[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

ATTEMPTS TO RESOLVE DERIVATIVES OF FLUORENE. PARA-AMINOBENZOPHENONE HYDRAZONE[1]

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Having failed to resolve 2-amino-9-diazofluorene[2] into its optical isomers, we turned our attention to the resolution of other 2,9-fluorene derivatives. A thorough examination of the literature revealed a single case only in which such a resolution had been attempted. Bader[3] attempted to resolve 2,9-diaminofluorene by the use of *d*-tartaric acid and also by the aldehyde condensation product with *d*-helecin. Neither of these agents, however, accomplished any separation. Since there is a possibility that other resolving agents might be more effective, it was decided to prepare his diamine and try other active acids. The reduction of 2-nitrofluorenone oxime following his directions gave only very small yields of impure material but the reduction of 2-aminofluorenone hydrazone by means of zinc dust in boiling glacial acetic acid gave, after hydrolysis of the intermediate acetyl derivative (m. p. 219°), an excellent yield of the beautiful crystals of 2,9-diaminofluorene, m. p. 160°, as described by Bader. The diamine could not be resolved by means of *d*-camphor sulfonic acid, *d*-phenyl-aminoacetic acid, nor *d*-hydroxy-methylene camphor.

Schmidt and Stützel had found[4] that the nitration of 9-acetaminofluorene by means of boiling nitric acid yielded 1,8-dinitrofluorenone, m. p. 197–198°, instead of the 1-nitro-9-acetaminofluorene desired. Modifications of their procedure in an attempt to obtain the desired derivative resulted in the formation of light yellow crystals, m. p. 236–238°. From the analyses, which were not wholly satisfactory, it appeared that the material was 1,8-dinitro-9-acetaminofluorene. Since this compound would be symmetrical, it was not further studied.

The resolution of 2-amino-9-hydroxyfluorene was also attempted by means of *d*-camphor sulfonic acid but no separation could be obtained.

Bader explained his inability to resolve 2,9-diaminofluorene by a rather novel theory based on an assumption that optical isomers do not exist in the case of this compound due to a mutual repulsion between the two amino groups which destroys the tetrahedral arrangement. Since there is no experimental basis for such an assumption, it seems just as likely that the failure to resolve this series of compounds is due to the fact that the right conditions have not yet been found, instead of an inherent lack of isomerism.

[1] Abstract of portions of a thesis submitted by C. W. Bennett in partial fulfilment of the requirements for the degree of Ph.D. at the University of Illinois.

[2] Bennett and Noyes, *Rec. trav. chim.*, **48**, 895–898 (1929).

[3] Bader, "Zur Stereochemie des Fluorens," Dissertation, Vienna, **1926**, pp. 53–54.

[4] Schmidt and Stützel, *Ann.*, **370**, 1–40 (1909).

These results have an interesting bearing on the fact that 2-amino-9-diazofluorene could not be resolved. Since none of the fluorene derivatives have been resolved, it is evident that resolution in this series is, at least, very difficult and the possibility of resolving such a derivative as the diazo compound would necessarily be remote. These results do not prove that the diazo carbon atom is not asymmetric in this compound nor that diazo compounds having an amino group in the molecule cannot be resolved.

In connection with these results, the fact that no substituted diphenylmethane derivatives of the type, $C_6H_5CHX\text{-}C_6H_4\text{-}Y$, have ever been resolved is of interest. Billon[5] has studied this problem and has so far been unsuccessful. Betti[6] and Berlingozzi[7] have, however, resolved α-naphtholphenylaminomethane and naphthylphenylaminomethane, respectively.

In an effort to obtain such a diazo derivative, the synthesis of *p*-aminophenyl phenyldiazomethane was attempted. The oxidation of *p*-aminobenzophenone hydrazone gave a beautiful purple solution which undoubtedly contains the diazo derivative but the latter was so unstable that only the ketazine of *p*-aminobenzophenone could be isolated.

Experimental Part

Preparation of 2-Aminofluorenone.—A suspension of 22.5 g. of 2-nitrofluorenone in 150 cc. of 95% alcohol with 0.2 g. of platinum oxide catalyst[8] was shaken in a bottle with hydrogen under pressure until there was no more absorption. Reduction was quite rapid and beautiful crystals of the amine were obtained. The suspension was heated to boiling and filtered to remove the catalyst and any unreacted nitrofluorenone. The product was purified by dissolving in hot dilute hydrochloric acid and reprecipitating with ammonia. The yield was 18.7 g. or 95% of the theoretical as compared with about 65%, the yield obtained by the use of ammonium sulfide, which is the only method described in the literature.[9] The purple crystals melt at 160°.

Preparation of 2,9-Diaminofluorene.—Bader's[3] method of reducing 2-nitrofluorenone oxime with zinc dust and hot glacial acetic acid yielded only a small amount of impure material. The reduction of 2-aminofluorenone hydrazone in the same manner, however, gave an excellent yield of the diamine.

Zinc dust was added gradually to a boiling solution of 5 g. of the hydrazone in 100 cc. of glacial acetic acid. After two hours the solution was completely decolorized and reduction was complete. The zinc was removed by filtration and ammonium hydroxide added to the cooled filtrate until alkalinity was reached. The resulting white precipitate was recrystallized from acetone, giving white needles, m. p. 219°. The crude material after refluxing for two hours with 20% hydrochloric acid and treating with norit was filtered and cooled. When ammonium hydroxide was added, beautiful silvery flakes were formed, m. p. 156°. Recrystallization from toluene yielded crystals melting at 160° as described by Bader. The first material was apparently the monoacetyl derivative of the diamine and resulted from the boiling with glacial acetic acid.

[5] Billon, *Ann. chim.*, [10] **7**, 314, 384 (1927).

[6] Betti, *Gazz. chim. ital.*, **37**, I, 62 (1907).

[7] Berlingozzi, *ibid.*, **50**, II, 281 (1920).

[8] Voorhees and Adams, THIS JOURNAL, **44**, 1397–1405 (1922).

[9] Diels, *Ber.*, **34**, 1760 (1901).

Anal. Calcd. for $C_{15}H_{14}N_2O$: N, 11.7. Found: N, 11.6.

The material melting at 160° was in all respects similar to Bader's 2,9-diaminofluorene and the synthesis and analysis prove that to be the correct formula; yield, 4.2 g., or 92.5% of the theoretical.

Anal. Calcd. for $C_{13}H_{12}N_2$: N, 14.29. Found: N, 14.4.

The diamine could not be resolved with *d*-camphor sulfonic acid, which gave a salt with a specific rotation of +15.05° for all fractions, the hydrolyzed amine from which was inactive. No salt was formed with *d*-phenylaminoacetic acid and the *d*-hydroxylmethylene camphor derivative could not be crystallized.

Nitration of 9-Acetaminofluorene.—Fluorenone oxime, prepared by the action of potassium ethylate on a mixture of amyl nitrite and fluorene according to Wislicenus' and Waldmüller's directions,[10] was reduced by zinc dust and acetic acid to the fluorenylamine by Schmidt and Stützel's method.[11] Their method of acetylating the amine with acetic anhydride was also used. No nitration occurred when 10 g. of the acetyl derivative was dissolved in 100 cc. of glacial acetic acid and 20 cc. of nitric acid and heated for one hour on the steam-bath. When 6 g. of the acetyl derivative was suspended in 200 cc. of glacial acetic acid and 1.7 g. of nitric acid added, there was no change after two months at room temperature and the acetyl derivative was recovered by the addition of water. Nitration did occur when 10 g. of the acetaminofluorene was added slowly to a mixture of 18 cc. of sulfuric acid and 37 cc. of nitric acid. The product was cooled and poured into ice water. The yellowish mass was recrystallized from boiling glacial acetic acid several times until a stable melting point of 236–238° was obtained. The analysis was not perfectly satisfactory but indicated that the compound was 1,8-dinitro-9-acetaminofluorene. The same compound was also formed when only enough nitric acid was used to obtain the mononitro derivative.

Anal. Calcd. for $C_{15}H_{11}O_5N_3$: C, 57.5; H, 3.51; N, 13.4. Found: C, 58.4; H, 3.79; N, 13.0.

***p*-Aminobenzophenone Hydrazone.**—Phthalanil prepared by Döbner's method[12] of distilling phthalic anhydride and aniline together, was converted into the benzoyl derivative by means of benzoyl chloride and zinc chloride. This material on hydrolysis by Torrey and Rafsky's method[13] gave *p*-aminobenzophenone, m. p. 124°. The hydrazone, which has not been previously described, was prepared by refluxing a mixture of 15 g. of *p*-aminobenzophenone, 15 cc. of 40% hydrazine hydrate and 50 cc. of 95% alcohol for four days with 10 g. of barium oxide. After this period, the filtered solution yielded yellow needles, m. p. 139–140°.

Anal. Calcd. for $C_{13}H_{13}N_3$: N, 19.91. Found: N, 20.2.

The filtrate on evaporation yielded a mixture of the new hydrazone and a yellow powder, m. p. 225°, which was shown to be the ketazine of *p*-aminobenzophenone. The same material was formed when a vacuum distillation of the hydrazone was attempted and also if the hydrazone was recrystallized too many times. Refluxing of the ketazine with 40% hydrazine hydrate solution and barium oxide gave no apparent change.

Anal. Calcd. for $C_{26}H_{22}N_4$: N, 14.3. Found: N, 14.01.

Attempts to oxidize the hydrazone to the diazo compound using mercuric oxide and mercuric acetamide in various solvents gave a purple solution from which the diazo derivative could not be isolated but instead the ketazine was obtained as its decomposition product.

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[10] Wislicenus and Waldmüller, *Ber.*, **41**, 3334–3340 (1908).

[11] Schmidt and Stützel, *ibid.*, **41**, 1246 (1908).

[12] Döbner, *Ann.*, **210**, 267 (1881).

[13] Torrey and Rafsky, THIS JOURNAL, **32**, 1489 (1910).

Summary

1. New syntheses for 2,9-diaminofluorene and for 2-aminofluorenone have been developed. Neither the diamine nor 2-amino-9-hydroxyfluorene could be resolved.

2. Attempts to prepare 1-nitro-9-aminofluorene by nitration of 9-acetaminofluorene resulted in the formation of a compound which was probably 1,8-dinitro-9-acetaminofluorene, m. p. 236–238°.

3. The failure to resolve any 2,9-fluorene compound may be due to a lack of asymmetry or to the fact that the right conditions have not been found. In any case, the failure to resolve 2-amino-9-diazofluorene does not demonstrate that the carbon atom bearing the diazo group is not asymmetric.

4. *p*-Aminobenzophenone hydrazone, m. p. 139–140°, was prepared along with the ketazine, m. p. 225°. The former, on oxidation, yielded an unstable diazo derivative which could not be isolated.

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[CONTRIBUTION FROM THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS]

A METHOD FOR THE STUDY OF TOXICITY USING GOLDFISH[1]

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The use of derris root as a fish poison by the inhabitants of the localities to which this plant is native suggested the use of fishes as test animals in the study of the comparative toxicity of rotenone, an active constituent of that plant, and its derivatives. The goldfish, being a member of the carp family and so at home in sluggish waters, is more adapted to conditions in still water tanks and jars than most of the native fishes. The fact that fishes accustomed to active, cool waters are liable to suffocate when kept in still, comparatively warm water is a factor to be considered. The goldfish is also more easily obtained in large quantity and is inexpensive. The species sold for aquaria, *Carassius auratus*,[2] is the one used here.

In 1915 Pittenger and Vanderkleed[3] and in 1919 Pittenger[4] found that the goldfish was a suitable test animal in the assay of digitalis preparations. In 1917 Powers[5] reported an investigation testing the validity of this method and the use in general of the goldfish as the test animal in the

[1] Presented as a part of the Insecticide Symposium before the Division of Agricultural and Food Chemistry at the 77th Meeting of the American Chemical Society, Atlanta, Georgia, April 7 to 11, 1930.

[2] U. S. Dept. of Commerce, Bureau of Fisheries Econ. Circ. No. 68. p. 1 (1929).

[3] Paul S. Pittenger and Chas. E. Vanderkleed, *J. Am. Pharm. Assocn.*, **4**, 427–433 (1915).

[4] Paul S. Pittenger, *ibid.*, **8**, 893–900 (1919).

[5] Edwin B. Powers, Ill. Biol. Mono., **4**, No. 2 (1917).