

nism for the reduction of other aromatic compounds by sodium in liquid ammonia and for the reduction of naphthalene by sodium in ethyl alcohol.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF IOWA STATE COLLEGE]

SYNTHESIS OF SOME NEW COMPOUNDS IN THE PYRROLE AND PYRROLIDINE SERIES

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A previous paper¹ reported the preparation of pyrrolidine, N-phenylpyrrolidine and N-cyclohexylpyrrolidine. In extending the series for the contemplated study of insecticidal action and physical properties, the benzyl, methyl, butyl and *p*-tolyl derivatives were desired.

The aliphatic N-substituted derivatives can be prepared by the general method of Britton² or by addition of RX to the free base. Contrary to the literature³ the yield by the latter method is low due to the formation of the quaternary derivative. The general method to be recommended for the preparation of N-substituted derivatives where R is a saturated aliphatic radical is to prepare the N-substituted pyrrole and reduce it catalytically as pyrrole was reduced. The presence of excess acid is necessary for a successful reduction. Substitution on the nitrogen appears to stabilize the ring toward polymerization by acid, eliminating the difficulty encountered with the carbon substituted derivatives.⁴ J. P. Wibaut⁵ reduced methylpyrrole catalytically with Adams and Shriner catalyst in glacial acetic acid, but his reduction required large amounts of catalyst and shaking for a long period of time. If alcohol acidified with hydrochloric acid is used as a solvent, the reduction requires only 0.2 g. of catalyst and is complete in three hours. The same catalyst may be used several times. N-Methylpyrrole has also been reduced successfully to N-methylpyrrolidine by passing its vapor over palladium⁶ at 160°.

Tadeus Reichstein⁷ gave a method for the characterization of N-substituted pyrroles by the use of a diazo reaction. Reduction can also be used for this purpose since the yield is practically quantitative and the resulting pyrrolidine derivative can easily be identified as the picrate.

In the N-butylpyrrole synthesis the formation of the substituted acid

¹ Craig and Hixon, *THIS JOURNAL*, **52**, 804 (1930).

² E. C. Britton, U. S. Patent 1,607,605, Nov. 23, 1926.

³ Schlinck, *Ber.*, **32**, 952 (1899); Ciamician and Magnaghi, *ibid.*, **18**, 2079 (1885).

⁴ Anderson and McElvain, *THIS JOURNAL*, **51**, 887 (1929).

⁵ Wibaut, *Rec. trav. chim.*, **44**, 1101-5 (1925); Dejong and Wibaut, *ibid.*, **49**, 237 (1930).

⁶ Zelinsky and Jerjew, *Ber.*, **62**, 2589 (1929).

⁷ Reichstein, *Helv. Chim. Acta*, **10**, 387 (1927).

amide is greater than with the N-methylpyrrole or pyrrole synthesis. By the use of reduced pressure in the distillation of the mucic acid salt, the yield of butylpyrrole was practically doubled.

p-Toluidine condenses smoothly with tetramethylene chloride to give satisfactory yields of N-*p*-tolylpyrrolidine.

Experimental

N-Normal-butylpyrrole.—The method of preparation was that of Reichstein except that mucic acid was used instead of saccharic. To 86 g. of mucic acid in enough water to make a thin paste, 60 g. of butylamine was added. Upon cooling the reaction mixture solidified. It was transferred to a 500-cc. Claisen flask and subjected to distillation under reduced pressure (35 mm.). The distillate contained 35 g. of an oil which was extracted with ether, dried and fractionated, giving 13.5 g. distilling at a temperature of 165–180°. This was used for reduction. It was a colorless oil and had a very disagreeable sharp odor.

N-Butylpyrrole- α -carboxy-normal-butylamide.—The high-boiling residue (21.5 g.) from above was subjected to distillation under reduced pressure (165–170° under 10–12 mm. pressure). The colorless distillate solidified. It melted at 57° and crystallized in needles from an alcohol-water mixture.⁸

An attempt to hydrolyze the substituted acid amide by refluxing over strong caustic was unsuccessful, as was also an attempt using alcoholic potash at 130°. The compound was finally hydrolyzed by heating for ten hours at 200°, 10 g. of the amide in an alcoholic solution containing 8 g. of potassium hydroxide in 4 cc. of 95% alcohol. After hydrolyzing, most of the alcohol was distilled off and water added to the residue. Fractionation of this mixture by solubility in ether, acid solution and basic solution yielded about 1 g. of unchanged amide, N-butylamine and an acid fraction. The oily acid fraction, which was N-butylpyrrole- α -carboxylic acid, was finally characterized by conversion to the acid amide. It is soluble in all organic solvents and insoluble in water. The calcium, barium and silver salts were too soluble to crystallize. Six grams of the free acid was subjected to distillation under 6 mm. pressure. From the distillate three grams of an alkali-insoluble oil was obtained that distilled at 165 to 178° and had all the characteristics of N-butylpyrrole. Two grams of the original acid was present in the distillate. Evidently carbon dioxide splits off quite readily from this acid.

N-Butylpyrrole- α -acid Amide.—To 1 cc. of the free acid an excess of thionyl chloride was added. After heating, as much of the excess thionyl chloride was evaporated as was possible using reduced pressure and heating on the water-bath. The residue was dropped into cold concentrated ammonia and the resulting oily mass extracted with ether. The ether extract was evaporated to dryness and the residue recrystallized from hot water. The yield is low; m. p. 108°.

Anal. Calcd. for $C_9H_{13}N_2O$: C, 64.9; H, 8.99. Found: C, 64.98, 65.00; H, 8.52, 8.88.

Reduction of N-Methylpyrrole and N-Butylpyrrole.—The N-methylpyrrole was prepared by the method of Bell and Lapper.⁹ To 10 cc. of pyrrole base in 100 cc. of absolute alcohol, 0.2 g. of Adams and Shriner catalyst and an equivalent of hydrochloric acid were added. In three hours in the case of N-methylpyrrole and five hours in the case of N-butylpyrrole the reduction was complete. The catalyst was filtered off and

⁸ Reichstein reported a compound, which corresponded to the above, as N-butylpyrrole- α -isobutylamide. This must be a typographical error, since normal-butylamine was used in the synthesis of his compound.

⁹ Bell and Lapper, *Ber.*, 10, 1861 (1877).

the alcohol removed by distillation. The residue was washed with ether and treated with solid potassium hydroxide until an oil separated. The oil was dried over solid potassium hydroxide and distilled. The N-methylpyrrolidine distilled entirely at 76–78°, the yield being almost the theoretical. N-Methylpyrrolidine has a stifling odor and a very high vapor pressure at room temperature. Its vapor pressure is 99 mm. at 25°. This may account for the emphasis in the literature placed on its physiological properties.

The yield of N-butylpyrrolidine is 88% of the theoretical. It is slightly soluble in water and has an odor similar to pyrrolidine. The picrate crystallized in leaflets from 95% alcohol and showed a constant melting point of 124°. An attempt was made to prepare a chloroplatinate by addition of a solution of chloroplatinic acid to the hydrochloride of the free base but the salt appeared to be too soluble to crystallize. A chloroaurate was prepared by this method using chloroauric acid. It was very soluble in alcohol but crystallized in yellow leaflets from hot water. It melted without decomposition at 78°.

Anal. Calcd. for $C_8H_{17}NHAuCl_4$: Au, 42.13. Found: Au, 42.14, 42.08.

N-*p*-Tolylpyrrolidine.—To 5 g. of tetramethylene chloride¹⁰ (boiling point 154–164°) 12.6 g. of *p*-toluidine was added. Upon heating on a steam-bath for ten hours, it formed a solid mass of crystals that entirely dissolved in dilute hydrochloric acid. The acid solution was washed with ether, made strongly alkaline and the oily layer run through a primary–secondary–tertiary amine separation with benzenesulfonyl chloride. A yield of 4.5 g. of a tertiary amine was obtained. It was dried over solid potassium hydroxide and distilled at a constant temperature of 120° under 8 mm. pressure. It crystallized in leaflets from an alcohol–water mixture and showed a constant melting point of 42.5°. It has a rather pleasant odor.

A chloroplatinate was prepared in the usual way but it could only be recrystallized from water containing considerable hydrochloric acid, as reduction took place in water alone. It showed a decomposition point of 175°. For analysis the material was recrystallized and dried at room temperature in a vacuum desiccator.

Anal. Calcd. for $(C_{11}H_{15}N)_2H_2PtCl_6$: Pt, 26.68. Found: Pt, 26.70, 26.67.

N-Benzylpyrrolidine.—This compound was first prepared by Schlinck.¹¹ He reported a nearly quantitative yield which could not be duplicated by the same method. To 5 cc. of pyrrolidine,¹² one-half equivalent of benzyl chloride was added (a full equivalent gave a lower yield of N-benzylpyrrolidine than a half). The mixture was warmed for two hours on a water-bath. Dilute hydrochloric acid was added and the unreacted halide removed by washing with ether. Upon addition of caustic solution, an oil separated; when solid potassium hydroxide was added, a third layer appeared. The top layer was drawn off and identified as N-benzylpyrrolidine. It amounted to 4 g. or a yield of 40% of the theoretical. Its picrate melted at 128° as reported by Schlinck.

The second layer (the larger) was viscous, insoluble in ether, very soluble in water and required a concentrated solution of potassium hydroxide to make it separate. It could not be prepared in a form suitable for analysis but its properties are what would be expected of dibenzylpyrrolidinium hydroxide.

Summary

*It has been shown that the N-substituted pyrroles can be reduced easily to the corresponding pyrrolidine compounds in alcohol–hydrochloric acid

¹⁰ Prepared from pyrrolidine by the method of Braun and Beschke, *Ber.*, 39, 4119 (1906).

¹¹ Schlinck, *Ber.*, 32, 952 (1899).

¹² Obtained by catalytic reduction of pyrrole.

solution. This method of preparation is to be preferred over that of condensation of RX with pyrrolidine as the yields are often low by the latter method due to formation of the quaternary derivative.

p-Toluidine condenses smoothly with tetramethylene chloride to give N-*p*-tolylpyrrolidine.

The compounds N-*p*-tolylpyrrolidine, N-*n*-butylpyrrole- α -carboxylic acid and N-*n*-butylpyrrole- α -acid amide are reported for the first time. The properties of N-*n*-butylpyrrolidine, N-*n*-butylpyrrole and N-*n*-butylpyrrole- α -carboxy-N-butyl amide are given.

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[CONTRIBUTION NO. 36 OF THE CHEMICAL LABORATORY OF THE UNIVERSITY OF UTAH]

THE CATALYTIC EFFECT OF MAGNESIUM ALCOHOLATES ON THE REACTION OF GRIGNARD REAGENTS WITH CARBON DIOXIDE¹

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Although many substances have been shown to have deleterious effects in Grignard reactions, nothing appears to be known about the effect of alcohols, which are often present in the organo halides from which the reagents are made. The catalytic behavior of alcohols or their magnesium derivatives was first brought to our attention by the variable yield of triphenylacetic acid obtained from triphenylmethylmagnesium chloride and carbon dioxide. A study of the reaction showed definitely that the presence of small amounts of triphenylcarbinol in the triphenylchloromethane used to make the reagent very materially lowered the yield of triphenylacetic acid.

The systematic addition of increasing quantities of triphenylcarbinol gave a yield curve shown in Fig. 1 as the lower curve, in which an addition of 15.3 mols per cent. of triphenylcarbinol caused the yield of triphenylacetic acid to drop from 75%² to 0%. The upper straight line in Fig. 1 represents the yield of acid to be expected based on the yield of acid without addition of the carbinol and subtracting an amount corresponding to the diminution in yield caused by the reaction of a part of the reagent with the carbinol.

The lowering in yield of acid was not caused by an interference in the reaction of the triphenylchloromethane with the magnesium to form the Grignard reagent, since the same amount of triphenylcarbinol (15.3 mole per cent.) when added *after the reagent had been prepared* prevented the reaction

¹ Parts of this paper have been presented at the Berkeley and Eugene meetings of the Pacific Division of the American Association for the Advancement of Science and at the Minneapolis meeting of the American Chemical Society.

² The maximum yield obtained was 87.5%, but the method used was not adaptable to the study at hand.