In Expts. II and III the solutions were allowed to ferment for eight weeks but it is not probable that any pentose was assimilated. A slightly higher value in favor of the distillation method is of course to be expected owing to the production of phloroglucide from other substances than pentoses.

It is significant that the blank gave no apparent pentose by the reduction method. The quantities found in the other cases were small and insufficient to account for the total free pentose found by Davis and co-workers. Still, they are of sufficient amount to introduce a very appreciable error in the determination of free pentose if its real amount is only slightly greater. Consequently, any extraction procedure involving the use of ammonia and perhaps other weak alkalies should be avoided, or used with caution.

Summary

It has been shown that refluxing with ammoniacal alcohol and extensive concentration of an alcoholic solution of pure sucrose and invert sugar give appreciable amounts of apparent pentoses by both the Krober-Tollens and the fermentation methods. These are not in sufficient quantity to account for the total quantities reported in plant extracts. In the absence of ammonia some apparent pentose is indicated by the Krober-Tollens method but none by the fermentation method.

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ACTION OF PHENYLMAGNESIUM BROMIDE ON ORGANIC ACIDS

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The investigation of the action of the Grignard reagent on free organic acids was undertaken as a result of an unsuccessful attempt to synthesize benzopinacol from oxalic acid and phenylmagnesium bromide. A review of the literature showed that little work had been done on the free acids, and such results as were published seemed to indicate that the reaction would be a general one. As a rule, the reactions discussed in the literature yielded tertiary alcohols as the chief products, although the conditions of the experiments often governed the products of the reactions. Thus it was found that in the action of carbon dioxide on arylmagnesium halides, low temperatures favored the formation of acids while higher temperatures tended to bring about the formation of ketones and tertiary alcohols.[1]

[1] Grignard, *Compt. rend.*, **138,** 152 (1904); *Bull. soc. chim.*, [3] **31,** 751 (1904). Shroeter, *Ber.*, **40,** 1585 (1907). Bodroux, *Compt. rend.*, **137,** 710 (1903). Houben, *Chem.-Ztg.*, **29,** 667 (1905). Zelinsky, *ibid.*, **28,** 303 (1904). Simmonis and Arand, *Ber.*, **42,** 3721 (1909). Ger. pat. 166,898.

In the present investigation the acids studied can be divided into the following groups; dibasic acids, monobasic acids, α-keto acids, halogenated acids, hydroxy acids and α-β unsaturated acids.

Dibasic Acids.—As indicated above, we were unable to cause a reaction to take place between oxalic acid and phenylmagnesium bromide. If this failure to react were due simply to the proximity of the carboxyl groups, then this inhibitory effect ought to be lessened by the introduction of methylene groups between them. We therefore tried malonic, succinic and adipic acids. With each acid an excess of the phenylmagnesium bromide was used, and the reaction mixtures were refluxed for a number of hours, since the work of other investigators indicates that higher temperatures favor further action on the acids. In no case was any reaction product other than phenol and diphenyl found. From each reaction mixture, practically all of the acid was recovered unchanged.

Monobasic Acids.—Propionic and benzoic acids were found to react readily with phenylmagnesium bromide to produce tertiary alcohols, as indicated in the patent literature. Phenylacetic acid also reacted readily, giving excellent yields of the product. The nature of this substance was not determined, but it was found, on oxidation with alkaline permanganate, to yield large amounts of benzoic acid and very small quantities of benzophenone. *iso*Butyric acid gave a 20% yield of the corresponding tertiary alcohol, and none of the acid was recovered. The analogous diphenyl acetic acid failed to react to any extent, 60% of the acid being recovered. A very small amount of an alkali-insoluble substance melting at 233–234° was formed. β,β-Diphenylpropionic acid, on the other hand, reacted very readily producing relatively good yields of the corresponding tertiary alcohol.

Alpha Keto Acids.—Phenylmagnesium bromide reacted with the α-keto acids, pyruvic and benzoylformic acids, to produce phenylmethylhydroxyacetic acid and benzilic acid, respectively. With these two acids the carboxyl groups were not attacked, reaction taking place only on the ketone groups.

Halogenated Acids.—Chloro-acetic acid reacted with phenylmagnesium bromide to produce the glycol and a very small quantity of a strongly lachrymatory substance, presumably chloro-acetophenone. α-Bromopropionic acid likewise yielded the glycol. Apparently, the hydrolysis of the Grignard reaction product was accompanied by the hydrolysis of the halogen also. No product was isolated in which the halogen was replaced by the phenyl group. With phenyl-chloro-acetic acid, however, the halogen is more reactive and the principal product when treated with an excess of phenylmagnesium bromide was that in which the halogen was replaced by the phenyl group.[2]

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[2] Drew and Martin, *J. Chem. Soc.*, **107**, 26 (1915).

Hydroxy Acids.—Mandelic acid and phenylmagnesium bromide reacted at the temperature of boiling ether to produce the glycol. When the reaction was carried out in boiling xylene, the yield of the glycol was practically doubled. Benzilic acid failed to react at all, and since the product of the reaction with pyruvic acid was phenylmethylhydroxyacetic acid, it is improbable that acid would react.

Alpha Beta Unsaturated Acid.—Cinnamic acid reacted with an excess of phenylmagnesium bromide to produce β,β-diphenyl-propionic acid in very good yields. With methylmagnesium iodide about half of the acid was recovered, but a small amount of an uncrystallizable oil was obtained. This oil formed a phenylhydrazone whose melting point corresponded with that of benzilidene-acetone-phenylhydrazone. Benzilidene-acetone would of course be formed if one molecule of methylmagnesium iodide added to the carbonyl group of the cinnamic acid.

In cases where phenylmagnesium bromide reacts with organic acids, the products are in general the same as those obtained from esters. With esters, however, the reactions usually take place more readily and produce better yields. Thus the aliphatic dicarboxylic acids do not react with phenylmagnesium bromide under ordinary conditions, while the esters under the same conditions, produce glycols.[3] The simpler members of the monocarboxylic acid series, both aliphatic and aromatic, react to produce tertiary alcohols, just as do the esters. The presence of a halogen or two aliphatic alkyl groups of low molecular weight on the alpha carbon does not interfere with this reaction of the carboxyl group. One phenyl group on the alpha carbon does not affect the reaction adversely, but two phenyl groups in that position are sufficient to prevent reaction completely. When two phenyl groups appear on the beta carbon, reaction proceeds in the normal manner. In alpha keto acids and in acids like phenyl-chloroacetic acid there are structures which react more readily with phenylmagnesium bromide than does the carboxyl group. The result is the formation of heavily substituted alpha carbons, so that there is no action on the carboxyl groups. With alpha keto esters a similar reaction takes place if an excess of Grignard reagent is avoided.[4] That this failure to react is due to structure rather than to ether insolubility of the compound containing the grouping —COOMgX, is shown by the experiments with benzilic acid. In this case the magnesium complex is entirely soluble in ether, but there was no reaction on the acid, 95% of it being recovered.

Cinnamic acid resembles certain other conjugated systems in its reaction with the Grignard reagent. It has been found[5] that in certain cases phenylmagnesium bromide adds to such a system in the 1,4-positions,

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[3] Dilthey and Last, *Ber.*, **37**, 2639 (1904).

[4] McKenzie, *J. Chem. Soc.*, **89**, 365, 688 (1906).

[5] Kohler, *Am. Chem. J.*, **36**, 529 (1906).

while methylmagnesium iodide adds to the carbonyl group in the 1,2 positions.

Experimental Part

In all cases except in the experiments with oxalic acid, the organic acid in dry ether solution or suspension was added slowly to the dry ether solution of the Grignard reagent. Thus the phenylmagnesium bromide was in excess at all times. The reaction flask was equipped with a mercury seal, and the reaction mixtures were stirred continuously by means of a motor stirrer during the additions of the acid and during the time of refluxing, which varied from one to five hours. In most of the cases the reaction mixtures were allowed to stand overnight. After hydrolysis by means of ice and hydrochloric acid, the ether layers were separated from the water solutions and were washed, first with sodium carbonate solutions to remove unchanged organic acid, then with potassium hydroxide solutions to remove phenol and finally were dried over anhydrous sodium sulfate and distilled. With acids relatively insoluble in ether, the acid hydrolysis solutions were made alkaline and evaporated to dryness on a water-bath, acidified and again evaporated to dryness and the dry solid was extracted with ether by means of a Soxhlet extractor. Unchanged acids obtained in this way were combined with whatever acids might be recovered from the ether solutions by means of washing with sodium carbonate solutions. This method was used only with the dicarboxylic acids. Unless otherwise noted, the amount of organic acid used in these experiments was 10 g.

Oxalic Acid and 4 Molecular Equivalents of Phenylmagnesium Bromide.—The only reaction product isolated was 4 g. of diphenyl.

Oxalic Acid and 7 Equivalents of Phenylmagnesium Bromide.—Twelve g. of the dried acid was used; 53 g. of benzene and 9.2 g. of diphenyl were obtained and 9.3 g. of the acid was recovered.

Malonic Acid and 7 Equivalents of Phenylmagnesium Bromide.—Using 10.4 g. of the dried acid, 40 g. of benzene and 3.1 g. of diphenyl were obtained; 7.7 g. of the acid was recovered.

Succinic Acid and 9 Equivalents of Phenylmagnesium Bromide.—Two and a half g. of diphenyl was obtained and 7.8 g. of the acid recovered.

Adipic Acid and 12 Equivalents of Phenylmagnesium Bromide.—Five g. of phenol and 2 g. of diphenyl were obtained; 7.5 g. of the acid was recovered.

Benzoic Acid and 4 Equivalents of Phenylmagnesium Bromide.—When 25 g. of the dried acid was used, 20 g. of triphenyl carbinol was obtained. There was no unchanged benzoic acid.

Propionic Acid and 3.5 Equivalents of Phenylmagnesium Bromide.—Twenty-five g. of the acid was used and the refluxing was continued for 35 minutes. Vacuum distillation of the product of the reaction yielded 4 g. of diphenyl and 14.5 g. of a substance melting at 89–90°. This latter after crystallization from alcohol yielded 10.3 g. of pure diphenyl-ethyl carbinol.

Phenylacetic Acid and 5 Equivalents of Phenylmagnesium Bromide.—The sodium carbonate washings on acidification yielded 8 g. of a white, curdy substance. This material was dissolved in hot glacial acetic acid, from which it separated on cooling as a white, curdy mass; m. p., 196°. Washing the substance with small quantities of hot benzene, ligroin and alcohol successively did not change this melting point.

Phenylacetic Acid and 2.5 Equivalents of Phenylmagnesium Bromide.—From 10 g. of the acid was obtained 9 g. of the product. After purification from glacial acetic acid it melted at 195°. Five g. was refluxed for several hours with alkaline permanganate. An ether extract of this reaction mixture yielded just a trace of benzophenone. The alkaline solution obtained after filtering off the manganese dioxide yielded a large quantity of benzoic acid. Five g. of this material was heated above the melting point in a test-tube. On cooling, a solid was obtained which, after purification, was identified as desoxybenzoin by means of a mixed melting point with some stock desoxybenzoin. A mixed melting point of the phenylhydrazones of the two desoxybenzoins confirmed the above conclusion. Ignition of 1 g. of the material left no inorganic residue.

*iso***Butyric Acid and 8 Equivalents of Phenylmagnesium Bromide.**—Twenty g. of the acid was used. The sodium carbonate washings gave only a faint odor of *iso*butyric acid on acidification. The ether solution was evaporated and the residue distilled in a vacuum. The temperature rose gradually to 170° (21 mm.), where it remained constant; yield, 10 g.

Anal. Subs., 0.2172: H_2O, 0.1567; CO_2, 0.6789. Calcd. for $C_{16}H_{18}O$: H, 7.96; C, 84.95. Found: H, 8.01; C, 85.22.

A mixture of 8.5 g. of the product with 24 g. of potassium dichromate and 175 cc. of dil. sulfuric acid (equal weights of acid and water) was refluxed for four hours. An ether extract of the reaction mixture yielded 4 g. of benzophenone.

Two equivalents of *iso*propylmagnesium iodide were permitted to act on benzophenone. The product of the reaction distilled at 167–168° (19 mm.), and 8.5 g. on oxidation yielded 5 g. of benzophenone. This product was therefore identical with that obtained in the reaction between *iso*butyric acid and phenylmagnesium bromide.

Diphenylacetic Acid and 6 Equivalents of Phenylmagnesium Bromide.—A very small quantity of an alkali-insoluble substance melting at 233–234° was obtained; 6 g. of the acid was recovered.

β,β-Diphenyl-propionic Acid and 6 Equivalents of Phenylmagnesium Bromide.—The solid material obtained on evaporation of the ether was crystallized from ligroin; m. p., 97–98°; yield, 7 g.

Anal. Subs., 0.2187: CO_2, 0.7133; H_2O, 0.1350. Calcd. for $C_{27}H_{24}O$: H, 6.59; C, 89.01. Found: H, 6.85; C, 88.94.

Three g. of the substance was oxidized with potassium dichromate and sulfuric acid. An ether extract of this reaction mixture yielded just a trace of benzoic acid and 1.5 g. of benzophenone.

Benzoyl-formic Acid and 8 Equivalents of Phenylmagnesium Bromide.—From 8.5 g. of the dried acid were obtained 3 g. of benzilic acid and 1 g. of triphenylmethane.

Pyruvic Acid and 7 Equivalents of Phenylmagnesium Bromide.—The reaction mixture was stirred for two hours without heating; yield, 5.5 g. of an acid melting at 91°. It was shown to be α-phenyl-α-hydroxypropionic acid by means of a mixed-melting-point determination with some of that acid prepared from acetophenone and hydrogen cyanide.

Chloro-acetic Acid and 7 Equivalents of Phenylmagnesium Bromide.—The evaporation of the ether left a semisolid which on filtration and crystallization from alcohol yielded a solid melting at 121°. It gave no test for chlorine.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.50; H, 6.54. Found: C, 78.29, 78.37; H, 6.45, 6.49.

Oxidation with alkaline permanganate yielded carbon dioxide and benzophenone. The reaction also yielded a very small quantity of an oil which was strongly lachrymatory. The quantity was too small to permit identification, but it was presumably chloro-acetophenone.

α-Bromopropionic Acid and 7 Equivalents of Phenylmagnesium Bromide.—Evaporation of the ether left a semi-solid which, after being filtered off and crystallized from alcohol, melted at 93°; yield, 4 g. The compound contained no halogen.

Anal. Subs., 0.1468: CO_2, 0.4250; H_2O, 0.0909. Calcd. for $C_{15}H_{16}O_2$: C, 78.94; H, 7.01. Found: C, 78.95; H, 6.88.

Oxidation with alkaline permanganate yielded acetic acid (identified by the Du Claux constant) and benzophenone.

Mandelic Acid and 7 Equivalents of Phenylmagnesium Bromide.—The product of the reaction was shown to be the glycol, α,β-dihydroxy-α,β,β-triphenylethane, by means of a mixed-melting-point determination with some of that substance prepared according to the method of Acree.[6]

Benzilic Acid and 7 Equivalents of Phenylmagnesium Bromide.—The addition of each drop of the ether solution of the benzilic acid to the Grignard reagent produced a white precipitate that at once redissolved. At the end of the addition a perfectly clear solution was obtained, that was refluxed for 45 minutes and allowed to stand overnight. No material separated during that time. From the reaction mixture 9.5 g. of the benzilic acid was recovered.

Cinnamic Acid and 8 Equivalents of Phenylmagnesium Bromide.—From the reaction mixture was obtained 8 g. of β,β-diphenylpropionic acid; m. p., 150°. On boiling this substance with alkaline permanganate, 3 g. yielded 1 g. of benzophenone.

Cinnamic Acid and 8 Equivalents of Methylmagnesium Iodide.—The clear solution obtained by treating the Grignard reagent with the acid was refluxed for two hours. No material separated during that time. From the reaction mixture 5 g. of cinnamic acid was recovered. A small quantity of an oil was also obtained, which was found to reduce permanganate instantly and to absorb bromine readily. It formed a phenylhydrazone which after crystallization melted at 155–156°. It was presumably benzilidene-acetone-phenylhydrazone; m. p., 156°.

Summary

1. The simpler members of the monocarboxylic acid series, both aliphatic and aromatic, react with phenylmagnesium bromide, forming tertiary alcohols in general. Alpha hydroxy and halogenated aliphatic acids react similarly.

2. The carboxyl groups of acids holding two phenyl groups on the alpha carbon, or containing structures which react with phenylmagnesium bromide to produce two phenyl groups on the alpha carbon, do not react.

3. Aliphatic dicarboxylic acids do not react with phenylmagnesium bromide.

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[6] Acree, *Ber.*, 37, 2753 (1904).