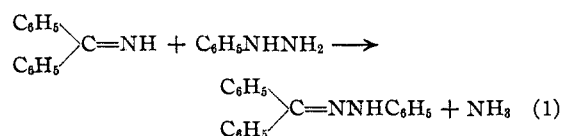# The Ammono Ketone-Alcohols. I. Benzophenoneimine

BY G. E. P. SMITH, JR., AND F. W. BERGSTROM

Cornell, and Bergstrom and Fulton[1] have shown conclusively that the nitriles are the anammonides of the carbazylic acids. Ammonolysis of the addition products of Grignard reagents with carbazylic acid derivatives should yield ammono ketones, the nitriles themselves yielding the ketimines or ammono ketone-alcohols, $\underset{R''}{\overset{R'}{\diagdown}}C=NH$, and the substituted acids (amidines) yielding the ammono ketone-ethers, $\underset{R''}{\overset{R'}{\diagdown}}C=NR'''$. Such an ammonolysis was in fact carried out with the addition product of benzonitrile and phenylmagnesium bromide on a small scale in a Faraday tube by Cornell. We have extended this method for larger scale operation, and have made it a general reaction for the preparation of a number of ketimines, including benzophenoneimine.[2]

The only general reaction of the ketimines reported in the literature is that of hydrolysis to the corresponding aquo ketones.[3] Hence a study is being made of their reactions from the standpoint of the ammonia system of compounds, the present paper dealing exclusively with benzophenoneimine.

As a result of the present investigation benzophenoneimine has been found to react vigorously with phenylhydrazine to give benzophenone phenylhydrazone

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NH + C_6H_5NHNH_2 \longrightarrow$$

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NNHC_6H_5 + NH_3 \quad (1)$$
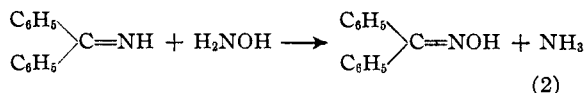
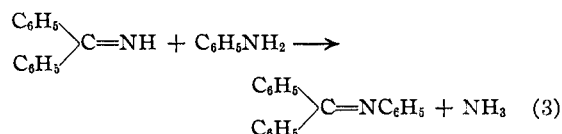with hydroxylamine in liquid ammonia to form benzophenone oxime

(1) "The Nitrogen System of Compounds," by E. C. Franklin, to be published by the Chemical Catalog Company, 1934; Cornell, THIS JOURNAL, 50, 3311 (1928); Bergstrom and Fulton, ibid., 53, 3092 (1931).

(2) Other methods of preparation of the ketimines are given in the following references: (a) ammonolysis of ketones, Moureu and Mignonac, Compt. rend., 169, 237 (1919), and Strain, THIS JOURNAL, 52, 820 (1930); (b) reduction of ketoximes, Moureu and Mignonac, Compt. rend., 170, 936 (1920); (c) pyrolysis of benzophenone oxime, Lachman, THIS JOURNAL, 46, 1477 (1924); and (d) hydrolysis of the addition products of Grignard reagents with nitriles, Moureu and Mignonac, Compt. rend., 156, 1801 (1913); ibid., 159, 149 (1914), and Ann. chim., 14, 322 (1920).

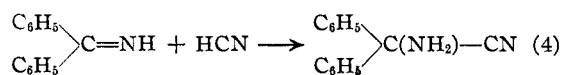(3) Thorpe and Best, J. Chem. Soc., 95, 1506 (1909); Moureu and Mignonac, Ref. 2.

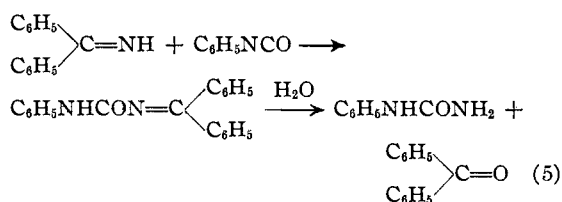$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NH + H_2NOH \longrightarrow \underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NOH + NH_3 \quad (2)$$

and with aniline to form benzophenone anil

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NH + C_6H_5NH_2 \longrightarrow$$

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NC_6H_5 + NH_3 \quad (3)$$

Benzophenoneimine readily adds hydrogen cyanide in absolute alcohol

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NH + HCN \longrightarrow \underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C(NH_2)-CN \quad (4)$$

Phenyl isocyanate reacts with benzophenoneimine producing benzohydrylidenephenylurea, which is easily hydrolyzed to phenylurea and benzophenone

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NH + C_6H_5NCO \longrightarrow$$

$$C_6H_5NHCON=C\underset{C_6H_5}{\overset{C_6H_5}{\diagup}} \overset{H_2O}{\longrightarrow} C_6H_5NHCONH_2 +$$

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=O \quad (5)$$

With potassium and sodium amides in liquid ammonia, benzophenoneimine forms highly colored and very soluble salts.[4]

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NH + NaNH_2 \longrightarrow \underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NNa + NH_3 \quad (6)$$

$$\underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C=NH + 2KNH_2 \longrightarrow \underset{C_6H_5}{\overset{C_6H_5}{\diagdown}}C\underset{NHK}{\overset{NHK}{\diagup}} + NH_3 \quad (7)$$
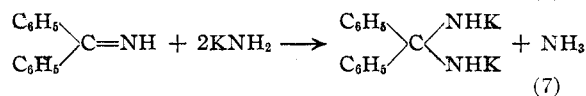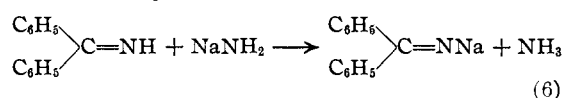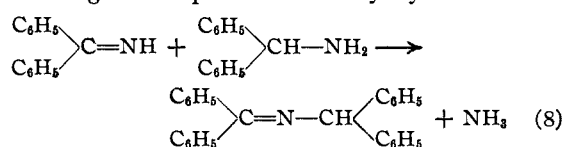
Solutions of metallic potassium and sodium in liquid ammonia give highly colored and very soluble products which cannot be freed from ammonia and an excess of metal for analysis. Hydrolysis of these reaction products produces a mixture of benzohydrylamine and benzophenone, the yield of benzohydrylamine reaching a maximum of about 50% of the theoretical even though a large excess of sodium is used in the reaction. A small amount of hydrogen is produced in the reaction, indicating a very slow replacement of

(4) For salts of aquo ketones, including benzophenone, see Strain, THIS JOURNAL, 52, 3383 (1930).

the hydrogen of the imine by sodium. The reactions of benzophenoneimine with sodium, potassium, sodium amide and potassium amide, all produce deep red liquid ammonia solutions of identical appearance. These facts indicate the formation of the monosodium ketyl of benzophenoneimine, followed by reaction with ammonia (ammonolysis) to an equimolecular mixture of amine and imine, just as the monosodium ketyl of benzophenone may be hydrolyzed to a mixture of alcohol and ketone. Sodium amide is formed in the ammonolysis, so that the reaction mixture should have the same color characteristics as the solutions formed from the alkali amides with benzophenoneimine. Some disodium ketyl may be formed and subsequently hydrolyzed to benzohydrylamine, but the ammonolysis of this ketyl should be at the most only partial on the basis of the "benzohydryl rule" of Wooster,[5] and if this were a major product of the reaction, the use of larger amounts of sodium should result in a larger yield of ketyl and of benzohydrylamine, contrary to the fact that the yield of benzohydrylamine reaches a maximum of about 50% of the theoretical regardless of the excess of sodium used.

Filtered phenylmagnesium bromide fails to reduce benzophenoneimine, probably due to the insolubility of the magnesium halide salt of the imine which is first formed. With the reducing system, $Mg-MgI_2$, however,[6] there is first formed a very stable complex of benzophenoneimine and magnesium iodide, $[(C_6H_5)_2C=NH]_2 \cdot MgI_2$, and on long heating followed by ammonolysis with liquid ammonia, some benzohydrylamine is formed as the reduction product.

In each of the reduction reactions that part of the benzophenoneimine left unreduced reacts readily with the product, benzohydrylamine, forming benzophenonebenzohydrylimine

$$\begin{array}{l} C_6H_5 \\ \Large{\rangle}\normalsize C=NH + \\ C_6H_5 \end{array} \begin{array}{l} C_6H_5 \\ \Large{\rangle}\normalsize CH-NH_2 \longrightarrow \\ C_6H_5 \end{array}$$

$$\begin{array}{l} C_6H_5 \\ \Large{\rangle}\normalsize C=N-CH\Large{\langle}\normalsize \begin{array}{l} C_6H_5 \\ C_6H_5 \end{array} + NH_3 \quad (8) \\ C_6H_5 \end{array}$$

This substance is also the product formed if any unfiltered Grignard reagent is allowed to react with benzophenoneimine at elevated temperatures in diamyl ether. In fact, a small amount of reduction takes place in ethyl ether if the solution is boiled for some time or if considerable iodine is

(5) Wooster and Ryan, THIS JOURNAL, 54, 2419 (1932); 56, 1133 (1934).

(6) Gomberg and Bachmann, ibid., 49, 236 (1927).

added in order to start the Grignard reaction. This reduction is not by the Grignard reagent itself, since the filtered reagent was found to have no reducing action on benzophenoneimine; neither is it by magnesium alone, as that was also found to be without action on benzophenoneimine, even when the two were boiled together for several days in ether and in benzene. Hence the reducing agent is in this case, as found by Gomberg and Bachmann with aquo ketones, the *combination* of magnesium with magnesium halide. The reduction product, however, is the ammono secondary alcohol, benzohydrylamine, in contrast to the benzopinacol produced by the reduction of aquo benzophenone. If any ammono benzopinacol or benzopinacolin is formed in these reduction reactions, it is unstable, or has not as yet been identified among the products.

Experimental

Preparation of Benzophenoneimine.—To a solution of filtered phenylmagnesium bromide prepared from 4.64 g. (0.191 mole) of magnesium was added 19.7 g. (0.191 mole) of benzonitrile in small portions with constant stirring. The white crystalline addition product was broken up thoroughly and, after lowering the temperature of the flask to the boiling point of ammonia, liquid ammonia was added directly to the flask, a little at a time, pouring from a well-made Pyrex Dewar tube down a stirring rod. After evaporation of excess liquid ammonia, the remaining solid was extracted with dry ether and filtered on a Buchner funnel. The suction caused boiling of the ether and loss of most of the remaining gaseous ammonia. The clear ether solution, treated with dry hydrogen chloride, produced 24.6 g. of the white benzophenoneimine hydrochloride, 59.2% of the theoretical. This hydrochloride was hydrolyzed in 95% yield to benzophenone. Treatment with dry gaseous ammonia in chloroform produced the pure imine, and samples of hydrochloride prepared from this imine were hydrolyzed quantitatively to benzophenone. The crude hydrochloride melted with decomposition from 250° up, but the pure material, crystallized from glacial acetic acid and from chloroform, showed no decomposition or softening below 310°.

Picrate, yellow grains from boiling alcohol, m. p. 281–282°, with slow decomposition; benzoyl chloride yields only benzophenoneimine hydrochloride and carbon dioxide forms no carbonate, in contradistinction to benzohydrylamine.

Reaction with Phenylhydrazine.—Two grams of benzophenoneimine was added to an equal volume of phenylhydrazine, and the homogeneous mixture heated to 60–70° for about forty-five minutes. On cooling, a mass of beautiful white crystals of benzophenone phenylhydrazone separated from the brown liquid; stubby white needles from boiling alcohol; yield, 1.44 g. or 47.9%; m. p. 138–139°.

Anal. Calcd. for $(C_6H_5)_2C=N_2HC_6H_5$: N, 10.32. Found: N (Dumas), 10.32.

Reaction with Hydroxylamine.—A solution of hydroxylamine in liquid ammonia was obtained in a Faraday tube by the action of ammonia on hydroxylamine sulfate, using technique described elsewhere.[7] Addition of 7.04 millimoles of benzophenoneimine to 6.87 millimoles of hydroxylamine in liquid ammonia solution produced no apparent change, and the oxime could not be crystallized from liquid ammonia solutions. After evaporation of the ammonia, however, benzophenone oxime crystallized from the resulting liquid mixture; yield, 1.32 g. or 97.5%; colorless needles from hot 50% alcohol, m. p. 142–143°.

Anal. Calcd. for $(C_6H_5)_2C=NOH$: N, 7.10. Found: N (Dumas), 7.04.

Reaction with Aniline.—A gram of benzophenoneimine was heated with excess aniline until most of the unreacted aniline had distilled away. Cooling produced crystalline benzophenone anil; crystals from ether and alcohol, m. p. 112–113°; yield, 0.5 g. or 35.3%.

Anal. Calcd. for $(C_6H_5)_2C=NC_6H_5$: N, 5.45. Found: N (Kjeldahl), 5.54, 5.45.

Reaction with Hydrogen Cyanide.—Dry liquid hydrogen cyanide was added in excess to 5.0 g. of benzophenoneimine dissolved in 5 cc. of absolute alcohol. At the end of an hour at 0°, the reaction liquid had set to a nearly solid mass of white crystals of cyanohydrin; yield of purified material, 4.4 g. or 76.5% of the theoretical. The substance is very soluble in alcohol, readily soluble in chloroform and carbon tetrachloride, and somewhat less soluble in ether and benzene, m. p. 101–102°.

Anal. Calcd. for $(C_6H_5)_2C(NH_2)CN$: N, 13.46; C, 80.77; H, 5.77. Found: N (Dumas), 13.66, 13.32; C, 80.33; H, 5.79.

In a Faraday tube a liquid ammonia solution of cyanohydrin could be titrated with a potassium amide solution, the end-point being the first permanent pink color caused by the formation of the characteristic red potassium salt of benzophenoneimine. The end-point corresponded approximately to the addition of equimolecular quantities of the reactants. Evaporation of the resulting solution yielded benzophenoneimine and crystals of potassium cyanide.

Reaction with Phenyl Isocyanate.—Addition of a slight excess of phenyl isocyanate to a solution of benzophenoneimine in an equal volume of dry benzene caused warming of the mixture, and final crystallization of the product, which was washed free of phenyl isocyanate with excess benzene. The benzohydrylidenephenylurea formed was very soluble in chloroform and acetone, less soluble in alcohol and ethyl acetate, and very slightly soluble in carbon tetrachloride. The concentrated solutions were bright yellow in color, but the dilute solutions were colorless. The nearly white crystal plates melted at 160–162° with decomposition.

Anal. Calcd. for $(C_6H_5)_2C=NCONHC_6H_5$: N, 9.33. Found: N (Kjeldahl), 9.25.

Crystallization three times from 95% alcohol separated the compound by hydrolysis into benzophenone of m. p.

48°, and phenylurea of m. p. 143–144°. Mixed melting points with authentic samples of materials showed no lowering in either case.

Formation of the Sodium and Potassium Salts of Benzophenoneimine.—A. In a Faraday tube, addition of 7.45 millimoles of benzophenoneimine in liquid ammonia to 7.40 millimoles of sodium amide produced a deep red solution, which after standing several days was decanted away from the unreacted excess of sodium amide. Attempts to crystallize the salt from liquid ammonia were unsuccessful, and evaporation of the ammonia left a dark red solid which partly crystallized on standing. It was impossible to remove the last of the ammonia from the precipitate, although the sample was dried *in vacuo* for analysis.

Anal. Calcd. for $(C_6H_5)_2C=NNa$: N, 6.90; Na, 11.34. Found: N (Kjeldahl), 8.87, 8.95; Na, 11.60.

B. Addition of 0.46 millimole of benzophenoneimine hydrochloride to 0.82 millimole of potassium amide produced a white precipitate of potassium chloride and a deep red solution similar to that of the sodium salt. The solution was decanted from the potassium chloride and the ammonia evaporated to give a partially crystalline salt. This was recrystallized several times by dissolving it in liquid ammonia, reprecipitating part of it by evaporation of some ammonia and then decanting the remaining solution. The sample, dried *in vacuo* for analysis, consisted, in large part at least, of deep-colored red crystals. A second sample was prepared in a similar manner, except that benzophenoneiminemagnesium bromide was ammonolyzed in the Faraday tube, and the extracted benzophenoneimine was allowed to react with potassium amide in the same tube.

Anal. Calcd. for $(C_6H_5)_2C(NHK)_2$: N, 10.2, K, 28.47. Found: Sample I: N (Kjeldahl), 11.40, 11.04; K, 25.44. Sample II: N, 9.61. 9.54; K, 25.93.

Reduction of Benzophenoneimine by Alkali Metals.—Attempts to separate the sodium and potassium ketyls from liquid ammonia solutions in Faraday tubes were unsuccessful. Using an apparatus in which larger amounts of materials could be handled in liquid ammonia at its boiling point,[8] 0.0276 mole of benzophenoneimine diluted with 5 cc. of dry benzene was added to 0.085 mole of sodium dissolved in liquid ammonia. The evolved gases were collected and amounted to 7.02 cc. measured at standard conditions, or 2.26% of the theoretical if assumed to be pure hydrogen. After evaporation of the ammonia the red solid was treated with benzene and water. Hydrolysis was vigorous and produced considerable gaseous ammonia. The benzene solution was separated and the benzene boiled away, leaving a brown liquid. This was taken up in dry ether from which 2.55 g. or 42.1% of the theoretical quantity of benzohydrylamine hydrochloride was obtained by treatment with dry hydrogen chloride. Attempted hydrolysis of 0.5 g. of this hydrochloride with boiling hydrochloric acid yielded less than 5 mg. of benzophenone and a sample of crystalline hydrochloride which melted with decomposition at 287–288°. This temperature was unchanged when the material was mixed with authentic benzohydrylamine hydro-

(7) Franklin, This Journal. **35**, 1460 (1913). See Browne, *ibid.*, **33**, 1728 (1911). for a similar preparation of hydrazine in liquid ammonia.

(8) White, *ibid.*, **45**, 779 (1923); Wooster, *ibid.*, **51**, 1856 (1929).

chloride.[9] The ether filtrate from the preparation of benzohydrylamine hydrochloride gave 1.37 g. or a 27.3% yield of benzophenone. In similar experiments (but without the hydrolysis as described above) samples of benzohydrylamine carbonate and picrate were prepared and identified by means of mixed melting points.

Anal. Calcd. for $(C_6H_5)_2CHNH_3Cl$: N, 6.38. Found: hydrochloride, N (Kjeldahl), 6.08, 6.34.

Reduction of benzophenoneimine by sodium in absolute alcohol solutions gave similar results.

Reaction of Benzophenoneimine with Phenylmagnesium Bromide.—In ethyl ether addition of benzophenoneimine to a filtered solution of phenylmagnesium bromide produced immediately the typical precipitate of benzophenoneiminemagnesium bromide. The result was the same in phenetol solutions heated to 130–140° for twenty-one hours. Ammonolysis of the resulting product gave an almost exactly theoretical recovery of benzophenoneimine.

The reaction of unfiltered Grignard reagents with benzophenoneimine gave benzophenonebenzohydrylimine in yields up to 20% of the theoretical. This compound was identified by complete analysis and by mixed melting point. The material for comparison was prepared from benzohydrylamine and benzophenoneimine; crystals from ether, m. p. 154–155°, mixed melting point 153.5–155°; picrate, prepared from warm benzene solutions, m. p. (with slow dec.), 203°; hydrochloride, from glacial acetic acid, m. p. (dec.) 255–258°.

Reduction of Benzophenoneimine by the System, Mg-MgI₂.—Five grams (0.028 mole) of benzophenoneimine in 20 cc. of benzene was added to a solution prepared from 0.058 gram atom of magnesium and 0.30 gram atom of iodine. On warming gently and shaking, the golden yellow addition product of benzophenoneimine and MgI₂ slowly settled out. In one experiment this was filtered, washed well with dry ether and dried for analysis: yield, 6.0 g. or 67.8%.

Anal. Calcd. for $[(C_6H_5)_2C{=}NH]_2{\cdot}MgI_2$: N, 4.37; Mg, 3.79. Found: N (Kjeldahl), 4.45, 4.37; Mg, 3.74, 3.79.

(9) The derivatives of benzohydrylamine used for comparison in this and following experiments were prepared from the amine obtained from hydrobenzamide and phenylmagnesium bromide: Busch and Leefhelm, *J. prakt. Chem.*, [2] **77**, 14 (1908). These derivatives included the hydrochloride, m. p. (with dec.) 290–292°; carbonate, m. p. (with dec.) 95–98°; picrate, m. p. (with dec.) 204°; benzoyl derivative, m. p. 170.5–171; benzohydrylphenylurea (from phenyl isocyanate), m. p. (with dec.) 224–225°; and benzophenone-benzohydrylimine (from benzophenoneimine), m. p. 154–155°.

Water and ammonia each cause immediate separation of the complex into its components. It is, however, very stable toward the action of heat, both dry and in the presence of organic solvents.

In a second experiment with the same amounts of starting materials, refluxing the reaction mixture caused no apparent change, so the solvents were distilled off and the residue ammonolyzed with liquid ammonia. From the warm ether extract of the resulting mixture was obtained 1.25 g. of benzophenonebenzohydrylimine, m. p. 152°, mixed melting point with authentic material without lowering. This was recrystallized unchanged from boiling phenyl isocyanate and hydrolyzed by hydrochloric acid to benzohydrylamine hydrochloride. The filtrate from the above material, treated with carbon dioxide, yielded 1.11 g. of benzohydrylamine carbonate; m. p. (with dec.), 97–100°, mixed melting point without lowering. In a similar experiment, by precipitating benzohydrylamine carbonate immediately from the ether solution after ammonolysis, 2.8 g. of precipitate was obtained, which, with ammonia in chloroform, yielded 1.8 g. of liquid benzohydrylamine, 36%. In the original experiment, the use of a large excess of Mg-MgI₂ appeared to make the addition complex more soluble on heating, but the products obtained after ammonolysis were identical with those already described.

Summary

Benzophenoneimine has been prepared in good yield by direct ammonolysis of the addition product of phenylmagnesium bromide and benzonitrile.

Benzophenoneimine has been shown to have the properties of a typical aromatic ammono ketone-alcohol: readily forming a phenylhydrazone, an oxime and an anil; adding hydrogen cyanide and phenyl isocyanate; forming salts with metallic amides in liquid ammonia; and being reduced by alkali metals and by the system Mg-MgI₂ to benzohydrylamine or the product of its reaction with benzophenoneimine, benzophenonebenzohydrylimine. The reduction to an ammono benzopinacol or benzopinacolin has not as yet been accomplished.

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