[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF TEXAS]

THE AMMONOLYSIS OF BENZIL BY LIQUID AMMONIA¹

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The first observations relative to the interaction of benzil and ammonia were recorded by Zinin (1) more than one hundred years ago. In the intervening years, a considerable body of information on the reactions between benzil and ammoniacal media consisting of aqueous ammonia, alcoholic ammonia, ammonium formate, and ammonium acetate has become available and has led to rather marked divergence of opinion, particularly with regard to the mechanism of these reactions.²

Staudinger and Binkert (3) attempted to prepare a metal salt of benzil by the reaction between the diketone and potassium in liquid ammonia at and below -33.5° , and observed that reaction between benzil and ammonia precluded the possibility of formation of a metal ketyl. Strain (4) heated benzil with ammonia for two hours at 200° (*i.e.*, considerably above the critical temperature of ammonia) and obtained a forty per cent yield of lophine (2,4,5-triphenylglyoxaline). Strain also reported that benzamide and "imabenzil" result from the reaction between benzil and liquid ammonia at room temperature, but gave no experimental data in support of this statement.

The present paper describes the action of liquid ammonia and liquid ammonia solutions of ammonium chloride (an acid) and potassium amide (a base) upon benzil at 103° and 35°. These studies represent an effort to determine the identity of the products and the quantity of each with a degree of accuracy not approached in earlier investigations, as a step preliminary to the study of a series of reactions designed to shed further light upon the mechanism of the reactions concerned.

EXPERIMENTAL

Materials. Benzil was prepared by the method of Adams and Marvel (5). Scholl's (6) color test for the detection of benzoin in the presence of benzil was used as a criterion of purity and only that material $(m.p. 95^{\circ})^3$ which failed to give a positive test for benzoin was employed. All other chemicals used were reagent grade materials.

Reaction with liquid ammonia at 103° . Benzil (10.5 g.) was placed in a Pyrex tube (55 x 2.5 cm.) together with approximately 100 cc. of anhydrous liquid ammonia and the tube was sealed. The tube and about 300 cc. of commercial liquid ammonia were placed in an auto-

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 $^{^{2}}$ For primary references, review, and discussion of possible reaction mechanisms see reference (2).

³ All melting points reported in this paper are corrected.

clave of the type described by Bergstrom (7) and the autoclave was heated by steam at 103° for forty-six hours. The tube was cooled, opened, and 10.05 g. of crude product was removed from the tube, dried, and ground to 60-mesh in an agate mortar. This material was extracted successively with 50-, 30-, and 20-cc. portions of hot water. The aqueous extracts were combined and boiled for one hour with an excess of aqueous potassium hydroxide.⁴ The resulting solution was acidified with hydrochloric acid and cooled. The benzoic acid which separated was removed by filtration, and that remaining in the aqueous solution was removed by extraction with ether. The two crops of acid were combined, dried, and weighed; m.p. 122°. Neutralization equivalent, 123 (calculated, 122).

The water-insoluble material was dried, powdered (60-mesh), and extracted for ten minutes with carbon disulfide in a Soxhlet apparatus. The material insoluble in carbon disulfide was identified as lophine, m.p. 276.5°.

Anal. Calc'd for C₂₁H₁₆N₂: C, 85.11; H, 5.44; N, 9.45.

Found: C, 84.97; H, 5.52; N, 9.51.

The melting point of this product was not depressed by mixing with lophine (m.p. 276.5°) prepared as described by Davidson and co-workers (2). Upon cooling the carbon disulfide solution, a small quantity of lophine separated.⁵ This was removed by filtration and combined with the main body of this product.

The solvent was evaporated from the carbon disulfide solution and the resulting gummy material was boiled with 95% alcohol. A small quantity of pale yellow crystalline material failed to dissolve.⁶ This product melted at 249-250° and the melting point was not raised by recrystallization from glacial acetic acid. A very small quantity of this product imparted an intense red coloration⁷ to concentrated sulfuric acid. A mixture of this product and tetraphenylpyrazine (m.p. 251.5°) prepared as described by Davidson, Weiss, and Jelling (8) melted at 250.5°.

The alcoholic solution was concentrated and cooled. Thus were obtained orange-colored needle-like crystals which, after recrystallization from petroleum ether, melted at 112–113°. This product was shown to consist of 2,4,5-triphenyloxazole by a mixed melting point determination using 2,4,5-triphenyloxazole (m.p. 112–113°) prepared by the method of Schönberg (9).

The yield data relating to products separated by the foregoing procedure as well as those to be described in the following paragraphs are summarized in Table I.

In the foregoing procedure, the ketone was initially in contact with liquid ammonia at -50° (the temperature at which the ammonia was condensed in the tube) and could therefore react with ammonia before the temperature of 103° was reached. To eliminate the possibility of reaction below 103° , the following experiment was conducted. Benzil (32.5 g.) was placed in a Pyrex test tube. The tube was then placed in an inclined position (with the mouth of the tube above the level of the liquid) in a bomb (made of Monel metal and similar

⁴ In a preliminary experiment, the aqueous extracts were cooled, whereupon benzamide, m.p. 127.5°, separated from the solution. The melting point was not depressed when the substance was mixed with an authentic specimen of pure benzamide, m.p. 128°. Thereafter, benzamide was converted to and weighed as benzoic acid by the procedure described above.

⁵ An estimation of the solubility of lophine in carbon disulfide resulted in a value of 0.03 g. of lophine/100 cc. of carbon disulfide at 25°.

⁶ The solubility of tetraphenylpyrazine in 95% alcohol was found to be 0.014 g./100 cc. of solvent, at 25°.

⁷ Laurent [Ann., **52**, 357 (1844)] observed that tetraphenylpyrazine imparts a red coloration to concentrated sulfuric acid and Leuckart [J. prakt. Chem. [2] **41**, 332 (1890)] reported a similar behavior for 2,4,5-triphenyloxazole. In the present investigation, Laurent's observations were confirmed and it was found that pure 2,4,5-triphenyloxazole gives no such color test. Undoubtedly, the oxazole used by Leuckart was contaminated by traces of tetraphenylpyrazine. in construction to an ordinary calorimeter bomb) containing about 200 cc. of liquid ammonia. After being heated (by steam) to 103°, the bomb was tilted and shaken so that the benzil and liquid ammonia might be mixed.⁸ The reaction mixture was heated for twentyfour hours at 103°, after which the solvent was evaporated and the products separated by the procedure previously described. The results of experiments conducted in this manner are listed in Table I.

Reaction with liquid ammonia at 103° in the presence of ammonium chloride. Benzil (34.3 g.) was brought into contact with a solution of ammonium chloride (26.2 g.) in liquid ammonia (approximately 200 cc.) at 103° and the resulting mixture heated at this temperature for twenty-four hours. The method used in separating the products (see Table I) was the same as that previously described excepting that the weight of water-soluble material was corrected for the presence of ammonium chloride in terms of halide ion found (as AgCl).

темр. (°с.)	ACID OR BASE	WT. OF CRUDE PRODUCT (G.)	YIELD (%) ³						
			Benzamide	Lophine	Tetra- phenyl- pyrazine	Tri- phenyl- oxazole	Imabenzil	Benzil- imide	Total
103 ^b	none	10.3	21.7	45.7	0.5	20.0			87.9
٥ 103	none	30.0	31.0	34.0	0.6	28.0		—	93.6
103 d	NH4Cl	34.1	30.5	39.3	0.5	20.5		_	90.8
103	KNH_2	20.6	65.0	19.0	trace	0.0	—		84.0
35	none	39.4	24.6	_	trace	10.0	29.8	13.4	81.1 °
30	none	41.9	22.7		trace	7.0	40.0	4.1	75.8 ^f
35	NH ₄ Cl	40.0	25.7		trace	8.3	27.0	16.4	84.10
35	KNH_2	24.5	60,0	_	trace	0.0	11.0	16.0	87.0 ^h

TABLE I

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^a All yield data are expressed as fractions of the total weight of dry crude product removed from the reaction vessel.

^b Average values from two experiments. Reactions in sealed tubes.

^c Average values from two experiments.

 d Average values from three experiments.

* Total includes 3.3% of carbon disulfide-insoluble product.

¹ Total includes 2.0% of carbon disulfide-insoluble product.

^o Total includes 6.7% of carbon disulfide-insoluble product.

^h No carbon disulfide-insoluble product found in these experiments.

In the course of a series of these experiments, it was found that the yields of lophine and triphenyloxazole vary markedly with variation in the ratio of ketone to ammonia.

Reaction with liquid ammonia at 103° in the presence of potassium amide. A solution of the potassium amide from 17.2 g. of potassium in approximately 200 cc. of liquid ammonia, and 21.0 g. of benzil were brought together at 103° and thereafter heated for twenty-four hours. The yields of the products isolated (benzamide, lophine, and traces of tetraphenylpyrazine) are given in Table I.

Reaction with liquid ammonia at 35° . A series of experiments conducted at or near room temperature showed that the yields of the various products varied considerably with temperature differences of only a few degrees. Consequently, the remaining experiments were conducted in the calorimeter-type bomb just as described previously excepting that the

⁸Benzil is unreactive toward gaseous ammonia. The ketone was recovered unchanged after having been heated in a stream of anhydrous ammonia for six hours at 78°.

bomb and its contents were placed in a thermostat and brought to a temperature of 35° (or 30°) $\pm 0.2^{\circ}$ before mixing the reactants and the temperature maintained throughout the reaction. In this manner, reproducible yield data were obtained readily.

Benzil (42.0 g.) and liquid ammonia (approximately 200 cc.) were mixed at 35° and held at this temperature for twenty-four hours. The solvent was evaporated and the dried and finely powdered crude product was stirred for one hour with 150 cc. of alcohol and filtered. The crude alcohol-insoluble imabenzil was recrystallized by dissolving it in the smallest possible volume of warm pyridine, followed by seven-fold dilution with toluene and cooling overnight in an ice-bath. This method of purification was found to be much more satisfactory than that of Japp and Wynne (10). The pure imabenzil appeared as a white, microcrystalline powder, m.p. 196°.

Anal. Calc'd for C₃₅H₂₈N₂O₃: N, 5.34. Found: N, 5.53.

The solvent was evaporated *in vacuo* from the alcoholic solution and the resulting hard, wax-like material was powdered and extracted with boiling water to remove benzamide, which was determined as benzoic acid. The water-insoluble material was extracted with carbon disulfide, and the small quantity of insoluble material (1.3 g.) was recrystallized from a large volume of alcohol; m.p. 184°. As yet, this product has not been identified. After evaporation of the carbon disulfide, the residues were stirred with 40 cc. of isopropyl ether⁹ for one hour. The insoluble material melted at 139°. The identity of this product as benzilimide [N-desylbenzamide (2)] was established by a mixed melting point determination using benzilimide prepared by the method of Henius (11). The isopropyl ether was recovered and the residual material was recrystallized from alcohol and found to consist of triphenvloxazole. The results of experiments conducted at 35° and 30° are shown in Table I.

Reactions with liquid ammonia at 35° in the presence of ammonium chloride and potassium amide. Experiments similar to those involving ammonium chloride and potassium amide at 103° were conducted at $35^{\circ}\pm0.2^{\circ}$, and the products were separated as described for the reactions with ammonia at 30° and 35° . The yield data are given in Table I.

The Radziszewski glyoxaline synthesis. A modification of Radziszewski's (12) synthesis of glyoxalines was carried out as follows. Benzil (14.0 g.) and benzaldehyde (7.20 g.) were treated with an excess of liquid ammonia for five hours at 35°. The solvent was removed and the crude product (23.2 g.) was extracted with water. The water-insoluble material was extracted with carbon disulfide. The carbon disulfide-insoluble material consisted of substantially pure 2,4,5-triphenyloxazole (lophine). Only traces of lophine could be isolated from the carbon disulfide solution. The yield was 9.75 g. or 42.0%. In a similar experiment conducted at 103° rather than 45°, 10.30 g. of lophine, corresponding to a 45.7 % yield, was isolated.

DISCUSSION

Two different mechanisms designed to account for the various products obtained from the interaction of benzil and ammoniacal media other than liquid ammonia have been proposed. Japp (10, 13) assumed an initial ammonolytic cleavage of benzil whereas the mechanism suggested by Davidson and co-workers (2) avoids this assumption. The latter mechanism was proposed primarily on the strength of the argument that Japp's explanation was inadequate in view of the unidirectional character of the reaction between benzil, benzaldehyde and ammonia in alcohol (Radziszewski's synthesis of glyoxalines). Since the present studies have shown that, *in liquid ammonia*, lophine is formed not quantitatively but only to the extent of 46 %, it seems reasonable to assume that neither of the previously proposed mechanisms will prove adequate finally to explain these apparently complex reactions in liquid ammonia. It is possible, of course, that

⁹ The solubility of benzilimide was found to be 0.10 g./100 cc. of isopropyl ether.

reaction may occur simultaneously in accordance with both mechanisms. The relatively high yields of benzamide obtained in reactions employing potassium amide support Japp's assumption concerning the cleavage of benzil, since a simple ammonolytic cleavage should be expected to be promoted by an increase in the concentration of amide ion. That the reaction between benzil and liquid ammonia should not be strictly analogous to the interaction of the diketone and other ammonolytic media is not unanticipated. The absence of such an analogy has been amply demonstrated in other cases (14).¹⁰

A general criticism of earlier work in this connection lies in the fact that, to the best of the present writers' knowledge, all of the various reaction products formed at any given temperature have not previously been isolated from a single controlled reaction. Neither has there been much attention given to the relative quantities of the various products formed under different conditions of temperature. Accordingly, the studies described in this paper have been concerned largely with the problem of developing methods for the separation and estimation of the various products. The quantities of product unaccounted for in this work are of such magnitude that the losses may reasonably be attributed to mechanical losses resulting from the numerous separations required.

Tetraphenylpyrazine has not been observed previously as a product of the reaction between benzil and ammonia, but Japp and Wilson (16) have identified tetraphenylpyrazine among the products obtained from the reaction between benzoin and ammonia. Since the quantities of tetraphenylpyrazine found in the present investigation were always very small, it is entirely possible that the benzil employed contained quantities of benzoin too small to be detected by Scholl's color test.

From an inspection of the data of Table I, it is seen that (A) lophine is not formed in reactions effected near room temperature; (B) imabenzil and benzilimide do not appear as products of reactions conducted at 103°, and (C) triphenyloxazole is not produced in reactions involving potassium amide. In addition, experiments not reported in this paper have shown that the yield of lophine is a function of the concentration of ammonium chloride present. Until additional studies can be made, efforts to explain these facts could be little more than mere speculation. However, it is believed that the results reported here suggest and serve as a basis for lines of investigation which will eventually lead to a clarification of the entire question of the mechanism of the interaction of benzil and ammonia.

SUMMARY

1. The identification of the products produced by the interaction of benzil and liquid ammonia under several different experimental conditions has been reported.

2. Methods for the separation and estimation of these products have been described.

¹⁰ For review and primary references see reference 15.

3. The Radziszewski glyoxaline synthesis has been shown to result in relatively low yields of lophine when liquid ammonia is used as the reaction medium.

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