

was cleared by filtration, then treated with 10 g. of methyl iodide and set aside until the scarlet color had disappeared. The pale yellow solution thus formed was extracted with ether, the ethereal solution dried over sodium sulfate and allowed to evaporate. It deposited a mixture of yellow needles and a pale yellow high-melting powder.

The yellow needles were extracted with cold acetone and ultimately purified by recrystallization from ether. Like the methyl ether of the Grignard product, this methyl ether of the methyl alcohol addition product loses formaldehyde at the melting point, 175–180°.

Anal. Calcd. for $C_{24}H_{21}O_3N$: C, 77.6; H, 5.7; OCH_3 , 16.7. Found: C, 77.3; H, 5.8; OCH_3 , 14.5.

Summary

1. The preparation of three purple anhydrides from the corresponding oximes is described.

2. These remarkably colored substances are shown to be highly phenylated pyrrolenine oxides—capable of addition to the $>C=NO$ system.

3. The mode of addition with Grignard reagents to these compounds is studied and an analogous addition reaction with sodium methylate is reported.

4. The evidence in favor of a "nitron" formulation as against the carbazoxy ring structure is summarized, support for the former proceeding from this study of the purple anhydrides.

5. The use of the term "nitron" and the method of representing the unsaturated system in nitrones are discussed, preference being given to $>C=NO$.

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A DELICATE COLOR TEST FOR MICHLER'S KETONE AND A LESS SENSITIVE TEST FOR PHOSGENE AND DIALKYL-ANILINES

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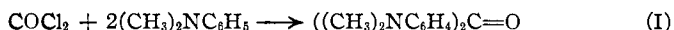
Introduction

The delicate color test of Gilman, Schulze and Heck¹ for reactive organometallic compounds, involving as it does the use of Michler's ketone, suggested its application as a test for Michler's ketone, and for phosgene, which is used in the preparation of the ketone. The test, which has found its widest application with organomagnesium compounds, is readily carried out by adding a very small quantity of the reactive organometallic com-

¹ (a) Gilman and Schulze, *THIS JOURNAL*, **47**, 2002 (1925); *Bull. soc. chim.*, [4] **41**, 1479 (1927); (b) Gilman and Heck, *Rec. trav. chim.*, **48**, 193 (1929); (c) Gilman and Heck, *Ber.*, **62**, 1379 (1929).

pound to Michler's ketone in benzene, hydrolyzing and then developing the color with a glacial acetic acid solution of iodine.

The limiting sensitivity for phosgene depends obviously on the delicacy of the test for Michler's ketone. It was first shown, in the present study, that it is possible to get a positive test with 1 cc. of Michler's ketone in a benzene solution which is 0.00001 molar, by means of a 2.25 molar solution of phenylmagnesium bromide. If it were possible to cause phosgene to react quantitatively with dimethylaniline, as follows



to give Michler's ketone, then it would be possible to get a positive test for a quantity as small as 0.000001 g. of phosgene. This order of sensitivity would be admirably suited for detecting less than toxic doses of phosgene.²

The possibility of getting a complete reaction between phosgene and dimethylaniline was rendered somewhat remote by the observation of Dyson³ that "phosgene reacts very reluctantly with aromatic tertiary amines save in the presence of anhydrous aluminum chloride." However, we found that there is a significant reaction between phosgene and dialkylanilines under ordinary conditions and in the absence of aluminum chloride. Unfortunately, the reaction is not quantitative. It is possible to get a positive test with a 0.202 molar solution of phosgene in benzene, a degree of sensitiveness which is quite inadequate.⁴ This concentration of phosgene is obviously not a limit for the detection by this method of the several dialkylanilines investigated, inasmuch as increasing concentrations of phosgene should favor the formation of ketone from the dialkylanilines. It was also found that tetraethyldiaminobenzophenone, $((\text{C}_2\text{H}_5)_2\text{NC}_6\text{H}_4)_2\text{CO}$, has no advantage over Michler's ketone in the detection of reactive organometallic compounds.

Experimental Part

Michler's Ketone.—The Michler's ketone solutions were prepared by dissolving 0.2682 g. (0.001 mole) of ketone in 100 cc. of dry benzene and by dissolving a like weight in 100 cc. of freshly distilled dimethylaniline. These stock solutions were progressively diluted with benzene and dimethylaniline, respectively, until no positive color test was obtained. A positive test was obtained with 1 cc. of a 0.00001 molar solution of

² Konowalow, *Z. ges. Schiess-Sprengstoffw.*, **22**, 152 (1927), [*C. A.*, **21**, 4033 (1927)], has shown that a concentration of 0.0003 g. of phosgene in a liter of air is toxic to animals. On this basis 3 cc. of such an air mixture would be adequate for a positive test, providing the phosgene could be made to react quantitatively with dimethylaniline.

³ Dyson, *Chemical Reviews*, **4**, 109 (1927), has recently reviewed the chemistry of phosgene. See particularly p. 147.

⁴ Admittedly there is the probability that a further study of the reaction between phosgene and dialkylanilines might result in a more complete reaction. It is doubtful if other noxious gases would interfere with the test because they would be destroyed by the subsequent addition of an excess of Grignard reagent or other reactive organometallic compounds.

the ketone in benzene, and with 1 cc. of a 0.000045 molar solution of the ketone in dimethylaniline. The test was carried out in the customary manner with 1 cc. of a 2.25 molar solution of phenylmagnesium bromide. Hydrolysis was effected by 3 cc. of water after the original mixtures were shaken for a moment at room temperature to effect intimate mixing. As the solutions became more dilute, it was necessary to add 2 cc. of glacial acetic acid containing just enough iodine to give the acetic acid a light brown color. With these low concentrations the appearance of color in only the water layer was taken as an indication of a weak but positive test.

Tetraethyldiaminobenzophenone.⁵—The test solutions of tetraethyldiaminobenzophenone were prepared by dissolving the freshly purified ketone, 0.3242 g. or 0.001 mole, in 100 cc. of benzene and diethylaniline, respectively. Using the procedure described above it was found possible to get a positive test with 1 cc. of a 0.000025 molar solution of the ketone in benzene and a weaker test with 1 cc. of a 0.000025 solution of the ketone in diethylaniline.

Phosgene.—The concentration of phosgene in the stock benzene solution was determined by the method of Kling and Schmutz,⁶ and this solution was progressively diluted with benzene until no positive color test was obtained. In carrying out the several tests, 1 cc. of the phosgene solution and 1 cc. of the dialkylaniline were placed in a test-tube, thoroughly shaken and then 1 cc. of a 2.25 molar solution of phenylmagnesium bromide solution was added and the resulting mixture again shaken for a moment at room temperature. When the mixture was directly hydrolyzed with water, it was possible to get a color test with a solution containing 0.0259 g. of phosgene per cc. of benzene. The delicacy of the test was not improved by allowing sealed tubes to stand for *sixty* hours prior to the addition of the Grignard reagent. By heating for one hour in a sealed tube⁷ at 118° it was possible to detect a concentration of 0.00129 g. of phosgene in 1 cc. of benzene. The same delicacy was noted when anhydrous aluminum chloride was added to the phosgene in the amine and benzene solution.⁸

With diethylaniline in place of dimethylaniline, a test was obtained with 0.0259 g. of phosgene per cc., with practically no time on standing. When heated for one hour in a sealed tube at 118°, a positive test was obtained with 0.0129 g. per cc.

With di-*n*-propylaniline a test was obtained with 0.0129 g. per cc. directly after mixing the solutions at room temperature.

With di-*n*-butylaniline a test was obtained with 0.0259 g. per cc., also directly after mixing the solutions at room temperature.

Effect of Different Grignard Reagents.—In order to ascertain whether the delicacy of the test could be enhanced by the use of a particular organomagnesium halide, the following results were obtained with several typical Grignard reagents and the tetraethyldiaminobenzophenone. A poor color test was obtained with a 0.001 molar solution of the ketone and 2 molar ethylmagnesium chloride, and negative tests were obtained with the same concentration of ketone and 3 molar *n*-butylmagnesium bromide and 2 molar benzylmagnesium chloride, respectively. Phenylmagnesium bromide of 0.35 molar concentration gave a weak test with 0.001 molar ketone, and an excellent test

⁵ The authors wish to thank Dr. E. K. Bolton and Mr. F. B. Holmes for this ketone.

⁶ Kling and Schmutz, *Compt. rend.*, **168**, 773 (1919). See, also, Scholvien, *Ber. pharm. Ges.*, **3**, 213 (1893).

⁷ In these cases the Grignard reagent was only added after the phosgene and amine were heated.

⁸ Aluminum chloride reacts with phenylmagnesium bromide. Apparently the sensitivity of this test was not increased by allowing the mixture to stand in a sealed tube for one hour prior to the addition of phenylmagnesium bromide.

with 0.01 molar ketone.⁹ In general, a concentrated solution (2.25 molar and upwards) of phenylmagnesium bromide appears to be best suited for the tests described in this paper.

Summary

The sensitive color test for reactive organometallic compounds can be used as a delicate test for Michler's and related ketones. It is less satisfactory for phosgene and dialkyl anilines.

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THE CHEMISTRY OF THE LIPOIDS OF TUBERCLE BACILLI. XIV. THE OCCURRENCE OF INOSITE IN THE PHOSPHATIDE FROM HUMAN TUBERCLE BACILLI¹

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Introduction

The phosphatide fraction, A-3, isolated from the human type of tubercle bacilli, strain H-37, after it had been hydrolyzed with dilute sulfuric acid, was found to yield about 67% of fatty acids and about 33% of water-soluble material.² On concentrating the aqueous solution, a thick sirup was obtained from which we isolated glycerophosphoric acid, a small quantity of a colorless crystalline substance, crude mannose phenylhydrazone³ and finally obtained a good yield of glucosazone.

We have recently examined the crystalline substance which separated from the concentrated sirup and it has been identified as ordinary inactive inosite. That inosite should be present in tubercle bacilli is not surprising, since it appears to be universally distributed in all living cells, but the occurrence of inosite in an ether-soluble lipid was unexpected. The nature of the inosite linkage in the phosphatide molecule is still unknown, but it must have been combined in some manner either with the carbohydrate complex or with fatty acids.

Experimental Part

The inosite crystals had been obtained in the following manner. After the phosphatide, A-3, had been hydrolyzed by boiling with dilute sulfuric acid, the fatty acids

⁹ This is in agreement with earlier work by Gilman and Heck (see Ref. 1b of this paper), who showed that the color was more pronounced with more concentrated solutions of Michler's ketone.

¹ The present report is a part of a coöperative investigation on tuberculosis; it has been supported partly by funds provided by the Research Committee of the National Tuberculosis Association.

² Anderson, *J. Biol. Chem.*, **74**, 537 (1927).

³ Anderson and Renfrew, *THIS JOURNAL*, **52**, 1252 (1930).