405. *The Lability of the Dimethylamino-group in Some Dimethylamino-ketones.*

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The lability of the dimethylamino-group in ω-dimethylaminoacetophenone and β-dimethylaminopropiophenone results in the formation of trimethylamine when these ketones are treated with methyl iodide in an alkaline medium. It also leads to the formation of abnormal products when they react with phenylhydrazine, *viz.*, the osazone of phenylglyoxal from the former and 1 : 3-diphenylpyrazoline from the latter. β-Dimethylaminoethyl methyl ketone reacting with phenylhydrazine forms 1-phenyl-3-methylpyrazoline. The reaction of these ketones with hydrazine is more complicated.

The alkaloid gramine (3-dimethylaminomethylindole), treated with methyl iodide in an alkaline medium, loses the dimethylamino-group and gives a compound, $C_{10}H_{11}ON$, which is probably 3-methoxymethylindole (see preceding paper). In order to find an analogous reaction some tertiary amines have been treated with methyl iodide under similar conditions.

ω-Dimethylaminoacetophenone forms with methyl iodide in a neutral medium the methiodide of the base. When the reaction is carried out in the presence of methyl-alcoholic potassium hydroxide, trimethylamine is formed; the only other product isolated is benzoic acid. ω-Dimethylaminoacetophenone methiodide, treated with alkali, yields the same products (cf. Rumpel, *Arch. Pharm.*, 1899, **237**, 225). β-Dimethylaminopropiophenone and methyl iodide in neutral solution also give the methiodide, but when the reaction is carried out in the presence of methyl-alcoholic potassium hydroxide trimethylamine and a nitrogen-free compound ($C_{18}H_{16}O_2$) are formed. The latter is probably 1 : 2-dibenzoyl*cyclo*butane, conceivably formed by the condensation of two molecules of phenyl vinyl ketone originating from the Hofmann degradation of the quaternary salt. β-Dimethylaminoethyl methyl ketone, reacting in methyl-alcoholic potassium hydroxide with methyl iodide, forms tetramethylammonium iodide and presumably vinyl methyl ketone (cf. Robinson, this vol., p. 53).

The reaction of ω-dimethylaminoacetophenone with phenylhydrazine also shows the lability of the dimethylamino-group: in 50% acetic acid solution, the osazone of phenylglyoxal is formed. The same substance has been obtained in a similar way from ω-aminoacetophenone. This reaction resembles the formation of glyoxalosazone from aminoacetaldehyde and phenylhydrazine (Fischer, *Ber.*, 1893, **26**, 95) and of methylglyoxalosazone from phenylhydrazine and aminoacetone (Gabriel and Pinkus, *ibid.*, p. 2202). Treatment of β-dimethylaminopropiophenone with phenylhydrazine in 50% acetic acid solution yields 1 : 3-diphenylpyrazoline (Auwers, *Ber.*, 1932, **65**, 833). Similarly, formation of 1-phenyl-3-methylpyrazoline takes place in the reaction between β-dimethylaminoethylmethyl ketone and phenylhydrazine.

The reaction of ω-dimethylaminoacetophenone with hydrazine in 50% acetic acid solution is more complicated. The *compound* obtained has the formula $C_{16}H_{16}N_6$. β-Dimethylaminopropiophenone and hydrazine in acetic acid solution give a crystalline yellow *substance*, $(C_6H_6N)_n$, m. p. 141°.

EXPERIMENTAL.

Action of Methyl Iodide and Potassium Hydroxide on ω-Dimethylaminoacetophenone.—The ketone (3 g.) (Stevens, Cowan, and MacKinnon, J., 1931, 2570) was dissolved in methyl alcohol (15 c.c.) and mixed with methyl iodide (3 c.c.) and 25% methyl-alcoholic potassium hydroxide (40 c.c.). After 1—2 days' standing at 37° a strong basic smell was noticed. Air was bubbled through the alcoholic solution and passed into alcoholic picric acid. The crystalline picrate obtained, after recrystallisation from alcohol, proved to be trimethylamine picrate, m. p. and mixed m. p. 216°. The methyl-alcoholic solution was then poured into water (*ca.* 300 c.c.), acidified with dilute hydrochloric acid, and extracted with ether. After being dried with sodium sulphate, the ether was removed on the water-bath; the residue separated from light petroleum (b. p. 60—80°) in crystals of benzoic acid, m. p. and mixed m. p. 121°.

ω-Dimethylaminoacetophenone methiodide was treated under the same conditions with methyl-alcoholic potassium hydroxide only; trimethylamine and benzoic acid were again formed.

Action of Methyl Iodide and Potassium Hydroxide on β-Dimethylaminopropiophenone.—The procedure was that described above [β-dimethylaminopropiophenone (Mannich and Heilner, *Ber.*, 1922, **55**, 356) 3 g., methyl alcohol 15 c.c.; 25% methyl-alcoholic potassium hydroxide 40 c.c., methyl iodide 4 c.c.]. Trimethylamine picrate, m. p. 215—216°, was obtained. The oily residue left on evaporation of the ethereal extract partly crystallised on cooling. Repeated crystallisation from carbon tetrachloride gave 0·6 g. of a *substance*, m. p. 172° [Found: C, 81·5, 81·6; H, 6·0, 6·1; *M* (Rast), 290. $(C_9H_8O)_2$ requires C, 81·8; H, 6·0%; *M*, 264], very soluble in alcohol, acetone, chloroform and ethyl acetate.

β-Dimethylaminopropiophenone methiodide, treated in the same way with methyl-alcoholic potassium hydroxide alone, gave the same two products.

Action of Methyl Iodide and Potassium Hydroxide on β-Dimethylaminoethyl Methyl Ketone.—Methyl-alcoholic potassium hydroxide (5 c.c.) and methyl iodide (20 drops) were added to a solution of 0·2 c.c. of β-dimethylaminoethyl methyl ketone (Mannich, *Arch. Pharm.*, 1917, **255**, 1566) in methyl alcohol (0·5 c.c.). After 1 hour a crystalline precipitate formed, m. p. above 340°. A small amount of this compound was dissolved in hot alcohol, and alcoholic picric acid added; the solution after concentration deposited long hairy needles, m. p. 290° (tetramethylammonium picrate has m. p. 312—313°).

Phenylhydrazine and ω-Dimethylaminoacetophenone.—The ketone (2 g.) and phenylhydrazine (3 c.c.) were dissolved in 50% acetic acid (20 c.c.) and heated on the water-bath; after 10 minutes a yellow solid separated. After 1 hour's heating, the mixture was poured into water, and the crystalline precipitate collected. Repeated crystallisation from alcohol gave yellow needles of the phenylosazone of phenylglyoxal, m. p. 155° (Found: N, 17·9. Calc. for $C_{20}H_{18}N_4$: N, 17·8%). The same osazone was obtained when aminoacetophenone hydrochloride (2 g.), dissolved in 50% acetic acid (20 c.c.), and phenylhydrazine (2 c.c.) were heated for ½ hour on the water-bath; the thick oil separating soon solidified. After being washed with water and recrystallised several times from alcohol, it had m. p. 155°.

Phenylhydrazine and β-Dimethylaminopropiophenone.—β-Dimethylaminopropiophenone hydrochloride (3 g.), sodium acetate (3 g.), and phenylhydrazine (3 g.) were dissolved in 50% acetic acid (30 c.c.) and heated on the water-bath for 1—2 hours. The clear solution soon became turbid and a thick oil separated, which crystallised on cooling. The mixture was poured into water (*ca.* 300 c.c.) and the solid was washed with water and recrystallised three times from alcohol, giving colourless crystals (1·5 g.), m. p. 151°, of 1 : 3-diphenylpyrazoline (Found: C, 81·1; H, 6·4; N, 12·8. Calc. for $C_{15}H_4N_2$: C, 81·1; H, 6·4; N, 12·6%).

Phenylhydrazine and β-Dimethylaminoethyl Methyl Ketone.—The ketone (2 c.c.) and phenylhydrazine (4 c.c.), treated as described above, gave a solid. This was dissolved in the minimum amount of alcohol, an equal volume of saturated alcoholic hydrogen chloride added, and the mixture refluxed for 2 hours on the water-bath. On cooling, a crystalline solid appeared. The product was poured into water and made alkaline with sodium hydroxide. After 12 hours a crystalline substance separated, which, recrystallised once from alcohol and twice from light petroleum (b. p. 60—80°), gave 1-phenyl-3-methylpyrazoline, m. p. 73° (Found: C, 74·8; H, 7·4; N, 17·6. Calc. for $C_{10}H_{12}N_2$: C 75·0; H, 7·6; N, 17·5%).

Hydrazine and ω-Dimethylaminoacetophenone.—The ketone (1 g.) and hydrazine hydrate (50% solution) (5 c.c.) were mixed with 70% acetic acid (10 c.c.) and heated on the water-bath for ½ hour. The thick oil obtained solidified on addition of water, and after two recrystallisations from alcohol colourless crystals, m. p. 206°, were obtained [Found: C 66·3; H, 5·4; N, 28·8; *M* (Rast), 258. $C_{16}H_{16}N_6$ requires C, 66·5; H, 5·5; N, 28·8%; *M*, 290].

Hydrazine and β-Dimethylaminopropiophenone.—The ketone hydrochloride (2 g.) and sodium acetate (2 g.) were dissolved in water (5 c.c.) and mixed with hydrazine hydrate (50% solution) (7 c.c.) and acetic acid (70%) (10 c.c.). After the treatment described above, the *product* was obtained in pale yellow needles, m. p. 141° [Found: C, 78·5; H, 6·6; N, 14·9; *M* (Rast), 93. C_6H_6N requires C, 78·2; H, 6·5; N, 15·2%; *M*, 92]. In spite of the molecular weight the substance seems to be a polymer.

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