substances are regarded as clues to the anabolic processes, and the following three types of reactions are being investigated: (a) $CH_3COOH + 2H_2O = 2CO_2 + 4H_2$; (b) $RCH_2COOH + NH_3 = RCH(NH_2)COOH + H_2$; (c) the production of higher homologs, such as the formation of succinic from acetic, which Quastel[2] mentions, followed by decarboxylation to propionic acid. The experimental evidence favors the first two reactions, operating probably in the form of a cycle with hydroxy acid, then amino acid production representing the anabolic phase, as in the animal body;[8] the reverse process, including oxidation by water, would be the catabolic phase. The production of hydroxy and amino acids would yield hydrogen, and the catabolic oxidation would explain the excess carbon dioxide observed in these experiments. Such a cycle has the added interest of involving alpha, and not beta, oxidation of the carbon chain.

Summary

1. A study has been made of the anaerobic breakdown of lower fatty acids by microörganisms converting them into methane and carbon dioxide.
2. Water has been shown to act as an oxidizing agent in this degradation, and a simple relation to exist between the number of carbon atoms in the acid and the number of participating water molecules.
3. Concurrent side reactions are demonstrated and their probable mechanisms discussed.

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THE PREPARATION OF MERCURY DIALKYLS FROM ORGANOMAGNESIUM HALIDES

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Introduction

Some improvements were described recently[1] for the preparation of mercury dialkyls from mercuric chloride and the Grignard reagent. This is one of the best methods for the synthesis of this class of compounds. The improvements suggested then were: first, the use of a Soxhlet extractor to facilitate manipulation of the mercuric halide; second, the use of a larger volume of ether to reduce caking; and, third, a marked extension in the time of heating.

In those experiments a liberal excess of Grignard reagent was used. We have now shown that it is possible to synthesize some typical mercury dialkyls with practically an equivalent quantity of organomagnesium

[8] Knopp, *Science*, **71**, 23 (1930).

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[1] Gilman and Brown, This Journal, **51**, 928 (1929). This article contains references to earlier studies, particularly those of Marvel and co-workers.

halide. Furthermore, the time required to obtain essentially equal (and in some cases markedly superior) yields can be drastically reduced.[2] These two improvements probably make this reaction the best now available for the preparation of mercury dialkyls on a laboratory scale.

Experimental Part

The appropriate Grignard reagent was decanted from unused magnesium into a two-liter, three-necked flask provided with a mercury-sealed mechanical stirrer and a Soxhlet extractor holding a water-condenser.[1] Dry ether was added to the reaction flask until its contents were 800 cc., and one-half mole of mercuric chloride[3] was placed in the extraction thimble. The flask was heated until the ether boiled gently, and when all of the mercuric chloride had been added to the Grignard reagent,[4] the extractor was replaced by a long condenser set for distillation. The water in the bath surrounding the reaction flask was slowly brought to boiling,[5] and then maintained at this temperature for one hour. Stirring was continued during the entire distillation and heating.

The water-bath was then cooled, and after returning the ether distillate to the reaction flask,[6] hydrolysis was effected with water or with an ammonium chloride solution containing a small quantity of ammonium hydroxide. The ether layer was separated and combined with two 25-cc. portions of ether which were used to wash the water layer. The combined ether solutions were dried over calcium chloride (about 10 g.) and then distilled through an efficient column.[1]

The troublesome, readily volatile butylmercuric halides were easily and almost completely removed by freezing them out (by ice and water cooling) from the mercury di-*n*-butyl after the ether was removed. This treatment is unnecessary with the methyl- and ethylmercuric halides because of their much lower volatility.

One experiment was carried out for the preparation of mercury diphenyl by a slight modification of the method just described. Because of the low solubility of aryl mercury compounds in ether, 500 cc. of benzene and 300 cc. of ether were added to the phenylmagnesium bromide prior to the introduction of mercuric chloride. The mercury diphenyl was extracted from the reaction mixture with chloroform, and twice recrystallized from this solvent. The yield of mercury diphenyl was 70.6% from 1.15 moles of phenylmagnesium bromide and 0.5 mole of mercuric chloride.

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[2] The improved yields reported in our first paper (Ref. 1) in which the time of heating was extended beyond that used by earlier investigators led us to believe that the yields then reported might have been increased significantly by a more protracted period of refluxing. From the present results it appears that the time might be reduced to an even greater extent if it were possible to add the mercuric chloride *in solution* more rapidly.

[3] The mercuric chloride was dried in a desiccator for these experiments. In the previous study (Ref. 1) the mercuric halide was used directly from a stock bottle. This added precaution of drying may be unnecessary.

[4] This required about four hours with the Soxhlet extractor used by us. When the experiment is carried out during winter or in a cool room, it is advisable to wrap a towel around the extractor to prevent separation of mercuric chloride in the small turn of the extractor.

[5] During this time practically all of the ether was removed by distillation.

[6] The ether distillate was returned to the flask in order to moderate, where necessary, the vigor of subsequent hydrolysis. Also, this serves to assemble any small quantity of lower molecular weight mercury dialkyl which might have been carried over with the ether.

The results are summarized in Table I and the footnotes which accompany it.

TABLE I

MERCURY DIALKYLS

Grignard reagent	Moles	Mercuric chloride, mole	% Yield of mercury dialkyl
CH_3MgI	1.2[a]	0.5	71.2
CH_3MgI	1.15	.5	70.2
C_2H_5MgI	1.15	.5	82.0, 80.4 and 84.4[b]
n-C_4H_9MgBr	1.15	.5	80.1 and 80.0[c]

[a] The number of moles of each Grignard reagent refers to the quantity of halide used, and not the actual quantity of RMgX compound available. When allowance is made for the small loss incidental to decantation from unused magnesium, and, more particularly, to the actual yields of Grignard reagents from a given weight of RX compound [see Gilman, Zoellner and Dickey, THIS JOURNAL, **51,** 1576 (1929)] it is altogether possible that we may not have had the required one mole of Grignard reagent. In order to be more certain on this point, an experiment was carried out with 1.1 mole of ethylmagnesium iodide and 0.5 mole of mercuric chloride. Here the Grignard reagent was estimated quantitatively by our titration method. The yield in this preparation was the 84.4% reported in Table I, and a positive color test[7] at the end of the reaction showed an excess of ethylmagnesium iodide.

[b] The yield of mercury diethyl obtained previously (Ref. 1) by us was about 88%.

[c] The maximum yield of mercury di-*n*-butyl reported previously by us was 66.7%.

Miscellaneous Observations.—In connection with interpretations of the reaction, mercury-diethyl, -di-*n*-butyl and -diphenyl were each treated with magnesium bromide and magnesium iodide, respectively. However, in no case (under our experimental conditions) was there a positive color test[7] to indicate the formation, in appreciable quantities, of an RMgX compound. Incidental to these studies, a highly interesting observation was made: namely, a few drops of mercury diethyl were sufficient to induce complete solution of a relatively large quantity of magnesium iodide-etherate in ether.

The stability of mercury dialkyls and diaryls varies greatly. Mercury dimethyl showed no signs of decomposition after five months' standing in a pyrex flask closed with a cork. Both mercury diethyl and mercury di-*n*-butyl showed signs of decomposition; *i. e.*, deposition of a gray film of metallic mercury, within a few days even in glass-stoppered, brown bottles. Solid pure mercury diphenyl appears to remain white indefinitely; however, even a slightly impure product turns yellow on standing.

The well-known physiologically deleterious properties of mercury dialkyls and diaryls were frequently noticed. Mercury dimethyl appeared to be the most objectional to work with, in part, because of its high vapor pressure at room temperature. The odor of mercury diphenyl is very per-

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[7] Gilman, Sweeney and Heck, THIS JOURNAL, **52,** 1604 (1930). This article contains references to earlier studies on the sensitive color test for reactive organometallic compounds.

sistent, and this disagreeable odor becomes more acute with continued exposure to the compound or its vapors. Some individuals appear to have an idiosyncrasy toward the vapor of organic mercurials, and are distinctly more affected than others.

Summary

Some improvements in the preparation of mercury dialkyls from mercuric chloride and the Grignard reagent make this synthesis the best for such compounds on a laboratory scale.

Miscellaneous observations have been reported on the stability, physiological action and behavior toward magnesium halides of mercury dialkyls and mercury diphenyl.

AMES, IOWA

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF SHARP AND DOHME]

AMINO-ALCOHOLS. II. HOMOLOGS AND ANALOGS OF PHENYLPROPANOLAMINE

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The preparation of phenylpropanolamine and its *p*-methyl derivative by reduction of the corresponding oximino ketones has been described.[1] By employing the same technique, it has been possible to prepare other members of the arylalkanolamine series from phenylethanolamine to phenyloctanolamine. Diphenylethanolamine was prepared by the catalytic reduction of benzoin oxime, both the α- and β-oximes yielding the amino-alcohol melting at 165°.

Procedure

The higher intermediate oximino ketones were prepared according to the method already described for isonitrosopropiophenone and its *p*-methyl derivative, with uniformly good results, although the longer the alkyl side chain, the poorer the yields of purified isonitroso ketone. The lower yields are probably caused by complications attending isolation of the product rather than by incomplete nitrosation, for in no case was it possible to recover unchanged ketone.

Isonitroso-acetophenone was best obtained according to the directions of Claisen and Manasse[2] by allowing butyl nitrite and acetophenone to react in an absolute alcoholic solution containing sodium ethoxide. The method which gave such excellent results with propiophenone and its higher homologs gave very poor yields with acetophenone—6 to 12%.

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[1] Hartung and Munch, THIS JOURNAL, **51**, 2262 (1929).

[2] Claisen and Manasse, *Ber.*, **20**, 2194 (1887).