ylamino-4,4-diphenylheptane, and *dl*-ethyl 4-dimethylamino-2,2-diphenylvalerate hydrochlorides have been prepared using *d*- and *l*-4-dimethylamino-2,2-diphenylvaleronitrile as the starting materials.

INDIANAPOLIS, INDIANA RECEIVED JULY 21, 1948

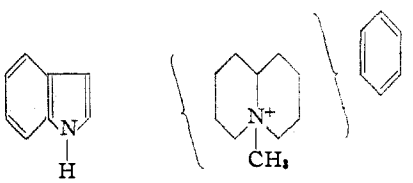
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Curariform Activity and Chemical Structure. III. Syntheses in the 3-Indolylmethylamine Series[1]

BY L. E. CRAIG[2] AND D. S. TARBELL

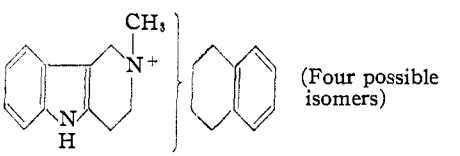
The most physiologically effective of the curare alkaloids belong to the calabash curare group. Of the eighteen alkaloids which have been isolated from calabash curare, the most active is C-toxiferine-I, which paralyzes frogs in doses of 0.005–0.009 mg./kg.[3]

Karrer and Schmid[4] showed that C-curarine-I chloride ($C_{20}H_{21}ClN_2$) contains a secondary, non-basic nitrogen, which is the nitrogen of an indole ring-system, and a quaternary nitrogen present in a tetrahydroisoquinoline ring system, common to two rings, and containing a methyl group. On the basis of this, the following structure can be drawn



Since the benzene ring must be attached in a position to give a tetrahydroisoquinoline, fourteen isomeric hexahydrobenzoindoloquinolizines are possible.

The most probable structures are those in which the quaternary nitrogen is separated from the indole ring by one carbon. On the basis of similarity of color reactions, Schmid and Karrer[3] postulated that C-toxiferine-I might be related to tetrahydro-9-pyrido(3,4-b)indoles, which would mean that the above proposed structure would have the β-carboline arrangement of the nitrogen atoms. Wieland, Witkop and Bähr[5] isolated isoquinoline, skatole and impure 3-ethylindole from a zinc dust distillation of another of the calabash curare alkaloids, C-dihydrotoxiferine-I chloride ($C_{20}H_{23}ClN_2$). The isolation of the 3-ethylindole supports the β-carboline structure proposed by Schmid and Karrer; however, the isolation of skatole suggests the γ-carboline structure, as follows:



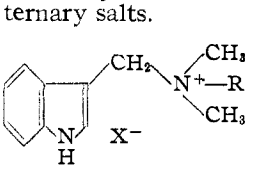
The present papers reports the synthesis of, and the preliminary pharmacological tests on, compounds containing a quaternary nitrogen in the γ-carboline structure, that is, 3-indolylmethylammonium salts.

The 3-indolylmethylamines were prepared conveniently by the Mannich reaction, essentially by the method of Kühn and Stein.[6]

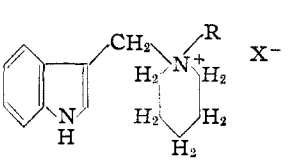
When the Mannich reaction was attempted with indole, formaldehyde and 1,2,3,4-tetrahydroisoquinoline hydrochloride, methylene-bis-(N,N'-1,2,3,4-tetrahydroisoquinoline) and a polymeric material[7] were obtained. The methylene-bis-compound was obtained in good yield when the amine hydrochloride and aqueous formaldehyde were heated together. Attempts to prepare derivatives of this previously unreported compound led to some anomalous results.

On treatment of the methylene-bis-compound with ethanolic picric acid, the picrate of 1,2,3,4-tetrahydroisoquinoline was obtained. Treatment of the bis-compound with methyl iodide yielded N,N-dimethyl-1,2,3,4-tetrahydroisoquinolinium iodide. The cleavage of the methylenediamine linkage with ethanolic picric acid is not without precedent, as Elderfield and Kreysa[8] reported a similar reaction.

The tertiary 3-indolylmethylamines were converted by conventional methods into various quaternary salts.



I, R = $-CH_3$
II, R = $-CH_2C_6H_5$
III, R = $-CH_2CH_2C_6H_5$



IV, R = $-CH_3$
V, R = $-CH_2C_6H_5$

(1) For the second paper of this series, see Craig and Tarbell, THIS JOURNAL, **70**, 2783 (1948).

(2) Aided by a Grant from the National Foundation for Infantile Paralysis. Present address, General Aniline and Film Corporation, Easton, Pennsylvania.

(3) Schmid and Karrer, *Helv. chim. acta*, **30**, 1162 (1947).

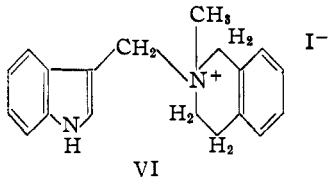
(4) Karrer and Schmid, *ibid.*, **29**, 1853 (1946).

(5) Wieland, Witkop and Bähr, *Ann.*, **558**, 144 (1947).

(6) Kühn and Stein, *Ber.*, **70**, 567 (1937).

(7) Indole has been reported to polymerize in the presence of acids; see Schmitz-Dumont, Hamann and Diebold, *ibid.*, **71**, 205 (1938).

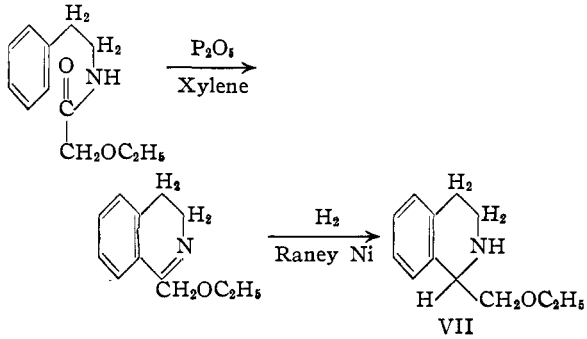
(8) Elderfield and Kreysa, THIS JOURNAL, **70**, 44 (1948).



VI

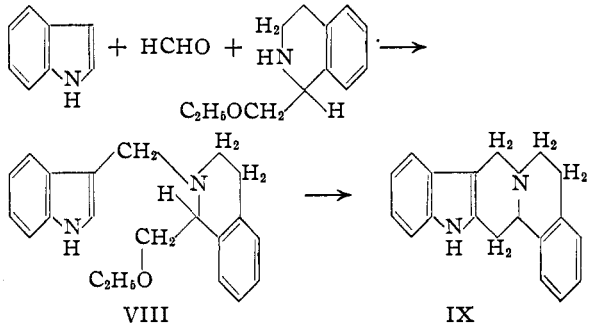
Compound VI is an open-chain analog of the γ-carboline ring system which was suggested for the calabash curare alkaloids.

Unsuccessful attempts were made to synthesize the complete hexahydrobenzoindoloquinolizine ring system (IX) by ring closure of 1-ethoxymethyl-2-(3-indolylmethyl)-1,2,3,4-tetrahydroisoquinoline (VIII). 1-Ethoxymethyl-1,2,3,4-tetrahydroisoquinoline (VII) was obtained by hydrogenation of the 1-ethoxymethyl-3,4-dihydroisoquinoline prepared by the Bischler–Napieralski reaction from N-(β-phenylethyl)-ethoxyacetamide; by condensation of VII with indole by the Mannich



VII

reaction, 1-ethoxymethyl-2-(3-indolylmethyl)-1,2,3,4-tetrahydroisoquinoline (VIII) was obtained in good yield.



VIII IX

Conventional methods for ether cleavage were applied to compound VIII with the hope that ring-closure to the indole ring might occur simultaneously with the cleavage of the ethoxyl group, thus forming the hexahydrobenzoindoloquinolizine (IX). The Mannich base (VIII) was treated with anhydrous aluminum bromide in refluxing benzene, concentrated hydriodic acid at reflux, boron tribromide[9,10] in refluxing benzene, zinc chloride in refluxing acetic acid, and phosphorus trichloride in refluxing benzene. Very dark tars were obtained which did not yield any desired product on attempted purifications by crystallizations and chromatography.

Compounds I, II, V and VI exhibited typical curare-like activity in mice. Compound VI was effective when injected intraperitoneally in doses of less than 16 mg./kg. and when given orally in doses of approximately 80 mg./kg. Compounds I, II and V were effective when injected intraperitoneally in doses of 40, 60 and 80 mg./kg., respectively. Compound III was ineffective in doses of 60 mg./kg. and Compound IV was a convulsant poison. While the most effective of these compounds, compound VI, has only a very small fraction of the activity of C-toxiferine-I, it is significant to note that the 3-indolylmethyl group greatly enhances curariform activity, because N,N-dimethyl-1,2,3,4-tetrahydroisoquinolinium iodide was found to be ineffective in doses of 200 mg./kg.[11]

Experimental[12]

3-Indolylmethyltrimethylammonium Iodide (Gramine Methiodide)[6,13] (I).—A solution of 25 g. (0.144 mole) of gramine and 21 g. (0.148 mole) of methyl iodide in 200 cc. of absolute ethanol was allowed to stand in the dark for twenty hours. The precipitate was collected, slurried with cold ethanol, and again collected by filtration to give 30.8 g. (97.5%) of colorless leaflets which darken at 150–200° but do not melt under 300°.[14]

Benzyldimethyl-3-indolylmethylammonium Bromide (II).—A solution of 1.74 g. (0.01 mole) of gramine and 1.71 g. (0.01 mole) of benzyl bromide in 25 cc. of absolute ethanol was allowed to stand at room temperature for sixteen hours. Upon adding ether to the orange solution, 1.2 g. (35%) of tan powder was obtained, which gave 1.0 g. (29%) of colorless crystals on recrystallization from methanol–ether. The product darkens at 130–135° and melts with decomposition over a temperature range between 145–155°. It is soluble in ethanol and methanol, only very slightly soluble in water and insoluble in ether.

Anal. Calcd. for $C_{18}H_{21}BrN_2$: C, 62.61; H, 6.13. Found: C, 62.22; H, 5.80.[15]

Dimethyl-3-indolylmethyl-β-phenylethylammonium Bromide (III).—A solution of 2.5 g. (0.014 mole) of gramine and 2.6 g. (0.014 mole) of β-phenylethyl bromide in 50 cc. of absolute ethanol was allowed to stand for six days at room temperature. The light pink precipitate (1.9 g., 37%) was collected and recrystallized from methanol–ether to give 1.6 g. (31%) of colorless needles, m. p. 171°. The product is soluble in methanol, only very slightly soluble in water and insoluble in ether and benzene.

Anal. Calcd. for $C_{19}H_{23}BrN_2 \cdot {}^1/_2H_2O$: C, 61.96; H, 6.57. Found: C, 61.76, 61.86; H, 6.30, 6.23.

N-(3-Indolylmethyl)-piperidine.—To a cooled solution of 8.5 g. (0.1 mole) of piperidine and 8.6 g. (0.1 mole of formaldehyde) of 35% formaldehyde in 100 cc. of 50%

(9) Gamble, Gilmont and Stiff, THIS JOURNAL, **62**, 1257 (1940).

(10) Benton and Dillon, *ibid.*, **64**, 1128 (1942).

(11) The authors are indebted to F. M. Berger, M.D., the University of Rochester School of Medicine and Dentistry, for the pharmacological tests on these compounds.

(12) All melting points are uncorrected; analyses by Mrs. G. L. Sauvage.

(13) Snyder, Smith and Stewart, THIS JOURNAL, **66**, 200 (1944).

(14) Kühn and Stein[6] reported that the compound darkens at 175° but does not melt under 350°.

(15) High hydrogen and low carbon values were obtained until the product was dried at elevated temperatures under reduced pressure. In subsequent experiments, the quaternary salts of the Mannich bases discolored and decomposed on heating, and the high hydrogen and low carbon values were assumed to be due to fractional molecules of water of crystallization.

acetic acid was added 11.7 g. (0.1 mole) of indole. A slight exothermic reaction occurred as the indole went into solution. After the light yellow solution had stood at room temperature for twelve hours, it was made strongly basic with sodium hydroxide and the precipitate collected by filtration. After recrystallization from dilute ethanol, 15.5 g. (74%) of colorless needles were obtained, m. p. 159–159.5°.[16]

N-(3-Indolylmethyl)-N-methylpiperidinium Iodide (IV).—A solution of 2 g. (0.0094 mole) of N-(3-indolylmethyl)-piperidine and 2 cc. (0.032 mole) of methyl iodide in 20 cc. of absolute ethanol was allowed to stand at room temperature for twenty-four hours. The oil which separated when ether was added crystallized slowly on standing in the refrigerator. Recrystallization of the product from methanol–ether gave 1.8 g. (55%) of colorless prisms, m. p. 142–143°. The product is soluble in methanol, ethanol and warm water, and insoluble in ether and petroleum ether.

Anal. Calcd. for $C_{15}H_{21}IN_2 \cdot {}^1/_4H_2O$: C, 49.94; H, 6.01. Found: C, 49.77; H, 5.98.

N-Benzyl-N-(3-indolylmethyl)-piperidinium Bromide (V).—A solution of 1 g. (0.0047 mole) of N-(3-indolylmethyl)-piperidine and 0.8 g. (0.0047 mole) of benzyl bromide was allowed to stand at room temperature for six days. The fine white powder that precipitated was recrystallized from ethanol–ether to give 1.1 g. (61%) of product, m. p. 147–151° with decomposition after darkening at 132–134°. The product is soluble in ethanol and warm water and insoluble in ether.

Anal. Calcd. for $C_{21}H_{25}BrN \cdot {}^1/_4H_2O$: C, 64.68; H, 6.59. Found: C, 64.92; H, 6.94.

Methylene-bis-(N,N′-1,2,3,4-tetrahydroisoquinoline).—A solution of 3.4 g. (0.02 mole) of 1,2,3,4-tetrahydroisoquinoline hydrochloride and 1 g. (0.02 mole) of 35% formaldehyde in 30 cc. of 20% acetic acid was heated on a steam-bath for one hour. The oil which separated when the solution was made basic was extracted from the mixture with two 50-cc. portions of ether. The light yellow oil left on evaporation of the ether was taken up in ethanol and crystallization induced by adding a few drops of water to give 2.1 g. (75%) of light tan powder, m. p. 88–88.5°.

Anal. Calcd. for $C_{19}H_{22}N_2$: C, 81.97; H, 7.97. Found: C, 82.30; H, 7.95.

A small amount of the above product was heated for a few minutes in saturated ethanolic picric acid. On cooling a picrate separated in long needles, m. p. 200–201° after softening and darkening at 185–190°.

Anal. Calcd. for the picrate of 1,2,3,4-tetrahydroisoquinoline, $C_{15}H_{14}N_4O_7$: C, 49.72; H, 3.89. Found: C, 50.00; H, 4.14.

As this analysis checked for the picrate of 1,2,3,4-tetrahydroisoquinoline, a mixed melting point of this picrate with that of an authentic sample of 1,2,3,4-tetrahydroisoquinoline (m. p. 201–202°) was taken. There was no depression.

A solution of 1 g. (0.0036 mole) of the bis-compound and 2.8 g. (0.02 mole) of methyl iodide in 25 cc. of dry ether was allowed to stand at room temperature for twenty-four hours. The light yellow needles which formed amounted to 0.4 g., m. p., after recrystallization from methanol–ether, 187–188°.[17] Evaporation of the filtrate to dryness left 0.5 g. of the unreacted bis-compound. The 0.4 g. of product, which was shown by analysis to be N,N-dimethyl-1,2,3,4-tetrahydroisoquinolinium iodide, represents a yield of 40% based on the unrecovered starting material.

Anal. Calcd. for N,N-dimethyl-1,2,3,4-tetrahydroisoquinolinium iodide, $C_{11}H_{16}IN$: C, 45.69; H, 5.59. Found: C, 45.97; H, 5.68.

N-(3-Indolylmethyl)-1,2,3,4-tetrahydroisoquinoline.—A water solution of 5 g. (0.03 mole) of 1,2,3,4-tetrahydroisoquinoline hydrochloride was made strongly basic with alkali and the free base taken up in ether. After removing the ether by distillation, the residue was taken up in 20 cc. of 50% acetic acid. To this solution was added 3.4 g. (0.04 mole) of 35% formaldehyde and 3.5 g. (0.03 mole) of indole. After the light yellow solution had stood at room temperature for twelve hours, it was made strongly basic and the mixture extracted with three 50-cc. portions of ether. The residue left from the evaporation of the ether solution was recrystallized from dilute ethanol to give 4.7 g. (60%) of essentially colorless product, m. p. 139–140°. It was necessary to purify the product by chromatography, using chloroform–petroleum ether as the solvent and alumina as the adsorbent, before a satisfactory carbon–hydrogen analysis could be obtained. The melting point was not raised by this purification, but consistently high carbon values were obtained until the product was chromatographed.

Anal. Calcd. for $C_{18}H_{18}N_2$: C, 82.41; H, 6.91. Found: C, 82.10; H, 7.05.

The hydrochloride of the Mannich base was prepared by passing dry hydrogen chloride gas through a dry ether solution. Upon recrystallization from ethanol–ether, pink prisms were obtained, m. p. 179.5–180°.

Anal. Calcd. for $C_{18}H_{19}ClN_2$: C, 72.34; H, 6.41. Found: C, 71.92; H, 6.45.

N-(3-Indolylmethyl)-N-methyl-1,2,3,4-tetrahydroisoquinolinium Iodide (VI).—A solution of 1 g. (0.0038 mole) of N-(3-indolylmethyl)-1,2,3,4-tetrahydroisoquinoline and 2 cc. (0.032 mole) of methyl iodide was allowed to stand for two hours at room temperature. The light tan, flaky precipitate amounted to 1.6 g. (quantitative), m. p. 75–80° with darkening. When the product was dissolved in methanol and a large amount of ether added, a gummy solid invariably formed, which became completely solid on washing with large amounts of ether. Several repetitions of this procedure gave an essentially colorless powder that melted at 110–112° with darkening and decomposition. The product is soluble in ethanol and methanol, rather insoluble in water and insoluble in ether.

Anal. Calcd. for $C_{19}H_{21}IN_2 \cdot {}^1/_4H_2O$: C, 55.82; H, 5.29. Found: C, 56.02; H, 5.32.

Ethoxyacetyl Chloride.—The preparation of ethoxyacetyl chloride by treatment of ethoxyacetic acid[18] with thionyl chloride according to the usual procedures was found to be unsatisfactory (13% yield), considerable cleavage of the ethoxyl group apparently taking place. The procedure used by Brown[19] for preparing various volatile acid chlorides was found to be the most satisfactory. In a 100-cc. flask, fitted with a short Vigreux column, were placed 56 g. (0.4 mole) of benzoyl chloride and 21 g. (0.2 mole) of ethoxyacetic acid. The flask was heated in an oil-bath so that a slow distillation was maintained. In one experiment, 19.8 g. (crude yield, 80%) of colorless liquid was obtained at 95–130°, the major portion coming over between 120–125°.[20] The best results were obtained when this product was used without refractionation in the subsequent experiment.

N-(β-Phenylethyl)-ethoxyacetamide.—The 19.8 g. (0.16 mole) of crude ethoxyacetyl chloride from the above experiment was added slowly with cooling to a solution of 48 g. (0.4 mole) of β-phenylethylamine in 100 cc. of benzene. After standing several hours, the precipitated β-phenylethylamine hydrochloride was removed by filtration. After drying the benzene solution over anhydrous magnesium sulfate, the benzene was removed by distillation and the residue distilled to give 15.3 g. (46%) of colorless liquid, b. p. 144–150° (0.6–0.9 mm.), $n^{23}D$ 1.5172.

(16) Kühn and Stein[8] reported a m. p. of 161°.

(17) Gulland and Virden, *J. Chem. Soc.*, 1791 (1929), reported a melting point of 192° for N,N-dimethyl-1,2,3,4-tetrahydroisoquinolinium iodide. They obtained the product as yellow leaflets from which it was very difficult to remove the color.

(18) Fuson and Wojcik, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 260.

(19) Brown, THIS JOURNAL, **60**, 1325 (1938).

(20) Rothstein, *Bull. soc. chim.*, **51**, 838 (1932), reported a b. p. of 123–124°.

Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27. Found: C, 69.36; H, 8.01.

1-Ethoxymethyl-3,4-dihydroisoquinoline.—To a solution of 12 g. (0.06 mole) of N-(β-phenylethyl)-ethoxyacetamide in 150 cc. of refluxing xylene was added portionwise, over a period of fifteen minutes, 14 g. (0.1 mole) of phosphorus pentoxide. Reflux was maintained for another fifteen minutes. After decanting the xylene from the dark brown solid, 150 cc. of water was added and the mixture shaken until all had gone into solution. The water solution was extracted with two 50-cc. portions of ether to remove the xylene and any other ether-soluble material. The mixture which formed when the water solution was made strongly basic with alkali was extracted with four 50-cc. portions of ether. After drying the ether solution and removing the ether by distillation, the dark red-brown residue was distilled to give 4.9 g. (45%) of colorless liquid, b. p. 106–115° (1–1.5 mm.), $n^{22}D$ 1.5495. The liquid rapidly turned yellow on exposure to air.

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.15; H, 7.99. Found: C, 75.48; H, 7.55. The sample had turned yellow before the analysis was made; oxidation could account for the low carbon–hydrogen values.

The picrate was obtained as yellow needles from ethanol, m. p. 138–139° with decomposition.

Anal. Calcd. for $C_{18}H_{18}N_4O_8$: C, 51.68; H, 4.34. Found: C, 51.94; H, 4.38.

The hydrochloride precipitated when dry hydrogen chloride gas was bubbled through a dry ether solution of the distilled free base. It was very hygroscopic and difficult to handle, recrystallization from ethanol–ether giving colorless needles, m. p. 85–86° with darkening and decomposition.

Anal. Calcd. for $C_{12}H_{16}ClNO \cdot {}^1/_4H_2O$: C, 62.60; H, 7.22. Found: C, 62.84; H, 7.28.

1-Ethoxymethyl-1,2,3,4-tetrahydroisoquinoline (VII).—A solution of 3.6 g. (0.019 mole) of the distilled 1-ethoxymethyl-3,4-dihydroisoquinoline in 50 cc. of absolute ethanol, in the presence of about 1.0 g. of Raney nickel, was shaken for five hours at room temperature under hydrogen at 3.8 atmospheres. After removing the catalyst by filtration and the ethanol by distillation, the residue was distilled under reduced pressure to give 3.4 g. (94%) of colorless liquid, b. p. 90–103° (0.5–0.6 mm.), $n^{21}D$ 1.5360. The liquid turned light yellow on standing.

Anal. Calcd. for $C_{12}H_{17}NO$: C, 75.35; H, 8.97. Found: C, 74.66; H, 8.83. The colorless sample had turned light yellow before the analysis was run.

The picrate formed very slowly as tiny yellow needles from ethanol, m. p. 164–165°.

Anal. Calcd. for $C_{18}H_{20}N_4O_8$: C, 51.43; H, 4.80. Found: C, 51.32; H, 4.50.

The hydrochloride was prepared by bubbling dry hydrogen chloride gas through an ethanol solution of the free base and adding ether to induce crystallization. Recrystallization from ethanol–ether gave colorless prisms, m. p. 155–156°.

Anal. Calcd. for $C_{12}H_{18}ClNO$: C, 63.28; H, 7.97. Found: C, 63.39; H, 7.80.

1-Ethoxymethyl-2-(3-indolylmethyl)-1,2,3,4-tetrahydroisoquinoline (VIII).—To a solution of 1.9 g. (0.01 mole) of 1-ethoxymethyl-1,2,3,4-tetrahydroisoquinoline in 30 cc. of 50% acetic acid was added 0.4 g. (0.05 mole) of 35% formaldehyde and 1.1 g. (0.01 mole) of indole. After the light yellow solution had stood at room temperature for seven hours, it was made basic with dilute sodium hydroxide, a light yellow oil separating. The mixture was extracted exhaustively with ether, and the ether removed from the combined extracts by distillation. The residue was taken up in 25 cc. of ethanol and a few cc. of water added dropwise until precipitation was complete. Recrystallization of the product from dilute ethanol gave 2.2 g. (69%) of tiny colorless needles, m. p. 100–102°. A small sample recrystallized again from dilute ethanol melted at 102–103°. Although the melting point was not changed, it was necessary to purify the product by chromatography (using chloroform–petroleum ether and a column of alumina) before a satisfactory analysis was obtained. Consistently high carbon values were obtained until this was done.

Anal. Calcd. for $C_{21}H_{24}N_2O$: C, 78.71; H, 7.55; N, 8.75. Found: C, 78.80; H, 7.50; N, 8.60.

Summary

A number of previously unreported 3-indolylmethylammonium salts, compounds which are analogous to the structures postulated for the calabash curare alkaloids, have been prepared. Some of these quaternary salts exhibit marked curariform activity, the most effective, N-(3-indolylmethyl)-N-methyl-1,2,3,4-tetrahydroisoquinolinium iodide, causing paralysis in mice in doses of 16 mg./kg.

ROCHESTER, N. Y. RECEIVED JULY 22, 1948

[CONTRIBUTION FROM THE DEPARTMENT CHEMISTRY, THE UNIVERSITY OF ROCHESTER]

Curariform Activity and Chemical Structure. IV. Syntheses in the Piperidine Series[1]

BY L. E. CRAIG[2] AND D. S. TARBELL

Substituted 4-piperidones, 4-hydroxypiperidines and various piperidinium salts have been reported to exhibit rather intense curariform activity.[3,4] The present paper reports the syntheses of and the results of preliminary pharmacological tests on 4-piperidonium and 4-hydroxypiperidinium salts.

Di-β-carbomethoxyethylmethylamine (I), obtained by the addition of methylamine to methyl acrylate by the method of Mozingo and McCracken,[5] was treated with powdered sodium in xylene by the procedure of McElvain[6] to give 1-methyl-3-carbomethoxy-4-piperidone (III). Compound III, on acid hydrolysis, gave 1-methyl-4-piperidone (V), which was readily converted to 1-

(1) For the third paper of this series see Craig and Tarbell, THIS JOURNAL, **71**, 462 (1949).

(2) Aided by a Grant from the National Foundation for Infantile Paralysis. Present address: General Aniline and Film Corporation, Easton, Pennsylvania.

(3) Craig, *Chem. Revs.*, **42**, 360, 390 (1948).

(4) von Oettingen, "The Therapeutic Agents of the Pyrrole and Pyridine Group," Edwards Brothers, Inc., Ann Arbor, Michigan, 1936, p. 116.

(5) Mozingo and McCracken, *Org. Syn.*, **20**, 35 (1940).

(6) McElvain, THIS JOURNAL, **46**, 1721 (1924).