and placing their research facilities at his disposal. He is especially grateful to Mr. J. A. Anderson, Jr., in whose section he worked, for expediting many things, Doctors M. A. Mosesman and L. W. Vernon for making room for him in their laboratory and office and Dr. B. H. Johnson for interpreting the infrared spectra.

BAYTOWN, TEXAS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ALBERTA]

The Behavior of 4-Methoxyphthalic Anhydride in Grignard Condensations

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The reactions between 4-methoxyphthalic anhydride and the Grignard reagents from bromobenzene, α-bromonaphthalene, *m*-bromoanisole and *p*-bromoanisole have been carried out. In every case the yield of the 4-methoxy-2-aroylbenzoic acid has been found to be higher than that of the 5-methoxy isomer. If the normal reaction of a Grignard reagent with an unhindered carboxylic acid anhydride involves addition at a carbonyl group, then the yields of the keto carboxylic acids can be explained by the electron-donating effect of the 4-methoxyl group.

In 1935, Weizmann, Bergmann and Bergmann[1] carried out reactions between 4-methoxyphthalic anhydride (I) and phenylmagnesium bromide and also between I and 1-naphthylmagnesium bromide. They reported high yields (70–80%) of 4(5?)-methoxy-2-benzoylbenzoic acid and 4(5?)-methoxy-2-α-napthoylbenzoic acid, respectively. In connection with the synthesis of some methoxy derivatives of anthracene and 1,2-benzanthracene, it was necessary for the present authors to characterize the compounds reported by Weizmann, *et al.* We have found them to be the compounds where reaction has occurred at the carbonyl group in position 2, *viz.*, 4-methoxy-2-benzoylbenzoic and 4-methoxy-2-α-naphthoylbenzoic acid. The authors have also carried out reactions between I and *m*-methoxyphenylmagnesium bromide and between I and *p*-methoxyphenylmagnesium bromide with consistently higher yields of the 4-methoxy-2-aroylbenzoic acid than of the 5-methoxy isomer. Again, Bauer[2] has shown that in the reaction between I and ethylmagnesium bromide, only the carbonyl *meta* to the methoxy group is attacked with the formation of 5-methoxy-3,3-diethylphthalide.

The results of the very careful and extensive work by Newman and co-workers on the reactions of Grignard reagents with carboxylic anhydrides[3] has been interpreted by them to indicate that the normal reaction between a carboxylic anhydride and a Grignard reagent takes place by addition at a carbonyl group. In the case of hindered anhydrides it is postulated that a metathetical reaction mechanism is involved.[4]

If the normal reaction of a Grignard reagent with an unhindered carboxylic acid anhydride involves addition at a carbonyl group, then a plausible explanation for the preferential reactivity of the 2-carbonyl function of I lies in the effect of the 4-methoxyl group. With the latter group the carbonyl in position 1 is stabilized by delocalization of the unshared electron pairs on oxygen. The reaction rate at the 1-carbonyl group is therefore less than the rate at the carbonyl group in position 2.[5]

Experimental

Reactions of 4-Methoxyphthalic Anhydride. (a) With Phenylmagnesium Bromide.—The Grignard reagent from bromobenzene (22 g.) in ether (150 ml.) was added during 15 minutes and at 50–60° to a well stirred solution of 4-methoxyphthalic anhydride (24 g., m.p. 96°) in benzene (400 ml.). After stirring for 3 hr. at 50–60° the reaction mixture was decomposed with saturated ammonium chloride solution (150 ml.) and dilute hydrochloric acid (10 ml.). The ether–benzene solution of the hydrolyzed reaction products was shaken with carbonate. The carbonate extract was acidified with acetic acid and yielded 17.5 g. of 2-benzoyl-4-methoxybenzoic acid, m.p. 150–169°. After one crystallization from benzene, the yield of pure keto acid was 14 g. (m.p. 172–174°, lit.[1] 167°). The 2-benzoyl-4-methoxybenzoic acid was characterized by decarboxylating in the presence of basic copper carbonate. This afforded 3-methoxybenzophenone, which was distilled and refluxed with 55% hydriodic acid. The demethylated material was crystallized from dilute ethanol and yielded 3-hydroxybenzophenone, m.p. 115°.

The acetic acid acidified filtrate from the above keto acid was treated with hydrochloric acid. This afforded 4.6 g. of 2-benzoyl-5-methoxybenzoic acid, m.p. 140–150°. One crystallization from benzene did not change the melting point. For that reason the crude material was dissolved in concentrated sulfuric acid (10 ml.) and heated at 60–70° for 1 hr., at which time it was cooled and poured into ice and water. The reaction mixture was made basic with sodium hydroxide and any cyclized material[6] derived from the isomeric keto acid was separated. The filtrate was acidified with hydrochloric acid and afforded 2-benzoyl-5-methoxybenzoic acid. One crystallization from alcohol gave 2.7 g. of pure compound, m.p. 155–156°. It did not depress the melting point of an authentic sample made from the known 2-benzoyl-5-nitrobenzoic acid (II).[7]

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[1] C. Weizmann, E. Bergmann and F. Bergmann, *J. Chem. Soc.*, 1367 (1935).

[2] H. Bauer, *Arch. Pharm.*, **249**, 450 (1911); *C. A.*, **5**, 3802 (1911).

[3] (a) L. F. Fieser and M. S. Newman, THIS JOURNAL, **58**, 2376 (1936); (b) M. S. Newman, *ibid.*, **59**, 1003 (1937); (c) M. S. Newman and M. Orchin, *ibid.*, **60**, 586 (1938); (d) M. S. Newman, *ibid.*, **60**, 1368 (1938); (e) M. S. Newman and M. Orchin, *ibid.*, **61**, 244 (1939); (f) M. S. Newman and McCleary, *ibid.*, **63**, 1542 (1941); (g) M. S. Newman and Wise, *ibid.*, **63**, 2109 (1941); (h) M. S. Newman and Lord, *ibid.*, **66**, 733 (1944).

[4] See also the interpretation by M. S. Kharasch and O. Reinmuth in their excellent treatise, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, p. 849.

[5] The nitro group, because of electron withdrawal, would be expected to be favorable for reaction at the carbonyl group in position 1. It is therefore interesting to note that R. Goncalves, M. R. Kegelman and E. V. Brown (*J. Org. Chem.*, **17**, 705 (1952)) report a yield of 34% and 19%, respectively, for 2-(2-thenoyl)-5- and 2-(2-thenoyl)-4-nitrobenzoic acids obtained from 4-nitrophthalic anhydride and the Grignard reagent from 2-bromothiophene.

[6] The authors have found that 2-benzoyl-4-methoxybenzoic acid undergoes a slow cyclization in sulfuric acid at 60–70° to afford 2-methoxyanthranquinone, m.p. 195°. The isomeric 2-benzoyl-5-methoxybenzoic acid under these conditions affords no detectable cyclized material.

[7] W. A. Lawrence, THIS JOURNAL, **42**, 1871 (1920).

2-Benzoyl-5-methoxybenzoic Acid (III) from II.—2-Benzoyl-5-aminobenzoic acid (IV), m.p. 192–193°, lit.[7] 193–194° was obtained in almost quantitative yield by the hydrogenation of II (10 g., m.p. 214°, lit.[7] 212°) in ethyl acetate (300 ml.) in the presence of Raney nickel and at 50 p.s.i. Amino-acid IV was dissolved in 50% sulfuric acid, diazotized and heated on a steam-bath until the evolution of gas had ceased. The reaction mixture afforded 2-benzoyl-5-hydroxybenzoic acid, yield 40% (m.p. 191–192°), pale yellow needles from dilute acetic acid and dilute alcohol.

Anal. Calcd. for $C_{14}H_{10}O_4$: C, 69.83; H, 4.13. Found: C, 69.29; H, 4.38.

The hydroxyacid was methylated with methyl sulfate without difficulty and afforded III, m.p. 155–156°.

Anal. Calcd. for $C_{15}H_{12}O_4$: C, 70.33; H, 4.72. Found: C, 70.05; H, 4.88.

(b) **With 1-Naphthylmagnesium Bromide.**—The procedure was that of Weizmann, *et al.*,[1] and afforded 2-α-naphthoyl-4-methoxybenzoic acid, m.p. 192–193°, lit.[1] 196°. The acid was characterized by decarboxylating to 1-naphthyl-3-methoxyphenyl ketone, b.p. 260–261° at 24 mm. The ketone was fused with potassium hydroxide according to Bachmann,[8] and the cooled mass was taken up in boiling water and filtered. The precipitate did not depress the m.p. of naphthalene. The warm alkaline filtrate was acidified and the resulting solid was immediately filtered. It proved to be 1-naphthoic acid, m.p. 156–157°. The filtrate was cooled in ice and water and afforded *m*-methoxybenzoic acid, m.p. 104–105°. It did not depress the m.p. of an authentic sample of the acid.

(c) **With *m*-Methoxyphenylmagnesium Bromide.**—The Grignard reagent from *m*-bromoanisole (18.7 g.) in ether was added to a well stirred solution of the anhydride (16 g., m.p. 96°) in benzene. After refluxing for 3 hr. the reaction mixture was treated with dilute hydrochloric acid. The ether–benzene solution of the hydrolyzed reaction products was shaken with carbonate. The yield of the total acid fraction recovered from the carbonate solution was 65%, and it melted from 140 to 150°. The original ether–benzene extract contained varying amounts of neutral material (2.5–5 g.) and was not further examined.

Crystallization of the above acid mixture from 50% acetic acid yielded 9.0 g. of almost pure 2-(3'-methoxybenzoyl)-4-methoxybenzoic acid. For analysis it was crystallized three times from benzene and melted at 173°.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.1; H, 4.9. Found: C, 67.1; H, 4.9.

The keto acid (8 g.) was characterized by heating with basic copper carbonate for 1 hr. at 260°. This afforded 3,3'-dimethoxybenzophenone (6 g.), b.p. 164–168° at 2 mm. One gram of the dimethoxy compound was refluxed for 3 hr. with 10 ml. of 55% hydriodic acid. The mixture was diluted with 50 ml. of water, decolorized with sodium bisulfite and the solid material filtered. Crystallization from water afforded 0.6 g. of 3,3'-dihydroxybenzophenone, m.p. 160–161°.[9]

The keto acid was dissolved in *cold* concentrated sulfuric acid and allowed to stand at room temperature for *five* minutes. Dilution with ice and water gave a 90% yield of almost pure 2,7-dimethoxyanthraquinone, m.p. 213°. A mixed melting point determination carried out with an authentic sample of the quinone showed no change.

The acetic acid mother liquors from the crystallization of the above keto acid contained a large amount of tarry material and a small amount (1.5 g.) of what the authors believe to be impure isomeric 2-(3'-methoxybenzoyl)-5-methoxybenzoic acid. The amount was too small for characterization. It melted unsharply at 136–140°, and repeated crystallization from dilute acetic acid failed to improve the melting point. The analytical results also indicate that the material was not quite pure.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.1; H, 4.9. Found: C, 66.2; H, 5.0.

This keto acid, unlike its isomer, did not undergo ring closure in cold concentrated sulfuric acid. However, heating for 3 hr. on a steam-bath afforded a good yield of yellow 2,6-dimethoxyanthraquinone, m.p. 250°.[10]

(d) **With *p*-Methoxyphenylmagnesium Bromide.**—The reaction between the Grignard reagent from *p*-bromoanisole and 4-methoxyphthalic anhydride has been shown to yield approximately a 3:1 ratio of the 4-methoxy-2-aroylbenzoic acid to the 5-methoxy isomer.[11]

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[8] W. E. Bachmann, THIS JOURNAL, **57**, 737 (1935).

[9] L. Gattermann and H. Rudt (*Ber.*, **27**, 2293 (1894)) have reported a m.p. of 162–163°.

[10] E. Schunck and H. Roemer (*Ber.*, **9**, 379 (1876)) report yellow needles, m.p. 250°; L. H. Briggs and G. A. Nichols (*J. Chem. Soc.*, 1138 (1951)) report almost colorless plates, m.p. 257°.

[11] Unpublished work by the authors.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ALBERTA]

The Hayashi Rearrangement of Substituted o-Benzoylbenzoic Acids

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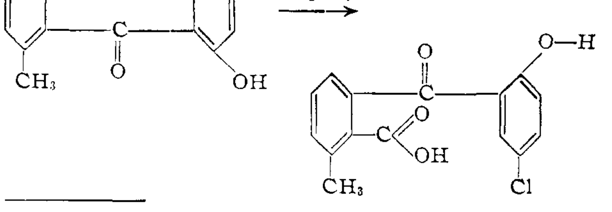
The rearrangement of some substituted *o*-benzoylbenzoic acids in concentrated sulfuric acid has been studied. It has been proposed that the rearrangement involves the rearrangement of an acyl carbonium ion in such a way that there is an increase in conjugation. It is also suggested that a non-classical phenonium cation type of structure is involved.

Hayashi,[1] in 1927, was the first to report the occurrence of a molecular rearrangement in the course of the ring closure of certain substituted *o*-benzoylbenzoic acids



Since 1927, several instances of this remarkable rearrangement have been recorded.[2] Cook[2b] working with 1-(1-naphthoyl)-2-naphthoic acid (I) found that on cyclization, instead of the expected 1,2,7,8-dibenzanthraquinone, compound I gave only 1,2,5,6-dibenzanthraquinone. Cook suggested that the rearrangement proceeded through the hydroxy lactone form of the keto acid.[3]

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[1] M. Hayashi, *J. Chem. Soc.*, 2516 (1927).

[2] (a) M. Hayashi, *ibid.*, 1513, 1520, 1524 (1930); (b) J. W. Cook, *ibid.*, 1472 (1932); (c) M. Hayashi, S. Tsuruoka, T. Morikawa and H. Namikawa, *Bull. Chem. Soc. Japan*, **11**, 184 (1936); (d) R. B. Sandin and L. F. Fieser, THIS JOURNAL, **62**, 3098 (1940); (e) R. Goncalves, M. R. Kegelman and E. V. Brown, *J. Org. Chem.*, **17**, 705 (1952).

[3] L. F. Fieser, "The Chemistry of Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1936, p. 95.