The liquid **dimethyl ester of *trans*-2-methyl-2-carboxycyclohexane-1-β-propionic acid** (V) obtained by evaporation of the filtered methanol solution was then cyclized in the same way as the *cis* isomer, seven hours being allowed for the reaction. The cyclic keto ester gave a bluish-violet color with an alcoholic solution of ferric chloride. Hydrolysis of the keto ester and decarboxylation was carried out as described and the ***trans*-8-methyl-1-hydrindanone** was obtained as a colorless liquid with a camphor-like odor by distillation at 116–120° at 35 mm.; weight, 1.14 g. On redistillation it boiled at 108–109° at 20 mm.; $n^{25.8}D$ 1.4807.

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.9; H, 10.6. Found: C, 78.8; H, 10.3.

The **semicarbazone** after recrystallization from *n*-butyl alcohol melted at 234° when the melting point tube was placed in the bath at 190°. A mixture of the semicarbazones of *cis*- and *trans*-8-methyl-1-hydrindanones melted at 206–208°.

Anal. Calcd. for $C_{11}H_{19}ON_3$: N, 20.0. Found: N, 20.1.

The **oxime** after recrystallization from aqueous alcohol melted at 113–115.5°. Mixed with the oxime of the *cis* cyclic ketone it melted at 74–90°.

Anal. Calcd. for $C_{10}H_{17}ON$: N, 8.4. Found: N, 8.2.

Summary

The synthesis of the *cis* and *trans* forms of 8-methyl-1-hydrindanone from cyclohexanone is described. The *cis* and *trans* forms of 2-methyl-2-carboxycyclohexane-1-acetic acid were prepared, the acetic acid side chain was lengthened to a propionic acid group through the Arndt–Eistert synthesis and the esters of the resulting products were cyclized by the Dieckmann method.

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

Synthetic Mydriatics. III

BY F. F. BLICKE AND H. M. KAPLAN[1,2]

Although atropine is the most outstanding mydriatic of the ester type, it is known that certain esters, simpler than the alkaloid in structure, produce strong mydriasis.[3] These esters, like atropine, represent combination of a basic alcohol with an arylhydroxy aliphatic acid. The basic alcohol may be as simple as β-dimethylaminoethanol, or somewhat more complex such as β,β-dimethyl-γ-piperidinopropanol. The acid may be a substituted acetic or propionic acid.

Hitherto, no systematic study has been made to determine which basic alcohols and arylhydroxy acids are most suitable for the preparation of esters which possess mydriatic properties. During this investigation fifty-two products have been synthesized which represent combinations of phenylhydroxyacetic (mandelic), diphenylhydroxyacetic (benzilic), α-phenyl-α-hydroxypropionic (atrolactic), α-phenyl-β-hydroxypropionic (tropic), β-phenyl-α-hydroxypropionic, β-phenyl-β-hydroxypropionic or β,β-diphenyl-β-hydroxypropionic acid with one of fourteen different basic alcohols.

The esters were obtained by interaction of the phenylhydroxy acid with the required basic alkyl halide according to the procedure of Horenstein and Pählicke.[4]

The compounds, in the form of hydrochlorides, hydrobromides, phosphates or methobromides, were tested by Dr. John G. Beall for mydriatic and local anesthetic activity by surface application of freshly-prepared 2% aqueous solutions to the rabbit's cornea. The pharmacological data are reported in Table I, column I.

It was found that most of the esters which are strong mydriatics are also strong local anesthetics. With the possible exception of compound 34, β,β-dimethyl-γ-dimethylaminopropyl α-phenyl-α-hydroxypropionate (27) was the only strongly active mydriatic found which did not produce local anesthesia. In view of the high activity of compound 27, it seems strange that compound 28, the next higher homolog,[5] should have been found to be completely inactive. The strong local anesthetics, compounds 22, 23, 48, 51 and 52, do not dilate the pupil.

Since tropyl mandelate (homatropine) is an

(1) This paper represents part of a dissertation submitted to the Horace H. Rackham School of Graduate Studies by H. M. Kaplan in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

(2) Lilly Endowment Fellow.

(3) (a) Blicke and Maxwell, THIS JOURNAL, **64**, 428 (1942); (b) **64**, 431 (1942).

(4) Horenstein and Pählicke, *Ber.*, **71**, 1654 (1938).

(5) Probably in the strict sense of the term, the next higher homolog of a compound which contains the dimethylamino group would be the corresponding methylethylamino, and not the diethylamino derivative.

active, widely-used mydriatic it was expected that some of the simpler basic-alkyl esters of mandelic acid would exhibit activity. However, every ester of this acid proved to be inactive as a mydriatic and, with three exceptions, these esters do not produce local anesthesia.

Several striking facts were discovered in the benzilic acid series. Six out of the eleven esters

TABLE I

ESTER SALTS AND METHOBROMIDES

The products were recrystallized from the following solvents: 2, 21 and 22 from ethyl acetate; 8 and 9 from dilute alcohol; 11 from alcohol; 1, 3, 4, 5, 6, 7, 10, 13, 14, 18, 19, 23, 24, 26, 31, 32, 34, 36, 38–46, 48, 50 and 51 from a mixture of alcohol and ethyl acetate; 12, 15, 16, 17, 20, 25, 27, 28, 29, 30, 33, 37, 47, 49 and 52 were precipitated from an alcoholic solution by ether; the oil, 35, after precipitation from an alcoholic solution by ether was washed repeatedly with absolute ether.

	R	I[a]	M. p., °C.	Formula	Halogen, % Calcd.	Found
	Esters of phenylhydroxyacetic acid (mandelic acid), $C_6H_5CH(OH)COOR$					
1	$CH_2CH_2N(C_3H_7)_2 \cdot HCl$	0 (I)	116–118	$C_{16}H_{26}O_3NCl$	11.23	11.13
2	$CH_2CH_2N(C_4H_9)_2 \cdot HCl$	0 (I)	104–106	$C_{18}H_{30}O_3NCl$	10.31	10.31
3	$CH_2CH_2NC_5H_{10} \cdot HBr$[b]	0 (I)	140–141	$C_{15}H_{22}O_3NBr$	23.21	23.29
4	$CH_2CH_2CH_2N(C_4H_9)_2 \cdot HCl$	0 (I)	92–93	$C_{19}H_{32}O_3NCl$	9.91	10.03
5	$CH_2CH_2CH_2NC_5H_{10} \cdot HCl$	0 (I)	136–137	$C_{16}H_{24}O_3NCl$	11.30	11.33
6	$CH_2C(CH_3)_2CH_2(CH_3)_2 \cdot HCl$	0 (I)	117–118	$C_{15}H_{24}O_3NCl$	11.75	11.79
7	$CH_2C(CH_3)_2CH_2N(CH_3)_2 \cdot CH_3Br$[c]	0 (S)	145–146	$C_{16}H_{26}O_3NBr$	22.18	22.12
8	$CH_2C(CH_3)_2CH_2N(C_2H_5)_2$ (base)[d]	0 (G)	66–67[e]	...	...	...
9	$CH_2C(CH_3)_2CH_2NC_5H_{10}$ (base)[d]	0 (G)	96–97	$C_{18}H_{27}O_3N$	(4.59	4.83 N)
	Esters of diphenylhydroxyacetic acid (benzilic acid), $(C_6H_5)_2C(OH)COOR$					
10	$CH_2CH_2N(CH_3)_2 \cdot HCl$	++++ (E)	183–185	$C_{18}H_{22}O_3NCl$	10.56	10.51
11	$CH_2CH_2N(C_3H_7)_2 \cdot HCl$	0 (G)	152–153	$C_{22}H_{30}O_3NCl$	9.05	8.96
12	$CH_2CH(CH_3)N(C_2H_5)_2 \cdot HCl$	+++ (G)	163–164	$C_{21}H_{28}O_3NCl$	9.38	9.42
13	$CH_2CH(CH_3)N(C_4H_9)_2 \cdot HCl$[f]	0 (G)	167–168	$C_{25}H_{36}O_3NCl$	8.17	8.13
14	$CH_2CH_2CH_2N(C_2H_5)_2 \cdot HCl$	+++++ (E)	145–146	$C_{21}H_{28}O_3NCl$	9.38	9.41
15	$CH\ CH\ CH_2N(C_3H_7)_2 \cdot HCl$	0 (G)	158–159	$C_{23}H_{32}O_3NCl$	8.73	8.75
16	$CH_2CH_2CH_2N(C_4H_9)_2 \cdot HCl$	0 (G)	114–115	$C_{25}H_{36}O_3NCl$	8.17	8.23
17	$CH_2CH_2CH_2N(C_4H_9)_2 \cdot CH_3Br$	0 (G)	166–167	$C_{26}H_{38}O_3NBr$	16.23	16.37
18	$CH_2C(CH_3)_2CH_2N(CH_3)_2 \cdot HCl$	++++ (E)	169–170	$C_{21}H_{28}O_3NCl$	9.38	9.33
19	$CH_2C(CH_3)_2CH_2N(CH_3)_2 \cdot CH_3Br$	++++ (E)	150–151	$C_{22}H_{30}O_3NBr$	18.31	18.40
20	$CH_2C(CH_3)_2CH_2N(C_2H_5)_2 \cdot HCl$[g]	++++ (E)	139–140[h]	$C_{23}H_{32}O_3NCl$	8.73	8.84
	Esters of α-phenyl-α-hydroxypropionic acid (atrolactic acid), $CH_3C(C_6H_5)(OH)COOR$					
21	$CH_2CH_2N(C_2H_5)_2 \cdot HCl$	0 (I)	108–109	$C_{15}H_{24}O_3NCl$	11.75	11.73
22	$CH_2CH_2N(C_4H_9)_2 \cdot HCl$	0 (E)	120–121	$C_{19}H_{32}O_3NCl$	9.91	9.91
23	$CH_2CH_2NC_5H_{10} \cdot HCl$	0 (E)	161–162	$C_{16}H_{24}O_3NCl$	11.30	11.35
24	$CH_2CH_2NC_5H_{10} \cdot CH_3Br$	0 (I)	149–150	$C_{17}H_{26}O_3NBr$	21.47	21.59
25	$CH_2CH_2CH_2N(C_4H_9)_2 \cdot HCl$	0 (G)	93–94	$C_{20}H_{34}O_3NCl$	9.53	9.70
26	$CH_2CH_2CH_2NC_5H_{10} \cdot HCl$	0 (S)	130–131	$C_{17}H_{26}O_3NCl$	10.82	10.77
27	$CH_2C(CH_3)_2CH_2N(CH_3)_2 \cdot HCl$	+++ (I)	128–129	$C_{16}H_{23}O_3NCl$	11.23	11.31
28	$CH_2C(CH_3)_2CH_2N(C_2H_5)_2 \cdot H_3PO_4$	0 (I	150–151	$C_{18}H_{32}O_7NP$	(3.46	3.51 N)
	Esters of α-phenyl-β-hydroxypropionic acid (tropic acid), $CH_2(OH)CH(C_6H_5)COOR$					
29	$CH_2CH_2N(C_2H_5)_2 \cdot CH_3Br$[i]	++ (I)	99–101	$C_{16}H_{26}O_3NBr$	22.18	22.24
30	$CH_2CH_2N(C_4H_9)_2 \cdot CH_3Br$	0 (I)	131–132	$C_{20}H_{34}O_3NBr$	19.19	19.19
31	$CH_2CH_2CH_2N(C_4H_9)_2 \cdot CH_3Br$	0 (I)	127–128	$C_{21}H_{36}O_3NBr$	18.57	18.62
32	$CH_2CH_2CH_2NC_5H_{10} \cdot HCl$	++ (S)	127–128[j]	$C_{17}H_{26}O_3NCl$	10.82	10.83
33	$CH_2C(CH_3)_2CH_2N(CH_3)_2 \cdot H_3PO_4$	++ (I)	143–144	$C_{16}H_{28}O_7NP$	(3.71	3.74 N)
34	$CH_2C(CH_3)_2CH_2N(C_2H_5)_2 \cdot H_3PO_4$[k]	++ to +++ (I)	139–141[l]	...	...	...
	Esters of β-phenyl-α-hydroxypropionic acid, $C_6H_5CH_2CH(OH)COOR$					
35	$CH_2CH_2N(C_2H_5)_2 \cdot CH_3Br$	0 (I)	oil	$C_{16}H_{26}O_3NBr$	22.18	22.16
36	$CH_2CH_2NC_5H_{10} \cdot HCl$	0 (I)	128–129	$C_{16}H_{24}O_3NCl$	11.30	11.34
37	$CH_2CH_2CH_2NC_5H_{10} \cdot CH_3Br$	0 (I)	116–118	$C_{18}H_{28}O_3NBr$	20.69	20.93
38	$CH_2C(CH_3)_2CH_2N(CH_3)_2 \cdot CH_3Br$	0 (I)	164–166	$C_{17}H_{28}O_3NBr$	21.35	21.46
39	$CH_2C(CH_3)_2CH_2N(C_2H_5)_2 \cdot HCl$	0 (I	99–100	$C_{18}H_{30}O_3NCl$	10.31	10.46

TABLE I (*Concluded*)

	R	I[a]	M. p., °C.	Formula	Halogen, % Calcd.	Found
	Esters of β-phenyl-β-hydroxypropionic acid, $C_6H_5CH(OH)CH_2COOR$					
40	$CH_2CH_2N(C_4H_9)_2 \cdot CH_3Br$	0 (I)	129–131	$C_{20}H_{34}O_3NBr$	19.19	19.06
41	$CH_2CH_2NC_5H_{10} \cdot HCl$	0 (I)	102–103	$C_{16}H_{24}O_3NCl$	11.30	11.38
42	$CH_2CH_2NC_5H_{10} \cdot CH_3Br$	0 (I)	113–115	$C_{17}H_{26}O_3NBr$	21.47	21.67
43	$CH_2CH_2CH_2N(C_4H_9)_2 \cdot CH_3Br$	0 (I)	87–89	$C_{21}H_{36}O_3NBr$	18.57	18.76
44	$CH_2CH_2CH_2NC_5H_{10} \cdot HCl$	0 (I)	143–144	$C_{17}H_{26}O_3NCl$	10.82	10.93
45	$CH_2C(CH_3)_2CH_2N(CH_3)_2 \cdot CH_3Br$	0 (I)	117–119	$C_{17}H_{28}O_3NBr$	21.35	21.40
46	$CH_2C(CH_3)_2CH_2N(C_2H_5)_2 \cdot HCl$	0 (I)	89–90	$C_{18}H_{30}O_3NCl$	10.31	10.35
	Esters of β,β-diphenyl-β-hydroxypropionic acid, $(C_6H_5)_2C(OH)CH_2COOR$					
47	$CH_2CH_2N(C_2H_5)_2 \cdot HCl$	++ (G)	144–146	$C_{21}H_{28}O_3NCl$	9.38	9.41
48	$CH_2CH_2N(C_3H_7)_2 \cdot HCl$	0 (E)	115–116	$C_{23}H_{32}O_3NCl$	8.73	8.77
49	$CH_2CH_2NC_5H_{10} \cdot HCl$	0 (G)	169–171	$C_{22}H_{28}O_3NCl$	9.09	9.12
50	$CH_2CH_2CH_2N(C_2H_5)_2 \cdot HCl$	0 (G)	143–145	$C_{22}H_{30}O_3NCl$	9.05	8.94
51	$CH_2CH_2CH_2NC_5H_{10} \cdot HCl$	0 (E)	127–128	$C_{23}H_{30}O_3NCl$	8.78	8.82
52	$CH_2C(CH_3)_2CH_2N(CH_3)_2 \cdot HCl$	0 (E)	136–138	$C_{22}H_{30}O_3NCl$	9.05	9.21

[a] Mydriatic activity: 0 = inactive; + = poor; ++ = moderate; +++ = good; ++++ = excellent. Local anesthetic activity: (I) = inactive; (S) = slight; (G) = good; (E) = excellent. [b] NC_5H_{10} = piperidino. Since we were rather surprised to find that the hydrochloride of this ester is inactive (Blicke and Maxwell, THIS JOURNAL, **64,** 432 (1942)) it was prepared again and tested as the hydrobromide. [c] Methobromide. [d] Tested pharmacologically in the form of the hydrochloride. [e] German Patent 594,085 (*C. A.*, **28,** 3417 (1934)), m. p. 67°. [f] Because of the relative insolubility of the hydrochloride a 0.5% solution, instead of 2%, was employed in the tests. [g] The hydrochloride, as well as the methosulfate, was described by Fromherz (*Arch. Exptl. Path. Pharmakol.*, **173,** 86 (1933)) as an active mydriatic. [h] German Patent 586,247 (*Chem. Zentr.*, **105,** I, 248 (1934)), m. p. 141–142°. [i] Hygroscopic. [j] Obtained as an oil by von Braun, Braunsdorf and Räth (*Ber.*, **55,** 1675 (1922)). [k] This substance is the commercial antispasmodic Syntropan. It has been recommended for diagnostic use in ophthalmology; see Fromherz, *J. Pharmacol. Exptl. Therap.*, **60,** 5 (1937). [l] Horenstein and Pählicke (*Ber.*, **71,** 1656 (1938)), m. p. 138–140°. The ester hydrochloride has been described in German Patent 594,085 (*Chem. Zentr.*, **105,** I, 3236 (1934)).

are very active as mydriatics and all eleven are strong anesthetics. In several instances the next higher homolog of a very effective mydriatic proved to be completely inactive. Thus the β-dimethylaminoethyl (10) and the β-diethylaminoethyl[3a] esters are very potent, while the β-dipropylaminoethyl (11) and the β-dibutylaminoethyl[3a] esters are inactive. Furthermore, the γ-diethylaminopropyl (14) ester produces strong dilation of the pupil but the γ-dipropylaminopropyl (15) and the γ-dibutylaminopropyl (16) esters are without effect.

Among the esters of α-phenyl-α-hydroxypropionic and α-phenyl-β-hydroxypropionic acids only one compound is a strong mydriatic.

All esters of β-phenyl-α-hydroxypropionic and β-phenyl-β-hydroxypropionic acid which we prepared possess neither mydriatic nor local anesthetic properties.

Only one ester (47) of β,β-diphenyl-β-hydroxypropionic acid shows some activity as a mydriatic; all of these esters are active anesthetics.

Since forty of the products prepared are entirely inactive as mydriatics, it is very evident that the mere presence of a basic nucleus in the alcoholic radical of the ester, and a phenyl and a hydroxyl group in the acyl radical do not ensure activity. The nature of the basic nucleus and the positions occupied by the phenyl and hydroxyl groups are of prime importance.

Experimental Part

No comments relative to the preparation of mandelic,[6] benzilic,[7] atrolactic,[8] tropic[9] and β,β-diphenyl-β-hydroxypropionic acid[10] are necessary.

β-Phenyl-β-hydroxypropionic acid was obtained by hydrolysis of the ethyl ester[11] with 20% potassium hydroxide solution.

β-Phenyl-α-hydroxypropionic acid was prepared in the following manner. Benzylmagnesium chloride was allowed to react with ethyl orthoformate, the phenylacetaldehyde diethylacetal hydrolyzed to the aldehyde, the latter converted to the cyanohydrin, and this substance hydrolyzed to the acid.

An ether solution of 148 g. of ethyl orthoformate was added slowly to benzylmagnesium chloride prepared from 126.5 g. of benzyl chloride, 600 cc. of ether and 24.3 g. of magnesium. The mixture was refluxed for five hours.

(6) Mandelonitrile ("Organic Syntheses," Coll. Vol. I, p. 336 (second edition)) was hydrolyzed with hydrochloric acid.

(7) "Organic Syntheses," Coll. Vol. I, p. 89 (second edition).

(8) McKenzie and Wood, *J. Chem. Soc.*, **115,** 833 (1919).

(9) Purchased from the Eastman Kodak Company. A synthetic procedure has just been described by Burtner and Cusic (THIS JOURNAL, **65,** 266 (1943)).

(10) Rupe and Busolt, *Ber.*, **40,** 4539 (1907).

(11) "Organic Syntheses," Vol. 21, p. 51.

During this time a precipitate formed and a secondary reaction[12] may set in, often quite suddenly; in this event external cooling is required to prevent the reaction from becoming uncontrollable.[13] The Grignard complex was decomposed with ammonium chloride solution, the ether layer separated and the aqueous layer extracted with ether. The ether solution was dried, the solvent removed and the phenylacetaldehyde diethylacetal distilled; b. p. 114–120° (15 mm.)[14]; yield 136 g. (70%).

A mixture of 87 g. of the acetal and 500 cc. of 10% sulfuric acid was boiled in a flask fitted with an inclined condenser. The aldehyde distilled from the mixture and was collected in a separatory funnel from which it was allowed to drop into a well-stirred saturated sodium bisulfite solution. The sulfuric acid solution was prevented from becoming too strong during the distillation by the addition of water at frequent intervals. The precipitated bisulfite addition product was filtered, washed with ether, made into a paste with water and then stirred with a saturated potassium cyanide solution. The cyanohydrin separated as an oil which solidified when cooled. The latter was placed in an evaporating dish and heated on a steam-bath with 100 cc. of 18% hydrochloric acid until solid material formed, and then allowed to remain at room temperature for twelve hours. Evaporation was continued until the pasty product solidified when cooled. The material was dried, powdered and the propionic acid extracted with benzene; yield 24 g.[15]; m. p. 95–96°.[15]

The basic alkyl chlorides were liberated from their hydrochlorides with saturated sodium carbonate solution, and distilled just prior to use.[16] The chloride hydrochlorides were obtained from the basic alcohols and thionyl chloride.[17a,b,c]

Most of the basic alkyl chlorides have been described in the literature: β-dimethylaminoethyl,[17b] β-diethylaminoethyl,[17a,b] β-dipropylaminoethyl,[18] β-dibutylaminoethyl,[19] β-piperidinoethyl,[20] β-diethylaminopropyl,[17b] β-dibutylaminopropyl,[21] γ-diethylaminopropyl,[22] γ-dipropylaminopropyl,[23] γ-dibutylaminopropyl,[24] γ-piperidinopropyl,[25] β,β-dimethyl-γ-dimethylaminopropyl,[26] β,β-dimethyl-γ-diethylaminopropyl,[27] β,β-dimethyl-γ-piperidinopropyl.[27]

In order to obtain the esters, molecular equivalent amounts (0.03–0.05 mole) of the hydroxy acid and the basic chloride were dissolved in 50 cc. of isopropyl alcohol, which had been dried over calcium oxide, and refluxed for twelve hours. The solvent was removed under reduced pressure and the ester hydrochloride washed repeatedly with absolute ether. After this operation the yield of crude ester hydrochloride often was as high as 80–90%. Usually the yield of recrystallized product was 50–60%, but the amount could have been increased by recovery of dissolved material in the mother liquors. In a few instances it was necessary, in order to obtain a crystalline salt, to treat the oily ester base with the calculated amount of concentrated hydrochloric or phosphoric acid.

Methobromides were produced when the ester bases, dissolved in absolute alcohol, were allowed to remain in contact with excess methyl bromide for twenty-four hours at ordinary temperature.

Summary

Fifty-two esters have been prepared which represent combination of phenylhydroxyacetic (mandelic), diphenylhydroxyacetic (benzilic), α-phenyl-α-hydroxypropionic (atrolactic), α-phenyl-β-hydroxypropionic (tropic), β-phenyl-α-hydroxypropionic, β-phenyl-β-hydroxypropionic or β,β-diphenyl-β-hydroxypropionic acid with one of fourteen different basic alcohols. Six esters of benzilic acid were found to be strong mydriatics as well as good topical anesthetics. All esters of β-phenyl-α-hydroxypropionic and β-phenyl-β-hydroxypropionic acids proved to be devoid of mydriatic as well as anesthetic properties.

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(12) See Smith and Bayliss, *J. Org. Chem.*, **6**, 437 (1934).

(13) In one instance the mixture was allowed to remain overnight at room temperature; during this time the secondary reaction took place and the contents were blown out of the flask.

(14) Tschitschibabin (*Ber.*, **37**, 188 (1904)) found 245–246°.

(15) The procedure described is slightly different from that employed by La Mer and Greenspan (THIS JOURNAL, **56**, 1494 (1934)); our yield is more than four times that reported by these investigators. They found the melting point to be 95–96°.

(16) Because of their tendency to cyclize, the chlorides were preserved as hydrochlorides.

(17) (a) Gough and King, *J. Chem. Soc.*, 2436 (1928); (b) Slotta and Behnisch, *Ber.*, **68**, 754 (1935); (c) Mason and Block, THIS JOURNAL, **62**, 1443 (1940).

(18) B. p. 77–79° (19 mm.).

(19) Blicke and Maxwell, THIS JOURNAL, **64**, 429 (1942).

(20) B. p. 69° (12 mm.). Dunlop (*J. Chem. Soc.*, **101**, 2002 (1912)) prepared the chloride hydrochloride, and stated that it melts at 231° although other investigators had reported 208°. We found the melting point to be 229–230°.

(21) B. p. 116–120° (29 mm.).

(22) Magidson and Strukow, *Arch. Pharm.*, **271**, 572 (1933).

(23) B. p. 99–102°. The alcohol was obtained from trimethylene chlorohydrin and diprepylamine according to the directions given by Samdahl and Weider (*Bull. soc. chim.*, (5) **2**, 2014 (1935)) for another substance.

(24) Blicke and Jenner, THIS JOURNAL, **64**, 1723 (1942). The chloroaurate melts at 143–146° after recrystallization from dilute alcohol. *Anal.* Calcd. for $C_{11}H_{25}NCl_3Au$: Au, 36.13. Found: Au, 36.06.

(25) Hörlein and Kneisel, *Ber.*, **39**, 1432 (1906).

(26) B. p. 44–49° (14 mm.). The chloride hydrobromide has been described by Blicke and Otsuki, THIS JOURNAL, **63**, 1947 (1941).

(27) Mannich and Baumgarten, *Ber.*, **70**, 210 (1937).