plosion peninsula, maximum in the reaction rate, "cool" flames) can be described by peroxide branching; and that peracid branching can describe the explosion limits of higher hydrocarbons at high temperatures.

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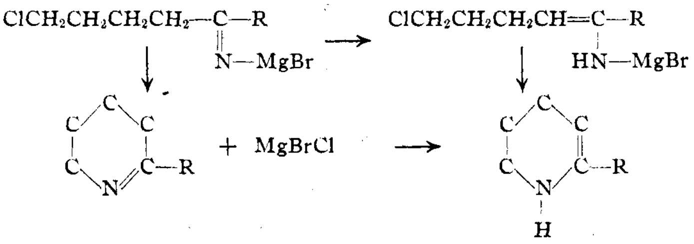
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

Synthesis of Some New Alpha-Substituted Tetrahydropyridines and Piperidines[1]

BY RICHARD SALATHIEL, J. MARVIN BURCH AND R. M. HIXON

A general method for the preparation of α-substituted tetrahydropyridines has been developed, a preliminary report of which was presented by Starr and Hixon,[2] who reported the preparation of α-phenyltetrahydropyridine. This preparation followed the general plan of the method used by Craig, Bulbrook and Hixon,[3] who reported the preparation of α-substituted pyrrolines by a modification of Cloke's reaction.[4] This paper extends this synthesis to the preparation of other compounds in this series, and to the preparation of the corresponding piperidines.

The reactions involved are first the reaction of a Grignard reagent with δ-chlorovaleronitrile to form the mixed magnesium bromide salt of a δ-chlorobutylketimine, $Cl(CH_2)_4CM + RMgBr \longrightarrow ClCH_2CH_2CH_2CH_2—CR{=}NMgBr$, and second the closing of the ring which is accomplished by replacing the ether in the reaction mixture with xylene and raising the temperature. Expressing this reaction by equations completely analogous to those proposed by Craig, Bulbrook and Hixon,[3] two possible mechanisms are shown.



Experimental Part

δ-Chlorovaleronitrile, b. p. 118–121° (25 mm.), was prepared as described by Starr and Hixon.[2]

α-Phenyltetrahydropyridine.—A Grignard reagent was prepared from 4.86 g. of magnesium, 34.5 g. of bromobenzene and 160 cc. of ether. A solution of 23.5 g. of δ-chlorovaleronitrile in 25 cc. of ether was added dropwise, as the reaction mixture was stirred and refluxed. The addition product, a heavy viscous colorless liquid, separated from the solvent. The ether was removed by distillation from an oil-bath, the volume in the flask being kept constant by the addition of xylene. When the temperature in the flask reached 130–135°, the liquid addition product quickly changed to a solid, semi-crystalline, yellow mass. Heating just sufficient to reflux the xylene was continued for an hour. The material was cooled and hydrolyzed, using 130 cc. of hydrochloric acid (sp. gr. 1.10). The xylene layer was separated and extracted again with hydrochloric acid. The acid solution was extracted with 20 cc. of petroleum ether to remove residual xylene, then made strongly basic with sodium hydroxide and extracted with ether. The ether extract was dried and fractionated. There was collected at 142–150° (20 mm.) 21 g. of a nearly colorless oil, which turns brown quickly on exposure to air. The yield is 66% of the theoretical.

The hydrochloride, precipitated from aqueous acetone, melted at 86–87° as reported by Gabriel[5] but when dried in a current of warm air the melting point becomes 152–153°. Other derivatives, the picrate, m. p. 181.5°, and the mercuric chloride–hydrochloride double salt, m. p. 165–166°, were prepared.

α-(*p*-Chlorophenyl)-tetrahydropyridine.—A Grignard reagent prepared from 2.43 g. of magnesium, 21.1 g. of *p*-chlorobromobenzene and 125 cc. of ether, was added to a solution of 11.8 g. of δ-chlorovaleronitrile. A procedure similar to that for α-phenyltetrahydropyridine yielded 9.5 g. of a colorless base boiling at 165° (13 mm.) which crystallized in the receiver, m. p. 54°. The yield is 49% of the theoretical.

A picrate, m. p. 177–178°, was crystallized from an alcohol solution. A mercuric chloride–hydrochloride double salt, m. p. 133–135°, a chloroplatinate, m. p. 192°, and a hydrochloride, m. p. 215–217°, were prepared from aqueous solutions.

Anal. Calcd. for $C_{11}H_{12}ClN \cdot HCl$: N, 6.09. Found: N, 6.19, 6.15.

α-(*p*-Tolyl)-tetrahydropyridine.—A Grignard reagent prepared from 2.5 g. of magnesium turnings, 21 g. of *p*-bromotoluene and 120 cc. of ether was treated with 11.7 g. of δ-chlorovaleronitrile. The product was obtained by a procedure similar to that for α-phenyltetrahydropyridine. The major portion of the 9 g. of the product distilled over at 145° (13 mm.). The yield is 52% of the theoretical.

The following derivatives were prepared: chloroplati-

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[1] Supported in part by grants from the Rockefeller Fluid Research Fund and from the Industrial Science Research Funds of the Iowa State College.

[2] Starr and Hixon, THIS JOURNAL, **56**, 1595 (1934).

[3] Craig, Bulbrook and Hixon, *ibid.*, **53**, 1831 (1931).

[4] Cloke, *ibid.*, **51**, 1174 (1929).

[5] Gabriel, *Ber.*, **41**, 2012 (1908).

nate, yellow needles from water, m. p. 186–187°; mercuric chloride–hydrochloride double salt, crystallized from water, m. p. 119.5°; picrate, yellow needles from alcohol, m. p. 178–179°; hydrochloride, crystallized from water solution, m. p. 137–137.5°.

Anal. Calcd. for $C_{12}H_{15}N \cdot HCl \cdot H_2O$: N, 6.15. Found: N, 6.10, 6.15.

In an oven at 100° the hydrochloride salt loses water and the melting point changes to 175–177°.

Anal. Calcd. for $C_{12}H_{15}N \cdot HCl$: N, 6.68. Found: N, 6.56, 6.61.

α-Cyclohexyltetrahydropyridine.—A Grignard reagent was prepared from 6 g. of magnesium turnings, 33 g. of chlorocyclohexane and 200 cc. of ether. A solution of 21.5 g. of δ-chlorovaleronitrile was added dropwise to the reagent and a viscous heavy liquid precipitated out. Following the usual procedure 7 g. of a light yellow oil, which darkens on exposure to air, boiling at 118–125° (17 mm.) was separated. The yield is 23% of the theoretical.

Anal. Calcd. for $C_{11}H_{19}N$: N, 8.48. Found: N, 8.50.

The hydrochloride, m. p. 222–224°, was prepared by passing hydrogen chloride gas into the free base and washing the resulting crystals with acetone. It loses hydrogen chloride slowly on standing in air.

α-(*n*-Butyl)-tetrahydropyridine.—To a Grignard reagent prepared from 4 g. of magnesium, 22 g. of *n*-butyl bromide and 170 cc. of ether, 15 g. of δ-chlorovaleronitrile was added dropwise. A liquid addition product separated out. The ether was replaced by xylene, the temperature raised and the resulting product hydrolyzed as in the α-phenyl preparation. The acid solution was made basic with sodium hydroxide and steam distilled. The distillate was made acid and concentrated by vacuum distillation, and then made basic with sodium hydroxide and extracted with ether. The dried ether extract was fractionated. The yield of a light yellow oil, boiling at 195–200°, which darkens quickly in contact with air, was 4 g. (22% of the theoretical).

Anal. Calcd. for $C_9H_{17}N$: N, 10.07. Found: N, 10.18, 10.00.

The hydrochloride decomposes easily, losing hydrogen chloride in air. The yellow crystalline chloroplatinate, m. p. 156°, was prepared from water solutions.

Anal. Calcd. for $(C_9H_{17}N)_2H_2PtCl_6$: C, 31.38; H, 5.27; Pt, 28.49. Found: C, 31.8; H, 5.32; Pt, 28.3.

α-Phenylpiperidine, in 6.5 g. yield, was prepared as described by Gabriel[5] by reduction of 9 g. of α-phenyltetrahydropyridine with tin and hydrochloric acid. It was characterized by the crystalline hydrate, m. p. 60–61°, and the hydrochloride, m. p. 200–201°.

α-(*p*-Chlorophenyl)-piperidine.—α-(*p*-Chlorophenyl)-tetrahydropyridine, 7 g., was reduced by refluxing with 60 cc. of hydrochloric acid (sp. gr. 1.10) and an excess of granulated tin for three hours. The reaction mixture was made basic with sodium hydroxide and steam distilled. The distillate was made acid with hydrochloric acid and concentrated by vacuum distillation. The hydrochloride salt crystallized out, and after recrystallization the yield was 5.3 g., m. p. 259–260°.

Anal. Calcd. for $C_{11}H_{14}ClN \cdot HCl$: N, 6.04. Found: N, 6.09, 6.02.

The base was freed from 4.7 g. of the hydrochloride with sodium hydroxide solution, extracted with ether and dried over sodium sulfate. The ether solution was fractionated, yielding 3.8 g. of a nearly colorless oil, boiling at 145° (8 mm.), which crystallized, on cooling in an ice-bath, m. p. 16°.

The chloroplatinate melted at 221° with decomposition.

α-(*p*-Tolyl)-piperidine.—A 6-g. portion of the α-(*p*-tolyl)-tetrahydropyridine was hydrogenated by refluxing for three hours with 80 cc. of hydrochloric acid (sp. gr. 1.10) and an excess of granulated tin. The reaction mixture was made basic, using a large excess of sodium hydroxide, and steam distilled. The distillate was made just acid with hydrochloric acid and concentrated by vacuum distillation to 50 cc. From this the base was set free with sodium hydroxide and extracted with ether. The dried ether extract was fractionated, yielding 5 g. of a nearly colorless oil boiling at 135° (8 mm.).

The hydrochloride, m. p. 209–210°, was prepared by passing hydrogen chloride gas into the free base and washing the resulting crystals with acetone.

Anal. Calcd. for $C_{12}H_{17}N \cdot HCl$: N, 6.62. Found: N, 6.71, 6.58.

α-Cyclohexylpiperidine.—A solution of 2.5 g. of α-cyclohexyltetrahydropyridine in 40 cc. of hydrochloric acid (sp. gr. 1.10) was refluxed with an excess of granulated tin for four hours. A separation procedure similar to that used for α-(*p*-tolyl)-piperidine yielded 1.5 g. of a pale yellow oil boiling at 135° (35 mm.).

The hydrochloride, prepared by passing hydrogen chloride gas over the base and washing the resulting crystals with acetone, melted sharply but not quite completely at 197–198°. It was apparent that there was a higher melting product present. Repeated crystallization from water of a rather large amount of the salt yielded a small amount melting at 250°. These two bodies are probably position isomers.

Anal. Calcd. for $C_{11}H_{21}N \cdot HCl$: N, 6.88. Found: N, (product melting at 197–198°) 6.90, (product melting at 250°) 6.91.

α-*n*-Butylpiperidine.—A solution of 1.8 g. of α-(*n*-butyl)-tetrahydropyridine in 20 cc. of hydrochloric acid (sp. gr. 1.10) was refluxed with an excess of granulated tin for three hours. By a separation procedure similar to that for α-(*p*-tolyl)-piperidine 1.5 g. of product, b. p. 185–192°, was obtained.

The hydrochloride, crystallized from water, melted at 185–186°. Löffler and Plöcker[6] reported 181–182° for this constant.

However, Winterfeld and Holschneider[7] reported 186–187°.

Anal. Calcd. for $C_9H_{19}N \cdot HCl$: N, 7.89. Found: N, 7.89, 7.84.

Summary

A satisfactory and convenient method for preparation of α-substituted tetrahydropyridines has been demonstrated.

The yields of the aromatic substituted com-

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[6] Löffler and Plöcker, *Ber.*, **40**, 1323 (1907).

[7] Winterfeld and Holschneider, *Ann.*, **499**, 109 (1932).

pounds are notably superior to those of the aliphatic and cycloparaffinic substituted compounds prepared.

The α-substituted tetrahydropyridines can be reduced easily to the corresponding piperidines with tin and hydrochloric acid.

The following new compounds have been prepared and suitable derivatives reported: α-*n*-butyltetrahydropyridine, α-cyclohexyltetrahydropyridine, α-cyclohexylpiperidine, α-(*p*-tolyl)-tetrahydropyridine, α-(*p*-tolyl)-piperidine, α-(*p*-chlorophenyl)-tetrahydropyridine and α-(*p*-chlorophenyl)-piperidine.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ARMOUR AND COMPANY]

The Preparation and Cracking of High Molecular Weight Nitriles

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Introduction

The present work was undertaken with the object of producing from high molecular weight fatty acids, straight chain aliphatic compounds containing less than thirteen carbon atoms per molecule. It was thought that a mixture of compounds containing only straight chains might be obtained if a fatty acid derivative which contained no oxygen were subjected to a cracking process similar to that used in the petroleum industry. The present paper is a report of the preparation and cracking of high molecular weight aliphatic nitriles and the partial identification and separation of the resulting compounds.

In undertaking a study of the cracking of high molecular weight nitriles a satisfactory method was essential for preparing such nitriles in considerable quantities from acids. The ordinary method of amide dehydration by means of agents such as phosphorus pentoxide or phosphorus oxychloride was not to be considered because of the expense of the reagents.

The pyrolysis of amides to produce nitriles in varying yields has been reported by several authors.[1] Weidel and Ciamician[2] obtained capronitrile by passing a mixture of ammonia and caproic acid vapor over red hot pumice. Mitchell and Reid[3] noted the formation of small amounts of nitriles incidental to the preparation of amides by passing ammonia through acids at 160–190°. These authors state that no amide was obtained from either palmitic or stearic acid and very little from lauric acid under their conditions.

Since lower amides are partially converted to nitriles upon distillation it seemed probable that stearamide with a high boiling point might be completely converted to nitrile in this manner. Accordingly, stearamide was distilled at atmospheric pressure. The distillate was found to consist of a mixture of stearonitrile and stearic acid together with some unchanged amide. Evidently the water formed by the dehydration of one molecule of amide had served to hydrolyze a second molecule. The ammonium stearate thus formed decomposed at the temperature of the distillation to ammonia and acid. The condition may be expressed by the following equilibria

$$\mathrm{RCOOH} + \mathrm{NH_3} \overset{\mathrm{I}}{\rightleftarrows}$$

$$\mathrm{RCOONH_4} \overset{\mathrm{II}}{\xrightleftharpoons[+\mathrm{H_2O}]{-\mathrm{H_2O}}} \mathrm{RCONH_2} \overset{\mathrm{III}}{\xrightleftharpoons[+\mathrm{H_2O}]{-\mathrm{H_2O}}} \mathrm{RCN}$$

In view of the above result, it seemed probable that stearonitrile could be prepared from stearic acid by heating the acid to a sufficiently high temperature in a stream of ammonia. The ammonia would serve to force reaction I to the right and also to sweep out water as it was formed in reactions II and III. This procedure was carried out and was found to produce stearonitrile in excellent yields.

Two methods were used for the cracking of nitriles. The first consisted in passing the nitrile vapors through a glass tube packed with various catalysts maintained at temperatures of 450 to 600°. The second method was to heat the material in a closed vessel to a temperature of approximately 420°. This procedure gave higher yields than the first method and for this

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[1] Wöhler and Liebig, *Ann.*, **3**, 249 (1832); Boehner and Andrews, THIS JOURNAL, **38**, 2503 (1916); Boehner and Ward, *ibid.*, **38**, 2505 (1916); Hurd, Dull and Martin, *ibid.*, **54**, 1974 (1932).

[2] Weidel and Ciamician, *Ber.*, **13**, 84 (1880).

[3] Mitchell and Reid, THIS JOURNAL, **53**, 1879 (1931).