[Contribution from the Department of Chemistry, University of Notre Dame]

THE ACTION OF GRIGNARD REAGENTS ON OXIMES. IV. ALIPHATIC GRIGNARD REAGENTS AND MIXED KETOXIMES[1]

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In previous papers from this Laboratory (1, 2, 3) it has been shown that aryl Grignard reagents react with aryl alkyl ketoximes to yield either ethylenimines or *beta*-amino alcohols, the product obtained depending on the conditions used in the hydrolysis of the Grignard complex. This reaction constitutes a new type of synthesis of ethylenimines.

It was of interest to determine whether the reaction could be extended to aliphatic Grignard reagents. This was found to be the case; ethylenimines have been obtained from acetophenone and propiophenone oximes with ethylmagnesium and propylmagnesium bromides. With the aromatic magnesium halides the optimum temperature appears to be about 135–145°, but with the aliphatic Grignard reagents the reaction is best carried out at 95–100° in toluene solution; higher temperatures cause extensive tar formation.

The ethylenimines obtained in the present work, like those reported earlier, did not reduce an acetone solution of potassium permanganate in the cold, and they were easily hydrolyzed by dilute acid to the corresponding amino alcohols, which were also synthesized by an independent reaction for comparison. Analytical data, molecular refraction and parachor values are in accord with the ethylenimine structures.

One of the ethylenimines (2-phenyl-2-ethylethylenimine) was synthesized in poor yield from the amino alcohol by treatment with thionyl chloride, followed by alcoholic potassium hydroxide. The product so obtained agreed in properties with the material obtained from acetophenone oxime and ethylmagnesium bromide.

EXPERIMENTAL

2-Phenyl-2-ethylethylenimine. A solution of ethylmagnesium bromide prepared from 24 g. of magnesium turnings, 115 g. of ethyl bromide, and 350 ml. of dry ether was distilled until 200 ml. of ether was removed; 200 ml. of dry toluene was added, and then a solution of 34 g. (0.25 mole) of acetophenone oxime in 200 ml. of dry toluene was added dropwise over a period of two hours. The oil-bath surrounding the flask was kept at 90–95° during the addition, and for thirty minutes afterwards. The mixture was hydrolyzed at once by pouring onto ice and ammonium chloride solution; the water layer was extracted several times with ether, and the combined ether solutions were dried over magnesium sulfate. The residue remaining after removal of the ether and toluene was distilled under reduced pressure to yield 14.4 g. of material of b.p. 85–86°/7 mm., n_D^{20}: 1.5318, d_4^{20}: 0.9811, MR_D obs., 46.4, MR_D calc'd, 46.2; parachor obs., 366, calc'd, 375. This is a yield of 37%; in other runs the yields ranged from 20–60%.

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[1] A part of this work was presented before the Organic Division at the St. Louis meeting of the American Chemical Society, April, 1941.

Anal. Calc'd for $C_{10}H_{13}N$: C, 81.63; H, 8.85; N, 9.52; mol. wt., 147.
Found: C, 81.52; H, 9.26; N, 9.21; mol. wt., 149.

The compound did not reduce an acetone solution of potassium permanganate at room temperature in fifteen minutes. It gave a red color with concentrated sulfuric acid.

Treatment of an anhydrous ether solution of the substance with dry hydrogen chloride in ether yielded a rather hygroscopic hydrochloride. After several recrystallizations from absolute alcohol-anhydrous ether mixture this melted at 191–191.5°.

Anal. Calc'd for $C_{10}H_{14}ClN$: Cl, 19.33. Found: Cl, 19.85.

The phenylthiourea of the amine melted at 99–100° after recrystallization from alcohol. The *alpha*-naphthylurea melted at 129–130°.

Hydrolysis. (a) The ethylenimine was refluxed with 4 *N* hydrochloric acid for five minutes or with 2 *N* sulfuric acid for ten minutes. A small amount of oil floating on the solution was removed by extraction with ether, the acid aqueous layer was made basic with ammonium hydroxide and the oil formed taken up in ether. Distillation of the residue remaining after evaporation of the ether yielded an oil, b.p. 108–112°/2 mm., n_D^{20}: 1.533. This oil gave a benzamide, m.p. 114–115.5°, and a hydrochloride, m.p. 181°. 2-Phenyl-1-amino-2-butanol was synthesized from phenacylamine hydrochloride and ethylmagnesium bromide by the method of Tiffeneau and Cahnmann (4). The product, obtained in 30% yield, had b.p. 109–111°/2 mm., n_D^{20}: 1.5331. Its hydrochloride melted at 181–182° and did not depress the melting point of the hydrochloride of the hydrolysis product. The benzamide of 2-phenyl-1-amino-2-butanol melted at 114–114.5° and did not depress the melting point of the hydrolysis product benzamide.

Anal. Calc'd for $C_{17}H_{19}NO_2$: N, 5.2. Found: N, 5.4.

(b) A 1-g. portion of the ethylenimine was refluxed with 6 *N* hydrochloric acid for thirty minutes. The acid solution was extracted with ether, and the ether extract after drying over magnesium sulfate was evaporated to dryness. The residual oil gave a semicarbazone, m.p. 152–153.5°, which did not depress the melting point of the semicarbazone (m.p. 152–152.5°) of *alpha*-phenylbutyraldehyde. The aldehyde was prepared from 2-phenyl-2-ethylethylene oxide by the method of Stoermer (5).

The acid solution remaining from the ether extraction was evaporated to dryness, and the solid so obtained was shown to be ammonium chloride.

Synthesis of 2-phenyl-2-ethylethylenimine from 2-phenyl-1-amino-2-butanol. A mixture of 5.5 g. of 2-phenyl-1-amino-2-butanol hydrochloride, 11 g. of redistilled thionyl chloride, and 100 ml. of dry chloroform was refluxed for three hours. Most of the solvent and excess thionyl chloride were removed by suction, and dry petroleum ether and diethyl ether were added to the residue. The solid so precipitated (3 g.) melted at 145–147° after recrystallization from absolute alcohol-anhydrous ether mixture. A solution of 2 g. of this compound in 60 ml. of absolute alcohol was treated with a solution of 2 g. of potassium hydroxide in 20 ml. of absolute alcohol. The mixture was allowed to stand at room temperature for eight hours, and was then poured into a large volume of water. The turbid solution was extracted several times with ether, and the ether extracts were dried over magnesium sulfate. Distillation of the oil remaining after evaporation of the ether yielded 0.5 g. of a colorless oil, b.p. 92–94°/8–9 mm., n_D^{20}: 1.5281. The hydrochloride of this oil melted at 189–191° and did not depress the melting point of the ethylenimine hydrochloride. The phenylthiourea melted at 99°.

2-Phenyl-2-propylethylenimine. This compound was prepared by the method described above for the ethyl compound, using 34 g. of acetophenone oxime and the Grignard reagent obtained from 24 g. of magnesium and 105 g. of *n*-propyl bromide. The product, isolated in 10–15 g. yield (23–35%) had b.p. 90–91°/3 mm., n_D^{20}: 1.5235, d_4^{20}: 0.9644, MR_D obs. 51.0, MR_D calc'd 50.8. Parachor, obs. 404, calc'd, 414.

Anal. Calc'd for $C_{11}H_{15}N$: C, 81.99; H, 9.32; N, 8.70; mol. wt., 161.
Found: C, 81.83; H, 9.6; N, 8.79; mol. wt., 165.

Like its lower homolog, this substance did not reduce an acetone solution of potassium permanganate in fifteen minutes at room temperature.

The hydrochloride melted at 68–69°.

Anal. Calc'd for $C_{11}H_{16}ClN$: Cl, 17.96.
Calc'd for $C_{11}H_{17}Cl_2N$: Cl, 30.04.
Found: Cl, 20.7, 20.4.

The phenylthiourea of the amine melted at 100° after recrystallization from absolute alcohol.

On hydrolysis of the amine with 2 *N* sulfuric acid a viscous oil was obtained, b.p. 119–122°/4 mm., n_D^{20}: 1.5335. The benzamide of the hydrolysis product melted at 112–113°.

1-Phenyl-1-propyl-2-aminoethanol was prepared in 7.5 g. yield from 0.5 mole of propylmagnesium bromide and 15.2 g. of phenacylamine hydrochloride. The amino alcohol boiled at 125–126°/7 mm. n_D^{20}: 1.5335.

Anal. Calc'd for $C_{11}H_{17}NO$: C, 73.74; H, 9.5; N, 7.82.
Found: C, 73.66; H, 9.66; N, 7.90.

The benzamide of this amino alcohol melted at 112–113° and did not depress the melting point of the benzamide obtained from the hydrolysis product.

Anal. Calc'd for $C_{18}H_{21}NO_2$: N, 4.94. Found: N, 5.12.

2-Phenyl-2-ethyl-3-methylethylenimine. This was obtained in 13.5 g. (50%) yield from the reaction of 26.8 g. of propiophenone oxime with 1 mole of ethylmagnesium bromide in toluene solution at 100°. The material was obtained as a clear, colorless oil, b.p. 77–79°/3 mm., n_D^{20}: 1.5205, d_4^{20}: 0.9614, MR_D obs. 50.9, MR_D calc'd 50.8. Parachor, obs. 408, calc'd, 414.

Anal. Calc'd for $C_{11}H_{15}N$: C, 81.99; H, 9.32; N, 8.70; mol. wt. 161.
Found: C, 81.84; H, 9.51; N, 8.62; mol. wt. 167.

The hydrochloride melted at 158–159°.

Anal. Calc'd for $C_{11}H_{16}ClN$: Cl, 17.96. Found: Cl, 17.72.

The phenylthiourea melted at 130–131°.

Hydrolysis of the compound with 2 *N* sulfuric acid yielded a viscous oil, b.p. 106–110°/6 mm., n_D^{20}: 1.5350. This material formed a hydrochloride, m.p. 228°, and a benzamide, m.p. 160°. At the time this work was done 1-phenyl-1-ethyl-2-aminopropanol was not described in the literature (6). It was synthesized, therefore, from *alpha*-aminopropiophenone hydrochloride and ethylmagnesium bromide. The substance so obtained had b.p. 106–108°/5 mm., n_D^{20}: 1.5347.

Anal. Calc'd for $C_{11}H_{17}NO$: C, 73.74; H, 9.5; N, 7.82.
Found: C, 73.81; H, 9.72; N, 7.78.

The hydrochloride melted at 230° and the benzamide at 160°. These derivatives did not depress the melting points of the corresponding derivatives obtained from the hydrolysis product of the ethylenimine. The benzamide was analyzed for nitrogen.

Anal. Calc'd for $C_{18}H_{21}NO_2$: N, 4.94. Found: N, 5.20.

SUMMARY

1. Ethylenimines are obtained by the action of aliphatic Grignard reagents on aryl alkyl ketoximes. Three such ethylenimines have been prepared and characterized.

2. The ethylenimines have been hydrolyzed to amino alcohols by dilute acid. The amino alcohols have been synthesized in other ways for comparison.

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