{11}H_{21}N_3O_3S$: C, 48.0; H, 7.7; N, 15.3. Found: C, 47.7; H, 7.5; N, 15.0.

1-Isopropylthioacetyl-4-sulfamylpiperazine.—Under a nitrogen atmosphere, 4.8 g (0.02 mole) of 1-chloroacetyl-4-sulfamylpiperazine was added to 2.3 g (0.03 mole) of 2-propanethiol and 2.2 g (0.04 mole) of sodium methoxide in 75 ml of methanol. The reaction mixture was allowed to stir for 2 hr, concentrated to one-fifth the original volume, and added to 75 ml of water. The resulting precipitate was filtered, dried, and recrystallized from ether; yield 2.3 g, mp 113–114°.

Anal. Calcd for $C_9H_{19}N_3O_3S_2$: C, 38.4; H, 6.8; N, 14.9. Found: C, 37.8; H, 6.8; N, 14.8.

1-Ethylcarbamoyl-4-sulfamylpiperazine.—To 9.9 g (0.06 mole) of 1-sulfamylpiperazine in 90 ml of DMF was added slowly 4.7 g (0.066 mole) of ethyl isocyanate and 6.6 g (0.066 mole) of triethylamine. After heating the reaction mixture for 1 hr on a steam bath it was cooled, and filtered. The desired product was recrystallized from ethanol, 7.0 g, mp 178–180°.

Anal. Calcd for $C_7H_{16}N_4O_3S$: C, 35.6; H, 6.8; N, 23.7. Found: C, 35.6; H, 6.7; N, 23.9.

1-Methylsulfonyl-4-sulfamylpiperazine.—To a solution of 1.7 g (0.01 mole) of 1-sulfamylpiperazine and 1.1 g (0.011 mole) of triethylamine in 15 ml of DMF was added 1.3 g (0.011 mole) of methanesulfonyl chloride. The reaction mixture was heated at steam bath temperatures for 1 hr followed by cooling and the addition of ether. The resulting precipitate was filtered and recrystallized from acetone, 1.0 g, mp 248–250°.

Anal. Calcd for $C_5H_{13}N_3O_4S_2$: C, 24.7; H, 5.4; N, 17.3. Found: C, 24.8; H, 5.2; N, 17.5.

Some Derivatives of Cyclododecane[1]

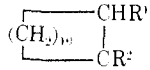
ALFRED BURGER AND CHARLES J. PAGET

Department of Chemistry, University of Virginia, Charlottesville, Virginia

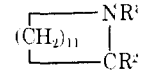
Received April 25, 1966

Many neuro- and psychopharmacologically active compounds contain planar, near-planar, or nonplanar cyclic moieties with acidic or basic functions in the rings or in side chains. In order to further delineate these requirements we have prepared a number of derivatives of cyclododecane with functional groups as they are encountered in typical drug molecules.

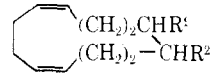
None of these compounds showed an interesting degree of biological activity in dose range studies in rats and mice.[2] Only at dose levels of 200 mg/kg in rats and 500–2000 mg/kg in mice did some of the derivatives produce overt effects such as decreased motor activity and hypotonia. None of the compounds was active in rat tests for antipyretic activity by the procedure



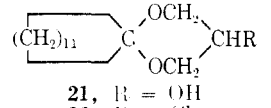
	R^1	R^2
1	$CH_2NC_5H_{10}$	=O
2	$CH_2N(CH_3)_2$	=O
3	NC_5H_{10}	H, OH
4	NC_5H_{10}	H, OAc
5	$N(CH_3)_2$	H_2
6	$NH(CH_2)_3N(C_2H_5)_2$	H_2
7	$NHCH_2C_6H_5$	H_2
8	$N^+(CH_3)_2(CH_2)_4N^-CH_3(C_2H_5)_2$	H_2
9	$N^+(CH_3)_2CH_2C_6H_5$	H_2
11	$O(CH_2)_2N(C_2H_5)_2$	H_2
12	H	OH, $(CH_2)_4N(CH_3)_2$
13	H	OH, C≡CH
14	H	OH, C≡CCH$_2$N(CH$_3$)$_2$
15	H	$OCONH_2$



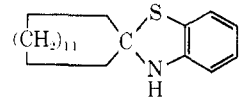
10, $R^1 = CH_3$; $R^2 = H$, $N^+(CH_3)_3$
16, $R^1 = (CH_2)_3N(CH_3)_2$; $R^2 = O$
17, $R^1 = (CH_2)_3N(CH_3)_2$; $R^2 = H_2$



18, $R^1 = OH$; $R^2 = NC_5H_{10}$
19, $R^1 = OAc$; $R^2 = NC_5H_{10}$
20, $R^1 = OH$; $R_2 = (CH_2)_3N(CH_3)_2$



21, R = OH
22, R = Cl
23, R = NC_5H_{10}



24

(1) Supported by a research grant from Smith Kline and French Laboratories to whom we express our appreciation.

(2) We wish to thank Drs. D. G. Tedeschi and L. Cook of Smith Kline and French Laboratories for the performance of these tests and for permission to quote their results.

TABLE I

PHYSICAL, ANALYTICAL, AND OTHER DATA

No.	Yield, %	Mp or bp (mm), °C	Solvent or method of purification	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H	Characteristic infrared bands, cm^{-1}
1	87	193–194	Subl 150° (0.2 mm)	$C_{18}H_{34}ClNO$	68.43	10.85	68.39	10.70	1710 (s) (C=O)
2	82	163–164	Subl 120° (0.2 mm)	$C_{18}H_{36}ClNO \cdot 0.5H_2O$	63.24	10.97	63.28	10.87	Doublet 1700, 1720 (s) (C=O)
3	56	99–99.5	Petr ether,[a] subl	$C_{17}H_{33}NO$	76.33	12.44	76.19	12.52	3380 (m) (NH)
4	87	220–222 (0.2)		$C_{19}H_{35}NO_2$	73.73	11.40	73.61	11.13	
5	37	154–155	EtOH–EtOAc	$C_{14}H_{30}ClN$	67.84	12.20	67.81	12.17	
6	58	206 (0.2)		$C_{19}H_{40}N_2$	76.95	13.60	77.03	13.65	3250 (w) (NH)
7	60	199.5–200	EtOH–EtOAc	$C_{19}H_{32}ClN$	73.63	10.41	73.54	10.42	1500 (m) (NH)
8	90	212–213	MeCN	$C_{22}H_{48}I_2N_2$	44.45	8.14	44.23	8.23	
9	79	210–211	MeCN	$C_{21}H_{36}IN$	58.74	8.47	58.77	8.53	
10	60	133.5–134	EtOH–EtOAc	$C_{18}H_{36}ClNO$	67.56	11.97	67.45	11.89	1110 (s) (COC)
11	64	212–213	MeCN	$C_{19}H_{42}I_2N_2$	41.31	7.66	41.12	7.68	
12	29	76–77	Petr ether, subl	$C_{17}H_{35}NO$	75.77	13.09	75.58	12.95	3150 (s) (OH), 2765 (m) [$(CH_3)_2N$]
13	33	98–98.5	Petr ether, subl	$C_{14}H_{24}O$	80.71	11.61	80.57	11.65	3400, 3240 (s) (≡CH)
14	10	103–104.5	Subl	$C_{17}H_{31}NO$	76.92	11.77	77.11	11.34	3095 (OH)
15	67	167–167.5	Diisopropyl ether	$C_{18}H_{25}NO_2$	68.68	11.08	68.48	10.97	3400 (s) (NH), 3190 (m), 3240 (m) (NH bonded)
16	74	160–166 (0.4)		$C_{17}H_{34}N_2O$	72.28	12.13	72.40	12.26	2740 (m), 2755 (m) [$(CH_3)_2N$], 1640 (s) (C=O)
17	86	135 (0.4)		$C_{17}H_{36}N_2$	76.05	13.52	76.27	13.60	2760 (m) [$(CH_3)_2N$]
18	88	266	EtOH–EtOAc	$C_{17}H_{30}ClNO$	68.08	10.08	68.05	9.70	3330 broad (OH)
19		229–229.5		$C_{19}H_{32}ClNO_2$	66.74	66.80	9.44	9.40	
20	62	130–130.5	EtOH–diisopropyl ether	$C_{28}H_{39}NO_8$	60.37	8.59	60.26	8.93	3475 (OH), 1725 (s), 1735 (s) (CO_2H), 1375 (s), 1590 (s) (COO)
21	70	55–55.5	Petr ether, subl 58° (0.3 mm)	$C_{16}H_{28}O_3$	70.27	11.01	70.08	10.77	3275 (s) (OH), doublet 1095, 1120 (s) (COC)
22	80	81.5–82	Petr ether	$C_{16}H_{27}ClO_2$	65.55	9.90	65.49	9.75	1085 (s), doublet 1120, 1110 (s) (COC)
23	83	53–54		$C_{20}H_{37}NO$	74.25	11.53	74.08	11.45	2730 (m) (CH_2N), doublet 1120, 1110 (s) (COC)
24	87	102–103	Petr ether	$C_{18}H_{37}NS$	74.40	9.40	74.52	9.43	3300 (m), 3330 (m) (NH), 1580 (m) (NH)

[a] Bp 30–60°.

of Winder, *et al.*,[3] and for the ability to antagonize pentylenetetrazole-induced seizures by the method of Bastian, *et al.*[4]

Experimental Section

Melting points were taken in a liquid bath and are corrected; boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer 337 spectrophotometer. Yields, physical data, analyses, and infrared absorption bands are listed in Table I. The derivatives of cyclododecane (ketones, olefins, dienes, lactams, etc.) used as starting materials were purchased from the Aldrich Chemical Co.

2-Piperidinomethylcyclododecanone hydrochloride (1) was prepared by a Mannich reaction.[5] A mixture of 9.1 g (0.05 mole) of cyclododecanone, 6.08 g (0.05 mole) of piperidinium chloride, 2.25 g (0.075 mole) of paraformaldehyde, 20 ml of absolute ethanol, and 10 drops of concentrated HCl was refluxed and stirred for 1 hr. Another 1.05 g (0.05 mole) of paraformaldehyde was added, and stirring and refluxing continued for 16 hr. Ethyl acetate (40 ml) was added, and the mixture was allowed to cool. The separated colorless crystalline solid (13.72 g, 87%) was filtered off and purified by sublimation.

2-Dimethylaminomethylcyclododecanone hydrochloride (2) was prepared in a similar manner.

2-Piperidinocyclododecanol Hydrochloride (3).—A mixture of 42.5 g (0.5 mole) of piperidine, 24.2 g (0.2 mole) of piperidinium chloride, 18.2 g (0.1 mole) of epoxycyclododecane, and 100 ml of ethylene glycol was refluxed for 7 days. On cooling, a colorless solid separated and was filtered off; additional quantities were obtained by dilution of the filtrate with water and extraction with ether.

2-Acetoxy-1-piperidinocyclododecane (4).—A mixture of 10.17 g (0.33 mole) of **3**, 33.66 g (0.33 mole) of acetic anhydride, 6 drops of H_2SO_4, and 100 ml of tetrahydrofuran (THF) was refluxed for 8 hr, cooled, and poured into 150 ml of water. Excess K_2CO_3 was added to pH 9 and the mixture was thoroughly extracted with ether. Work-up gave 8.90 g of viscous oil, bp 147° (0.3 mm), which was redistilled through a 50 × 1.25 cm column packed with 62-mm glass helices.

Dimethylaminocyclododecane Hydrochloride (5).—Using a modification of a method by Moore,[6] a mixture of 51 ml (0.8 mole) of dimethylformamide (DMF), 18.4 g (0.1 mole) of cyclododecanone, 10 g of $MgCl_2 \cdot 6H_2O$, and 38 ml (46 g, 1.0 mole) of 99% formic acid was refluxed and distilled. During the first 3 hr, 95 ml was allowed to distil off, and the temperature reached 145°; it stayed at this point for the remainder of the reflux period. An additional 50 ml of DMF was added, refluxing was continued for 48 hr, and the cooled mixture was poured over ice, made alkaline, and extracted well with ether. Work-up gave 8.80 g of an oil which was converted to the hydrochloride in anhydrous ether.

1-(3-Diethylaminopropylamino)cyclododecane (6).—Working by the general method of Billman, *et al.*,[7] a mixture of 37.6 g (0.2 mole) of cyclododecanone, 22 g of 3-diethylaminopropylamine, 400 mg of *p*-toluenesulfonic acid, and 150 ml of benzene was refluxed for 18 hr under a Dean–Stark trap to remove water. The mixture was cooled, excess solid KOH was added for 2 hr, the liquid was filtered, and the benzene was removed *in vacuo*. The residual oil was dissolved in 300 ml of dry methanol and reduced by careful addition of 7.56 g (0.2 mole) of $NaBH_4$ in small portions to the ice-cooled stirred mixture. After stirring at 25° for 16 hr the methanol was removed *in vacuo* and the liquid was added to 200 g of ice–water. It was acidified, extracted well with ether to remove 8.55 g of crude cyclododecanol, made basic, saturated with NaCl, extracted with ether, and worked up. Fractional distillation through a 50 × 1.25 cm column packed with 62-mm glass helices yielded an oil.

Benzylaminocyclododecane hydrochloride (7) was prepared analogously using benzylamine. Acidification of the reduction mixture with 10% HCl gave an insoluble salt which was filtered off and dried.

1-[1-(N,N-Dimethylammonium)-3-(N,N-diethyl-N-methyl)-N-propylammonium]cyclododecane Diiodide (8).—To a mixture

(3) C. V. Winder, J. Wax, B. Werrano, L. Scotti, S. P. Stockhouse, and R. H. Wheelock, *J. Pharmacol. Exptl. Therap.*, **133**, 117 (1961).

(4) J. W. Bastian, W. E. Krause, S. A. Ridlon, and N. Ercoli, *ibid.*, **127**, 75 (1959).

(5) F. F. Blicke, *Org. Reactions*, **1**, 329 (1942).

(6) M. L. Moore, *ibid.*, **5**, 319 (1949).

(7) J. H. Billman and A. C. Diesing, *J. Org. Chem.*, **22**, 1068 (1957).

of 7.14 g (0.025 mole) of **6**, 25 ml of anhydrous methanol, and 4 g of NaOH was added dropwise, with stirring, 6.2 ml (0.1 mole) of methyl iodide. The mixture was refluxed for 5 hr, and then an additional 2 ml of CH_3I was added. After stirring overnight at 25°, another 2 ml of CH_3I was added, and the mixture was refluxed for 3 hr and taken to dryness. The residue was crystallized from ethanol–ether and then from acetonitrile.

In a similar way, **N-benzyl-N-cyclododecyl-N,N-dimethylammonium iodide (9)** (from **7**), and **1-[N-(2-azacyclotridecyl)-N-methyl)-3-(N,N,N-trimethylammonium)] diiodide (10)** were prepared.

(2-Diethylaminoethoxy)cyclododecane Hydrochloride (11).—A mixture of 18.4 g (0.1 mole) of cyclododecanol, 4.93 g (0.11 mole) of 50% NaH in mineral oil, and 200 ml of anhydrous toluene was refluxed for 5 hr; it was cooled, and 12.54 g (0.1 mole) of β-diethylaminoethyl chloride in 100 ml of toluene was added. After stirring and refluxing for another 15 hr, the mixture was decomposed with ice, acidified, and extracted continuously for 18 hr. From this ether extract 10.15 g of cyclododecanol was recovered. The aqueous portion was made basic, saturated with NaCl, and extracted continuously for 12 hr. The residue from the ether extract was distilled, bp 155° (0.2 mm), and converted to the hydrochloride in anhydrous ether.

1-(3-Dimethylaminopropyl)cyclododecanol (12).—Using the general directions of Marxer,[8] 36.4 g (0.3 mole) of 3-dimethylaminopropyl chloride suspended in 100 ml of dry ether, was added to a stirred slurry of 7.2 g (0.3 g-atom) of Mg turnings (activated with CH_3I) and 30 ml of boiling ether over a period of 45 min. The mixture was refluxed for an additional 2 hr, and then 54.6 g (0.3 mole) of cyclododecanone in 125 ml of ether was added. After another 24 hr of refluxing the mixture was decomposed with saturated NH_4Cl solution, made basic, and extracted with ether for 12 hr. Removal of the ether gave 23.4 g of product which was recrystallized and finally sublimed at 65° (0.2 mm).

1-Ethynylcyclododecanol (13).—Magnesium acetylide was prepared from 9.6 g (0.4 g-atom) of Mg, 43.6 g (0.4 mole) of ethyl bromide in 260 ml of THF, and acetylene, by the method of Jones, *et al.*[9] To the metallic-looking suspension was added 36.4 g (0.2 mole) of cyclododecanone in 75 ml of THF at 0°. The mixture was stirred at 26° for 4 hr and then refluxed for 2 hr, decomposed with NH_4Cl solution, extracted with ether and worked up. The oily residue from the dried ether solution weighed 14 g.

1-(3-Dimethylamino-1-propynyl)cyclododecanol (14).—By a modification of a patented method,[10] a stirred mixture of 125 mg of $CuSO_4$, 5.2 g (0.025 mole) of **13**, 3.26 g (0.04 mole) of dimethylammonium chloride, and 3.7 ml (0.05 mole) of 40% formaldehyde solution was refluxed for 3 hr, and allowed to stand overnight. Another 3.7 ml of formaldehyde solution and 125 mg of $CuSO_4$ were added, stirring and refluxing was resumed for 3 hr, and the mixture was cooled and at pH 5 extracted with ether to remove 2.88 g of starting alcohol. The mixture was now made basic to pH 10, extracted with ether, and worked up. The colorless residue from the ether extract was sublimed at 90° (0.4 mm).

Carbamoylcyclododecane (15).—By the method of Loev and Kormendy,[11] 7.75 ml (0.105 mole) of trifluoroacetic acid was added dropwise to a stirred mixture of 9.2 g (0.05 mole) of cyclododecanol, 6.5 g (0.1 mole) of sodium cyanate, and 50 ml of dry benzene over a 1-hr period. After being stirred for 16 hr, 20 ml of water was added, and the mixture was extracted with ether and worked up.

1-(3-Dimethylaminopropyl)-2-oxoazacyclotridecane (16).—In a nitrogen atmosphere 9.6 g (0.2 mole) of 50% NaH in mineral oil was added slowly to a refluxing mixture of 39.4 g (0.2 mole) of 2-azacyclotridecanone, 50 ml of dry toluene, and 150 ml of ethylene glycol dimethyl ether (diglyme). The mixture was refluxed for 4 hr and then 24 g (0.2 mole) of 3-dimethylaminopropyl chloride in 50 ml of diglyme was added at once. The mixture was refluxed for 11 hr and then stirred at room temperature for 12 hr. It was worked up by adding 20 ml of methanol, removing all solvent, diluting with 400 ml of water, acidifying to pH 1, and extracting with ether. The aqueous extract was made basic, saturated with NaCl, extracted with ten 100-ml portions of ether, and dried (Na_2SO_4). The oil from the ether was fractionally distilled.

1-(3-Dimethylaminopropyl)-1-azacyclotridecane (17).—To a stirred and refluxing mixture of 9 g of $LiAlH_4$ in 500 ml of dry ether was added dropwise 28.48 g (0.1 mole) of **16** in 150 ml of ether. The mixture was stirred at room temperature for 14 hr and worked up by the addition of 25 ml of water, followed by 50% NaOH. It was filtered, the filter cake was washed with ether, the combined ether extract was dried (K_2CO_3), and the remaining oil was distilled.

2-Piperidino-5,9-cyclododecadien-1-ol Hydrochloride (18). A mixture of 100 ml of ethylene glycol, 42.5 g (0.5 mole) of piperidine, 18.8 g (0.106 mole) of 1,2-epoxy-5,9-cyclododecadiene, and 24.2 g (0.2 mole) of piperidinium chloride was refluxed for 7 days. It was poured into 400 ml of ice water and 100 ml of 10 *N* NaOH was added. The mixture was extracted with ether and worked up. The oil from the ether yielded two fractions, 2.85 g boiling at 50–66° (0.7 mm) and 24.43 g (88%) boiling at 147–156° (0.3 mm). The high-boiling oil was converted to the hydrochloride using ethereal HCl.

The **acetate ester hydrochloride (19)** was prepared with acetic anhydride (see **4**).

2-(3-Dimethylaminopropyl)-5,9-cyclododecadien-1-ol Monocitrate (20).—To 4.86 g (0.2 g-atom) of Mg turnings was added 15 ml of THF, one crystal of iodine, and 4 drops of methyl iodide. When the reaction had begun, 24.25 g (0.2 mole) of 3-dimethylaminopropyl chloride in 50 ml of THF was added to maintain refluxing. The mixture was refluxed for 1 additional hr, and then 18.8 g (0.100 mole) of 1,2-epoxy-5,9-cyclododecadiene in 50 ml of THF was added all at once and refluxing continued an additional 48 hr under a nitrogen atmosphere. The ice-cooled mixture was decomposed with excess saturated NH_4Cl solution, made alkaline (pH 11) with NaOH, and extracted with ether. The oil from the ether was distilled through a 50 × 1.25 cm column packed with 62-mm glass helices to yield 17.51 g (62%) of product, bp 201–215° (0.2 mm). This was converted to the monocitrate salt by allowing it to react with a saturated ethereal solution of citric acid.

Spiro(4-hydroxymethyl-1,3-dioxolane)-2,1′-cyclododecane (21).—A stirred mixture of 36.84 g (0.4 mole) of glycerol, 18.4 g (0.1 mole) of cyclododecanone, 800 mg of *p*-toluenesulfonic acid, and 300 ml of benzene was refluxed for 30 hr under a Dean–Stark trap to remove water and then cooled. After addition of 100 ml of saturated K_2CO_3 solution, the mixture was extracted with seven 100-ml portions of ether. The combined ether extract was washed with three 100-ml portions of water, dried (Na_2SO_4), and evaporated. The residual oil crystallized from low-boiling petroleum ether.

Spiro(4-chloromethyl-1,3-dioxolane)-2,1′-cyclododecane (22).—A mixture of 33.15 g (0.3 mole) of 3-chloro-1,2-propanediol, 36.4 g (0.2 mole) of cyclododecanone, 400 mg of *p*-toluenesulfonic acid, and 250 ml of benzene was refluxed for 24 hr with removal of water, and worked up as described for **22**.

Spiro(4-piperidinomethyl-1,3-dioxolane)-2,1′-cyclododecane (23).—A mixture of 13.74 g (0.05 mole) of **22**, 22 ml (0.4 mole) of piperidine, and 150 ml of DMF was refluxed for 2 hr. The solvent was removed, and the residual oil was acidified and extracted with ether. The aqueous extract was made alkaline, extracted with five 100-ml portions of ether, and dried (Na_2SO_4). After removing the ether, the basic extract was distilled to yield fractions distilling at 35–55° (0.3 mm) and about 200° (0.3 mm). The high-boiling fraction was redistilled through a 50 × 1.25 cm column packed with 62-mm glass helices to yield an analytical sample, bp 188–193° (0.2 mm). This fraction crystallized on standing.

2,1′-Spirobenzothiazolinylcyclododecane (24) was prepared by a modification of the method of Elderfield and McClenachen.[12] A mixture of 25 g (0.2 mole) of freshly distilled 2-aminobenzenethiol, 36.4 g (0.2 mole) of cyclododecanone, and 100 ml of dry methanol was refluxed for 8 hr under a nitrogen atmosphere. Then 70 ml of the methanol was distilled off, while maintaining a nitrogen atmosphere. The warm flask containing the mixture was purged with nitrogen, stoppered tightly, and kept at 4° overnight. The solid that had formed was ground up, washed with 50 ml of methanol on the filter, and dried to yield colorless crystals.

(8) A. Marxer, *Helv. Chim. Acta*, **24**, 223E (1941).

(9) E. H. R. Jones, L. Skattebol, and M. C. Whiting, *J. Chem. Soc.*, 4765 (1956).

(10) P. Dimroth, P. Doffner, R. Oster, and H. Pasedach, German Patent 1,100,617 (1961); *Chem. Abstr.*, **55**, 19960h (1961).

(11) B. Loev and M. F. Kormendy, *J. Org. Chem.*, **28**, 3421 (1963).

(12) R. Elderfield and E. J. McClenachen, *J. Am. Chem. Soc.*, **82**, 1982 (1960).