TABLE I

1,3-DIOXOLANES

Compounds 1, 2, 5 and 7 were recrystallized from isopropyl alcohol; 3 from methyl ethyl ketone; 4 from acetone; 6 and 8 from ethanol

	Substituent	Salt	B.p., base °C.	Mm.	M.p., °C. salt	Formula	Nitrogen, % Calcd.	Found	Hydrogen, % Calcd.	Found
					4-Substituted 2,2-diphenyl-					
1	$CH_2NC_6H_{12}$[a]	HCl	175–177	.01	183–184	$C_{22}H_{28}O_2NCl$	3.75	3.69	9.48	9.45
2	$CH_2NC_6H_{12}$	CH_3Br			203–205	$C_{23}H_{30}O_2NBr$	3.24	3.35	18.48	18.50
3	$CH_2NC_7H_{14}$[b]	HCl	183–185	.01	173–175	$C_{23}H_{30}O_2NCl$	3.61	3.67	9.14	9.04
					2-Substituted 4,5-diphenyl-					
4	$CH_2NC_5H_{10}$[c]	HCl			201–202	$C_{21}H_{26}O_2NCl$	3.89	3.86	9.87	9.84
5	$CH_2NC_6H_{12}$	HCl	178–180	.05	163–165[d]	$C_{22}H_{28}O_2NCl$	3.75	3.77	9.48	9.40
6	$CH_2NC_6H_{12}$	CH_3Br			223–225[d]	$C_{23}H_{30}O_2NBr$	3.24	3.25	18.48	18.53
7	$CH_2NC_7H_{14}$	HCl	173–175	.05	157–159	$C_{23}H_{30}O_2NCl$	3.61	3.63	9.14	9.30
8	$CH_2NC_7H_{14}$	CH_3Br			226–228[d]	$C_{24}H_{32}O_2NBr$	3.14	3.20	17.90	18.07

[a] NC_6H_{12} = 1-hexamethylenimino. [b] NC_7H_{14} = 4-methyl-1-hexamethylenimino. [c] NC_5H_{10} = piperidino. [d] Melts with decomposition.

methylenimine[7] was heated in a pressure bottle on a steam-bath for 5 days. The mixture was washed with a solution of 10 g. of sodium hydroxide in 50 cc. of water. The organic layer was separated, dried over magnesium sulfate, the solvent and excess imine were removed by distillation and the residue was fractionated; yield 24.1 g. (91%).

The hydrochloride was prepared by addition of the calculated amount of ethereal hydrogen chloride to the base dissolved in ether.

In order to obtain the methobromide, excess methyl bromide was added to the base dissolved in ether.

2,2-Diphenyl-5-methyl-5-(1-hexamethyleniminomethyl)-(9) and 2,2-Diphenyl-5-methyl-5-(4-methyl-1-hexamethyleniminomethyl)-1,3-dioxane (10) Hydrochlorides.—By the process described above, 13.4 g. of 2,2-diphenyl-5-methyl-5-iodomethyl-1,3-dioxane,[4a] 16.9 g. of hexamethylenimine and 100 cc. of benzene yielded 5.0 g. (40.3%) of product after three recrystallizations from absolute ethanol; m.p. 68–70°.

The hydrochloride melted at 215–217° after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{24}H_{32}O_2NCl$: N, 3.48; Cl, 8.82. Found: N, 3.55; Cl, 8.86.

From 15.0 g. of the iodomethyl compound, 43.0 g. of 4-methylhexamethylenimine and 100 cc. of benzene, 12.0 g. (83.3%) of product was obtained after recrystallization from methanol with the use of charcoal; m.p. 66–68° after recrystallization from absolute ethanol.

The hydrochloride melted at 214–215° dec. after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{25}H_{34}O_2NCl$: N, 3.37; Cl, 8.52. Found: N, 3.30; Cl, 8.47.

ANN ARBOR, MICHIGAN

(7) F. F. Blicke and N. J. Doorenbos, THIS JOURNAL, **76**, 2317 (1954).

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

Antispasmodics. XXI. Basic 1,3-Dioxolanes

BY F. F. BLICKE AND H. E. MILLSON, JR.[1,2]

RECEIVED AUGUST 24, 1954

One series of basic 4,5-diphenyl-1,3-dioxolanes and two series of basic spiro-1,3-dioxolanes were prepared. In a number of these compounds the basic substituent was a hexa-, hepta- or octamethylenimino radical. The antispasmodic activity of some of the compounds has been reported.

Three types of basic 1,3-dioxolanes were prepared for pharmacological study.

Basic 4,5-diphenyl-1,3-dioxolanes (Table I) were obtained by interaction of 2-bromomethyl-4,5-diphenyl- (I) or 2-(β-chloroethyl)-4,5-diphenyl-1,3-dioxolane (II) with an amine. Among the amines employed were hexa-, hepta- and octamethylenimine. The required intermediate I was prepared from hydrobenzoin and bromoacetal by a described procedure.[3] The second intermediate II was synthesized by interaction of hydrobenzoin with β-chloropropionaldehyde diethylacetal.

Under the conditions described in the experimental part, a 1-alkyl-4-piperidone hydrochloride was heated with ethanol and then with hydrobenzoin with the formation of a basic spirodioxolane (Table II). For example, 1-methyl-3-phenyl-4-piperidone hydrochloride, after treatment with ethanol and hydrobenzoin, yielded 2,3,6-triphenyl-8-methyl-1,4-diox-8-azaspiro[4.5]decane. Presumably, a hemiketal is the first intermediate in this series of reactions.

Another type of basic spirodioxolane (Table III) was obtained by the use of 1-(hydroxymethyl)-cyclohexanol. Interaction of this substance with bromoacetal yielded 2-bromomethyl-1,3-dioxaspiro-[4.5]decane which condensed with amines to form the corresponding 2-basically substituted products; thus, reaction with dimethylamine produced 2-dimethylaminomethyl-1,3-dioxaspiro[4.5]decane.

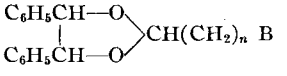
Some of the compounds (Table I) were tested in the Wm. S. Merrell Company laboratories on the isolated rabbit jejunum against acetylcholine-induced spasm. The minimum effective concentra-

(1) This paper represents part of a dissertation submitted by H. E. Millson, Jr., in partial fulfillment of the requirements for the Ph.D. degree in the University of Michigan, 1954.

(2) The Wm. S. Merrell Company Fellow.

(3) F. F. Blicke and G. R. Toy, THIS JOURNAL, **77**, 31 (1955).

TABLE I

2-BASICALLY SUBSTITUTED 4,5-DIPHENYL-1,3-DIOXOLANES  B

Cpd. no.[g]	n	B	B.p., °C. base	Mm.	Yield, %	Salt	M.p., °C.	Formula salt	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Halogen Calcd.	Halogen Found
1	1	NH_2	145–146	0.2	64	HCl	216[a]	$C_{16}H_{18}O_2NCl$	65.86	66.14	6.22	6.37	4.80	4.67	12.15	12.00
2	1	$NHCH_3$	145	.4	95	HCl	244–245[a]	$C_{17}H_{20}O_2NCl$	66.77	66.79	6.59	6.86	4.58	4.69	11.59	11.62
3	1	NHC_2H_5	141	.3	84	HCl	210–211	$C_{18}H_{22}O_2NCl$	67.59	67.52	6.93	7.10	4.38	4.58	11.09	10.98
4	1	$NHCH(CH_3)_2$	144–153	.3	100	HCl	218–219[a]	$C_{19}H_{24}O_2NCl$	68.35	68.56	7.24	7.28	4.20	4.10	10.62	10.88
5	1	$NHCH_2CH{=}CH_2$	165–169	.8	86	HCl	170–171	$C_{19}H_{22}O_2NCl$	68.76	68.78	6.68	6.83	4.22	4.16	10.68	10.81
6	1	$N(CH_3)_2$	137–140	.5	99	HCl	211–213[a]	$C_{18}H_{22}O_2NCl$	67.59	67.48	6.93	6.97	4.38	4.32	11.09	11.06
7	1	$N(CH_3)_2$				CH_3Br	213–214	$C_{19}H_{24}O_2NBr$	60.32	60.55	6.39	6.48	3.70	3.59	21.12	20.90
8	1	$N(C_2H_5)_2$	157–163	.5	84	HCl	130–133[b]	$C_{20}H_{26}O_2NCl$	69.04	68.80	7.53	7.44	4.03	4.02	10.19	10.34
9	1	$N(C_2H_5)_2$				CH_3Br	164–165	$C_{21}H_{28}O_2NBr$	62.06	62.23	6.94	6.84	3.45	3.47	19.67	19.69
10	1	$N(C_3H_7)_2$	167–169	.5	78	HCl	179–180	$C_{22}H_{30}O_2NCl$	70.28	70.50	8.04	8.20	3.73	3.64	9.43	9.52
11	1	$N<(CH_2)_4$	167–170	.4	99	HCl	181–183	$C_{20}H_{24}O_2NCl$	69.45	69.38	6.99	7.02	4.05	4.04	10.25	10.18
12	1	$N<(CH_2)_4$				CH_3Br	159–160	$C_{21}H_{26}O_2NBr$	62.37	62.50	6.48	6.78	3.46	3.37	19.76	19.79
13	1	NC_4H_8O[c]	176–180	.3	88	HCl	214–216[a]	$C_{20}H_{24}O_3NCl$	66.38	66.10	6.68	6.90	3.87	3.80	9.80	9.73
14	1	$N_2C_4H_9$[d]	202–208	1.0	59	HCl	213–215[a]	$C_{20}H_{26}O_2N_2Cl_2$					7.05	6.85	17.85	17.72
15	1	$N<(CH_2)_7$	165–170	0.6	79	HCl	183–184	$C_{23}H_{30}O_2NCl$	71.21	71.10	7.79	7.79	3.61	3.63	9.14	9.28
16	1	$N<(CH_2)_7$				CH_3Br	215–217	$C_{24}H_{32}O_2NBr$	64.57	64.60	7.22	7.35	3.14	3.21	17.90	18.03
17	1	$N<(CH_2)_8$	175–185	0.5	84	HCl	164–166	$C_{24}H_{32}O_2NCl$	71.71	71.68	8.02	8.06	3.48	3.41	8.82	8.80
18	1	$N<(CH_2)_8$				CH_3Br	219–221	$C_{25}H_{34}O_2NBr$	65.21	65.35	7.44	7.58	3.04	3.13	17.36	17.28
19	1	$NH(CH_2)_2N(CH_3)_2$	181–185	.3	80	2HCl	208–209[a]	$C_{20}H_{28}O_2N_2Cl_2$					7.01	7.01	17.76	17.79
20	1	$NH(CH_2)_2N(C_2H_5)_2$	188–193	.4	94	2HCl	206–207[a]	$C_{22}H_{32}O_2N_2Cl_2$					6.56	6.61	16.59	16.50
21	1	$N(CH_3)(CH_2)_2N(CH_3)_2$				$2CH_3Br$	208–210[a]	$C_{23}H_{34}O_2N_2Br_2$					5.28	5.31	30.14	30.25
22	1	$NH(CH_2)_2N(C_2H_5)_2$				$2CH_3Br$	183–185	$C_{24}H_{36}O_2N_2Br_2$					5.15	5.24	29.36	28.96
23	1	[e]			42	2HCl	240–241[a]	$C_{36}H_{42}O_4N_2Cl_2$	67.81	68.11	6.64	6.70	4.39	4.32		
24	2	NH_2	160–162	.2	45	HCl	190–192	$C_{17}H_{20}O_2NCl$	66.77	66.30	6.59	6.88	4.58	4.58	11.59	11.57
25	2	NHC_2H_5	167–169	.2	96	HCl	187–189	$C_{19}H_{24}O_2NCl$	68.35	68.67	7.25	7.30	4.20	4.17	10.62	10.59
26	2	$N(CH_3)_2$	154–155	.3	81	HCl	171–173	$C_{19}H_{24}O_2NCl$	68.35	68.38	7.25	7.42	4.20	4.17	10.62	10.72
27	2	$N(CH_3)_2$				CH_3Br	181–183	$C_{20}H_{26}O_2NBr$	61.22	61.03	6.68	6.96	3.57	3.61	20.37	20.18
28	2	$N(C_2H_5)_2$	719–183	.7	95	HCl	170–172	$C_{21}H_{28}O_2NCl$	69.69	69.85	7.80	7.95	3.87	4.02	9.80	9.67
29	2	$N<(CH_2)_4$	188–193	.5	90	HCl	195–198	$C_{21}H_{26}O_2NCl$	70.08	70.08	7.28	7.54	3.89	3.82	9.85	9.89
30	2	$N<(CH_2)_4$				CH_3Br	186–188	$C_{22}H_{28}O_2NBr$	63.15	62.89	6.75	6.84	3.35	3.35	19.10	18.97
31	2	$N<(CH_2)_6$	196–198	.3	85	HCl	202–204[a]	$C_{23}H_{30}O_2NCl$	71.20	71.20	7.79	7.95	3.61	3.80	9.14	9.06
32	2	$N<(CH_2)_6$				CH_3Br	184–186	$C_{24}H_{32}O_2NBr$	64.57	64.64	7.22	7.33	3.14	3.19	17.90	17.74
33	2	NC_7H_{14}[f]	208–212	.7		HCl	189–190	$C_{24}H_{32}O_2NCl$	71.71	71.63	8.02	8.06	3.48	3.50	8.82	8.82
34	2	NC_7H_{14}[f]				CH_3Br	208–210	$C_{25}H_{34}O_2NBr$	65.21	65.29	7.44	7.76	3.04	3.16	17.36	17.24

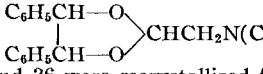
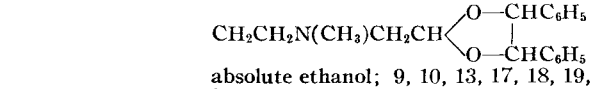
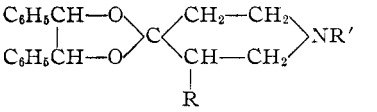
[a] Melts with decomposition. [b] Two melting points were observed: 95° and 130–133°. [c] NC_4H_8O is morpholino. [d] $N_2C_4H_9$ is piperazino. [e]  $CHCH_2N(CH_3)$-  . [f] NC_7H_{14} is 4-methyl-1-hexamethylenimino. [g] Compounds 2, 3, 4, 5, 6, 7, 14, 20, 23, 26, 28, 29, 30, 35 and 36 were recrystallized from absolute ethanol; 9, 10, 13, 17, 18, 19, 21, 22, 24, 27, 31, 32, 33 and 34 from ethanol–ether; 11 and 12 from ethanol–benzene; 1 from ethanol–toluene; 25 from ethanol–water; 8 from ethyl acetate.

TABLE II

2,3-DIPHENYL- AND 2,3,6-TRIPHENYL-8-ALKYL-1,4-DIOX-8-AZASPIRO[4.5]DECANES



Cpd. no.[c]	R	R′	Salt	M.p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Halogen Calcd.	Halogen Found
1	H	CH_3	HCl	227–229	$C_{20}H_{24}O_2NCl$	69.45	69.24	6.99	6.86	4.05	4.21	10.25	10.41
2	H	CH_3	CH_3Br	285–287[a]	$C_{21}H_{26}O_2NBr$	62.37	62.41	6.48	6.61	3.46	3.45	19.77	19.85
3	H	CH_3	CH_2=$CHCH_2Br$	200–202	$C_{23}H_{28}O_2NBr$	64.18	64.13	6.56	6.78	3.25	3.26	18.57	18.61
4	H	CH_3	C_4H_9Br	207–210	$C_{24}H_{32}O_2NBr$	64.56	64.63	7.23	7.52	3.14	3.20	17.90	17.74
5	H	C_2H_5	HCl	197–199[b]	$C_{21}H_{26}O_2NCl$	70.08	70.10	7.29	7.10	3.89	3.91	9.85	9.83
6	H	C_2H_5	CH_3Br	264–268	$C_{22}H_{28}O_2NBr$	63.15	63.40	6.75	6.91	3.35	3.37	19.10	19.13
7	H	C_2H_5	C_2H_5Br	243–245[a]	$C_{23}H_{30}O_2NBr$	63.88	63.48	6.99	7.13	3.24	3.37	18.48	18.45
8	H	C_2H_5	CH_2=$CHCH_2Br$	206–207[a]	$C_{24}H_{30}O_2NBr$	64.86	64.91	6.80	6.83	3.15	3.22	17.98	17.87
9	C_6H_5	CH_3	HCl	274–276[a]	$C_{26}H_{28}O_2NCl$	74.00	73.74	6.69	6.93	3.32	3.42	8.40	8.67
10	C_6H_5	CH_3	CH_3Br	280–282	$C_{27}H_{30}O_2NBr$	67.49	67.00	6.29	6.50	2.92	3.00	16.63	16.89

[a] Melted with decomposition. [b] Two melting points were noted for this compound: 107–110° and 197–199°. [c] Compounds 1, 3, 4, 5, 6, 7 and 8 were recrystallized from ethanol–ether; 2 and 10 from absolute ethanol; 9 from isopropyl alcohol.

tions were found to be as follows: 1:1,000,000 for 10 and 12; 1:310,000 for 7; 1:100,000 for 1, 2 and 3; 1:31,000 for 6 and 11 (1:80,000,000 for atropine). The following minimum effective concentrations were found for barium chloride-induced spasm: 1:310,000 for 10 and 12; 1:100,000 for 1, 2, 3, 6 and 11; 1:10,000 for 7 (1:100,000 for papaverine).

Experimental

2-(β-Chloroethyl)-4,5-diphenyl-1,3-dioxolane.—A mixture of 20.0 g. of hydrobenzoin and 15.5 g. of β-chloropropionaldehyde[4] was placed in a small distillation flask and heated at 120° (bath temperature) until the ethanol (about 11 cc.), formed during the reaction, had distilled from the mixture. The hot residue was dissolved in 50 cc. of isopropyl alcohol and the product, which separated from the cold solution, was recrystallized from ethanol; yield 12.0 g. (44%), m.p. 85–87°.

Anal. Calcd. for $C_{17}H_{17}O_2Cl$: C, 70.67; H, 5.93; Cl, 12.28. Found: C, 70.70; H, 6.24; Cl, 12.33.

General Procedure for the Preparation of 2-Basically substituted 4,5-Diphenyl-1,3-dioxolanes.—A solution of 10.0 g. (0.031 mole) of 2-bromomethyl-4,5-diphenyl-1,3-dioxolane or 10.0 g. (0.035 mole) of 2-(β-chloroethyl)-4,5-diphenyl-1,3-dioxolane in 50 cc. of toluene and a two to five molar excess of the required amine were placed in a pressure bottle. Sodium iodide (24 g.) and 5 g. of sodium carbonate were added and the mixture was heated on a steam-bath at 100° for a week. The mixture was treated with 100 cc. of 5% sodium hydroxide solution, the organic layer was separated and the water layer was extracted with ether. The ether extract and the toluene layer were combined, dried over sodium carbonate, the solvents were removed by distillation and the residue was fractionated.

The hydrochlorides were prepared by treatment of a solution of the base in ether with the calculated amount of ethereal hydrogen chloride.

The methobromides were obtained by the addition of a five-molar excess of methyl bromide to a solution of the amine in 2-butanone at 0°.

Compounds which were synthesized by different processes are described below.

2-Aminomethyl- (Table I, 1) and 2-Methylaminomethyl-4,5-diphenyl-1,3-dioxolane (2) Hydrochlorides.—A solution of 10.0 g. of 2-bromomethyl-4,5-diphenyl-1,3-dioxolane in 100 cc. of absolute alcohol, which had been saturated with ammonia at 0°, was heated at 100° for 8 days in a pressure bottle. The subsequent procedure was the same as that described above.

(4) E. J. Witzemann, W. L. Evans, H. Hass and E. F. Schroeder, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 137.

In order to obtain the 2-methylaminomethyl compound, a mixture of 10.0 g. of the 2-bromomethyl derivative, 23.3 g. of sodium iodide, 4.3 g. of sodium carbonate and 100 cc. of absolute ethanol, which had been saturated with methylamine at 0° was heated in a pressure bottle for 7 days at 100° and then treated in the described manner.

2-(N-Methyl-N-β-dimethylaminoethylaminomethyl)-4,5-diphenyl-1,3-dioxolane Dimethobromide (21).—Three grams of 2-(dimethylaminoethylaminomethyl)-4,5-diphenyl-1,3-dioxolane (Table I, 19), prepared by the general method, was dissolved in 30 cc. of ether and 5 cc. of methyl bromide was added. After 2 days, the precipitate was recrystallized from ethanol–ether; m.p. 187–189° dec. The product was dissolved in ethanol at 0°, 5 g. of anhydrous sodium carbonate and 5 cc. of methyl bromide were added and the mixture, which was shaken occasionally, was allowed to remain at 0° for 1 day. The methyl bromide was removed by distillation, the hot solution was filtered, concentrated and 50 cc. of ether was added. The precipitate was recrystallized from ethanol; yield 1.5 g. (33%).

N,N′-Dimethyl-N,N′-bis-[2-(4,5-diphenyl-1,3-dioxolanyl)-methyl]-ethylenediamine Dihydrochloride (23).—A solution of 22.0 g. of 2-(methylaminomethyl)-4,5-diphenyl-1,3-dioxolane in 200 cc. of isopropyl alcohol was refluxed and 4.0 g. of ethylene bromide, dissolved in 100 cc. of isopropyl alcohol, was added, dropwise. The mixture was refluxed for 10 hours, the solvent was removed and the residue was treated with 50 cc. of 5% sodium hydroxide solution. After extraction with ether, the ether layer was dried over sodium carbonate, the solvent was removed and the unreacted 2-(methylaminomethyl) compound was removed *in vacuo* (0.01 mm.). The dihydrochloride precipitated upon the addition of the calculated amount of ethereal hydrogen chloride; yield 5 g.

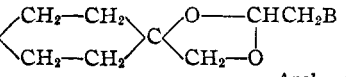
2-β-Aminoethyl-4,5-diphenyl-1,3-dioxolane Hydrochloride (24).—A mixture of 15.0 g. of 2-β-chloroethyl-4,5-diphenyl-1,3-dioxolane, 24 g. of sodium iodide, 5 g. of sodium carbonate and 100 cc. of ethanol, which had been saturated with ammonia at 0°, was heated on a steam-bath at 100° for 4 days. After treatment in the described manner, 6.3 g. (45%) of base was obtained.

The numbers after the names of the salts indicate their position in Table II.

2,3-Diphenyl-8-methyl-1,4-diox-8-azaspiro[4.5]decane, Hydrochloride (1), Methobromide (2), Allobromide (3) and Butobromide (4).—A solution of 26.0 g. of 1-methyl-4-piperidone hydrochloride[5] in 150 cc. of absolute ethanol was boiled in a flask to which a side-arm, reflux condenser and dropping funnel were attached. About 500 cc. of absolute ethanol was added from the dropping funnel over a 4-hour period, and alcohol was distilled from the mixture at the same rate it was added. Then about 200 cc. of xylene was dropped into the mixture and the distillation of alcohol was continued until practically all of the alcohol had been removed. Hydrobenzoin (38.0 g.) was added, the mixture

(5) S. M. McElvain and K. Rorig, THIS JOURNAL, **70**, 1820 (1948).

TABLE III

BASIC 1,3-DIOXASPIRO[4.5]DECANES 

Cpd. no.[a]	B	B.p., °C. base	Mm.	Yield, %	Salt	M.p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Halogen Calcd.	Halogen Found
1	$N(CH_3)_2$	69–71	0.2	85	HCl	150–152	$C_{11}H_{22}O_2NCl$	56.04	55.87	9.41	9.27	5.94	6.10	15.04	14.86
2	$N(CH_3)_2$				CH_3Br	173–175	$C_{12}H_{24}O_2NBr$	48.98	49.40	8.22	8.46	4.76	4.75	27.16	26.89
3	$N(C_2H_5)_2$	68–71	.2	97	HCl	101–102	$C_{13}H_{26}O_2NCl$	59.18	58.97	9.94	9.50	5.31	5.35	13.44	13.39
4	$NHCH_2CH_2N(CH_3)_2$	104–106	.4	73	2HCl	152–153	$C_{13}H_{28}O_2N_2Cl_2$					8.88	8.79	22.49	22.68

[a] Compounds 1, 2 and 4 were recrystallized from ethanol–ether; 3 from toluene–ether.

was refluxed and about 500 cc. of xylene was added, dropwise, while the xylene was distilled from the mixture at the same rate that it was added. This operation required about 5 hours. The product was a red, amorphous solid. After the addition of 100 cc. of 10% sodium hydroxide solution, the mixture was heated until all of the material had dissolved. The layers were separated and the aqueous layer was extracted with ether. The solvents were removed from the combined extract and xylene layer, and the residue was fractionated; b.p. 168–178° (0.2 mm.), yield 44.0 g. (78%). In this instance, and in the case of the two spirodecanes described below, a sharp boiling point could not be obtained by further fractionation, therefore, the crude amine was converted into the hydrochloride by treatment with ethereal hydrogen chloride. The base, liberated from the pure salt, boiled at 175–178° (0.6 mm.); m.p. 72–75°.

Anal. Calcd. for $C_{20}H_{23}O_2N$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.50; H, 7.41; N, 4.49.

The hydrochloride was obtained by the use of ethereal hydrogen chloride.

The methobromide was prepared by the addition of excess methyl bromide at 0° to a solution of the base in methyl ethyl ketone; after 7 days the precipitate was filtered.

The allobromide and the butobromide were obtained in the same manner as the methobromide.

2,3-Diphenyl-8-ethyl-1,4-diox-8-azaspiro[4.5]decane.—1-Ethyl-4-piperidone hydrochloride[6] (42.0 g.) and 55.0 g. of hydrobenzoin were allowed to react in the manner described above for the 8-methyl homolog; b.p. 180–184° (0.7 mm.), m.p. 60–63°, yield 74.0 g. (89%).

Anal. Calcd. for $C_{21}H_{25}O_2N$: C, 77.99; H, 7.79; N, 4.33. Found: C, 77.86; H, 8.03; N, 4.35.

2,3,6-Triphenyl-8-methyl-1,4-diox-8-azaspiro[4.5]decane.—1-Methyl-3-phenyl-4-piperidone hydrochloride[7] (18.0 g.) and 21.3 g. of hydrobenzoin were treated in the described manner. However, in this instance, after the xylene had been added, the mixture was refluxed for 21 hours; b.p. 228–232° (0.5 mm.), m.p. 149–150°, yield 12.0 g. (39%).

Anal. Calcd. for $C_{26}H_{27}O_2N$: C, 81.00; H, 7.06; N, .63. Found: C, 81.01; H, 7.18; N, 3.67.

2-Bromomethyl-1,3-dioxaspiro[4.5]decane.—A mixture of 27.0 g. of 1-(hydroxymethyl)-cyclohexanol[8] and 41.0 g. of bromoacetal was heated at 130° until nearly the calculated amount of ethanol had distilled from the mixture, and the residue was then fractionated; b.p. 128–130° (14 mm.), yield 40.0 g. (82%).

Anal. Calcd. for $C_9H_{15}O_2Br$: C, 45.97; H, 6.43; Br, 33.99. Found: C, 45.64; H, 6.41; Br, 33.83.

2-Dimethylaminomethyl-1,3-dioxaspiro[4.5]decane.—A mixture of 10.0 g. of 2-bromomethyl-1,3-dioxaspiro[4.5]-decane, 15 g. of dimethylamine, 24 g. of sodium iodide, 5 g. of sodium carbonate and 50 cc. of toluene was heated on a steam-bath in a pressure bottle for 6 days and then treated in the described manner; yield 7.2 g. (85%), b.p. 69–71° (0.2 mm.).

The bases of compounds 3 and 4 (Table III) were prepared by a process similar to that described above.

(6) This base was obtained in 52% yield from ethyl di-(β-carbethoxyethyl)-amine (A. Ziering, L. Berger, S. Heineman and J. Lee, *J. Org. Chem.*, **12**, 894 (1947)) and sodium hydride by a described method.[5]

(7) B. Barna, Dissertation, University of Michigan, 1952.

(8) Obtained as a by-product (3% yield) during the preparation of cycloheptanone (F. F. Blicke, N. J. Doorenbos and R. H. Cox, THIS JOURNAL, **74**, 2924 (1952)).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA]

Preparation of Some 1-Alkyl-1,2-dihydro-3-hydroxybenzo[g]quinoxaline-5,10-diones

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It has been shown that aliphatic secondary amines react with 2-chloro-3-chloroacetamido-1,4-naphthoquinone to form 1-alkyl-1,2-dihydro-3-hydroxybenzo[g]quinoxaline-5,10-diones. Except in the case of diethylamine, the intermediate 2-dialkylamino-3-chloroacetamido derivatives can be isolated. Morpholine reacted in a similar manner to form 1-β-chloroethoxyethyl-1,2-dihydro-3-hydroxybenzo[g]quinoxaline-5,10-dione.

During the course of a recent study of 1-H-naphthimidazole-4,9-diones[1] it was observed that diethylamine reacted with 2-chloro-3-chloroacetamido-1,4-naphthoquinone in dry benzene solution in an anomalous manner. Instead of the expected replacement product, 2-diethylamino-3-chloroacetamido-1,4-naphthoquinone, a compound was obtained which contained no chlorine and whose physical properties were different from those expected of the normal replacement product. Repetition of this work and analysis of a carefully purified sample showed a difference in carbon, hydrogen and chlorine, from the expected product, equivalent to ethyl chloride. This suggested the intermediate formation of an intramolecular quaternary ammonium salt which subsequently lost a molecule of ethyl chloride according to the reaction shown.

The work has now been extended to reactions with di-*n*-propylamine, di-*n*-butylamine and morpholine under similar conditions. These amines reacted with 2-chloro-3-chloroacetamido-1,4-naphthoquinone to form the corresponding 2-dialkylamino-3-chloroacetamido derivatives. The di-*n*-propylamino and di-*n*-butylamino derivatives when heated in a polar solvent, such as ethylene glycol or nitrobenzene, rapidly changed color and products were isolated which corresponded to that ob-

(1) J. R. E. Hoover and A. R. Day, THIS JOURNAL, **76**, 4148 (1954).