[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

# The Reaction of Hydrazine with Some α-Dimethylaminoacetophenones

BY ROBERT L. LETSINGER AND ROBERT COLLAT

The hydrazone of α-dimethylaminoacetophenone may be prepared by refluxing a mixture of the ketone and 85% hydrazine hydrate for a short time. It decomposes when heated with potassium hydroxide to give N,N-dimethylphenethylamine. When the aminoketone is heated for a longer period of time with hydrazine hydrate, the amino group is lost and acetophenone hydrazone is formed. Deamination occurs more readily with the hydroxydimethylaminoacetophenones than with the parent compound. A course for these cleavage reactions is proposed, and the data are correlated with related reactions reported in the literature.

Apparently the Wolff–Kishner reaction has not been used for the reduction of α-aminoacetophenones to the corresponding phenethylamines.[1] In fact, no account of the preparation of an α-aminoacetophenone hydrazone has been noted by the authors, although some reactions of hydrazine with these ketones have been reported. For example, Darapsky and Spannagel[2] obtained diphenyldihydropyrazine, aminoacetophenone azine and anhydrobisphenacylamine from some reactions between hydrazine and aminoacetophenone, and Jacob and Madinaveitia[3] isolated an unidentified compound, I (analyzed as $C_{16}H_{16}N_6$), from a reaction of hydrazine with α-dimethylaminoacetophenone in acetic acid.

We have observed, however, that α-dimethylaminoacetophenone hydrazone can be prepared conveniently in good yield by refluxing the aminoketone or its hydrochloride for a short time with 85% hydrazine hydrate. These conditions had been employed successfully by Lock and Stach[4] for the preparation of hydrazones of acetophenone and the hydroxyacetophenones. The dimethylaminoacetophenone hydrazone decomposed normally when heated with powdered potassium hydroxide to give N,N-dimethylphenethylamine (73%).

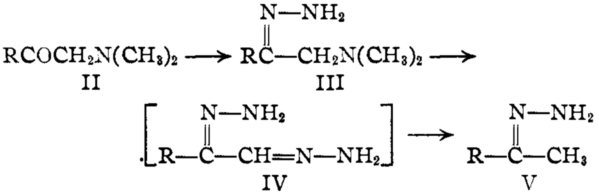
An attempt was then made to extend this procedure to the reduction of *o*- and *p*-hydroxy-α-dimethylaminoacetophenone. But with these compounds it was found that nitrogen gas was evolved during the period of heating with hydrazine; and in place of the expected products, the hydrazones of *o*- and *p*-hydroxyacetophenone were isolated. These hydrazones were obtained directly from the reaction in a relatively pure state, contaminated with only small amounts of the corresponding ketazines. For every mole of cleaved hydrazone which was formed approximately one mole of nitrogen and a little under three moles of a volatile base were liberated. The volatile base consisted of ammonia and dimethylamine (isolated as their picrates). These data are in accord with the equation for the hydrazine reaction

$$\mathrm{RCOCH_2N(CH_3)_2 + 3N_2H_4 \longrightarrow RC(CH_3){=}NNH_2 + N_2 + 2NH_3 + HN(CH_3)_2 + H_2O} \quad (1)$$

As a result of this deamination, the attempts to reduce the hydroxydimethylaminoacetophenones to the corresponding phenethylamines were generally unsuccessful. A low yield (12%) of *o*-hydroxy-N,N-dimethylphenethylamine was realized by refluxing the aminoketone with hydrazine hydrate and carrying out the potassium hydroxide decomposition directly in this mixture.

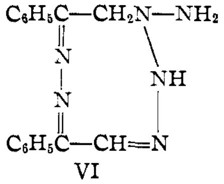
Subsequently it was found that on long heating with hydrazine hydrate, dimethylaminoacetophenone itself underwent cleavage to give acetophenone hydrazone. The rate of this reaction was accelerated by small amounts of hydrochloric acid (*i.e.*, the amine hydrochloride reacted faster than the free base) and by using relatively more hydrazine.

It appears likely that these cleavage reactions involve the formation and partial decomposition of a bishydrazone (IV).[5] This view is in agreement with reaction 1, and is supported by the chemistry of related compounds. Thus the formation of a bishydrazone might be expected since phenylhydrazine converts α-dimethylaminoacetophenone to phenylglyoxal bisphenylhydrazone,[3] and the lability of the aldehydic hydrazone is plausible in view of the unusual ease of decomposition of glyoxal α-monohydrazone.[6] Furthermore, we have found that compound I obtained by Jacob and Madinaveitia is the same as a substance isolated by Stolle[7] from a reaction of phenacyl bromide and hydrazine in alcohol. Stolle proposed structure VI for this compound. Although this particular cyclic formulation might be questioned, the general structural features appear correct. This substance (rewritten in VIa to emphasize the hydrazone character) therefore corresponds to the azine form of the proposed intermediate IV. Jacob and

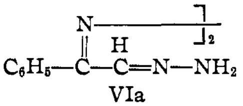


$$\underset{\text{II}}{\mathrm{RCOCH_2N(CH_3)_2}} \longrightarrow \underset{\text{III}}{\mathrm{R\overset{\overset{\displaystyle N-NH_2}{\|}}{C}-CH_2N(CH_3)_2}} \longrightarrow$$

$$\underset{\text{IV}}{\left[\mathrm{R-\overset{\overset{\displaystyle N-NH_2}{\|}}{C}-CH{=}N-NH_2}\right]} \longrightarrow \underset{\text{V}}{\mathrm{R-\overset{\overset{\displaystyle N-NH_2}{\|}}{C}-CH_3}}$$



VI



VIa

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[1] D. Todd. "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., p. 378.

[2] A. Darapsky and H. Spannagel, *J. prakt. Chem.*, **92**, 290 (1915).

[3] A. Jacob and J. Madinaveitia, *J. Chem. Soc.*, 1929 (1937).

[4] G. Lock and K. Stach, *Ber.*, **77**, 293 (1944). See also G. Lock, *et al.*, *Osterr. Chem. Ztg.*, **50**, 5 (1949).

[5] For R = phenyl, it is known that hydrazone formation occurs more rapidly than cleavage, so the reaction sequence indicated probably represents the major course of the reaction. For R = hydroxyphenyl, cleavage of the dimethylamino group prior to the reaction of the carbonyl group with hydrazine could be significant.

[6] L. Wolff, *Ann.*, **394**, 33 (1912).

[7] R. Stolle, *J. prakt. Chem.*, **131**, 275 (1931).

Madinaveitia carried out their reaction in an aqueous acetic acid solution. It now appears reasonable that VI should be formed under these conditions because the temperature was low (steam-bath), the time of reaction short (30 minutes), and the acid should both favor the cleavage of the dimethylamino group and retard the decomposition of the aldehydic hydrazone to V (by reducing the base concentration to a very low value). Also, their conditions would favor ketazine rather than hydrazone formation at the β-carbon.[4a] In view of the proposed transformation, IV → V, one would expect VI to decompose readily in the presence of a suitable base; and indeed this was found to be true. It decomposed smoothly when heated with a solution of potassium hydroxide in ethanol to give two mole equivalents of nitrogen and an oil from which was isolated acetophenone azine.

## Experimental

**α-Dimethylaminoacetophenone.**—A cold solution of 50.3 g. (0.253 mole) of phenacyl bromide in 200 ml. of ether was added in portions to 176 ml. of a chilled, 20% dimethylamine solution in anhydrous ether. The mixture was allowed to stand with occasional shaking for 12 hours at 0°, then filtered to remove inorganic salts and distilled. There was obtained 27.2 g. (66%) of α-dimethylaminoacetophenone, b.p. 83.5–84° (15 mm.).

In a similar run, the hydrochloride salt was precipitated from the ether solution by the addition of alcoholic hydrochloric acid; weight of salt, 37.6 g. (75%). Recrystallization afforded 29.6 g. (59%) of the hydrochloride, m.p. 176–178°; reported m.p., 174°.[8]

The semicarbazone of this aminoketone was prepared from semicarbazide hydrochloride and sodium acetate; m.p. 132.5–133°.

*Anal.* Calcd. for $C_{11}H_{16}ON_4$: N, 25.4. Found: N, 25.2.

**o-Hydroxy-α-dimethylaminoacetophenone.**—To a cold solution of 23.3 g. (0.155 mole) of sodium iodide in 100 ml. of dry acetone was added a solution of 26.5 g. (0.155 mole) of *o*-hydroxy-α-chloroacetophenone[9] (m.p. 71–71.5°). After the mixture had stood at 0° with occasional shaking for a half-hour, a solution of dimethylamine (0.326 mole) in 200 ml. of ether was added. This mixture was then allowed to stand for 14 hours at 0°, after which an additional 400 ml. of anhydrous ether was added. The precipitated salts were removed by filtration and the filtrate concentrated to a volume of 400 ml. under vacuum. From this solution was obtained the aminoketone hydrochloride (28.6 g.) by the addition of alcoholic hydrochloric acid. Two recrystallizations from isopropyl alcohol yielded 20.5 g. (61%) of white crystals, m.p. 105–107°.

*Anal.* Calcd. for $C_{10}H_{14}O_2NCl$: N, 6.49. Found: N, 6.38.

**p-Hydroxy-α-dimethylaminoacetophenone.**—This compound was prepared from *p*-hydroxy-α-chloroacetophenone[9] (15.0 g., m.p. 151–152°) in a manner similar to that used for the ortho isomer. In this case, however, as a result of the lesser solubility of the para compound, a considerable portion of the amine precipitated from the ether solution along with the inorganic salts. Therefore, this precipitate was extracted exhaustively with large portions of ether, and the amine hydrochloride then precipitated from the ether solutions by addition of alcoholic hydrochloric acid. In this way there was obtained altogether 8.16 g. (43%) of the aminoketone hydrochloride (m.p. 233–235°). Recrystallization from isopropyl alcohol yielded 6.35 g. (33%) of purified product, m.p. 242–243° (reported, 233–235°).[10]

**α-Dimethylaminoacetophenone Hydrazone.**—A mixture of 9.2 g. of dimethylaminoacetophenone and 18.5 ml. of 85% hydrazine hydrate was vigorously refluxed for 70 minutes, cooled, and extracted with ether. Distillation of the ether extract, which had been dried over potassium hydroxide, yielded 7.63 g. (76%) of the hydrazone derivative; b.p. 116–124° (3 mm.), m.p. 31–40°. After two recrystallizations from hexane, a sample which melted at 50–51.5° was obtained.

*Anal.* Calcd. for $C_{10}H_{15}N_3$: N, 23.7. Found: N, 24.0.

**N,N-Dimethylphenethylamine.**—An intimate mixture of 5.9 g. of the hydrazone (m.p. 31–40°) and 2.9 g. of powdered potassium hydroxide was heated on an oil-bath at 110–125°. At the end of one hour 50% of the theoretical amount of nitrogen had been liberated. After eight hours of heating (98% of the theoretical nitrogen had been evolved), the mixture was cooled, treated with 25 ml. of water, and extracted with ether. The ether extract was dried and distilled to give 3.55 g. (73%) of dimethylphenethylamine; b.p. 92–93° (18 mm.) (reported b.p., 89–91° at 16 mm.),[11] $n^{25}_D$ 1.5003. The picrate melted at 136–136.5° (reported 135–136°),[12] and the chloroplatinate, at 203–205° (reported 206–208°).[13]

**Cleavage of Dimethylaminoacetophenone with Hydrazine.**—A sample of the aminoketone (3.0 g.) evolved nitrogen slowly at a uniform rate (3.2 cc. per hour) when refluxed with 6 cc. of 85% hydrazine hydrate. At the end of 21 hours only 14% of the theoretical volume of nitrogen (calculated on the basis of one mole of nitrogen per mole of aminoketone) had been liberated. When a 2.0-g. sample of the aminoketone was similarly treated with 20 cc. of the hydrazine hydrate, the rate of reaction was greater; thus the percentages of nitrogen given off at the end of 12, 24, 48, 60 and 72 hours was 30, 62, 89, 99 and 99, respectively. The reaction occurred even more rapidly when the aminoketone hydrochloride was used, as shown by the following example.

A mixture of 2.55 g. of dimethylaminoacetophenone hydrochloride and 20 cc. of 85% hydrazine hydrate was refluxed for 18 hours. At the end of 1, 2, 6 and 18 hours, nitrogen evolution had amounted to 12, 21, 58 and 109% of the theoretical. The reaction had ceased by the end of this time. Extraction and distillation of the reaction product yielded 1.33 g. (78%) of acetophenone hydrazone, b.p. 81–82° (0.3 mm.), m.p. 16–20°. The 2,4-dinitrophenylhydrazone prepared from 0.167 g. of this material weighed after recrystallization 0.25 g. (67%) and melted at 246–247°. It did not depress the melting point of an authentic sample of acetophenone 2,4-dinitrophenylhydrazone. Another sample of the hydrazone (1.07 g.) on recrystallization from benzene–pentane yielded 0.43 g. of the purified acetophenone hydrazone, m.p. 23–24° (reported m.p. 26°).[4]

**Cleavage of o-Hydroxydimethylaminoacetophenone (a) (As the Free Base).**—The free base was liberated from 4.4 g. of the aminoketone hydrochloride by shaking it with 10 ml. of hydrazine hydrate (85%). After extraction from the hydrazine with ether and then removal of the solvent, the residual aminoketone was added to 8 ml. of fresh 85% hydrazine hydrate, which was soon brought to reflux. Exit gases were passed through a saturated alcoholic solution of picric acid and collected in a gas buret over water. Fifty per cent. of the theoretical nitrogen had collected by the end of three hours, and 85% by the end of seven hours. At this point gas evolution had practically ceased, and yellow crystals had formed in the picric acid solution. The reaction mixture was cooled and extracted with ether. The extracts were dried, and the ether boiled off on a steam-bath. There was left an oily residue which solidified on cooling to give 2.6 g. (85%) of light yellow needles, m.p. 78–82°. One recrystallization from ethanol afforded thick, colorless needles of *o*-hydroxyacetophenone hydrazone, m.p. 83–84° (reported, 84°)[4] admixed with a very few fine yellow needles of the azine, m.p. 197–198° (reported, 197°).[4] A 1-g. portion of the hydrazone was hydrolyzed with a mixture of acetic and hydrochloric acids, and then converted to the oxime; m.p. 111.5–112° (reported for *o*-hydroxyacetophenone oxime, 112°).[14] The crystals in the picric acid bubbler were filtered, washed with ethanol and dried; m.p. 245–260° with decomposition. A sample of ammonium picrate prepared independently decomposed similarly. On long standing, the filtrate deposited large yellow crystals of dimethylammonium picrate, m.p. 158–160° (reported 158–159°).[15]

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(8) E. Eidebenz, *Arch. Pharm.*, **280**, 49 (1942).

(9) K. Fries and W. Pfaffendorf, *Ber.*, **43**, 212 (1910).

(10) J. Corrigan, M. Langerman and M. Moore, THIS JOURNAL, **67**, 1894 (1945).

(11) J. N. Brann and L. Neumann, *Ber.*, **49**, 1286 (1916).

(12) K. Kindler, *Ann.*, **431**, 219 (1923).

(13) H. Decker and P. Becker, *Ber.*, **45**, 2407 (1912).

(14) W. Dunstan and T. Henry, *J. Chem. Soc.*, 69 (1899).

(15) G. Jerusalem, *ibid.*, 1279 (1909).

(b) (As the Hydrochloride).—The refluxing of a mixture of 4.4 g. of the aminoketone hydrochloride and 18 ml. of 85% hydrazine hydrate yielded 52% of the theoretical nitrogen after two hours, and 85% after six hours. Gas evolution had virtually ceased by the end of this time. On working up as in the previous case there was obtained 2.7 g. (88%) of crude product, m.p. 80.5–83°. One recrystallization from ethanol gave, as before, needles of the hydrazone, m.p. 83–84°, interspersed with a few yellow needles of the azine, m.p. 197–198°. In this experiment the exit gases had been passed through 100 ml. of 1.16 *N* sulfuric acid. Titration showed that 2.6 moles of amine had been adsorbed per mole of nitrogen collected.

**Cleavage of *p*-Hydroxydimethylaminoacetophenone.**—A mixture of 1.1 g. of the aminoketone hydrochloride and 5 ml. of 85% hydrazine hydrate was refluxed in an oil-bath maintained at 130–140°. After two hours 53% of the theoretical nitrogen had been collected, and after six hours, the evolution had practically ceased (83%). The reaction mixture solidified on cooling. It was broken up, filtered, and washed with cold water. There remained 0.5 g. (66%) of crude *p*-hydroxyacetophenone hydrazone, m.p. 145–152°. The filtrate and wash water were extracted with ether and yielded an additional 0.11 g. (14%) of the crystalline hydrazone, m.p. 145–150°. Recrystallization from ethanol afforded colorless, stout prisms of the pure hydrazone, m.p. 154–155°. A mixed melting point with *p*-hydroxyacetophenone hydrazone (m.p. 154–155°), prepared directly from *p*-hydroxyacetophenone, showed no depression.

***o*-Hydroxy-N,N-dimethylphenethylamine.**—To a mixture of 7.6 g. of the aminoketone hydrochloride and 7 ml. of 85% hydrazine hydrate which had refluxed for one hour was added 36 g. of powdered potassium hydroxide. After 90 minutes of continued heating, 104% of the theoretical nitrogen (on basis of the hydrazone decomposition without deamination) had been evolved. The reaction mixture was cooled, although nitrogen was still being evolved, and poured into water. The solution was acidified, washed with ether, made basic with sodium bicarbonate and extracted with four portions of ether. On drying and evaporation of the ether there was obtained 1.2 g. of oily residue, which yielded 0.7 g. (12%) of product; b.p. 82–85° (0.5 mm.).

*Anal.* Calcd. for $C_{10}H_{15}ON$: N, 8.48. Found: N, 8.46.

The product was not very soluble in water, but dissolved in 10% sodium hydroxide and in dilute hydrochloric acid. It formed a chloroplatinate, m.p. 159–161°, and a picrate, m.p. 148–149°.[16]

*Anal.* of picrate. Calcd. for $C_{16}H_{18}O_7N_4$: N, 14.21. Found: N, 14.32.

**Identity of I and VI.**—α-Dimethylaminoacetophenone, hydrazine, acetic acid and water were permitted to react under the conditions specified by Jacob and Madinaveitia.[8] There was isolated a solid compound which melted after two recrystallizations from alcohol at 209–210°. Stolle's directions[7] for the preparation of VI were followed, and yielded a compound melting at 209–210°. The melting point of a mixture of these two compounds was also 209–210°.

**Base Decomposition of VI.**—Compound VI (1.76 g.) was added to a solution of approximately 1 g. of potassium hydroxide in 15 cc. of absolute ethanol. The major portion of VI remained undissolved. When the mixture was refluxed on a steam-bath, nitrogen was evolved at a constant rate (1.14 cc. per min.) until 93% of the theoretical amount (base on two moles of nitrogen per mole of compound) had been liberated. At this point gas evolution abruptly ceased and no more gas was evolved even though the refluxing was continued. During this heating period compound VI dissolved and formed a red-brown solution in the alcohol. Extraction and distillation (0.3 mm.) of the brownish-yellow oil which formed when the solution was added to water gave a light yellow distillate that crystallized to a large extent on standing. Recrystallization of the solid portion from alcohol yielded a yellow solid, m.p. 122–122.5°. The melting point of acetophenone azine prepared independently[4] and also a mixed melting point for these two substances was the same.

Stolle describes a similar reaction in which he isolated material which melted at 121°, but he failed to characterize it as the azine, apparently as a result of a faulty combustion analysis.

**Acknowledgment.**—This work was supported by the Research Corporation. Analyses were made by C. Brauer and J. Sorensen.

[16] J. v. Braun and O. Bayer, *Ber.*, **57**, 913 (1924), reported melting points of 144° and 142° for the chloroplatinate and picrate, respectively. Analyses were reported for neither.

EVANSTON, ILLINOIS RECEIVED JULY 20, 1951

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE]

# The Effect of Oxygen on the Polymerization of Acrylonitrile[1]

BY KENNETH C. SMELTZ AND ELIZABETH DYER

Studies were made of the effect of oxygen on acrylonitrile in aqueous solutions using potassium persulfate, in non-aqueous solutions with benzoyl peroxide, in bulk systems with benzoyl peroxide and in photosensitized systems with diacetyl as initiator. In all cases normal polymerization was inhibited if the mixture was agitated in the presence of 100% oxygen. The rate of absorption of the oxygen varied with the initial concentrations of the initiator and of the acrylonitrile, and with the solvent. In aqueous systems the absorption of oxygen was initially first order with respect to the persulfate concentration and three-halves order with respect to the acrylonitrile. Over long periods of time the order with respect to persulfate changed from first order for the lowest concentration to three-halves order for the highest. A highly unstable peroxide, of molecular weight approaching that of a trimer, was isolated from non-aqueous experiments. This was shown to give the same decomposition products as were obtained from the aqueous experiments, namely, hydrogen cyanide, carbon dioxide, formaldehyde, the cyanohydrin of glycolic aldehyde and glycolic acid. Evidence was also obtained for the presence of carbon monoxide and a solid substance with terminal unsaturation. Quantitative data from experiments in aqueous solution showed that for every three moles of oxygen absorbed, three moles of hydrogen cyanide, one mole of formaldehyde and one mole of carbon dioxide were produced.

Because of the increasing interest in the effect of oxygen on vinyl polymerizations,[2] an investigation was made of this effect with acrylonitrile. Bacon[3] showed that oxygen inhibited the aqueous solution polymerization of acrylonitrile by causing an induction period which varied with the oxygen content of the system, the temperature and the concentration of initiator. Morgan[4] found that the induction period was inversely proportional to the initial persulfate concentration. Baxendale, Evans and Park,[5] who studied the polymerization of acrylonitrile with hydrogen peroxide–ferrous salt

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[1] From the Ph.D. dissertation of Kenneth C. Smeltz, University of Delaware, June, 1951. This research was supported in part by the Office of Naval Research under contract N7-onr-492.

[2] (a) F. A. Bovey and I. M. Kolthoff, THIS JOURNAL, **69**, 2143 (1947); (b) C. E. Barnes, R. M. Elofson and G. D. Jones, *ibid.*, **72**, 210 (1950); (c) V. Gutmann, *J. Polymer Sci.*, **3**, 336 (1948); (d) H. E. Worrell, M. S. Thesis, University of Delaware, June, 1950.

[3] R. G. R. Bacon, *Trans. Faraday Soc.*, **42**, 141 (1946).

[4] L. B. Morgan, *ibid.*, **42**, 169 (1946).

[5] J. H. Baxendale, M. G. Evans and G. S. Park, *ibid.*, **42**, 155 (1946).