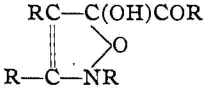
with phenylhydrazine hydrochloride. A yellow precipitate formed which was identified as the phenylhydrazone of phenyl glyoxylic acid by comparison with an authentic sample.

Cleavage of Bases.—A solution of a small quantity of the dimolecular compound in methyl alcohol containing a trace of sodium hydroxide was boiled down, cooled and diluted with water. It deposited the unsaturated amino ester VI. The filtrates from the ester later also deposited a small quantity of desoxybenzoin. This unsaturated amino ester was obtained also when the ferric chloride double salt was shaken with ice and methyl alcoholic sodium hydroxide. In this case the yield of ester was 82%.

Summary

1. In the pseudo bases which are formed from isoxazolinium salts that are completely substituted and have an acidic group in the 5-position, the hydroxyl group occupies the 5-position:



$$\begin{array}{l} \mathrm{RC{-}C(OH)COR} \\ \quad \| \qquad \rangle \mathrm{O} \\ \mathrm{R{-}C{-}NR} \end{array}$$

Owing to the ease with which they are cleaved, their behavior is quite different from that of the pseudo bases derived from other tri-substituted isoxazoles.

2. The pseudo bases derived from β,γ-diphenyl isoxazole likewise have an hydroxyl group in the 5-position. They undergo a characteristic rearrangement into open-chained compounds.

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THE INFLUENCE OF ACID CHLORIDES AND OF PYRROLE ON THE COLOR TEST FOR REACTIVE ORGANOMETALLIC COMPOUNDS. THE CONSTITUTION OF PYRRYLMAGNESIUM HALIDES

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Introduction

In continuation of studies[1] on the reaction between acid halides and the Grignard reagent, it was noted that some acid chlorides appeared to interfere with the sensitive color test[2] for reactive organometallic compounds. This prompted an investigation of the effect of several typical acid halides on the color test. It has been found that such interference is not general.

Fortunately, the occasional interference of acid halides need not be of serious consequence for several reasons. First, the reaction between RMgX

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[1] Gilman, Fothergill and Parker, *Rec. trav. chim.*, **48**, 748 (1929); Gilman and Fothergill, This Journal, **51**, 3501 (1929).

[2] (a) Gilman and Schulze, *ibid.*, **47**, 2002 (1925); (b) Gilman and Schulze, *Bull. soc. chim.*, [4] **41**, 1479 (1927); (c) Gilman and Heck, *Rec. trav. chim.*, **48**, 193 (1929); (d) Gilman and Heck, *Ber.*, **62**, 1379 (1929); (e) Gilman, Sweeney and Heck, This Journal, **52**, 1604 (1930); and (f) Gilman and Heck, *Rec. trav. chim.*, **49**, 218 (1930).

compounds and acid halides is rapid.[3] Second, it is possible to use equivalent quantities of acid halide and Grignard reagent, the former being weighed out and the latter titrated before use. Third, in reactions involving *alkyl*-magnesium halides having an alkyl group of low weight, it is possible to detect a slight excess of such an RMgX compound by observing the evolution of gas when a small sample of the reaction mixture is removed and hydrolyzed.

However, in a very special and rarely met with case there is another source of interference with some acid halides. Such interference might arise when a part or all of the commonly used diethyl ether is replaced by an amine like dimethylaniline.[4] Amines of this type may give, in some cases, products with acid halides whose color might interfere with the colors developed in testing for reactive organometallic compounds.[5] These are considered in the "Experimental Part."

We have had occasion to test the reliability of the color reaction with an unusually comprehensive and varied series of compounds. In addition to the occasional interference of acid halides, we directed attention recently[2f] to the infrequent interference of a few amino compounds by the production of colors which obscure those otherwise normally developed. The peculiar effects of pyrrole are of considerable interest in connection with the constitution of pyrrylmagnesium halides. It is known that when an RMgX compound reacts with a compound containing active hydrogen, the hydrogen is replaced by the –MgX group. Accordingly, the structure of a pyrrylmagnesium halide should be that represented by Formula (A). However, pyrrylmagnesium halides give reaction products which generally have the new grouping attached to carbon and not to nitrogen, and most frequently attached to an α-carbon atom. Consequently, a question has been raised[6] concerning the possibility of such types having Formula (B), either prior to or during its reaction with other compounds like carbon dioxide.

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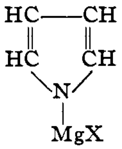
[3] See Gilman, Heck and St. John, *Rec. trav. chim.*, **49**, 212 (1930), for the relative rates of some reactions involving organomagnesium halides. Obviously, the rate of reaction might be affected considerably in some cases by steric influences of groups about the acid halide grouping.

[4] See Gilman and McCracken, *ibid.*, **46**, 463 (1927), for the effect of some solvents on the yields of Grignard reagents.

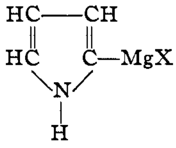
[5] Michler, *Ber.*, **9**, 716 (1876); Michler and Dupertuis, *ibid.*, **9**, 1899 (1876); Michler and Gradmann, *ibid.*, **9**, 1912 (1876); Michler and Moro, *ibid.*, **12**, 1168 (1879); Michler and Meyer, *ibid.*, **12**, 1791 (1879); Staudinger and Stockmann, *ibid.*, **42**, 3485 (1909). Some references to colored products from Michler's ketone and acid halides are: Baither, *ibid.*, **20**, 1731 (1887), and Staudinger, *ibid.*, **42**, 3966 (1909).

See Pfeiffer, Goebel and Angern, *Ann.*, **440**, 265 (1924), for a reference to colored complexes formed from amino-ketones and some amines.

[6] The following are some selected, recent and pertinent citations: (a) McCay and Schmidt, THIS JOURNAL, **48**, 1933 (1926); (b) Nenitzescu, *Bul. soc. chim. Romania*, **11**, 130 (1930); (*Chem. Abstracts*, **24**, 2458 (1930)).



(A)



(B)

It has been suggested[6b] that the pyrrylmagnesium iodides might be represented in accordance with Formula (B) because they, unlike the related indylmagnesium halides, give a color test. This is an ingenious application of the color test. However, it may be open to the criticism that a compound of Formula (A) might give the color test, not because of the –NMgX grouping (which is known not to give a color test) but because the amine itself (which is liberated from –NMgX compounds by hydrolysis incidental to the completion of the color test) might be the cause of the color. Actually, pyrrole (in the absence of Grignard reagent) does give a blue coloration with iodine and glacial acetic acid, the reagents used to develop the color in testing for reactive organometallic compounds. However, because a more marked color is obtained from a mixture of an RMgX compound and an *excess* of pyrrole, it appears that the –MgX group is attached to carbon and not to nitrogen. This must not, however, be construed to mean that Formula (B) is necessarily the correct one *prior* to its reactions with a miscellany of compounds. It is entirely possible that no chemical reaction can differentiate between (A) and (B), because the *product* of reaction gives us no clue as to the original position of the –MgX group. We need only recall a simple illustration: namely, sodium acetoacetic ester which has the sodium attached to oxygen, and yet which (in a reaction with an RX compound) gives a product with the R group attached to carbon and not to oxygen.[7]

Another suggestion for deciding between Formulas (A) and (B) involves the chemiluminescence induced by the oxidation of organomagnesium halides. McCay and Schmidt[6a] observed no luminescence when a small stream of oxygen was played on pyrrylmagnesium iodide. This observation has been confirmed by us in connection with a miscellany of studies on the chemiluminescence of Grignard reagents.[8] We have

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[7] This is open to two usual reservations. First, the sodium used need not be attached to oxygen, electronically speaking—in the same way that some would consider no formal valence bond between sodium and chlorine in sodium chloride. Second, some RX compounds react with sodium acetoacetic ester to give an R–O and not an R–C combination.

[8] Gilman, McGlumphy and Fothergill, *Rec. trav. chim.*, **49**, 526 (1930). Also Gilman, Fothergill and McGlumphy, *ibid.*, **49**, 726 (1930). Other references are to be found in these papers. The *p*-chlorophenylmagnesium bromide was selected because it gives an intense luminescence with oxygen. An answer to the question of the position of the –MgX group in pyrroles and related compounds may be found in absorption spectra studies.

shown that when a known excess of dry and freshly distilled pyrrole is treated with methylmagnesium iodide, phenylmagnesium iodide and *p*-chlorophenylmagnesium bromide, respectively, and oxygen is then passed into the mixture there is no chemiluminescence. These observations, however, are not to be taken as incontrovertible evidence for the –NMgX linkage, because there is still a possibility that a pyrrole –CMgX linkage may not luminesce.

Perhaps the best present way of deciding the position of the –MgX group is by means of the Zerewitinoff reaction. If the –MgX is attached to carbon in accordance with Formula (B), then pyrrole should show at least two active hydrogen atoms inasmuch as another active hydrogen (–NH) is present when the –MgX group in Formula (B) is attached to carbon. If Formula (A) is correct, then but one equivalent of methane should be liberated when pyrrole is treated with an excess of methylmagnesium iodide. Using di-*n*-butyl ether as a solvent, the number of active hydrogens determined at 29° with freshly distilled pyrrole was 1.049 and 1.045. At a more elevated temperature (heating in a boiling water-bath for one hour) the number was 1.125 and 1.216. These values confirm other related studies.[9] From them one may conclude with definiteness that the –MgX group is attached to nitrogen in accordance with Formula (A), and that in a reaction of the pyrrylmagnesium halide the substituent finds itself generally on the α-carbon atom. This applies to pyrrylmagnesium iodide in di-*n*-butyl ether under the temperature conditions stated above.

Experimental Part

To those who may be unfamiliar with the carrying out of the color test, it might be stated that it is done very simply by adding a very small volume[2c] of the organometallic mixture to be tested to Michler's ketone in benzene, hydrolyzing with water, and then developing the color with a glacial acetic acid solution of iodine. In the results to be described, no organometallic compound was used. Unless otherwise stated, a benzene solution of Michler's ketone was used.

Acetyl Chloride.—Michler's ketone in benzene and acetyl chloride gave a pale blue color which disappeared in one-half minute. The ketone in dimethylaniline with acetyl chloride gave a dark blue color which did not disappear on standing; however, the addition of water destroyed the color. No color was observed when dimethylaniline and acetyl chloride stood for fifteen minutes.

Benzoyl Chloride.—With benzoyl chloride and the ketone a blue color only developed after five minutes. The same mixture with water gives a blue color which reaches maximum intensity in five minutes, and the addition of iodine in glacial acetic acid gives a deeper color, which changes rapidly to brown on the further addition of iodine–glacial acetic acid solution and so would not be confused with the colors given by reactive organometallic compounds.

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[9] Oddo, *Ber.*, **44**, 2048 (1911); Ciusa, *Gazz. chim. ital.*, **50**, II, 53 (1920); (*Chem. Abstracts*, **15**, 837 (1921)); Fischer and Postowsky, *Z. physiol. Chem.*, **152**, 300 (1926). See also, Chelintzev and co-workers, *J. Russ. Phys.-Chem. Soc.*, **47**, 1224 (1915); **48**, 127 (1916).

Essentially the same color effects were noted when Michler's ketone was replaced by its ethyl homolog, *p,p'*-tetraethyldiaminobenzophenone. Both ketones in dimethylaniline give colors which are destroyed by the iodine solution.

No color was observed after ten minutes, with a mixture of dimethylaniline, benzoyl chloride and water.

Benzoyl Bromide.—Benzoyl bromide appears to have a more pronounced interfering effect than benzoyl chloride.

Furoyl Chloride, C_4H_3OCOCl.—A mixture of the ketone, furoyl chloride and water gave, after ten minutes, a pale green color to the upper layer. This would not be confused with a positive test for an organometallic compound because of the long time required for the development of color subsequent to hydrolysis.

Phosgene, $COCl_2$.—The phosgene solution was that used earlier in a related study.[2e] The colors noted with phosgene may be definitely stated to interfere.

Oxalyl Chloride, $(COCl)_2$.—There is an unmistakable color interference with oxalyl chloride. It is interesting to note that as small a quantity as 0.05 cc. of a 1% solution of oxalyl chloride in benzene gives a pale but distinct blue color with 1 cc. of a 0.01 *M* solution of Michler's ketone.

Benzene Sulfochloride, $C_6H_5SO_2Cl$.—The colors obtained with benzene sulfochloride and Michler's ketone (and *p,p'*-tetraethyldiaminobenzophenone, respectively) should not interfere because they are not the greens and blues obtained with RMgX compounds. Furthermore, even these colors disappear when sufficient iodine–glacial acetic acid solution is added ultimately.

Thionyl Chloride, $SOCl_2$.—A very poor but positive color test is obtained with 1 cc. of a saturated Michler's ketone solution and 0.1 cc. of a 1% thionyl chloride solution in benzene. The color is more pronounced with a larger quantity of thionyl chloride.

Sulfur Chloride, S_2Cl_2.—Neither Michler's ketone nor its ethyl homolog in benzene or dimethylaniline gives a positive or conflicting test with sulfur chloride.

Chloromethyl Sulfate, $ClCH_2OSO_2OCH_3$.—A reddish-purple color is obtained with chloromethyl sulfate.

Phosphorus Pentachloride.—The blue-green color obtained with phosphorus pentachloride definitely interferes in the sense that it would be mistaken for a positive color test with reactive organometallic compounds. This interference was noted with both Michler's ketone and its ethyl homolog.

Pyrrole.—The following facts clarify the observations reported previously.[2f] First, pyrrole and Michler's ketone in benzene give no characteristic color; second, pyrrole and iodine in glacial acetic acid give a blue coloration which might be mistaken for a positive test; third, pyrrole and glacial acetic acid give no characteristic color; and, fourth, an organomagnesium halide (ethylmagnesium chloride or phenylmagnesium bromide) and a definitely known excess of pyrrole with Michler's ketone and glacial acetic acid (without iodine) give what can be regarded as an excellent test.

Miscellaneous.—The following compounds gave no interfering colors: concd. hydrochloric acid, phosphorus trichloride, antimony tri-iodide, anhydrous aluminum chloride, sulfuryl chloride, vanadium oxytrichloride,[10] picryl chloride, di-chloromethyl sulfate [$(ClCH_2)_2SO_4$], cinnamoyl chloride [$C_6H_5CH{=}CHCOCl$], tetranitromethane and *p*-toluene sulfochloride.

Summary

A study has been made of the possible interference of some acid halides on the sensitive color test for organometallic compounds. In connection with interfering colors, evidence has been presented for the attachment of

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[10] Kindly provided by Dr. F. E. Brown and F. A. Griffitts.

the –MgX group to nitrogen in pyrrylmagnesium halides. The ultimate disposition of substituents on the α-carbon is accordingly no proof for a –CMgX linkage.

AMES, IOWA

[CONTRIBUTION FROM THE EVANS MEMORIAL AND BOSTON UNIVERSITY SCHOOL OF MEDICINE]

A NEW SERIES OF HALOGENATED SULFONEPHTHALEINS

BY WILLIAM CLOUSER BOYD WITH ALLAN WINTER ROWE

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Introduction

Sulfonephthaleins with halogen substituted in the phenolic residues have been prepared by several investigators since the initial discovery of the parent body by Remsen.[1] Since certain of the phthaleins and sulfonephthaleins have interesting application as dyes, as indicators, and in certain clinical procedures, a study was begun in 1927 of the preparation of a series of sulfonephthaleins having halogen substituted in the *o*-sulfobenzoic anhydride residue. The selective elimination by the kidney of phenolsulfonephthalein offered a potential lead to direct pyelography if this property were retained in compounds rendered opaque to x-rays by substituted halogen.

In 1929 there appeared a paper by Harden and Drake[2] describing some work on such a series, including four of the compounds described here. They gave but meager details of the preparation, however, and it was felt that the compounds and methods described below might still prove of interest.

Preparation and Properties of the Parent Substances (Tetra-iodo-*o*-sulfobenzoic Anhydride and Tetrabromo-*o*-sulfobenzoic Anhydride.— As has evidently been the experience of other workers, it was found that halogen could be not introduced directly into the *o*-sulfobenzoic anhydride residue of a sulfonephthalein. Attempts to do so resulted in the destruction of the molecule. Consequently the halogen was substituted in the *o*-sulfobenzoic anhydride molecule before condensation, using a slight modification of the Juvalta method, as described by Pratt and Shupp.[3] Iodine and bromine derivatives were thus prepared with comparative ease. No attempt was made to prepare the fluorine or chlorine derivatives, though the latter could doubtless have been made, as Harden and Drake[2] report the preparation of some of them.

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[1] Remsen, *Am. Chem. J.*, **6**, 180 (1884); Lubs and Acree, THIS JOURNAL, **38**, 2773 (1916); White and Acree, *ibid.*, **41**, 1190 (1919); Orndorff and Sherwood, *ibid.*, **45**, 486 (1923); Orndorff and Shapiro, *ibid.*, **46**, 2856 (1924).

[2] Harden and Drake, *ibid.*, **51**, 562 (1929).

[3] Pratt and Shupp, *ibid.*, **40**, 254 (1918).