primary allylic bromides the term **propargylic rearrangement** is proposed. However, the explanation of how such a rearrangement takes place is not attempted on the basis of the presented experimental facts. Present research is being extended in this direction and includes also the behavior of secondary and tertiary bromides.

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Summary

For the first time, Grignard reagents have been prepared in practicable yields from primary β-acetylenic bromides. Carbonation of these reagents gave mixtures of acetylenic and allenic acids, which have been isolated, characterized, and identified.

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The Course of the Oxidation of Propiophenone with Alkaline Hypobromite Solution and Certain Related Reactions[1]

BY ROBERT LEVINE AND JAMES R. STEPHENS

The advantages of hypohalite oxidation[2,3] of methyl ketones are well recognized, yet apparently little is known of the behavior of higher alkyl ketones under similar conditions.[4] In a recent communication[5] from this laboratory, it was shown that alkaline hypochlorite solution may be used to cleave higher alkylaryl and alkylheterocyclic ketones in high yields. Thus, propiophenone has been oxidized to benzoic acid and *n*-propyl 2-thienyl ketone has been converted to 2-thiophenic acid.

The present investigation is concerned with the course of such oxidations. We have studied in detail the reaction of propiophenone with alkaline sodium hypobromite solution. From the data which we have accumulated as a result of our study, it seems that the oxidation of propiophenone follows the course indicated in the equations.

$$\underset{\text{(I)}}{\mathrm{C_6H_5COCH_2CH_3}} + \mathrm{2NaOBr} \longrightarrow \underset{\text{(II)}}{\mathrm{C_6H_5COCBr_2CH_3}} + \mathrm{2NaOH} \quad (1)$$

$$\underset{\text{(II)}}{\mathrm{C_6H_5COCBr_2CH_3}} + \mathrm{2NaOH} \longrightarrow \underset{\text{(III)}}{\mathrm{C_6H_5COCOCH_3}} + \mathrm{2NaBr} + \mathrm{H_2O} \quad (2)$$

$$\underset{\text{(III)}}{\mathrm{C_6H_5COCOCH_3}} + \mathrm{NaOBr} + \mathrm{2NaOH} \longrightarrow \underset{\text{(IV)}}{\mathrm{C_6H_5CO_2Na}} + \underset{\text{(V)}}{\mathrm{CH_3CO_2Na}} + \mathrm{NaBr} + \mathrm{H_2O} \quad (3)$$

$$\mathrm{C_6H_5COCH_2CH_3} + \mathrm{3NaOBr} + \mathrm{2NaOH} \longrightarrow \mathrm{C_6H_5CO_2Na} + \mathrm{CH_3CO_2Na} + \mathrm{3NaBr} + \mathrm{2H_2O} \quad (4)$$

In agreement with equation (4), we have shown that the conversion of propiophenone, (I), to sodium benzoate, (IV), requires about three equivalents of sodium hypobromite per equivalent of benzoic acid produced. That the other end-product of the oxidation is acetic acid was definitely shown by extracting acetic acid from the reaction mixture after the benzoic acid was removed.

Evidence is available from the literature that certain propiophenone derivatives may be treated with alkaline hypobromite solution and the α,α-dibromoketones may then be isolated. Thus, Fisher, Snyder and Fuson[6] have treated propionylmesitylene with sodium hypobromite solution and obtained α,α-dibromopropionylmesitylene, which they isolated as the 3,5-dinitro derivative. This reaction is analogous to the conversion of I to II which is postulated above.

The dibromo derivative (II) is then believed to be converted in the alkaline medium to 1-phenyl-1,2-propanedione (III) which is then cleaved to a mixture of benzoic and acetic acids (as their sodium salts). That II is probably converted to III finds support in the recent work of Ayres and Hauser.[7] These workers have definitely shown that phenylglyoxal is an intermediate when α,α-dibromoacetophenone is converted to mandelic acid by means of aqueous alkali.

In order to determine whether hypobromite is required for the cleavage of II via III or whether alkali alone is sufficient to effect this transformation, two types of experiments were performed. An authentic sample of II was prepared and subjected to reaction with both 20 and 2% aqueous sodium hydroxide. In neither case was any benzoic acid isolated. From the former experiment, a high yield (85%) of atrolactic acid (VI) and a trace of 2,5-diphenyl-1,4-benzoquinone

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[1] This paper is based on a thesis submitted by James R. Stephens in partial fulfillment of the requirements for the degree of Master of Science at the University of Pittsburgh, August, 1949.

[2] Newman and Holmes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 428.

[3] Fuson and Bull, *Chem. Revs.*, **15**, 275 (1934).

[4] Haworth (*J. Chem. Soc.*, 1127 (1932)) has used alkaline hypobromite to oxidize β-1-naphthoylisobutyric acid to 1-naphthoic acid. However, the course of the oxidation was not investigated.

[5] Farrar and Levine, THIS JOURNAL, **71**, 1496 (1949).

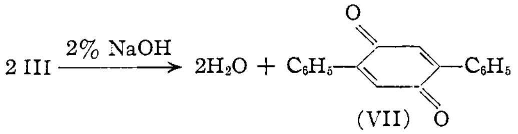
[6] Fisher, Snyder and Fuson, *ibid.*, **54**, 2669 (1932).

[7] Ayres and Hauser, *ibid.*, **65**, 1095 (1943).

(VII) were obtained. From the latter only VII (13%) was obtained. However, when II was treated with alkaline sodium hypobromite solution, benzoic acid was isolated in 92% yield and if any VI or VII were formed, not enough of either was present to be detected. These experiments indicate that hypobromite is required to cleave III which is formed from II. Titration data also indicate that approximately one equivalent of hypobromite is required to cleave II via III. When an authentic sample of the diketone (III) was treated with alkaline hypobromite, it also gave benzoic acid in high yield (91%). Titration indicated that between one and two moles of sodium hypobromite are required to oxidize each mole of III to benzoic acid.[8]

The quinone (VII) was probably formed by a double aldol condensation involving two moles of III per mole of quinone formed. Earlier von Pechman[9,10] reported that the interaction of III with dilute sodium hydroxide in the presence of potassium ferricyanide gave the quinone. The atrolactic acid was probably formed from III by a benzilic acid type rearrangement.[11,12] The following equations indicate how VI and VII may be formed.

$$\text{III} + H_2O \xrightarrow[\text{then } H^+]{20\%\ \text{NaOH}} C_6H_5C(OH)CH_3CO_2H \quad \text{(VI)}$$



(VII)

It was then of interest to determine what structures the higher alkylaryl ketones should have in order that they might be oxidized to acids by alkaline hypobromite solution. Therefore, butyrophenone, isobutyrophenone and pivalophenone were subjected to the oxidation reaction. Butyrophenone was oxidized to benzoic acid in good yield (48%) while pivalophenone was recovered unchanged. In the oxidation of isobutyrophenone, a small amount (5%) of benzoic acid was isolated but most of the ketone was recovered unchanged. It is quite possible that the isobutyrophenone was contaminated with a small amount of butyrophenone from which the benzoic acid may have been formed. Finally, to show that caustic alone would not cleave ketones to acids under the conditions of our experiments, samples of propiophenone and isobutyrophenone were treated with 10% sodium hydroxide solution. No benzoic acid was obtained and the ketones were recovered unchanged.

It appears, then, that if alkaline hypobromite solution is to be used successfully for the oxidation of the higher alkylaryl ketones to acids, the ketone should have two hydrogen atoms on the carbon atom alpha to the carbonyl group.

Experimental

Preparation of α,α-Dibromopropiophenone (II).—This ketone was prepared by a modification of the synthesis reported in the literature.[13] To 13.4 g. (0.1 mole) of propiophenone contained in a 500-ml. erlenmeyer flask maintained at 18° in a water-bath was added 16 g. (0.1 mole) of bromine dissolved in 100 ml. of chloroform. After standing at 18° for twenty-five minutes with no apparent reaction, the temperature of the water-bath was raised to 21°. A very rapid reaction took place with the evolution of large amounts of hydrogen bromide. After one hour, a solution of 17.6 g. of bromine in 40 ml. of chloroform was added over a period of five minutes. The temperature of the bath was raised slowly until the boiling point of the chloroform was reached. The mixture again evolved large amounts of hydrogen bromide. After the evolution of the gas had ceased (about two hours), the reaction mixture was washed with two 80-ml. portions of water. The wet reaction mixture was distilled at atmospheric pressure to remove the solvent and the residue was then distilled in vacuum to give 24.3 g. (83%) of α,α-dibromopropiophenone, b. p. 180° at 64 mm., m. p. 28–30.5°.[13]

Reaction of Ketones with Sodium Hypobromite Solution: (a) Preparation and Standardization of Sodium Hypobromite Solution.—All the solutions were freshly prepared at 0–10° by adding 28 ml. (87.5 g., 0.55 mole) of bromine with stirring to a solution of 88 g. (2.2 moles) of sodium hydroxide dissolved in 364 ml. of water. The standardized solutions[14] were about 1.3 *M*.

(b) Determination of the Oxidation Ratio, (R_{OX}), of the Ketones.—After the completion of the oxidation of the ketone, a 10-ml. aliquot from the reaction mixture was titrated and its hypobromite content determined.

An oxidation ratio (R_{OX}), which is an expression for the number of moles of hypobromite required to produce one mole of benzoic acid, may then be written as shown by the expressions

$$R_{OX} = \frac{\text{moles of OBr}- \text{ reduced}}{\text{moles of ketone oxidized}} = \frac{\text{moles of OBr}- \text{ reduced}}{\text{fraction of benzoic acid recovered} \times \text{moles of starting ketone}}$$

(c) Oxidation of Propiophenone.—The apparatus used for the oxidation of this and the other ketones consisted of a 500-ml. three-neck, round-bottom flask equipped with a thermometer, an addition funnel and an efficient mechanical stirrer. Stirring must be sufficiently rapid so that the reaction mixture exists as an emulsion throughout the oxidation. Otherwise, the yields of benzoic acid are low and much of the ketone is recovered unchanged

To 390 ml. of a rapidly stirred sodium hypobromite solution (0.512 mole) at 22°, 20.1 g. (0.15 mole) of propiophenone was added over a five-minute period. Stirring

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[8] Actually, 1.7 moles of hypobromite was consumed per mole of benzoic acid formed. According to equation three (see above), one mole of hypobromite should have been consumed. The high value may be explained on the basis that the diketone was contaminated with some propiophenone from which it was prepared. A small amount of propiophenone would increase greatly the amount of hypobromite reduced.

[9] von Pechman, *Ber.*, **21**, 1411 (1888).

[10] Muller and von Pechman, *ibid.*, **22**, 2127 (1889).

[11] See Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1940, p. 321.

[12] It should be pointed out, however, that in the conversion of II to atrolactic acid via III, the concentration of III is not very great at any time but probably reacts as rapidly as it is formed since an authentic sample of III, when treated with 20% sodium hydroxide, gave a large amount of tar and only a small amount of atrolactic acid.

[13] Krohnke and Timmler, *Ber.*, **69B**, 614 (1936).

[14] Kolthoff and Sandell, "Textbook of Quantitative Inorganic Analysis," revised ed., The Macmillan Company, New York, N. Y., 1946, pp. 587, 622 and 627.

was continued for two and one-half hours longer and the mixture kept at 24–25° by immersing the flask in an ice-bath when necessary. The solution then contained 0.043 mole of unreacted sodium hypobromite. After destroying the excess hypobromite with sodium bisulfite solution, the basic solution was extracted several times with ether to remove unreacted ketone. From the aqueous phase, acidified with concentrated hydrochloric acid, there was obtained 17.6 g. (96%) of benzoic acid, m. p. 121.5–122° alone and when mixed with an authentic sample. Part (200 ml.) of the residual aqueous solution (648 ml.) was extracted with ether for eleven hours in a continuous extraction apparatus[15] to give 0.7 g. (27%) of acetic acid, b. p. 105–120° which was converted to acetanilide, m. p. 113–114° alone and when mixed with an authentic sample. The R_{OX} in this experiment is 3.3, *i.e.*, 0.469/0.96 × 0.15.

(d) **Oxidation of α,α-Dibromopropiophenone (II).**—To 191 ml. of a rapidly stirred sodium hypobromite solution (0.250 mole) at 31° was added 21.9 g. (0.075 mole) of II over a five-minute period. Stirring was continued for three and one-half hours and the mixture was worked up as described above. From the yield of benzoic acid (8.4 g., 92%, m. p. 121°) and the amount of unreacted hypobromite (0.160 mole), the R_{OX} for converting II to benzoic acid is 1.3, *i.e.*, 0.09/0.92 × 0.075.

(e) **The Oxidation of 1-Phenyl-1,2-propanedione (III).**—To 80.5 ml. of sodium hypobromite solution (0.106 mole) at 0° was added with stirring 5 g. (0.0338 mole) of III (b. p. 107–111° at 12 mm.,[16] m. p. of the dioxime, 230–233°[17]) over a period of fifteen minutes. The temperature was kept at 22–25° by means of an ice-bath and stirring continued for forty-five minutes longer before working up the mixture in the regular way. From the unreacted hypobromite (0.054 mole) and the yield of benzoic acid (3.74 g., 91%), the R_{OX} for converting III to benzoic acid is 1.7, *i.e.*, 0.052/0.91 × 0.0338.

(f) **Oxidation of Butyrophenone, Isobutyrophenone and Pivalophenone.**—Using the procedure described for propiophenone, butyrophenone was oxidized to benzoic acid in 48% yield. When isobutyrophenone was treated similarly, the starting ketone (85%) and benzoic acid (5%) were isolated. Pivalophenone, prepared in 78% yield by the methylation of isobutyrophenone,[18] was not oxidized and was recovered unchanged when treated similarly.

Reactions of Ketones with Aqueous Alkali: (a) Treatment of α,α-Dibromopropiophenone (II) with 20% Sodium Hydroxide; Formation of Atrolactic Acid (VI).—To a rapidly stirred solution of 80 g. of sodium hydroxide in 320 ml. of water was added 20 g. (0.0685 mole) of II. The temperature of the solution, which was 31° at the start of the reaction, rose slowly to 39° during the first ninety minutes of stirring. During this time, the color of the reaction mixture went from colorless to orange to dark red. Stirring was continued for ninety minutes longer and the mixture was then extracted with ether and the phases separated. The aqueous phase was acidified with concentrated hydrochloric acid and filtered to remove the small amount of tar which precipitated. From this solution, which was placed in a refrigerator overnight, there precipitated 10.2 g. (85%) of atrolactic acid hemihydrate, m. p. 68–69°[19]; m. p. of the calcium salt 215° with decomposition.[20] The acid was dehydrated at 75° at 2 mm. to give atrolactic acid, m. p. 91–92.5°.[19] The original ether extract was dried over Drierite and the solvent distilled. The residue consisted of a few yellow crystals, m. p. 204–212°. When recrystallized from a mixture of benzene and alcohol, it melted at 214°[10] alone and when mixed with an authentic sample of 2,5-diphenyl-1,4-benzoquinone.

(b) **Treatment of α,α-Dibromopropiophenone (II) with 2% Sodium Hydroxide; Formation of 2,5-Diphenyl-1,4-benzoquinone (VII).**—To 350 ml. of 2% aqueous sodium hydroxide solution in a 500-ml. erlenmeyer flask, was added 9.25 g. (0.0317 mole) of II. The flask was stoppered and allowed to stand with occasional shaking for one week. During this time, the solution developed a red color and a solid had started to precipitate. The reaction mixture was stirred for twelve hours and then extracted with a mixture of ether and benzene. The phases were separated and the solvents distilled from the organic phase to give a semi-crystalline residue which was recrystallized from a mixture of benzene and alcohol. There was obtained 0.54 g. (13%) of VII, m. p. 213–214°.[10] A mixed melting point with an authentic sample of VII showed no depression.

(c) **Treatment of 1-Phenyl-1,2-propanedione (III) with 20% Sodium Hydroxide.**—This reaction was tried under the same conditions described above with II but only tar resulted from the long reaction time. The reaction was repeated as follows. To a rapidly stirred solution of 60 g. of sodium hydroxide in 240 ml. of water was added 7 g. (0.0472 mole) of III over a five-minute period. The temperature of the solution, which was −3° (ice-salt-bath) at the start of the reaction, rose to 2° by the time the ketone had been added to the alkali. Three minutes later the reaction seemed to be over as evidenced by the presence of only one phase. Tar had also started to form. The reaction mixture was worked up as described above in the experiment in which II was treated with 20% alkali. In this way, 0.4 g. of atrolactic acid which was dehydrated to the anhydrous form, m. p. 91–92.5°,[19] was obtained.

Summary

It has been shown that the probable course of the oxidation of propiophenone with sodium hypobromite solution involves bromination to form α,α-dibromopropiophenone, hydrolysis of the halogenated ketone to 1-phenyl-1,2-propanedione and cleavage of this α-diketone to a mixture of acetic and benzoic acids.

Butyrophenone is also oxidized by hypobromite solution to benzoic acid in good yield, but isobutyrophenone and pivalophenone are recovered from the reaction unchanged.

The reaction of α,α-dibromopropiophenone with 20% sodium hydroxide solution results in the formation of atrolactic acid in high yield, while its treatment with 2% alkali results in the production of 2,5-diphenyl-1,4-benzoquinone.

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[15] Lande and Wagner, *Ind. Eng. Chem., Anal. Ed.*, **6**, 300 (1934).

[16] Wegmann and Dahn, *Helv. Chim. Acta*, **29**, 1248 (1946).

[17] Gudeman, *Ber.*, **22**, 563 (1889).

[18] Haller and Bauer, *Compt. rend.*, **148**, 70 (1909).

[19] Grignard, *Ann. chim. phys.*, [7] **27**, 557 (1902).

[20] Smith, *J. prakt. Chem.*, [2] **84**, 738 (1911).