[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Alkylations with Quaternary Salts of 2-Aminomethylindoles

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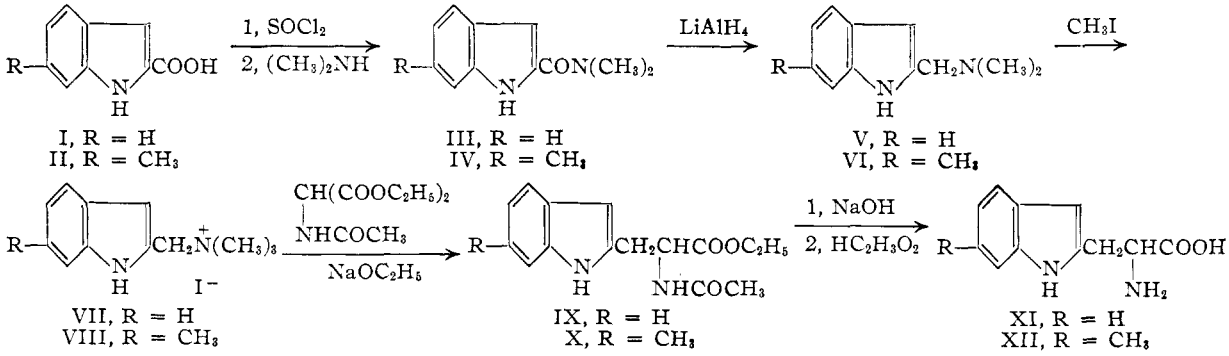
An improved synthesis of α-amino-β-(2-indole)-propionic acid, isotryptophan, as well as the synthesis of the analog, 6-methylisotryptophan, is described. The quaternary salts of gramine and isogramine are compared with respect to their action as alkylating agents. Some amine exchange reactions with the methiodides of 2-aminomethylindoles are reported.

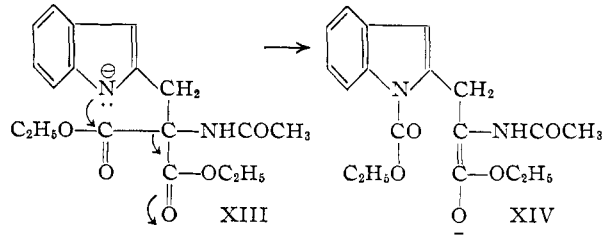
The synthesis of isotryptophan[2] (XI) and the report of its bacteriological activity suggested the preparation of other analogs of tryptophan having the alanine side chain in the β-position of the indole nucleus and with additional substituents in the molecule. It was also of interest to isolate quaternary salts of the isogramine type (VII and VIII), used in the synthesis, for comparison of chemical properties with those of gramine methiodide.

By a modification of the procedure of Kornfeld,[2] isotryptophan (XI) was prepared in improved yield, and the synthesis was extended to the 6-methyl homolog XII.



The chief change from the previous synthesis[2] was the use of the isolated quaternary salts (VII and VIII) as the alkylating agents. Kornfeld prepared the methosulfate corresponding to VII *in situ*, treating isogramine with methyl sulfate in methanol at temperatures below 35° and adding a solution of the sodio derivative of acetamidomalonic ester within a few minutes; the mixture so obtained was allowed to stand at room temperature for twelve days, although it was suggested that a reaction time of a day or two might have been adequate. In the present work the alkylation of acetamidomalonic ester with VII was carried out in refluxing ethanol over a period of 16–18 hours. A surprising result of the change was that the product isolated was not the expected malonic ester derivative; one of the carbethoxyl groups had been cleaved and the substituted propionic ester IX was obtained in a yield of over 70%. A similar result was encountered in the alkylation with the homolog VIII, the ester X being formed.

It seemed possible that the facile cleavage of the carbethoxyl group in the intermediate malonic ester is related to the proximity of the –NH function of the indole nucleus. In the presence of the base used in the alkylation the anionic center formed at this point, by attack on one of the carbethoxyl groups, could facilitate the decarbethoxylation through the formation of an intermediate N-carbethoxyl derivative. Such a transformation might occur *via* a pseudo-cyclic process similar to that postulated recently for the conversion of normal Michael reaction products into the abnormal isomers,[3] leading to XIV which would then lose the N-carbethoxyl group by ethanolysis. An alternative is the direct ethanolysis of the malonic ester function, similar to that observed, for example, in the ethanolysis of ethyl phenyl malonate.[4] A second alternative involving the formation and cleavage of a lactam XV must be considered unlikely, because of the resistance to cleavage of the similar lactam derived from the pyrrole compound.[5]



A simple test of the pseudo-cyclic mechanism postulated above could be made by employing 1-methylisogramine methiodide as the alkylating agent. This salt was prepared, but its low solubility in absolute ethanol precluded its use under the conditions of the earlier experiments. However, it could be used in a mixture of ethanol and dimethylformamide (1:5) and under these conditions

(1) The material here reported is taken from a dissertation presented by Paul L. Cook in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Illinois.

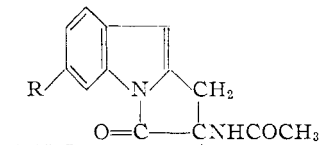
(2) E. C. Kornfeld, *J. Org. Chem.*, **16**, 806 (1951).

(3) J. W. Baker and E. Rothstein, *Chemistry & Industry*, 776 (1955).

(4) A. C. Cope and S. M. McElvain, THIS JOURNAL, **54**, 4319 (1932).

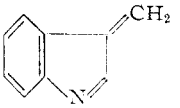
(5) W. Herz, K. Dittmer and S. Cristol, *ibid.*, **70**, 504 (1948).

the alkylation product isolated, in 28% yield, had undergone decarbethoxylation. Thus it appears that the decarbethoxylation leading to IX and X is a simple ethanolysis of the malonic ester structure.

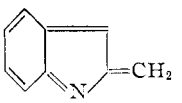


XV, R = H
XVI, R = CH_3

As indicated above, part of the purpose of the present work was to compare isogramine and its methiodide with gramine and its methiodide. In the preparation[6,7] of gramine methiodide great care must be exercised to suppress the disproportionation leading to diskatyldimethylammonium iodide, occurring as a result of the transfer of a β-indolemethyl group from a molecule of the methiodide to a molecule of gramine.[8] Geissman and Armen minimized this reaction by the use of an overwhelming excess of methyl iodide; in this Laboratory, Lovejoy[9] has controlled the reaction by operating at low temperatures or in the presence of weak acids. The extraordinary alkylating power of gramine methiodide has been attributed to the loss of the trimethylamine residue and the formation of the 3-methyleneindolenine (XVII), which rapidly undergoes conjugate addition of the reagent to give the alkylation product. The corresponding intermediate XVIII from isogramine cannot form without destroying the aromaticity of



XVII



XVIII

the benzene portion of the indole nucleus. Accordingly, isogramine methiodide would be expected to resemble a simple quaternary benzylammonium salt in its alkylation reactions, and the free base, isogramine, would not be expected to serve as an alkylating agent under mild conditions.[10] These predictions were borne out. In the alkylation of acetamidomalonic ester with isogramine methiodide, trimethylamine was still being evolved after 16 hours, indicating the reaction to be quite slow. Isogramine and 6-methylisogramine were converted to their methiodides in excellent yields, with no indication of the occurrence of disproportionation. Isogramine did not undergo amine exchange upon heating with piperidine; the methiodide, as expected, did give 2-piperidinomethylindole. 1-Methylisogramine methiodide also reacted, yielding 1-methyl-2-piperidinomethylindole.

In the reaction of N-methylisogramine methiodide with the sodio derivative of acetamidomalonic ester in a mixture of ethanol and dimethylformamide it was observed that the rate of reaction, as judged by the evolution of trimethylamine, was much slower than might have been expected for a reaction conducted in such a polar solvent mixture. That the lower rate was related to the presence of the methyl group in the 1-position is indicated by the much more rapid evolution of trimethylamine when the ester was alkylated with 6-methylisogramine methiodide in the same solvent mixture. This reaction led to a mixture of products; the only pure substance isolated (less than 10% yield) had the composition of the lactam XVI, and its infrared spectrum is in harmony with this structure.

(6) C. Schöpf and J. Thesing, *Angew. Chem.*, **63**, 377 (1951).

(7) T. Geissman and A. Armen, THIS JOURNAL, **74**, 3916 (1952).

(8) H. Snyder, R. Carnahan and E. Lovejoy, *ibid.*, **76**, 1301 (1954).

(9) E. R. Lovejoy, Thesis, Doctor of Philosophy, University of Illinois, 1953.

(10) For a discussion of alkylation with amines and quaternary salts see J. Brewster and E. Eliel in Adams, "Organic Reactions," Vol. VII, John Wiley and Sons, Inc., New York, N. Y., p. 99.

Experimental

Isogramine (V) (2-Dimethylaminomethylindole).—The preparation of this compound is amply described by Kornfeld.[2] In this work it was found that the isogramine obtained by the cyclization of chloroacet-*o*-toluidide was contaminated with this material even after careful distillation, so the alternative procedure[2] by the lithium aluminum hydride reduction of N,N-dimethylindolecarboxamide was used.

Isogramine Methiodide (VII) (2-Dimethylaminomethylindole Methiodide).—To a cooled solution of 15 ml. of methyl iodide in 100 ml. of dry benzene was added a solution of 13.6 g. of 2-dimethylaminomethylindole (V) in 100 ml. of dry benzene. The dropwise addition was carried out while the solution was stirred rapidly. The ice-bath was removed after the addition was complete and stirring was continued for 4 hours. The white, finely divided methiodide was filtered and thoroughly washed with benzene. The weight of the crude product was 23 g. (93.5%). An analytical sample was purified by dissolving the methiodide in a minimum quantity of absolute alcohol and reprecipitating by the addition of anhydrous ether. The granular white powder melted at 154–155°.

Anal. Calcd. for $C_{12}H_{17}N_2I$: N, 8.86. Found: N, 8.65.

Ethyl α-Acetamido-β-(2-indole)-propionate (IX).—Freshly cut sodium (1.68 g.) was dissolved in 100 ml. of absolute ethanol in a flask equipped with nitrogen inlet and protected from moisture with a soda-lime drying tube. When the sodium had completely dissolved, 15.85 g. of ethyl acetamidomalonate was added and the mixture shaken until a clear solution was obtained. A solution of 23 g. of 2-dimethylaminomethylindole methiodide (VII) in 100 ml. of absolute ethanol was added rapidly and the solution was refluxed for 16 hours. During this period a slow stream of nitrogen was passed through the flask. The odor of trimethylamine was apparent shortly after reflux was initiated. Even after 16 hours the odor was still detectable. The ethanolic solution was concentrated *in vacuo* to a volume of approximately 150 ml., poured into 300 ml. of water and cooled for a few hours in a refrigerator. A pink-colored precipitate was collected on a büchner funnel and dried. The yield of crude IX was 14.8 g. An additional quantity of 1 g. was obtained by concentration of the filtrate. The total yield was 15.8 g. (74%), m.p. 133–135°. Recrystallization from xylene raised the m.p. to 135–136°.

Anal. Calcd. for $C_{15}H_{18}O_3N_2$: C, 65.67; H, 6.61; N, 10.22. Found: C, 65.56; H, 6.67; N, 9.96.

Isotryptophan (XI) (α-Amino-β-(2-indole)-propionic Acid).—To a solution of 24 g. of sodium hydroxide in 175 ml. of water in a copper flask, 15.8 g. of ethyl α-acetamido-β-(2-indole)-propionate (IX) was added. The mixture was then refluxed for 23 hours. Just before the reaction was terminated Darco was added. The Darco was filtered, the filtrate cooled and brought to *p*H 6 with glacial acetic acid. A yield of 9 g. of crude isotryptophan (XI) was obtained. The product thus obtained decomposed at 213°. A small sample, which was recrystallized from water only after prolonged standing, melted with decomposition at 220° (reported m.p. 220–222°).[2]

6-Methylindole-2-carboxylic Acid (II).—This acid was prepared according to the method outlined by Snyder and

Pilgrim.[11] The details of an alternative synthesis are given by Williams.[12]

6-Methylindole-2-carboxylic Acid Dimethylamide (IV).—To a suspension of 29 g. of crude II in 500 ml. of anhydrous ether was added 59.5 g. of thionyl chloride. The flask was protected from moisture with a calcium chloride drying tube. The dark colored mixture was allowed to stand for 24 hours. The ethereal solution containing an excess of thionyl chloride was concentrated to dryness *in vacuo* at room temperature. Another 500 ml. of dry ether was added to the dry residue which remained. A small amount of insoluble material was removed by filtration. The red colored ethereal solution was cooled in an ice-bath and a cold solution containing 33.5 g. of dimethylamine in 250 ml. of dry ether added cautiously. Almost immediately a copious precipitate of the amide IV and dimethylamine hydrochloride formed. After one hour the precipitate was collected and washed by stirring with 200 ml. of water to remove the dimethylamine hydrochloride. The weight of crude product which melted at 210–212° was 26 g. (78%). After purification by recrystallization from 95% ethanol, the compound melted at 216–217°.

Anal. Calcd. for $C_{12}H_{14}ON_2$: N, 13.85. Found: N, 14.01.

6-Methylisogramine (VI) (2-Dimethylaminomethyl-6-methylindole).—In a Soxhlet extraction apparatus, a slurry of lithium aluminum hydride was made by suspending 26.6 g. of powdered hydride in 1 l. of anhydrous ether. Pure IV (35 g.) was placed in the Soxhlet thimble and extracted continuously for a period of 44 hours. While the flask was cooled in an ice-bath, 200 ml. of acetone was added to decompose the excess hydride. Enough 20% sodium hydroxide was added to dissolve the precipitated alumina. The ether layer was separated and the aqueous solution thoroughly extracted with ether. The ether extracts were combined and dried over magnesium sulfate and, after removal of the ether, the residue was fractionated. The portion boiling at 115–120° (0.7 mm.) was collected. One gram of forerun, b.p. 70–115° (0.7 mm.), was discarded. Redistillation of the main fraction yielded 22.6 g. (90%) of pure VI, b.p. 116–117° (0.8 mm.). The product was a colorless, viscous oil, which turned yellow on standing overnight.

Anal. Calcd. for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; N, 14.88. Found: C, 76.28; H, 8.71; N, 14.58.

6-Methylisogramine Methiodide (VIII) (2-Dimethylaminomethyl-6-methylindole Methiodide).—A solution of 17 g. of methyl iodide in 50 ml. of dry benzene was added in one portion to a solution of 11.2 g. of VI in 50 ml. of dry benzene. The reaction was exothermic and the mixture had to be cooled to prevent the methyl iodide from escaping. Crystallization did not take place immediately, but after overnight refrigeration a crystalline white solid was obtained. The granular material was washed with benzene and dried to give nearly a quantitative yield of VI. The decomposition point of the material was not sharp, decomposition occurring over a range of 115–125°. Recrystallization from absolute ethanol did not narrow this range. Analysis agreed with that calculated for the monomethiodide of 6-methylisogramine.

Anal. Calcd. for $C_{13}H_{19}N_2I$: C, 47.28; H, 5.80. Found: C, 47.51; H, 6.17.

Ethyl α-Acetamido-β-(6-methyl-2-indole)-propionate (X).—To 50 ml. of absolute ethanol was added 1.61 g. of clean sodium. After complete solution had occurred, 15.2 g. of ethyl acetamidomalonate was dissolved in the ethanolic solution. A solution of VIII in 150 ml. of warm absolute ethanol was then added and the mixture heated at the temperature of reflux for 18 hours. A stream of nitrogen was passed through the flask during the course of the reaction. After cooling, the contents of the flask were poured into 400 ml. of water. The light pink precipitate which had settled after 3 hours in the refrigerator was filtered, washed with water, dried and weighed. A small sample recrystallized several times from xylene melted at 149–150°. The yield of crude product was 18.5 g. (91%).

Anal. Calcd. for $C_{16}H_{20}O_3N_2$: C, 66.64; H, 6.99; N, 9.72. Found: C, 66.24; H, 6.87; N, 9.61.

(11) H. Snyder and F. Pilgrim, THIS JOURNAL, **70**, 3787 (1948).

(12) J. K. Williams, Thesis, Doctor of Philosophy, University of Illinois, 1953.

On another run the product isolated melted, after purification, at 135–136°. The analysis of this product was essentially the same as the above analysis. Infrared curves on chloroform solutions of the two products were superimposable.

Anal. Found: C, 66.63; H, 6.90; N, 9.52.

6-Methylisotryptophan (XII) (α-Amino-β-(6-methyl-2-indole)-propionic Acid.—Crude X (11 g.) was added to a solution of 16 g. of sodium hydroxide in 150 ml. of water in a copper flask. The mixture was heated at the temperature of reflux for 18 hours. Darco was added shortly before the reaction was halted. The Darco was filtered and the stirred filtrate acidified with hot glacial acetic acid to *p*H 5–6. The finely divided white precipitate was separated by filtration, washed with both water and ethanol and then dried. The product which melted at 233° with decomposition was further purified by reprecipitation from warm sodium hydroxide solution with glacial acetic acid. The decomposition point, after this purification, was raised to 235°, the yield being 6.43 g. (77%). A sample for analysis was prepared by dissolving the amino acid in hot water and concentrating the solution by evaporation until enough material for analysis was obtained (m.p. 239–240°).

Anal. Calcd. for $C_{12}H_{14}O_2N_2$: C, 66.03; H, 6.47; N, 12.84. Found: C, 65.78; H, 6.32; N, 12.55.

1-Methylindole-2-carboxylic Acid.—The method of preparation was essentially that of Fischer and Hess.[13] Crude pyruvic acid methylphenylhydrazone (37 g.) was suspended in 550 ml. of 10% hydrochloric acid. As the mixture was heated on the steam-bath, the solid gradually dissolved with the development of an orange-red color in solution. Soon thereafter, the tan colored solid began to crystallize. Heating was continued for about 1 hour after which the reaction mixture was cooled, the solid filtered, and washed free of mineral acid with cold water. The weight of acid obtained, after drying, was 22.3 g. (66%).

1-Methylindole-2-carboxylic Acid Dimethylamide.—Without further purification the above acid (22.3 g.) was suspended in 500 ml. of anhydrous benzene and 47.6 g. of thionyl chloride added. The mixture, which darkened soon after the addition of the acid chloride, was refluxed for 5 hours and then allowed to stand for 12 hours. The solvent and excess thionyl chloride were removed under reduced pressure at room temperature and the residue was taken up in 700 ml. of dry ether. A small amount of insoluble material was removed by filtration. A solution of 18 g. of dimethylamine in 150 ml. of dry ether was then poured into the cooled ethereal solution of the acid chloride and the mixture set aside for 30 minutes. One hundred milliliters of water was added to dissolve the precipitated amine hydrochloride, the ether layer was separated and washed successively with two 50-ml. portions of 10% sodium bicarbonate and 50 ml. of water. After drying over magnesium sulfate, the ether solution of the amide was concentrated *in vacuo* to dryness, a dark oil remaining. The addition of high boiling petroleum ether with stirring induced crystallization. A brown impure solid weighing 24 g. was isolated. This was extracted with 400 ml. of hot high boiling petroleum ether, a dark gummy material remaining undissolved. From the petroleum ether solution 13.2 g. (51%) of nearly pure amide was recovered. An analytical sample was prepared by recrystallization from petroleum ether, m.p. 94–95°.

Anal. Calcd. for $C_{10}H_9O_2N$: N, 13.85. Found: N, 14.02.

1-Methyl-2-dimethylaminomethylindole.—Lithium aluminum hydride (9.9 g.) was suspended in 350 ml. of anhydrous ether in a flask equipped with a condenser and dropping funnel. A solution of 13.2 g. of the above amide in 250 ml. of anhydrous ether was added dropwise at such a rate that normal reflux was maintained. After all the solution of the amide had been added, external heat was applied and reflux continued for 2 hours. Acetone (50 ml.) and water (50 ml.) were added consecutively, with caution, to decompose the excess hydride. The precipitated alumina was partially dissolved by the addition of 400 ml. of 20% sodium hydroxide. The remaining precipitate was allowed to settle and most of the ether layer decanted. More ether was added to the residue in the flask and again the ether layer was separated by decantation. The aqueous suspension of alumina was then filtered with the aid of Filter-Cel through

(13) E. Fischer and O. Hess, *Ber.*, **17**, 561 (1884).

a büchner funnel and washed with ether. The combined ether extracts and washing were extracted with 10% hydrochloric acid, the aqueous extracts neutralized with sodium carbonate and again extracted with ether. Fractionation of the ether extracts after drying yielded 8.6 g. (70%) of amine, b.p. 105° (1.1 mm.). The oil was colorless when pure but turned yellow after standing.

Anal. Calcd. for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; N, 14.88. Found: C, 76.43; H, 8.15; N, 14.72.

1-Methyl-2-dimethylaminoindole Methiodide.—The preparation of this methiodide was accomplished in the usual manner. In contrast to the previously prepared methiodides the methiodide of 1-methylisogramine was only slightly soluble in hot absolute ethanol and recrystallization was accomplished with difficulty. The product before recrystallization began to decompose at 212°. No higher decomposition point was obtained after recrystallization from absolute ethanol.

Anal. Calcd. for $C_{13}H_{19}N_2I$: C, 47.28; H, 5.80; N, 8.49. Found: C, 47.48; H, 5.79; N, 8.22.

Alkylation of Ethyl Acetamidomalonate with 1-Methylisogramine Methiodide in Dimethylformamide.—Pared sodium (0.28 g.) was dissolved in 20 ml. of absolute ethanol. After complete solution of the sodium, 2.6 g. of acetamidomalonic ester was added and the mixture shaken until no suspended solid remained. A solution of 4.02 g. of 1-methylisogramine methiodide in 80 ml. of dimethylformamide was then added in one lot and the mixture heated to reflux. (Dimethylformamide was used as the solvent because it readily dissolved the methiodide of 1-methylisogramine.) After 22 hours the reaction mixture was cooled, diluted with 200 ml. of water and the resulting cloudy solution was placed in the refrigerator for 5 hours. Since no crystallization had occurred, the mixture was extracted with ether. After drying and concentration *in vacuo* of the ether extracts, an oil began to separate. More ether was added until the oil redissolved and then a portion of petroleum ether until cloudiness was induced. The mixture was then allowed to stand for two days in the refrigerator. At the end of this time one gram of crystalline material was isolated. The solid was purified by recrystallization from a petroleum ether–benzene mixture, m.p. 122–124°. The analysis indicated the compound to be ethyl α-acetamido-β-(1-methyl-2-indole)-propionate; yield 28%.

Anal. Calcd. for $C_{16}H_{20}O_3N_2$: C, 66.64; H, 6.99; N, 9.72. Found: C, 66.43; H, 7.09; N, 9.69.

Alkylation of Ethyl Acetamidomalonate with 6-Methylisogramine Methiodide in Dimethylformamide.—The conditions for this alkylation were exactly analogous to those reported in the preceding reaction. The quantities of materials used were as follows: 20 ml. of absolute ethanol; 0.28 g. of sodium; 2.6 g. of acetamidomalonic ester; 4.02 g. of 6-methylisogramine methiodide in 80 ml. of dry dimethylformamide. The evolution of gaseous amine was much more rapid than when ethanol alone was used as the solvent. After one hour had elapsed the amine could no longer be detected by odor or with moist red litmus. The reaction was continued, however, for 22 hours. The reaction mixture was then cooled and diluted with 300 ml. of water. After the cloudy solution had been refrigerated for 5 hours, a light brown precipitate (0.35 g.) was removed by filtration. Two recrystallizations from benzene–petroleum ether yielded a white crystalline compound, m.p. 242–244°. An analysis of the compound corresponded to that for a compound with an empirical formula $C_{14}H_{14}O_2N_2$. Infrared absorption analysis indicated (1) the presence of a monosubstituted amide group; (2) substitution on the nitrogen of the indole ring; (3) the presence of a sharp carbonyl peak at 1755 cm.$^{-1}$; (4) the absence of any ester groups. The structure which best fits the analytical data is the lactam XVI.

Anal. Calcd. for $C_{14}H_{14}O_2N_2$: C, 69.43; H, 5.83; N, 11.57. Found: C, 69.33; H, 5.58; N, 11.39.

Extraction of the aqueous filtrate with ether furnished 0.39 g. of material melting over the range 140–150°. Recrystallization from benzene–petroleum ether failed to sharpen the melting point. Infrared analysis of this material indicated it to be a mixture of the lactam described and an ester, probably X.

2-Piperidinomethylindole.—When 0.25 g. of isogramine (V) was heated with an excess of piperidine for a period of 3 hours, amine exchange did not occur. There was no evidence of dimethylamine having been liberated and a picrate made from the residual oil after removal of excess piperidine was identical with the picrate of V. The methiodide of isogramine, however, reacted with piperidine readily.

To 10 ml. of piperidine, 0.93 g. of isogramine methiodide was added. The methiodide soon dissolved and the odor of trimethylamine was evident. The mixture was heated under reflux for 2 hours, cooled, and the crystalline piperidine hydriodide recovered by filtration.

The filtrate was concentrated to a volume of 2 ml. and diluted with water. An oil separated which crystallized after a short period of refrigeration. After filtration and drying, the product weighed 0.75 g. Recrystallization from an ethanol–water mixture gave a white crystalline material which melted at 80–83°. That this material was a hydrate was indicated by the analysis and by the fact that drying in an Abderhalden apparatus at room temperature caused partial liquefaction. The liquid again solidified upon exposure to air.

Anal. Calcd. for $C_{14}H_{18}N_2 \cdot {}^1/_2H_2O$: C, 75.29; H, 8.58; N, 12.55. Found: C, 74.96; H, 8.46; N, 12.79.

Preparation of 1-Methyl-2-piperidinomethylindole.—To 50 ml. of piperidine was added 0.56 g. of crude 1-methyl-2-dimethylaminomethylindole methiodide. The methiodide was very insoluble even in hot piperidine. The mixture was brought to reflux and heating was continued over a period of 12 hours. At the end of this time, no more solid remained in suspension. The amber-colored solution was cooled in an ice-bath for 5 minutes with the result that crystals of piperidine hydroiodide precipitated. The precipitate was washed free of piperidine with ether and dried. The weight of crude material was 0.44 g. Purification by recrystallization from benzene gave a product which began to soften at 172°, most of it melting at 185–187°. It was water soluble and a pale yellow precipitate, insoluble in dilute nitric acid, was formed when silver nitrate was added to the aqueous solution. Analysis of the product recrystallized from benzene showed it to be piperidine hydriodide.

Anal. Calcd. for $C_5H_{11}N \cdot HI$: C, 28.18; H, 5.68; N, 6.57. Found: C, 28.31; H, 5.52; N, 6.48.

After filtration of the piperidine hydriodide, the solution was diluted with 50 ml. of water. After several hours of refrigeration, 0.34 g. of a crystalline product was removed by filtration. Following recrystallization from an ethanol–water mixture the compound melted at 82–83°. An analysis of the white needles thus obtained corresponded to that calculated for 1-methyl-2-piperidinomethylindole.

Anal. Calcd. for $C_{15}H_{20}N_2$: C, 78.90; H, 8.83; N, 12.27. Found: C, 78.68; H, 8.74; N, 12.08.

URBANA, ILLINOIS