

with 50 cc. of carbon tetrachloride, filtered and the product recrystallized from dilute alcohol; yield 49 g. (quantitative), m. p. 99–101°.

Anal. Calcd. for $C_5H_8N_2O_2Cl_2$: Cl, 35.67. Found: Cl, 35.75.

N-Phenyl-N'-methacrylylurea.—A solution of 25 cc. of methyl methacrylate in 30 cc. of acetone was treated with 15.8 g. (0.1 mole) of sodium phenylurea. Considerable heat was liberated with the formation of a transparent semi-solid mass. After twelve hours a small amount of water was added and the white crystalline precipitate filtered. Upon crystallization from alcohol, beautiful white crystals, m. p. 130–131°, were obtained; yield 8.8 g. (43%).

Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.70; H, 5.88; N, 13.72. Found: C, 64.40; H, 5.97; N, 14.09.

N-Phenyl-N'-methacrylylurea was also conveniently prepared by slowly treating a solution of 90 g. (0.66 mole) of phenylurea in 1 liter of liquid ammonia with 15.2 g. of sodium. The sodium phenylurea remained in solution, in contrast to sodium urea, which is only slightly soluble in liquid ammonia. A solution of 90 g. of methyl methacrylate in 50 cc. of acetone was then added by means of a dropping funnel. The ammonia was allowed to evaporate and the residue treated as described above; yield 80 g. (58.8%).

Methacrylylaniline.—Sodium aniline was prepared³ by treating 31 g. (0.33 mole) of aniline with 13 g. (0.33 mole) of powdered sodamide. A solution of 40 g. of methyl methacrylate in 100 cc. of benzene was slowly added and this mixture gently refluxed for one hour, cooled, diluted with water, and the upper benzene layer separated. Concentration of the solution on a steam-bath yielded methacrylylaniline (22 g.) which upon crystallization from ligroin melted at 84–85°. Although white at first, the crystals darkened somewhat on standing.

(3) Titherley, *J. Chem. Soc.*, 71, 460 (1897).

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.53; H, 6.83; N, 8.69. Found: C, 74.08; H, 6.63; N, 9.00.

N-Methacrylyl-N'-phenylhydrazine.—A suspension of sodium phenylhydrazine in benzene was prepared⁴ by treating a solution of 27 g. of phenylhydrazine in 200 cc. of benzene with 10 g. of powdered sodamide. The mixture was refluxed for one hour and 35 g. of methyl methacrylate slowly added. The mixture was cooled, diluted with water, and acidified with hydrochloric acid. The mixture was filtered and the solid material crystallized from dilute alcohol. N-Phenyl-N'-methacrylylhydrazine was obtained as scale-like crystals, m. p. 130.5–131.5°, yield 10 g. (22%). The compound is soluble in hydrochloric acid but reprecipitated by sodium hydroxide.

Anal. Calcd. for $C_{10}H_{12}N_2O$: C, 68.18; H, 6.81; N, 15.90. Found: C, 68.67; H, 7.29; N, 15.25.

Summary

1. Methacrylylurea and N-phenyl-N'-methacrylylurea have been prepared by the reaction of methyl methacrylate with monosodium urea and monosodium phenylurea, respectively. The latter is easily prepared by the action of sodium upon the urea in liquid ammonia.

2. Methacrylylurea polymerizes readily when heated in alcohol solution in the presence of benzoyl peroxide. The polymer is insoluble in water and in organic solvents.

3. Methacrylylaniline and N-methacrylyl-N'-phenylhydrazine have been obtained from methyl methacrylate and the sodium derivatives of aniline and phenylhydrazine, respectively.

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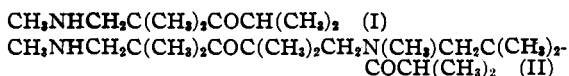
[CONTRIBUTION NO. 171 FROM THE CHEMICAL DEPARTMENT, E. I. DU PONT DE NEMOURS & COMPANY]

The Mannich Reaction: β -Aminoketones from Diisopropyl Ketone

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This paper deals with the preparation of several new β -aminoketones¹ from diisopropyl ketone by means of the Mannich reaction.

The reaction of diisopropyl ketone with aqueous formaldehyde and methylamine hydrochloride yielded methylamino-*t*-butyl isopropyl ketone (I) and a diketone having the empirical formula $C_{19}H_{28}N_2O_2$. The method of preparation and analytical data suggest that the diketone has the structure (II) and was formed from two molecules each of methylamine and diisopropyl ketone and three molecules of formaldehyde. A small amount of non-distillable sirupy resin was also obtained, indicating that further condensation had proceeded to a limited extent.



It is of interest that the same aminoketone (I) was obtained when ammonium chloride was substituted for methylamine hydrochloride in the

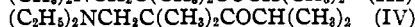
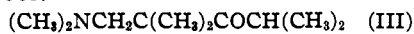
(1) Jacobson, U. S. Patent 2,179,215.

above condensation. The explanation lies in the fact that ammonium chloride and aqueous formaldehyde yield substantial amounts of methylamine when heated.² The equivalence of the monomeric products from the two reactions was indicated by the similarity of their physical constants and demonstrated by the preparation of identical hydrochlorides. While the high-boiling fraction obtained from ammonium chloride, formaldehyde and diisopropyl ketone appeared to contain more than one compound, at least one of them was identical with II. This fact was established by the preparation of identical aminodiketone hydrochlorides from the high-boiling fractions of both reactions.

The formation of diketones analogous to II is obviously precluded in the case of a secondary amine. Dimethylamine hydrochloride and diethylamine hydrochloride yielded the aminoketones, dimethylamino-*t*-butyl isopropyl ketone (III) and diethylamino-*t*-butyl isopropyl ketone (IV), respectively, upon condensation with form-

(2) Werner, *J. Chem. Soc.*, 121, 844 (1917).

aldehyde and diisopropyl ketone. However, the secondary amines reacted much more slowly than the primary amines and the yields of aminoketone were poor.



Isobutyraldehyde, aqueous formaldehyde and ammonium chloride reacted readily to give a complex sirupy product. A small part of this sirup was volatile upon attempted distillation at low pressures but the main portion invariably resinified. The sirup responded to tests for the amine and aldehyde groups. It appears likely that the sirup consisted of secondary derivatives resulting from the condensation of the aminoaldehyde initially formed.

Experimental

Condensation of Diisopropyl Ketone, Formaldehyde and Methylamine.—A mixture of 114 g. (1 mole) of diisopropyl ketone, 135 g. (2 moles) of methylamine hydrochloride and 300 g. (3.7 moles) of 37% formaldehyde solution was gently refluxed and stirred thoroughly. The ketone at first formed an immiscible layer on the surface of the reaction mixture but gradually disappeared during twelve hours. The mixture was extracted with ether to remove unchanged diisopropyl ketone (9 g.) and made alkaline with 50% potassium hydroxide solution. The upper layer was separated, the aqueous portion extracted several times with ether, and the combined product and extracts dried with magnesium sulfate. Upon distillation two products were obtained, boiling, respectively, at 80° (18 mm.) (13 g.) and 155° (3.5 mm.) (100 g.). The analytical data indicate that the lower boiling compound was the expected methylamino-*t*-butyl isopropyl ketone and the higher boiling product a diketone corresponding to formula (II). The refractive index, n_D^{20} , of the monomer was 1.4350 and of the diketone 1.4585.

The reaction proceeded much more slowly when stirring was not employed. In a run similar to the above, but without stirring, a small layer of unchanged ketone remained after 140 hours. It is also of interest that the simple aminoketone was formed in much the larger amount, the ratio of aminoketone to diketone being 3.5 to 1 as compared with a ratio of 1 to 8 when stirring was employed.

Anal. Calcd. for $\text{C}_9\text{H}_{19}\text{NO}$ (I): C, 68.79; H, 12.10; N, 8.91; mol. wt., 157. Found: C, 69.51; H, 11.91; N, 9.19; mol. wt., 161.

Anal. Calcd. for $\text{C}_{15}\text{H}_{33}\text{N}_2\text{O}_2$ (II): C, 69.93; H, 11.65; N, 8.58; mol. wt., 326. Found: C, 70.08; H, 11.67; N, 8.93; mol. wt., 284.

The hydrochloride of (I) melted at 165° and the dihydrochloride of (II) at 160°. *Anal.* Calcd. for $\text{C}_9\text{H}_{20}\text{NOCl}$ (hydrochloride of I): C, 55.81; H, 10.33; Cl, 18.34. Found: C, 55.40; H, 10.33; Cl, 19.00. Calcd. for $\text{C}_{15}\text{H}_{40}\text{N}_2\text{O}_2\text{Cl}_2$ (dihydrochloride of II): Cl, 17.79. Found: Cl, 18.27.

Condensation of Diisopropyl Ketone, Formaldehyde and Ammonium Chloride.—A mixture of 342 g. (3 moles) of diisopropyl ketone, 163.5 g. (3 moles) of ammonium chloride and 870 g. (10.7 moles) of 37% formaldehyde solution was gently refluxed and vigorously stirred for twenty-five hours. The subsequent treatment followed the procedure described above. Unchanged ketone amounting to 45 g. was recovered. Two main products, boiling, respectively, at 73–74° (15 mm.) (81 g.) and at 140–170° (3.5 mm.) (228 g.) were obtained. When stirring was not employed and the reaction permitted to continue for several days the ratio of ketone to diketone was approximately 2 to 1. The refractive indices, n_D^{20} of the two fractions were 1.4348 and 1.4573, respectively.

The physical constants and analytical data indicated that the products of this and the preceding condensation were the same. Confirmation was obtained by preparation of the hydrochlorides.

Anal. of the aminoketones. Calcd. for $\text{C}_9\text{H}_{19}\text{NO}$ (I): C, 68.79; H, 12.10; N, 8.91; mol. wt., 157. Found: C, 69.53; H, 11.67; N, 8.67; mol. wt., 161. Calcd. for $\text{C}_{15}\text{H}_{33}\text{N}_2\text{O}_2$ (II): C, 69.93; H, 11.65; N, 8.58. Found: C, 69.64; H, 10.99; N, 8.88.

The hydrochlorides of the ketone and diketone melted at 164–165 and 159.5°, respectively, and the melting points were not depressed by the addition of the corresponding hydrochlorides from the previous run.

Anal. of the hydrochlorides. Calcd. for $\text{C}_9\text{H}_{20}\text{NOCl}$: C, 55.81; H, 10.33; Cl, 18.34. Found: C, 56.00; H, 9.91; Cl, 18.66. Calcd. for $\text{C}_{15}\text{H}_{40}\text{N}_2\text{O}_2\text{Cl}_2$: Cl, 17.79. Found: Cl, 18.34.

Dimethylamino-*t*-butyl Isopropyl Ketone (III).—This compound was prepared from 171 g. (1.5 moles) of diisopropyl ketone, 122 g. (1.5 moles) of dimethylamine hydrochloride and 432 g. of 37% formaldehyde solution. Much of the ketone (150 g.) remained unreacted after ninety-three hours of stirring and refluxing. The dimethylamino-*t*-butyl isopropyl ketone (10 g.) was obtained as a colorless liquid, b. p. 81–83° (14 mm.), n_D^{20} 1.4338.

Anal. Calcd. for $\text{C}_{10}\text{H}_{21}\text{NO}$: C, 70.17; H, 12.28; N, 8.18. Found: C, 69.17; H, 12.00; N, 8.06.

Diethylamino-*t*-butyl Isopropyl Ketone (IV).—This amino ketone was obtained from 114 g. (1 mole) of diisopropyl ketone, 73 g. (1 mole) of diethylamine, 98.6 g. of strong hydrochloric acid (sp. gr. 1.1878), and 287 g. of 37% formaldehyde solution. The unreacted diisopropyl ketone at the end of sixty-seven hours amounted to 61 g. The diethylamino-*t*-butyl isopropyl ketone (37 g.) was obtained as a colorless liquid, b. p. 100–102° (12 mm.), n_D^{20} 1.4390.

Anal. Calcd. for $\text{C}_{12}\text{H}_{25}\text{NO}$: C, 72.37; H, 12.56; N, 7.04. Found: C, 71.40; H, 12.49; N, 7.48.

Condensation of Isobutyraldehyde, Formaldehyde and Ammonium Chloride.—In an attempt to prepare methylaminomethylisobutyraldehyde ($\text{CH}_2\text{NHCH}_2\text{C}(\text{CH}_3)_2\text{CHO}$), a mixture of 107 g. (2 moles) of ammonium chloride, 400 g. (4.9 moles) of aqueous formaldehyde (37%) and 160 g. of isobutyraldehyde was gently refluxed for four hours in an atmosphere of nitrogen. The product (206 g.), obtained by the procedure already described, was an oily yellow non-distillable reactive sirup exhibiting both aldehyde and amine reactions. Upon standing, considerable unidentified solid material (40 g.) melting at 160° separated.

Anal. of the sirup: C, 57.66; H, 10.76; N, 9.94; mol. wt., 153. Of the solid, m. p. 160°: C, 62.45; H, 10.23; N, 12.10; mol. wt., 253.

Summary

1. The condensation of diisopropyl ketone with aqueous formaldehyde solution and methylamine hydrochloride yielded methylamino-*t*-butyl isopropyl ketone, $\text{CH}_3\text{NHCH}_2\text{C}(\text{CH}_3)_2\text{COCH}(\text{CH}_3)_2$, and a diketone, $\text{CH}_3\text{NHCH}_2\text{C}(\text{CH}_3)_2\text{CO}-\text{C}(\text{CH}_3)_2\text{CH}_2\text{N}(\text{CH}_3)\text{CH}_2\text{C}(\text{CH}_3)_2\text{COCH}(\text{CH}_3)_2$, in varying ratios depending upon the experimental conditions.

2. Ammonium chloride can be substituted for methylamine hydrochloride in this reaction with formation of the same products.

3. Dimethylamino-*t*-butyl isopropyl ketone and diethylamino-*t*-butyl isopropyl ketone were obtained from dimethylamine hydrochloride and diethylamine hydrochloride, respectively, by condensation with diisopropyl ketone and formaldehyde. Secondary amines reacted much more slowly than primary amines.

4. A complex sirupy product was obtained from isobutyraldehyde, formaldehyde and ammonium chloride.