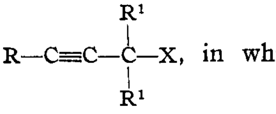
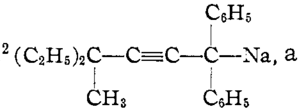
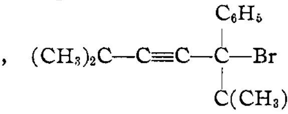
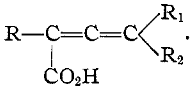
[CONTRIBUTION NO. 736 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

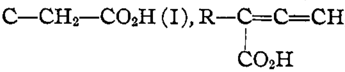
# The Propargylic Rearrangement. I. The Carbonation Products of Grignard Reagents from Primary Propargylic Bromides

BY JOHN H. WOTIZ

In a series of papers dealing with the synthesis and properties of hexasubstituted ethane compounds, Marvel and co-workers[1] have prepared halides of the type  $R—C\equiv C—C(R^1)_2—X$, in which R and $R_1$ were phenyl, *t*-butyl, or alkynyl groups. These halides were converted to organometallic derivatives which were then carbonated. The acids formed exhibited the acetylenic linkage and were identified by oxidation. However, the carbonation of diphenyl-(3-methyl-3-ethyl-1-pentynyl)-methyl sodium[2]  $(C_2H_5)_2C(CH_3)—C\equiv C—C(C_6H_5)_2—Na$, and the Grignard reagent of phenyl-*t*-butyl-*t*-butylethynylbromomethane,  $(CH_3)_3C—C\equiv C—C(C_6H_5)(C(CH_3)_3)—Br$, yielded allenic acids of the type  $R—C(CO_2H)=C=C(R_1)(R_2)$. In no case was the formation of a mixture of the acetylenic and the allenic acid reported.

The only $\beta$-acetylenic halides that were successfully converted into organometallic compounds were the tertiary halides prepared by Marvel and co-workers[1,2] which had no hydrogen atoms on the $\alpha$-carbons. In attempts to prepare organometallic reagents from other $\beta$-acetylenic halides, the coupled hydrocarbon was the main product. Thus, Campbell[3] was unable to prepare a Grignard reagent from tertiary $\beta$-acetylenic halides. Lai[4] studied the reaction of primary propargylic bromides with magnesium, but the Grignard reagent, $RC\equiv CCH_2MgBr$, could not be isolated due to the great reactivity of the halide. The reported products were $\gamma$-diacetylenic hydrocarbons, $RC\equiv C—CH_2CH_2C\equiv CR$. The products were obtained even when the reactions were carried out slowly and at high ether dilution. The reaction of 1,4-dichloro-2-butyne with magnesium[5] gave only traces of a Grignard reagent.

The only previous successful preparation of Grignard reagents from primary $\beta$-acetylenic bromides was carried out by this author,[6] and the present research represents an enlargement upon and an extension of that work. The apparatus and method developed by Rowlands, Greenlee, and Boord[7] for the preparation of Grignard reagents in high ether dilution were used. The halides used were of the type $RC\equiv CCH_2Br$, where R was the normal propyl, butyl, or amyl group. They were prepared from the corresponding primary alcohols using the procedure of Lai,[8] and each was repeatedly distilled under vacuum until the major part had a constant refractive index.

The Grignard reagents were carbonated by pouring them on an excess of Dry Ice. Three types of acids were isolated from the reaction product, $R—C\equiv C—CH_2—CO_2H$ (I),  $R—C(CO_2H)=C=CH_2$ (II), and $R_2C_7H_5O_2CO_2H$ (III). The yields of the combined acid fractions ranged from 3 to 73%, depending on various factors. The products and yields of some representative runs are listed in Table I, and some analytical data in Table II.

A considerable difference in the yield of acids was observed when *n*-butylpropargyl chloride (IV) was used to prepare the Grignard reagents. Using the optimal experimental conditions found for the corresponding bromide, the chloride yielded only 22% of combined acids and the ratio of acid I to II changed from 1:5 to 1:3.

## Experimental

**Identification of Products.**—Acids of the type I and II were characterized by their melting and boiling points and by converting them into the solid amides (Table I). Mixed melting points of isomeric amides showed large depressions. Neutral equivalents (Table II) were determined by potentiometric titrations against 0.1 *N* sodium hydroxide using a Beckman, Model H, *p*H meter. The carbon skeleton was established by hydrogenation to the corresponding saturated straight-chain acids, in the case of acids of type I, and to $\alpha$-alkylbutyric acids, in the case of acids of type II. The semi-quantitative hydrogenation was carried out in absolute ethanol using Adams platinum catalyst under pressures slightly above atmospheric. The theoretical amount of hydrogen (Table II) was absorbed very quickly with acids of type I, but slowly in the case of acids of type II. The hydrogenated acids were identified by their neutral equivalents, boiling points, and indexes of refraction. These values were in excellent agreement with those listed in the literature and with the measured properties of authentic samples of acids commercially available, or synthesized by the malonic ester synthesis. The hydrogenated acids were also converted into amides which

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(1) Ford, Thompson and Marvel, THIS JOURNAL, **57**, 2619 (1935); see also references listed therein.

(2) Harmon and Marvel, *ibid.*, **55**, 1716 (1933). Simultaneously with the submission of the present manuscript a paper on a similar subject was submitted by G. R. Lappin and has been published (THIS JOURNAL, **71**, 3966 (1949)).

(3) Campbell and Eby, *ibid.*, **62**, 1798 (1940).

(4) Lai, *Bull. soc. chim.*, **53**, 1543 (1933).

(5) Johnson, *J. Chem. Soc.*, 1009 (1946).

(6) Newman and Wotiz, THIS JOURNAL, **71**, 1292 (1949).

(7) Daniel C. Rowlands, M.S. Thesis, The Ohio State University, 1948, done under the supervision of K. W. Greenlee and C. E. Boord. A detailed description of this method is now being prepared for publication.

(8) Lai, *Bull. soc. chim.*, **53**, 682 (1933).

TABLE I

PHYSICAL PROPERTIES AND YIELDS OF PRODUCTS

| | $-C\equiv C-CH_2-Br$ | | | | $R-C\equiv C-CH_2-CO_2H$ (I) | | | | | $\underset{CO_2H}{R-C}=C=CH_2$ (II) | | | | Dimer (III) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| R- | B. p.,[a] °C. (4 mm.) | $n^{25}D$ | Moles used | Total yield of acids, % | Yield, % | M. p.,[b] °C. | B. p.,[a] °C. (2 mm.) | $n^{25}D$ | Amide m. p., °C. | Yield, % | M. p.,[b] °C. | B. p.,[a] °C. (2 mm.) | Amide, m. p., °C. | Yield, % | M. p.,[a] with dec., °C. | Residue, % |
| $C_3H_7$ | 38 | 1.4886 | 0.2 | 72 | 16 | 14 | 102 | 1.4635 | 67 | 38 | 53 | 94 | 70 | 12 | 113 | 6 |
| $C_4H_9$[e] | 54 | 1.4844 | .3 | 57 | 9 | 18[d] | 110[d] | 1.4577[d] | 53[d] | 41 | 70 | 102 | 63 | [c] | 99 | 7 |
| $C_5H_{11}$ | 68 | 1.4818 | .1 | 52 | 13 | 14 | 118 | 1.4603 | 54 | 23 | 47 | 110 | 73 | 3 | 105 | 13 |

[a] Boiling points represent cuts taken for analysis. [b] Melting points are uncorrected, over one-degree range, upper limit listed. [c] Isolated and characterized in a different run. [d] Previously reported; see footnote 6. [e] Compare with the product described in footnote 9.

TABLE II

ANALYTICAL DATA OF PRODUCTS

| | | $-C\equiv C-CH_2-CO_2H$ (I) | | | $-C\equiv C-CH_2CONH_2$ | | | $\underset{CO_2H}{-C}=C=CH_2$ (II) | | | $\underset{CONH_2}{-C}=C=CH_2$ | | | Dimer (III) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| R = | | $C_3H_7-$ | $C_4H_9-$ | $C_5H_{11}-$ | $C_3H_7-$ | $C_4H_9-$ | $C_5H_{11}-$ | $C_3H_7-$ | $C_4H_9-$ | $C_5H_{11}-$ | $C_3H_7-$ | $C_4H_9-$ | $C_5H_{11}-$ | $C_3H_7-$ | $C_4H_9-$ | $C_5H_{11}-$ |
| C,[a] % | Theory | 66.6 | (d) | 70.1 | 67.1 | (d) | 70.5 | 66.6 | 68.6 | 70.1 | 67.1 | 69.1 | 70.5 | 66.6 | 68.6 | 70.1 |
| | Found | 66.7 | | 70.4 | 67.0 | | 70.3 | 66.3 | 68.7 | 70.2 | 66.9 | 68.6 | 70.4 | 66.6 | 68.6 | 70.3 |
| H,[a] % | Theory | 7.9 | (d) | 9.1 | 8.8 | (d) | 9.8 | 7.9 | 8.6 | 9.1 | 8.8 | 9.3 | 9.8 | 7.9 | 8.6 | 9.1 |
| | Found | 7.7 | | 9.3 | 8.6 | | 9.9 | 7.6 | 8.5 | 9.1 | 8.6 | 9.3 | 9.5 | 7.6 | 8.2 | 9.1 |
| N,[a] % | Theory | .... | ... | .... | 11.2 | (d) | 9.2 | .... | .... | .... | 11.2 | 10.1 | 9.2 | ... | ... | ... |
| | Found | .... | ... | .... | 11.3 | | 9.3 | .... | .... | .... | 11.3 | 10.1 | 9.3 | ... | ... | ... |
| N. eq.[b] | Theory | 126 | (d) | 154 | .. | ... | .. | 126 | 140 | 154 | .. | .. | .. | 252 | 280 | 308 |
| | Found | 126 | | 154 | .. | ... | .. | 126 | 140 | 154 | .. | .. | .. | 252 | 280 | 308 |
| Vol. (cc.) of $H_2$ absorbed | Theory[c] | 599 | (d) | 250 | .. | ... | .. | 615 | 1360 | 250 | .. | .. | .. | .... | 885 | ... |
| | Found | 550 | | 247 | .. | ... | .. | 600 | 1300 | 247 | .. | .. | .. | ... | 880 | ... |
| | Wt. of acid | 1.68 | (d) | 0.86 | .. | ... | .. | 1.73 | 4.2 | 0.86 | .. | .. | .. | ... | ... | ... |
| | Time, min. | 30 | | 20 | .. | ... | .. | 270 | 240 | 190 | .. | .. | .. | ... | ... | ... |

[a] Duplicate microanalyses by G. L. Stragand and J. Corrado at the Microchemical Analytical Laboratory of the University of Pittsburgh. The better value is reported to conserve space. [b] Determined using a Beckman *p*H meter and 0.1 *N* sodium hydroxide. [c] Semiquantitative determination. Volume of hydrogen corrected to standard temperature and pressure. [d] Previously reported; see footnote 4. [e] Calculated for two double bonds per molecule.

did not depress the melting points of authentic samples of the same amides.

The position of unsaturation in acids I and II was established by ozonolysis of the products in which R was the *n*-butyl group. The acid I was found to be identical with the one prepared by the hydrolysis of the nitrile and previously described.[6] Acid II was ozonized in glacial acetic acid at room temperature to α-ketohexanoic acid. Its dinitrophenylhydrazone did not depress the melting point of an authentic sample. Acid II (R = $C_4H_9$) was also converted to its methyl ester and its infrared absorption spectrum was determined (Fig. 1). It shows the allenic structure conjugated with the carboxyl group by the absorption band at 1950 cm.$^{-1}$. The spectrum of the methyl ester of acid I (R = $C_4H_9$) was recently published.[9] Both spectra are consistent with the structures determined by chemical means. Neither the isolated single bond nor the conjugated double bond system were indicated, even in the infrared analysis of thicker samples.

The structures of acids of type III were not established and will be the subject of a future study. They were characterized by elementary analyses, melting point determinations (with decomposition), and neutralization equivalents, which were double those of the corresponding acids of type I and II.

**Isolation of Products.**—The carbonation products, after acid hydrolysis, were extracted from the ether by dilute aqueous sodium hydroxide solution and recovered by acidification. The neutral portion boiled over a wide range well above the boiling point of the starting material. When the chloride IV was used, a large part of it was recovered from the ethereal residue and was identified by its boiling point. When alkylpropargyl bromides were used, none were recovered.

The separation of acids, I, II and III was achieved by means of fractional crystallization from a mixture of ether and petroleum ether (30–60°). The acid II was the least soluble and separated in large, well developed crystals. The mother liquors, concentrated to smaller volume, deposited crystals of acid III that melted about 50° higher than acid II. Acid I was separated by vacuum distillation of the mother liquor of acid III. A distillation residue whose amount varied with the success in isolating acid III was observed in most cases (see Table I). A simpler separation was achieved by direct vacuum distillation of the crude acidic portion. Acids I and II distilled without decomposition, but acid III was decomposed under these conditions and the distillation residue was increased. It is to be noted that acid II boiled lower than acid I, although it melted considerably higher. A low-temperature fractional crystallization from petroleum ether completed the separation of acid I from acid II in the distillate.

**1-Bromo-2-alkynes.**—The procedure of Lai[8] using 2-alkyn-1-ols and phosphorus tribromide was used. Each product was rectified in a 90-cm. helices-packed column until the major part had a constant boiling point and refractive index; the yields of pure products were 62 to 67%. The boiling points and refractive indices are listed in Table I. Along with each bromide some dibromide was always obtained. Two of these dibromides have already been reported[6]; the one obtained from 2-octyn-1-ol (assumed structure $C_5H_{11}CBr=CHCH_2Br$) is new: b. p. 105° at 6

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(9) Wotiz and Miller, THIS JOURNAL, **71**, 3441 (1949).

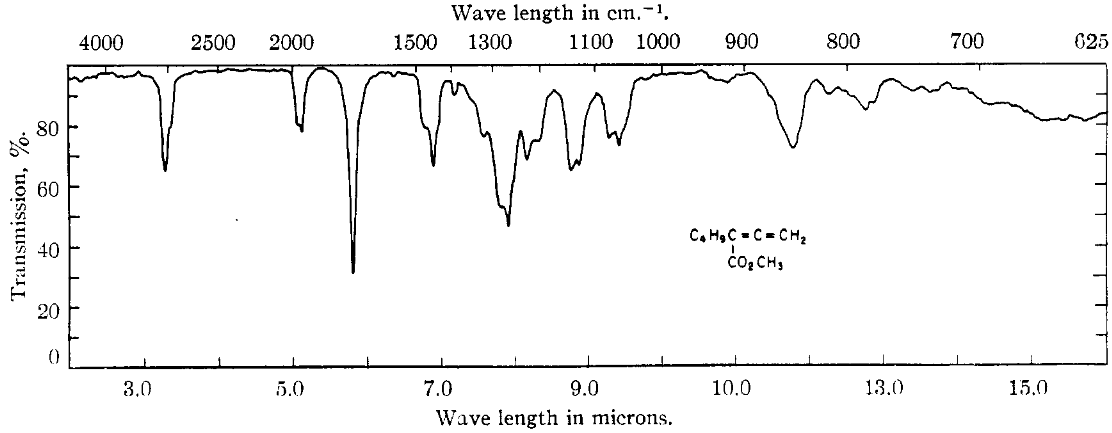


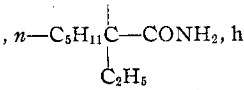
Fig. 1.

mm., $n^{25}D$ 1.5093. *Anal.* Calcd. for $C_8H_{12}Br_2$: C, 35.8; H, 4.5; Br, 59.8. Found: C, 36.1; H, 4.8; Br, 59.4.

**3-Heptynoic Acid I** (R = $C_3H_7$) and **1,2-Hexadiene-3-carboxylic Acid** (II) (R = $C_3H_7$).—1-Bromo-2-heptyne (32 g. or 0.2 *M*) was treated with magnesium in dry ether by a method[7] which achieves extremely high dilution in the reaction zone without using large quantities of solvent. The ethereal solution of Grignard reagent was poured on 1 kg. of powdered Dry Ice, and the product was brought to room temperature overnight. After hydrolysis with a concentrated solution of ammonium chloride followed by dilute hydrochloric acid, the ether solution was extracted with sodium carbonate. The aqueous layer was added to a mixture of ice and hydrochloric acid and the liberated organic acids taken into ether. The ether solution was washed with water, saturated sodium chloride solution, dried over anhydrous sodium sulfate, and filtered. The ether was evaporated under vacuum at room temperature to a volume of 50 cc. and diluted with an equal volume of petroleum ether (30 to 60°). On standing at 0° overnight, 8 g. of II separated as large, well-developed crystals. They were recrystallized from a mixture of petroleum ether and ether to a constant melting point. The mother liquor of II, concentrated to 30 cc., deposited 3 g. of III which was recrystallized from benzene. The mother liquor of III was distilled under vacuum to yield 5.5 g. of a distillate and 2 g. of a residue. The distillate, mixed with petroleum ether and kept ice-cold overnight, separated an additional 1.5 g. of II which was separated by filtration. The mother liquor, redistilled, yielded 4 g. of I. The per cent. yields and physical properties of these products are listed in Table I, and analyses in Table II.

Under similar conditions 1-bromo-2-octyne yielded **3-nonynoic acid** (I) (R = $C_5H_{11}$) and **1,2-octadiene-3-carboxylic acid** (II) (R = $C_5H_{11}$); also 1-bromo-2-heptyne yielded **3-octynoic acid** (I) (R = $C_4H_9$) and **1,2-heptadiene-3-carboxylic acid** (II) (R = $C_4H_9$) (see Table I and II).

**Preparation of Amides** (Table I and II).—Phosphorus pentachloride was added in parts to the acid until the evolution of hydrogen chloride ceased and the reaction mixture was added to ammonium hydroxide. The formed white solid was dissolved in ether and the solution purified by washing with water and drying over calcium chloride. The amide was recrystallized to a constant melting point from petroleum ether (30–60°) if unsaturated, or from benzene when the amide was saturated.



**2-Ethylheptanamide**, $n\text{—}C_5H_{11}\overset{\displaystyle H}{\underset{\displaystyle C_2H_5}{C}}\text{—}CONH_2$, has not been previously reported. An authentic sample was also prepared (m. p. 98–99°) from 2-ethylheptanoic acid (b. p. 100° at 2 mm., $n^{25}D$ 1.4258) prepared by the malonic ester synthesis. *Anal.* Calcd. for $C_9H_{19}NO$: C, 68.8; H, 12.1; N, 8.9. Found: C, 68.7; H, 11.8; N, 9.8.

**Methyl 1,2-Heptadiene-3-carboxylate.**—A solution of 14 g. of II (R = $C_4H_9$) in 60 cc. of methyl alcohol was refluxed with 0.5 g. of *p*-toluenesulfonic acid (catalyst) overnight. Most of the alcohol was distilled off under vacuum, the residue dissolved in ether and washed with dilute sodium carbonate. Distillation yielded 13 g. (76%) of the ester, b. p. 65° at 3 mm., $n^{25}D$ 1.4600. *Anal.* Calcd. for $C_9H_{14}O_2$: C, 70.1; H, 9.1. Found: C, 70.2; H, 9.1. This product was also used for infrared analysis (Fig. 1).

**Ozonization.**—Through a solution of 2.8 g. of II (R = $C_4H_9$) in 50 cc. of acetic acid was passed for seven hours a mixture of unknown concentration of ozone and oxygen. The ozone was not completely absorbed as apparent from the immediate liberation of iodine from potassium iodide. The product was poured on ice and 0.9 g. (32%) of the starting acid was recovered as a white solid (m. p. 70°). The filtrate was evaporated to dryness under vacuum at room temperature. A part (0.56 g.) of the oily residue was refluxed for three hours with 1.5 g. of 2,4-dinitrophenylhydrazine in 70 cc. of ethanol. The solution was mixed with 150 cc. of dilute hydrochloric acid and 0.87 g. (66% yield) of the hydrazone separated. Recrystallized from benzene it melted at 152–153°. *Anal.* Calcd. for $C_{12}H_{14}N_4O_6$: C, 46.5; H, 4.5; N, 18.1. Found: C, 46.6; H, 4.5; N, 18.2. A mixed melting point with an authentic sample of the 2,4-dinitrophenylhydrazone of α-ketohexanoic acid[10] showed no depression.

## Discussion of Results

Recently[6] it was shown that 1-bromo-2-hexyne can be converted into *n*-4-octynoic acid by the malonic ester synthesis, and 1-bromo-2-heptyne into 1-cyano-2-heptyne which on hydrolysis yielded *n*-3-octynoic acid. The carbon structure of both acids was proven by reduction to *n*-octanoic acid, and unsaturation was located by ozonization. No isomeric products were found in either reaction. Since in the present paper it was demonstrated that the same primary propargylic bromides yield a mixture of acetylenic and allenic acids on carbonation of their Grignard reagents, a rearrangement has to be considered.

In order to stress the great similarity in the behavior of primary propargylic bromides to

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(10) Prepared by the method of Adickes and Andresen, *Ann.*, **555**, 41 (1944).

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.

**Acknowledgment.**—The author wishes to express his gratitude to Dr. Foil A. Miller of Mellon Institute, for the determination and interpretation of the infrared spectrum, and to Drs. M. S. Newman and Kenneth W. Greenlee of the Ohio State University for advice.

## 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.

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

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

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

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

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).