(4) β-N-piperidino-ethyl phenyl ether (5) its hydrochloride, and (6) its hydrobromide (7) γ-N-piperidinopropyl phenyl ether (8) its hydrobromide, and (9) its hydrochloride are discussed. Of these compounds, 2, 3, 4, 5, 6, 7, 8 and 9 have anesthetic properties.

OXFORD, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF IOWA STATE COLLEGE]

SOME REACTIONS OF SUBSTITUTED MERCAPTOMAGNESIUM HALIDES

BY HENRY GILMAN AND W. BERNARD KING[1]

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Introduction

The reaction between organomagnesium halides and organic sulfur compounds is generally associated with the intermediate formation of the mercaptomagnesium halide group (—SMgX). In connection with studies concerned with the mechanism of reaction and the proof of structure, it was necessary to find some reliable reagent that will replace the —MgX group attached to sulfur by another in order to get a compound that lends itself to ready identification. Accordingly, a study has been made of the reactions of several substituted mercaptomagnesium halides with some compounds that undergo ready reaction with the more commonly known Grignard reagents. Some of the results, as might have been predicted, have been extended successfully to the chemistry of the —OMgX group.

Although many reactions have been carried out between organic sulfur compounds and the Grignard reagent, comparatively little work has been done on the chemistry of mercaptomagnesium halides. Taboury,[2] in connection with the reaction between RMgX compounds and sulfur, treated the intermediate mercaptomagnesium halides with various reagents. With acid halides and acid anhydrides the —MgX group was replaced by acyl, giving the corresponding thiol esters (RCOSR); with alkyl halides, particularly the iodides, and with dimethyl sulfate the —MgX group was replaced by an alkyl group, giving the corresponding sulfides. Houben and Schultze[3] treated the bromomagnesium salts of dithio acids (RCSSMgBr) with acid halides and obtained mixed anhydrides of the dithio and carboxylic acids (RCS_2COR). In earlier work, Houben and Pohl[4] suggested the probable formation of thioketones and mercaptans from the reaction between RCSSMgX and an excess of Grignard reagent.

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[1] This paper is an abstract of a thesis presented by W. Bernard King in partial fulfilment of the requirements for the degree of Master of Science in Chemistry at Iowa State College.

[2] Taboury, *Ann. chim. phys.*, [8] **15**, 5 (1908). This paper comprises essentially all of the earlier work reported by him in the *Bull. soc. chim.*, **29**, 761 (1903); **31**, 646, 1183 (1904); **33**, 836 (1905); **35**, 668 (1906); and in the *Compt. rend.*, **138**, 982 (1904).

[3] Houben and Schultze, *Ber.*, **43**, 2481 (1910); also *Ber.*, **44**, 3226 (1911). N. J. Beaber in this Laboratory has prepared ethyl dithiobenzoate from bromomagnesium dithiobenzoate ($C_6H_5CS_2MgBr$) and diethyl sulfate.

[4] Houben and Pohl, *Ber.*, **39**, 3219 (1906).

Borsche and Lange[5] obtained methyl camphyl sulfide when the reaction product from camphylmagnesium chloride and sulfur was heated with methyl iodide.

Ferrario and Vinay,[6] in a study of the reaction between sulfur chlorides and RMgX compounds, interpreted the formation of organic polysulfides as involving a secondary reaction between mercaptomagnesium halides and the sulfur chlorides.

Hepworth and Clapham[7] analyzed ethylmercaptomagnesium iodide (C_2H_5SMgI) prepared from ethyl mercaptan and methylmagnesium iodide. From ethylmercaptomagnesium bromide with acetyl chloride, benzoyl chloride and ethyl chloroformate, they obtained ethyl thiolacetate, ethyl thiolbenzoate and ethyl thiolcarbonate (C_2H_5-$SCO_2C_2H_5$), respectively.

Gilman and Kinney[8] prepared ethyl *p*-tolyl sulfide and ethyl benzyl sulfide from diethyl sulfate and *p*-tolylmercaptomagnesium iodide ($CH_3C_6H_4SMgI$) and benzylmercaptomagnesium iodide. Also, S-methyl- and S-ethyl-thiobenzanilide were obtained in a like manner when the reaction product of phenyl isothiocyanate and phenylmagnesium bromide was treated with dimethyl and diethyl sulfates.

Gilman, Smith and Parker[9] treated *p*-tolylmercaptomagnesium iodide with ethyl and phenyl benzoates, ethyl and phenyl *p*-toluenesulfonates and di-*p*-tolyl disulfoxide.

Discussion of Reactions

The —SMgX group undergoes practically all of the important reactions of salts of mercaptans; it shows some variations from the analogous —OMgX group; and it probably has no reactions in common with Grignard reagents where the —MgX is attached to carbon.

The —MgX group in the mercaptomagnesium halides undergoes ready replacement, as might have been expected, with compounds having a highly reactive halogen attached to carbon. Sulfides are formed in this manner from allyl bromide, benzyl bromide and chloro- and bromo-acetophenone, according to the following reaction: $RSMgX + R'X \longrightarrow RSR' + MgX_2$.

The standard reaction for the preparation of disulfides from salts of mercaptans and halogens also applies to the mercaptomagnesium halides. A smooth coupling reaction of this type occurs when iodine is added to the solution of —SMgX compound in ether. If the order of addition were reversed, then a sulfur halide (RSX) would probably result.[10] Mercaptomagnesium halides also undergo a coupling reaction to form disulfides when cupric chloride is used.[11]

Oxygen, under varying conditions, was found to have no apparent effect on the —SMgX group. Also, carbon dioxide appears to undergo no reaction with the mercaptomagnesium group. The work of Hepworth and Clapham[7] shows that the carboxyl group can be directly attached to

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[5] Borsche and Lange, *Ber.*, **39**, 2346 (1906).

[6] Ferrario and Vinay, *Bull. soc. chim.*, **7**, 518 (1910).

[7] Hepworth and Clapham, *J. Chem. Soc.*, **119**, 1188 (1921).

[8] Gilman and Kinney, THIS JOURNAL, **46**, 493 (1924).

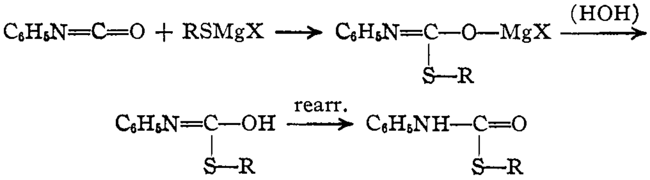
[9] Gilman, Smith and Parker, *ibid.*, **47**, 851 (1925). The work reported in this paper on mercaptomagnesium halides was done by W. B. King.

[10] Datta and Mitter, *ibid.*, **41**, 287 (1919).

[11] Gilman and Parker, *ibid.*, **46**, 2823 (1924).

sulfur if the mercaptomagnesium halide is treated with ethyl chloroformate. It is possible to replace an —MgX group attached to nitrogen[12] and to arsenic[13] by the carboxyl group by means of carbon dioxide.

Previous work proved that RMgX compounds added to the carbonyl group in phenyl isocyanate to give anilides.[8] Apparently the same type of reaction occurs, in an equally smooth manner, with mercaptomagnesium halides. The products so formed are S-esters of phenyl-thiolcarbamic acid ($C_6H_5NHCOSR$), according to the following reaction.



$$C_6H_5N{=}C{=}O + RSMgX \longrightarrow C_6H_5N{=}\underset{S-R}{\underset{|}{C}}{-}O{-}MgX \xrightarrow{(HOH)}$$

$$C_6H_5N{=}\underset{S-R}{\underset{|}{C}}{-}OH \xrightarrow{\text{rearr.}} C_6H_5NH{-}\underset{S-R}{\underset{|}{C}}{=}O$$

No addition takes place at the carbonyl group of esters.[9] The —OR group of the ester combines with the —MgX group as follows: $C_6H_5C(=O)-OC_2H_5 + RSMgX \longrightarrow C_6H_5C(=O)-SR + MgX(OC_2H_5)$. With esters of sulfonic acids, the mercaptomagnesium halides undergo the same reactions shown by RMgX compounds.[9]

Essentially no reaction takes place between benzonitrile and *p*-tolylmercaptomagnesium iodide.

It appears highly probable that the first reaction with aldehydes and ketones is one of condensation. Delacre[14] showed that zinc diethyl under varying conditions causes acetophenone to condense to dypnone and dypnopinacone. Very recently, Grignard and Dubien[15] started a comprehensive study of the condensing action of ROMgX compounds on aldehydes and ketones. Inasmuch as their compounds are analogous to the mercaptomagnesium halides (RSMgX), a correspondence in properties is to be expected. They treated iodomagnesium ethylate (C_2H_5OMgI) with five equivalents of butanal, and in addition to dibutanal, which was the principal product formed by an aldol condensation, they obtained some ethyl butyrate and butyl butyrate. No butanal was recovered.

With ethylmercaptomagnesium iodide (C_2H_5SMgI) and butanal no products other than some unchanged butanal and ethyl mercaptan were identified. The major portion of the oily reaction product did not boil where dibutanal does, and it showed a slight test for sulfur.

However, by working with aldehydes and ketones which give solid condensation products it was shown that the reaction is strictly analogous to

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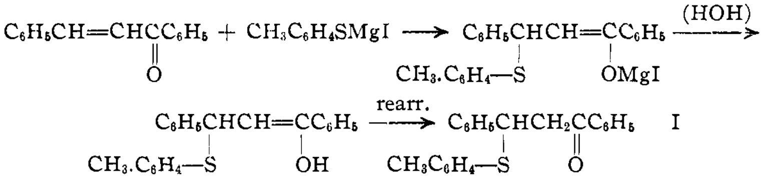
[12] Houben, *Ber.*, **37**, 3978 (1904).

[13] Job and Reich, *Compt. rend.*, **177**, 56 (1923). Also, *Bull. soc. chim.*, **35**, 1404 (1924).

[14] Delacre. in Beilstein, third ed., **1897**, vol. III, p. 249.

[15] Grignard and Dubien, *Compt. rend.*, **177**, 299 (1923). Also, Grignard and Fluchaire, *Bull. soc. chim.*, **35**, 1079 (1924).

that observed by Grignard and co-workers[15] First, it was shown that phenyl- and *p*-tolylmercaptomagnesium iodides will add readily to benzalacetophenone.



$$C_6H_5CH{=}CH\underset{\overset{\|}{O}}{C}C_6H_5 + CH_3C_6H_4SMgI \longrightarrow C_6H_5\underset{\overset{|}{CH_3.C_6H_4{-}S}}{CH}CH{=}\underset{\overset{|}{OMgI}}{C}C_6H_5 \xrightarrow{(HOH)}$$

$$C_6H_5\underset{\overset{|}{CH_3.C_6H_4{-}S}}{CH}CH{=}\underset{\overset{|}{OH}}{C}C_6H_5 \xrightarrow{rearr.} C_6H_5\underset{\overset{|}{CH_3C_6H_4{-}S}}{CH}CH_2\underset{\overset{\|}{O}}{C}C_6H_5 \qquad \text{I}$$

Then it was shown that a mixture of benzaldehyde and acetophenone with the mercaptomagnesium iodide gives the same final product obtained in (I). Very probably, the benzaldehyde and acetophenone first condensed to benzalacetophenone which then added the mercaptomagnesium iodide.

The constitution of these sulfides was verified in two ways. First, they were shown to be identical with the compounds obtained by Ruhemann[16] by condensing benzalacetophenone with thiophenols in the presence of small amounts of piperidine. Second, they were oxidized to the corresponding sulfones, one of which had been prepared previously by Posner.[17] These sulfones in turn were shown to be identical with the sulfones obtained by Kohler and Reimer[18] in the unusually smooth addition of sulfinic acids to conjugated systems. Incidentally, this correlation of compounds is additional confirmatory evidence for the sulfone structure of Kohler and Reimer's compounds. Because of the probable tautomeric forms of sulfinic acids, and because of the ready hydrolysis of these sulfones by alkalies into the sulfinic acid and unsaturated ketone, there was a possibility that the compounds might be sulfinic esters.

Benzaldehyde and acetophenone do react separately with *p*-tolylmercaptomagnesium iodide. However, the reaction is probably not one of simple addition to the carbonyl group. With benzaldehyde the reaction is incomplete, and although practically all of the thiocresol is recovered, about one-third of the aldehyde appears to be used up in condensation reactions. With acetophenone, the reaction is more nearly complete; very little thiocresol is recovered, but the sulfur-containing oil has not yet been identified. Probably it is an addition product of the type obtained from a mixture of benzaldehyde and acetophenone.

Experimental Part

p-Tolylmercaptomagnesium iodide was used in most of the experiments. This was selected largely because of the ease of recovery from reaction mixtures and partly because of the less offensiveness of *p*-thiocresol. Preliminary experiments showed that the iodide was quite soluble in

[16] Ruhemann, *J. Chem. Soc.*, **87**, 461 (1905).

[17] Posner, *Ber.*, **35**, 799 (1902).

[18] Kohler and Reimer, *Am. Chem. J.*, **31**, 163 (1904).

ether, the chloride sparingly soluble and the bromide intermediate in solubility.

The mercaptomagnesium iodide was readily prepared by adding *p*-thiocresol in ether to ethylmagnesium iodide. Using equivalent weights, the mercaptan was generally in excess because the yield of ethylmagnesium iodide is probably under 95%.[19] All yields in which this mercaptomagnesium halide was used are based on the quantity of *p*-thiocresol actually employed.

Reactions of *p*-Tolylmercaptomagnesium Iodide

Allyl Bromide.—Twenty-one and seven-tenths g. or 0.18 molecular equivalent of allyl bromide in ether was slowly added to an ether solution containing approximately 0.2 equivalent of *p*-tolylmercaptomagnesium iodide. Slow refluxing commenced after the first addition of allyl bromide. After hydrolysis by dil. sulfuric acid, the ether layer was washed with dil. sodium hydroxide to remove unaltered *p*-thiocresol; 17.3 g. or a 52.7% yield of *p*-tolyl allyl sulfide was obtained; b. p., 77–79° (2 mm.)[20]; d_4^{20}, 1.0044.

Anal. Calcd. for $C_{10}H_{12}S$: S, 19.51. Found: 19.22.

Some of the same compound was prepared according to a recent general method by Fromm and Siebert[21] from *p*-thiocresol, allyl bromide and sodium hydroxide; b. p., 81–84° (5 mm.); d_4^{20}, 1.0039. The compound undergoes decomposition when distillation is attempted at atmospheric pressure.

Benzyl Bromide.[22]—Thirty-three g. or 0.19 molecular equivalent of benzyl bromide in ether was added to about 0.2 equivalent of the well-stirred solution of the mercaptomagnesium iodide in ether. There was considerable refluxing throughout the addition, but the reaction mixture evidenced no change other than a slight turbidity. After hydrolysis, the ether layer was washed with dil. sodium hydroxide solution to remove unaltered *p*-thiocresol. The solid obtained by concentration of the dry solution melted at 44° after recrystallization from ligroin. It was further identified as benzyl *p*-tolyl sulfide by a mixed-melting-point determination.

Bromo-acetophenone.[22]—A very vigorous reaction occurred when an ether solution containing 8.2 g. or 0.04 molecular equivalent of bromo-acetophenone was added slowly to about 0.1 equivalent of the iodide, and two layers soon formed. The reaction product was worked up in the usual manner. In addition to unchanged *p*-thiocresol, a solid was obtained melting at 37°. The same compound was formed when chloro-acetophenone was used. It was obviously the expected keto-sulfide, for a mixed-melting-point made with a preparation from bromo-acetophenone, *p*-thiocresol and dil. sodium hydroxide showed no depression. Also, when oxidized by hydrogen peroxide in a mixture of acetic acid and acetic anhydride it gave the known keto-sulfone melting at 110°. This sulfone was identified by a mixed-melting-point determination made with the compound prepared from chloro-acetophenone and sodium *p*-toluene-sulfinate.

Iodine.—Iodine in ether was added slowly to about 0.2 molecular equivalent of *p*-tolylmercaptomagnesium iodide until the color due to a slight excess of iodine persisted; 8.5 g. of *p*-thiocresol was recovered in addition to 14 g., or a 91.5% yield, of di-*p*-tolyl disulfide that melted at 45.5°. The identity of the compound was further confirmed by a mixed-melting-point determination.

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[19] Gilman and Meyers, THIS JOURNAL, **45**, 159 (1923).

[20] The temperatures reported in this work are uncorrected.

[21] Fromm and Siebert, *Ber.*, **55**, 1015 (1922).

[22] Work done by F. Schulze.

Oxygen.—Dry oxygen was passed over the surface of the iodide for six hours. There was no evidence of a reaction, and a practically quantitative yield of *p*-thiocresol was recovered.

Carbon Dioxide.—Dry carbon dioxide was passed over the surface of the iodide, cooled by an ice-and-salt mixture, for three hours. Because there was no indication of a reaction, the ether was replaced in large part by dry xylene, and carbon dioxide was passed over the surface for an additional four hours near the boiling point of xylene. Again there was no evidence of a reaction, and 90% of the thiocresol was recovered.

In a similar experiment in which *p*-tolylmercaptomagnesium chloride was used, over 95% of *p*-thiocresol was recovered.

Phenyl Isocyanate.—Twenty and eight-tenths g. or 0.17 molecular equivalent of phenyl isocyanate in ether was added to about 0.2 equivalents of the iodide. A white precipitate formed at once, and refluxing occurred during the entire addition; 36.2 g. or a 75.4% yield of *p*-tolyl phenyl-thiolcarbamate was obtained; m. p., 127°.

Anal. Calcd. for $C_{14}H_{13}ONS$: S, 13.16. Found: 13.01.

When boiled for several hours with dil. potassium hydroxide, the compound was hydrolyzed to aniline and *p*-thiocresol.

When equivalent amounts of phenyl isocyanate and *p*-thiocresol were allowed to stand in a dry ether solution for six months, 90% of the thiocresol was recovered. In addition, a very small amount of the *p*-tolyl phenyl-thiolcarbamate was obtained, and much carbanilide. The carbanilide undoubtedly was formed from unaltered phenyl isocyanate which reacted with water during the working up of the reaction products. This experiment was done to show that the S-ester was formed from the *p*-tolylmercaptomagnesium iodide, and not from the *p*-thiocresol which results in the customary hydrolysis of the reaction mixture.

Benzonitrile.—Twenty-one and five-tenths g. or 0.2 molecular equivalent of benzonitrile in ether was added to about 0.2 equivalent of the iodide. The reaction mixture became turbid and gentle refluxing set in. When all of the benzonitrile had been added, the mixture was boiled for two hours.

After working up the mixture in the customary manner, about 90% of the benzonitrile and about 80% of the thiocresol were recovered. Apparently, addition had taken place to only a small extent. The physical evidences of reaction may be due, in part, to the formation of loose molecular complexes that break down readily into the original components.[23]

A Mixture of Benzaldehyde and Acetophenone.—An ether solution containing 21.2 g. or 0.2 molecular equivalent of benzaldehyde and 24 g. or 0.2 equivalent of acetophenone was slowly added to about 0.2 equivalent of the iodide. A yellow-green precipitate formed at once and refluxing soon set in. Two layers formed when addition was complete and the refluxing had stopped. After standing overnight, the mixture was hydrolyzed by iced, dil. sulfuric acid. An extraction of the ether layer with alkali gave 3 g. of *p*-thiocresol.

Steam distillation of the apparently intractable oil gave an additional 10 g. of *p*-thiocresol. The non-distillable portion when crystallized from alcohol gave 11 g. of a solid that melted at 110–111°.

Anal. Calcd. for $C_{22}H_{20}OS$: S, 9.63. Found: 9.58, 9.56.

The same compound was obtained from the reaction between benzalacetophenone and *p*-tolylmercaptomagnesium iodide. Its identity was confirmed by preparing it from benzalacetophenone, *p*-thiocresol and piperidine according to the general method of Ruhemann[16] for the preparation of corresponding compounds.

Additional evidence for the correctness of the structure of the 1,3-diphenyl-1-*p*-

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[23] v. Braun and Kirschbaum, *Ber.*, **52B**, 1725 (1919).

thiocresyl-3-ketopropane (see I) was obtained by its oxidation to the corresponding sulfone. When the keto-sulfide, dissolved in acetic acid and acetic anhydride, was treated with 30% hydrogen peroxide and the solution allowed to stand for a few hours at room temperature, fine, needle-like crystals were obtained; m. p., 179–180°. Several crystallizations from alcohol raised the melting point to 182–183°, and decomposition set in at a temperature slightly above the melting point. This sulfone was identified by a mixed-melting-point determination with the compound prepared by Kohler and Reimer[18] from benzalacetophenone and *p*-toluenesulfinic acid.[24] It was also prepared in alcoholic solution from benzalacetophenone, sodium *p*-toluenesulfinate and hydrogen chloride.

In order to confirm the correctness of the mechanism given in (I) and to correlate it with the work of others, benzalacetophenone was treated with phenyl-mercaptomagnesium iodide (C_6H_5SMgI). The 1,3-diphenyl-1-thiophenyl-3-ketopropane so obtained was shown to be identical with the compound prepared by the method of Ruhemann.[16] Furthermore, this keto-sulfide when oxidized at room temperature by means of 30% hydrogen peroxide in a mixture of acetic acid and acetic anhydride gave a compound which agreed in melting point (160–161°) with the sulfone prepared by Posner[17] by means of potassium permanganate.

Benzaldehyde.—Twenty-one and two-tenths g. or 0.2 molecular equivalent of benzaldehyde was added in ether to about 0.2 equivalent of the iodide. A reaction took place at once as was evident by the refluxing and the formation of a white precipitate that soon dissolved. With the addition of the last of the benzaldehyde a black precipitate formed and the solution became yellow. The color changed to faint red when the mixture was allowed to stand overnight. On working up the reaction mixture in the usual way there was obtained about 88% of the *p*-thiocresol, 66% of the benzaldehyde and a small amount of an apparently intractable oil.

Acetophenone.—Thirty-six g. or 0.3 molecular equivalent of acetophenone was added to about 0.3 equivalent of the iodide. Refluxing occurred shortly after the first addition of ketone, and the reaction mixture was further refluxed for 12 hours. The oil obtained from the ether layer subsequent to hydrolysis was subjected to steam distillation. Most of the product remained as a highly viscous oil which has not yet been identified.

Ethylmercaptomagnesium Iodide and Butanal.—Fifty-seven and six-tenths g. or 0.8 molecular equivalent of freshly distilled butanal was added in ether solution to about 0.2 equivalent of ethylmercaptomagnesium iodide. The mixture was refluxed for several hours and then worked up in the customary way. The oil was vacuum distilled and the first fraction of 18.5 g. distilled below 103° (10 mm.). It consisted largely of butanal with some ethyl mercaptan that had not been removed by the alkali extraction. The second fraction of 10 g. boiled at 103–135° (10 mm.), with no apparent fraction of constant boiling point. This gave a slight test for sulfur. The residue of 18 g. was not distilled. It contained no sulfur. Apparently only small amounts of dibutanal were present, for this compound boils at 103–105° (14 mm.).[15]

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[24] The melting point given by Kohler and Reimer for this compound is 169–170°. Very likely this is a typographical error, for the first melting points observed in our work are 179–180°. Their melting point for the keto-sulfone obtained from dibenzalacetone and *p*-toluenesulfinic acid was checked, namely, 189–190°.

No mention was made by them of the melting point of the keto-sulfone obtained from benzalacetone and *p*-toluenesulfinic acid. Because their reaction of sulfinic acids with such conjugated systems is unusually good for purposes of identification, we prepared the compound from benzalacetone and *p*-toluenesulfinic acid and found that it melted at 147–148°, decomposition setting in about 10° above the melting point.

Benzylmercaptomagnesium Iodide ($C_6H_5CH_2SMgI$) and Phenyl Isocyanate.—Twenty-one and two-tenths g. or 0.18 molecular equivalent of phenyl isocyanate in ether was added to about 0.2 equivalent of benzylmercaptomagnesium iodide; 19.5 g., or a 40.6% yield, of benzyl phenyl-thiolcarbamate, m. p. 94.5°, was obtained.

Anal. Calcd. for $C_{14}H_{13}ONS$: S, 13.16. Found: 13.01.

β-Naphthylmercaptomagnesium Iodide and Carbon Dioxide.—Dry carbon dioxide was passed for four hours over the surface of 0.125 molecular equivalent of the iodide, cooled by ice and salt. Since there was no evidence of a reaction, the ether was replaced by xylene and the mixture refluxed for four hours during which the passage of carbon dioxide was continued. A white precipitate formed. The alkali extract of the ether solution yielded 17 g. of β-thionaphthol. In addition, 1.5 g. of di-β-naphthyl disulfide was obtained. This may have been formed by air oxidation of the mercaptan subsequent to hydrolysis.

Summary

A study has been made of some reactions of mercaptomagnesium halides (RSMgX).

The —SMgX group can be identified satisfactorily by acylating agents, alkyl sulfates, RX compounds such as benzyl bromide and bromo-acetophenone which have very active halogens,[25] and phenyl isocyanate.[26]

AMES, IOWA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

DERIVATIVES OF PARA-HYDROXYMETHYL-BENZOIC ACID
I. ESTERS[1,2]

BY FRANCIS H. CASE[3]

RECEIVED JANUARY 15, 1925 PUBLISHED APRIL 4, 1925

Within recent years the search for a non-toxic cocaine substitute adapted to anesthesia of the mucous membrane has resulted in the discovery of "butyn,"[4] "tutocaine,"[5] and "psicain,"[6] all of which are now being marketed. Among the alcohol derivatives, Sollman[7] introduced benzyl al-

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[25] Conant and Kirner, THIS JOURNAL, **46**, 232 (1924).

[26] It is probable that phenyl-carbamic bromide ($C_6H_5NHCOBr$) is even better, for it reacts more readily than phenyl isocyanate with —OMgX compounds.

[1] Presented before the Division of Organic Chemistry, 68th Meeting of the American Chemical Society at Ithaca, N. Y., 1924.

[2] This investigation has been carried out in collaboration with the National Research Council Sub-committee on Local Anesthetics (A. J. Hill, Chairman). The physiological properties of the new compounds will be subsequently reported by Dr. A. D. Hirschfelder of the University of Minnesota.

[3] National Research Fellow.

[4] Adams, Kamm and Volwiler, U. S. Pat. 1,358,751.

[5] Schulemann, *Klin. Wochschr.*, **3**, 676 (1924).

[6] Willstätter, *Münch. med. Wochschr.*, **71**, 849 (1924).

[7] Sollman, *J. Pharmacol.*, **13**, 355 (1919).