silver on p-phenylenediamine. With the other developing agents it eliminated the effect of the silver on the total oxygen absorption, showing that the halogen ion interferes with the silver catalysis of the decomposition of hydrogen peroxide and of the oxidation of the developing agents by hydrogen peroxide. The effect of halogen ion on the shortening of the induction period, e. g., of metol, is much less pronounced.

According to the present results, a catalytic effect of silver in photographic development of the type suggested by Volmer, i. e., a catalysis which directly affects the reactivity of the developing agents is most unlikely with developing agents of the types of dioxybenzene and aminophenol. It may possibly play some role in development with p-phenylenediamine and its derivatives. For the discrimination between exposed and unexposed grains in general, however, the other mechanisms indicated in the introductory remarks should be responsible.

Summary

1. The oxygen absorption of hydroquinone at various rates of shaking was investigated to check the conditions under which the concentration of oxygen in the liquid phase remains constant.

2. In agreement with results in earlier papers of this series and in disagreement with Green and Branch, it was shown that the rate of autoxidation of hydroquinone between pH 7 and 8.2 increases with the square of the hydroxyl-ion concentration.

3. Silver accelerates the autoxidation of hydroquinone, catechol, p-aminophenol, and glycine only to a very small degree. With these developing agents, therefore, the catalysis suggested by Volmer is most unlikely to be of significance for photographic development.

4. The autoxidation of p-phenylenediamine and p-dimethylaminoaniline shows a more considerable catalysis by silver.

5. The addition of silver strongly diminishes the total amount of oxygen which is absorbed by the developing agents in alkaline solutions. This is chiefly caused by a catalytic effect of the silver on reactions of peroxide formed in the autoxidation.
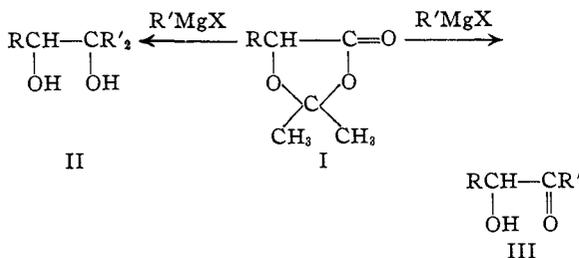

Reductive Cleavage of Dioxolones by the Grignard Reagent

By Reynold C. Fuson and A. I. Rachlin

Dioxolones, acetone derivatives of α-hydroxy acids (I), are known to react with the Grignard reagent to form glycols (II).[1] It seemed probable that if the reagent had a very highly branched radical, acyloins (III) might be produced.

In an attempt to obtain the latter type of compound, the acetone derivative of mandelic acid (IV) was treated with t-butylmagnesium chloride. The product was not the acyloin, however, but α-isopropoxymandelic acid (V). Isobutylene was evolved.

(1) Freudenberg, Todd and Seidler, Ann., **501**, 210 (1933).
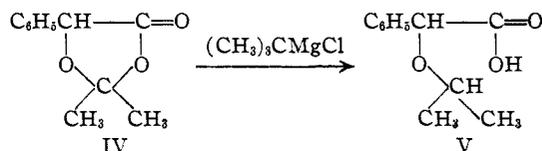
The reaction is a hydrogenolysis of the dioxolone ring and appears to be new in type. Moreover, it has no parallel among the reactions between the Grignard reagent and esters or lactones.

The structure of the product was established by synthesis. The following series of reactions was employed
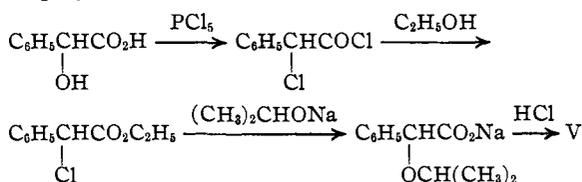
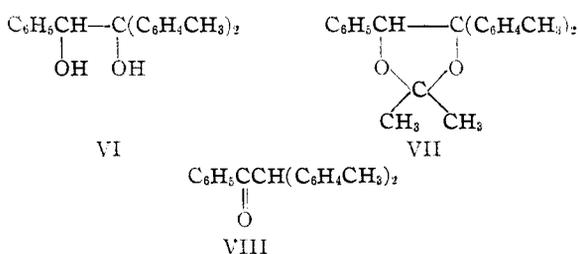It has been found that the reaction is general for acetone derivatives of α-hydroxy acids. The iso-

propyl ethers of mandelic, *p*-methylmandelic, *p*-bromomandelic, α-mesitylglycolic, lactic and α-hydroxyisobutyric acids have been prepared by this method in yields of 57, 66, 71, 80, 20 and 50%, respectively. All these acids are new compounds.

Unsuccessful attempts were made to produce the cleavage with the binary mixture (Mg + MgI₂),[2] aluminum isopropoxide, the zinc–copper couple and hydrogen in the presence of platinum. Hydrogen with copper chromite has been reported[3] to convert dioxolones into a mixture of compounds none of which is analogous to the product described here.

Attempts to effect the reduction of the acetone derivative of mandelic acid by use of other alkyl Grignard reagents were unsuccessful, indicating that the reaction may be peculiar to *t*-butylmagnesium halides.
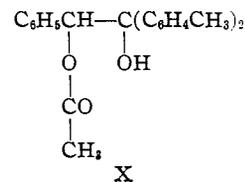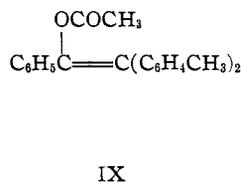
No evidence of reduction was observed in reactions involving aryl Grignard reagents. Normal addition was the principal reaction, with steric hindrance playing an interesting role. For example, phenylmagnesium bromide gave a 66% yield of triphenylethylene glycol as reported by Freudenberg, Todd and Seidler.[1]

Mesitylmagnesium bromide produced an intractable oil. On the other hand, *o*-tolylmagnesium bromide converted the dioxolone into the glycol (VI). Small amounts of the corresponding dioxolane (VII) and the ketone (VIII), formed from the glycol by dehydration, were also isolated.

$$C_6H_5CH-C(C_6H_4CH_3)_2$$
$$\underset{OH}{|} \quad \underset{OH}{|}$$
VI

$$C_6H_5CH-C(C_6H_4CH_3)_2$$
with dioxolane ring
$$\underset{CH_3}{} \quad \underset{CH_3}{}$$
VII

$$C_6H_5CCH(C_6H_4CH_3)_2$$
$$\underset{O}{\|}$$
VIII

The glycol (VI) was transformed readily into the ketone (VIII) by acids. Treatment of the glycol with acetic anhydride in the presence of a mineral acid produced an acetate (IX) obtained by similar treatment of the ketone (VIII). On the other hand, acetic anhydride in pyridine produced a different acetate (X), which was readily dehydrated to the other acetate (IX) by acetyl chloride. The glycol had two active hydrogen atoms.
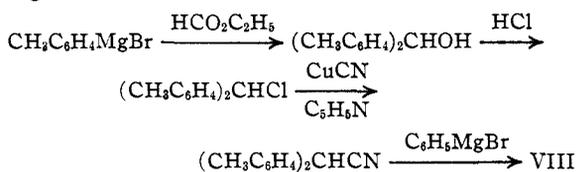
OCOCH₃
$$C_6H_5C═══C(C_6H_4CH_3)_2$$
IX

$$C_6H_5CH-C(C_6H_4CH_3)_2$$
$$\underset{O}{|} \quad \underset{OH}{|}$$
$$\underset{CO}{|}$$
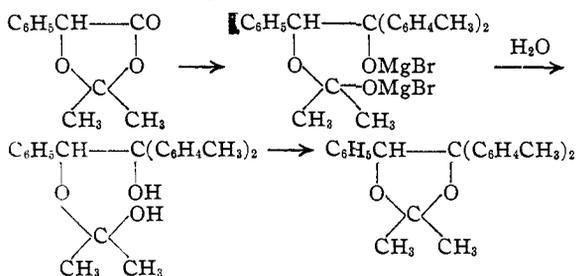$$\underset{CH_3}{|}$$
X

An attempt to synthesize the glycol by treating methyl mandelate with *o*-tolylmagnesium bromide resulted in the formation of an oil. A similar experience was reported by Roger and McKay[4] who used the ethyl ester.

The structure of the dioxolane (VII), an acetal, is based on the analysis, the transformation to the ketone (VIII) in the presence of acid and the synthesis by condensing the glycol (VI) with acetone. The dioxolane had no active hydrogen atom. When it was treated with acetic anhydride and acid, the acetate (IX) was formed.

The ketone (VIII) was synthesized in the following manner.

$$CH_3C_6H_4MgBr \xrightarrow{HCO_2C_2H_5} (CH_3C_6H_4)_2CHOH \xrightarrow{HCl}$$

$$(CH_3C_6H_4)_2CHCl \xrightarrow[C_5H_5N]{CuCN}$$

$$(CH_3C_6H_4)_2CHCN \xrightarrow{C_6H_5MgBr} VIII$$

The formation of the dioxolane may be explained by assuming that the behavior of the original dioxolone toward *o*-tolylmagnesium bromide resembles that of lactones. The transformation may be represented as
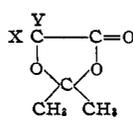
$$C_6H_5CH-CO \rightarrow [C_6H_5CH-C(C_6H_4CH_3)_2 \xrightarrow{H_2O}$$

$$C_6H_5CH-C(C_6H_4CH_3)_2 \rightarrow C_6H_5CH-C(C_6H_4CH_3)_2$$

Experimental

The dioxolones were made by condensing acetone with the appropriate α-hydroxy acids by means of concentrated sulfuric acid. The method, essentially that of Audrieth and Sveda,[5] was modified in order to give a pure product. The following directions for making acetonemandelic acid illustrate the general procedure.

A solution of 304 g. of mandelic acid in 880 cc. of dry acetone was cooled to −10° in an ice–salt-bath. The solution was stirred vigorously while 196 g. of concentrated sulfuric acid was added. The addition was made over a period of one hour and the unused acid was neutralized by

(2) Gomberg and Bachmann, This Journal, 49, 237 (1927).

(3) Oeda, Bull. chem. soc. Japan, 10, 531 (1935).

(4) Roger and McKay, J. Chem. Soc., 2232 (1931).

(5) Audrieth and Sveda, "Organic Syntheses," 20, 62 (1940).

TABLE I

$$\begin{array}{c} Y \\ X \overset{|}{C} \!-\! C\!=\!O \\ \underset{O}{\big|} \underset{C}{\diagdown} \underset{O}{\big|} \\ \diagup \diagdown \\ CH_3 \quad CH_3 \end{array}$$

Compound, with substituents at X and Y in the formula		M. p. or b. p., °C.	Yield (%)	Analyses, %[6]			
				Carbon		Hydrogen	
X and Y	CH₃ CH₃			Calcd.	Found	Calcd.	Found
C₆H₅	H	45[a]	77	...	...	..	..
CH₃C₆H₄	H	56–57	32	69.55	69.92	7.29	7.07
BrC₆H₄	H	65–66	35	48.75	49.01	4.06	4.26
Mes[b]	H	92	72	71.76	71.70	7.74	7.89
CH₃	H	58–60 (18 mm.)[c,d]	30	...	...	..	..
CH₃	CH₃	71 (42 mm.)[e]	35	58.31	58.76	8.39	8.69

[a] Described by Audrieth and Sveda.[5]   [b] "Mes" is used to represent mesityl.   [c] Described by Oeda.[3]   [d] The reaction mixture was poured into benzene. The benzene layer was treated with diethylamine to neutralize the acid, dried over magnesium sulfate and distilled.   [e] n^{20}D 1.4065.

pouring the reaction mixture into an ice-cold solution of 400 g. of anhydrous sodium carbonate in 3500 cc. of water. The curdy white product was collected on a suction filter and sucked dry. Purification was effected by washing the solid with four 250-cc. portions of ether. The ether solution was dried over calcium chloride and the solvent was removed by distillation. Removal of the last traces of ether *in vacuo* caused the acetone compound to solidify in a white mass. The hard cake was pulverized and used without further purification.

The physical constants, yields and analytical data for this and similar compounds are given in Table I.

The Action of *t*-Butylmagnesium Chloride on Dioxolones.—The procedure, illustrated for the reaction of *t*-butylmagnesium chloride on acetone-mandelic acid, was the same in all cases.

t-Butylmagnesium chloride was made by adding 55.8 g. of *t*-butyl chloride to a mixture of 14.4 g. of magnesium and 150 cc. of ether. To this well-stirred solution was added 38.4 g. of acetone-mandelic acid dissolved in 100 cc. of ether. The time of addition was one-half hour. The solution was stirred and refluxed for an additional hour before decomposition with 200 cc. of concentrated hydrochloric acid and 1000 g. of ice. After separation of the layers, the aqueous part was extracted with 200 cc. of ether. The combined ethereal solution was extracted repeatedly with 10% potassium bicarbonate. Acidification of the alkaline solution with hydrochloric acid caused the α-isopropoxymandelic acid to precipitate as an oil. The oil solidified when the mixture was allowed to stand for a few hours; yield, 22 g., 57% of theoretical.

One experiment was devoted to the examination of the gaseous by-product. By means of a stream of nitrogen the gas was forced through a series of wash bottles containing the following solutions in order: 64 g. of bromine in 200 cc. of carbon tetrachloride (0°); 10 g. of bromine in 100 cc. of carbon tetrachloride (0°); 25 cc. of sodium sulfite in 300 cc. of water; an empty trap at dry-ice temperature. The reaction was carried out as described above, using the Grignard reagent made from 24 g. of magnesium, 92 g. of *t*-butyl chloride, 250 cc. of ether and a solution of 76.8 g. of acetone-mandelic acid in 200 cc. of ether. The solution was refluxed a total of two hours, after the addition of the acetone compound. No other

effort was made to drive the gas out of the ether. The carbon tetrachloride solutions were combined, washed with sodium sulfite solution, water and distilled. There was produced 20 g. (24%) of pure dibromoisobutane; b. p. 146–147°; n^{20}D 1.508. The absence of a condensate in the dry-ice trap indicated that no saturated hydrocarbon was formed. The reaction mixture was worked up as described above and yielded 34 g. (45%) of isopropoxymandelic acid; m. p. 57–58°.

The physical constants, yields and analyses of the isopropoxy acid and their *p*-phenylphenacyl esters are given in Table II.

Synthesis of α-Isopropoxymandelic Acid.—Phenylchloroacetyl chloride was made, according to the directions of Bischoff and Walden,[7] by heating mandelic acid with phosphorus pentachloride at 140°. This compound was converted to ethyl phenylchloroacetate, reported by Findlay and Turner,[8] by heating it with absolute ethanol. A sodium isopropoxide solution, prepared by dissolving 8 g. of sodium in 120 cc. of dry isopropyl alcohol, was refluxed on a steam-bath while 30 g. of phenyl chloroacetate was added. The mixture was heated for four hours, cooled and filtered. The solid was dissolved in water and the solution acidified with hydrochloric acid. The oily product was isolated by extraction with ether, drying the ethereal extract with calcium chloride and removing the solvent by distillation. Treatment of the residual oil with low-boiling petroleum ether caused the separation of 14 g. of white acid; m. p. 41–55°. Several recrystallizations from low-boiling petroleum ether resulted in a pure product melting at 58–59°—alone or when mixed with the compound obtained by the other method.

The Reaction of *o*-Tolylmagnesium Bromide with Acetone-mandelic Acid.—To an *o*-tolylmagnesium bromide solution, prepared from 342 g. of *o*-bromotoluene and 48 g. of magnesium in 500 cc. of ether, was added, with vigorous stirring over a period of one hour, a solution of 96 g. of acetone-mandelic acid in 300 cc. of ether. The solution was stirred and refluxed for an additional three hours after which it was cooled and decomposed with 400 cc. of concentrated hydrochloric acid and 1500 cc. of ice. The ether was distilled from the organic layer and the residue was subjected to steam distillation in order to remove the toluene. The residue was dissolved in ether and repeatedly extracted with 10% potassium bicarbonate

(6) The microanalyses reported in this paper were carried out by Miss Mary S. Kreger, Miss Margaret McCarthy, Miss Theta Spoor and Mr. L. G. Fauble.

(7) Bischoff and Walden, *Ann.*, 279, 122 (1894).

(8) Findlay and Turner, *J. Chem. Soc.*, 87, 756 (1905).

TABLE II

ACIDS AND p-PHENYLPHENACYL ESTERS[a]

Compound, with substituents at X and Y in the formula	Y X—CCOOH | OR[b]	Yield %	M. p. or b. p., °C.	Neutral equivalent Calcd.	Found	Carbon Calcd.	Found	Hydrogen Calcd.	Found
C₆H₅	H	57	58–59	194	191	68.02	68.29	7.27	7.33
Ester		..	114–115	..	..	77.29	77.53	6.23	6.28
CH₃C₆H₄	H[c]	66	...	..	..	...	...	..	..
Ester		..	93–94	..	..	77.58	77.55	6.51	6.45
BrC₆H₄	H[c]	71	...	..	..	...	...	..	..
Ester		..	90–91	..	..	63.24	63.46	4.96	4.93
Mes	H[d]	80	83–84	236	242	71.15	71.52	8.53	8.69
CH₃	H[e]	20	72–75 (2 mm.)	132	134	54.53	54.62	9.15	8.80
CH₃	CH₃[f]	50	102–103 (15 mm.)	146	146	57.51	57.18	9.65	9.72
Ester		..	88	..	..	74.15	73.96	7.06	7.33

[a] The p-phenylphenacyl esters were made from p-phenylphenacyl bromide according to the method described in Shriner and Fuson, "Identification of Organic Compounds," 2nd Edition, John Wiley and Sons, New York, N. Y., 1940. p. 132. [b] R is used to represent isopropyl. [c] The product was a clear uncrystallizable oil. [d] "Mes" is used to represent mesityl. [e] n^{20}D 1.4158. [f] n^{20}D 1.4196.

solution. Acidification of the alkaline solution with hydrochloric acid produced 3 g. of mandelic acid.

The ether was distilled from the organic layer after it was washed with water and dried over calcium chloride. The residue was treated with 150 cc. of methanol and cooled in an ice-bath. A solid product (39 g.) melting at 118–132° was removed by filtration. Concentration of the mother liquor followed by cooling and filtration produced 3 g. of a solid (VIII), m. p 100–102°. The pure compound, recrystallized from methanol, melted at 104–106°.

Anal. Calcd. for C₂₂H₂₀O: C, 87.96; H, 6.71. Found: C. 88.25; H, 6.88.

The crude solid melting at 118–132° was washed with 200 cc. of low-boiling petroleum ether. The insoluble residue (VI) weighed 30.5 g. and melted at 139–141°. After recrystallization from methanol, it melted at 146°.

Anal. Calcd. for C₂₂H₂₂O₂: C, 82.99; H, 6.99. Found: C, 83.23; H, 7.19.

A Zerewitinoff determination showed the presence of two active hydrogen atoms in the molecule.

The wash solution was evaporated to an oily residue. Treatment of the oil with methanol produced 8.5 g. of a solid (VII), melting at 104–106°. The dioxolane, recrystallized from methanol, melted at 108–109°.

Anal. Calcd. for C₂₈H₂₆O₂: C. 83.76; H, 7.31. Found: C, 83.97; H, 7.69.

A Zerewitinoff determination showed the absence of active hydrogen.

The Condensation of 1-Phenyl-2,2-di-*o*-tolylethylene Glycol (VI) with Acetone.—To a solution of 0.6 g. of the glycol in 10 cc. of anhydrous acetone was added 0.4 cc. of concentrated sulfuric acid and 1 g. of anhydrous sodium sulfate. The reaction flask was allowed to stand with occasional shaking for twenty-four hours. The solution was filtered and the solvent was removed by a stream of air. The residue, dissolved in ether. was washed with 10% potassium bicarbonate solution and water, dried over calcium chloride and evaporated to an oil. Treatment of the oil with methanol caused the separation of a solid; m. p. 104–106°. The compound was recrystallized from

methanol and melted at 108–109° alone or mixed with other samples of the dioxolane. The yield of pure product was 0.4 g.

Reaction of 1-Phenyl-2,2-di-*o*-tolylethylene Glycol with Acetic Anhydride and Pyridine.—Five grams of the glycol was dissolved in 50 cc. of a 20% solution of acetic anhydride in pyridine. The solution was heated on a steam-bath for twelve hours. About 35 cc. of the solvent was removed by distillation and the residue was added to 100 cc. of water. The solution was digested for fifteen minutes, cooled and extracted with ether. The ethereal solution was dried over calcium chloride and concentrated to an oil. Treatment with methanol produced 4 g. of a solid (X), which melted at 153–155°. The acetate, recrystallized from methanol, melted at 158–160°.

Anal. Calcd. for C₂₄H₂₄O₃: C, 79.97; H, 6.71. Found: C, 80.01; H, 6.81.

The compound had one active hydrogen atom.

Reaction of 1-Phenyl-2,2-di-*o*-tolyl Ethylene Glycol with Acetic Anhydride and Hydrochloric Acid.—Three grams of the glycol was refluxed for eighteen hours with 30 cc. of acetic anhydride and 3 drops of concentrated hydrochloric acid. The reaction mixture was poured into 100 cc. of water and digested for fifteen minutes, cooled and extracted with ether. The ethereal solution was dried over calcium chloride and evaporated to an oil. Treatment of the oil with methanol produced 2.5 g. of a white solid (IX) which melted at 133–135°. The acetate, recrystallized from methanol, melted at 138.5–140°.

Anal. Calcd. for C₂₄H₂₂O₂: C, 84.20; H, 6.48. Found: C, 84.09; H, 6.53.

The Reaction of Acetyl Chloride with the Acetate (X).—Two grams of the acetate (X) was heated at the refluxing temperature for four hours with 20 cc. of acetyl chloride. The reaction mixture was poured on ice and allowed to come to room temperature. The organic matter was extracted with ether. The ethereal solution was washed with 10% potassium bicarbonate solution and water and then dried over calcium chloride. The solvent was removed and the residue was taken up in hot methanol. Cooling caused the precipitation of 1.2 g. of a compound

melting at 135–136°. Recrystallized from methanol, it melted at 138.5–140° alone or mixed with the acetate (IX).

Reaction of the Dioxolane (VII) with Acetic Anhydride and p-Toluenesulfonic Acid.—Two grams of the dioxolane was heated at the refluxing temperature for four hours with 20 cc. of acetic anhydride and a few crystals of p-toluenesulfonic acid. The reaction mixture was worked up in the usual manner; yield, 1.5 g. of a white compound melting at 129–132°. Recrystallization from methanol gave a melting point of 138.5–140° alone or mixed with other samples of the acetate (IX).

Transformation of 1-Phenyl-2,2-di-o-tolylethylene Glycol and the Dioxolane in Acid Solution.—One gram of the compound was dissolved in 4 cc. of methanol and three drops of concentrated hydrochloric acid. The solution was refluxed for twelve hours and the solvent was removed by distillation. The residue was 0.75 g. of a solid identified as ω,ω-di-o-tolylacetophenone (VIII).

Treatment of the dioxolane (VII) with hydriodic acid, 30% sulfuric acid, phosphoric acid or p-toluenesulfonic acid gave practically quantitative conversion to ω,ω-di-o-tolylacetophenone. Treatment of the 1-phenyl-2,2-di-o-tolylethylene glycol with hydrochloric acid or p-toluenesulfonic acid gave similar results.

Reaction of ω,ω-Di-o-tolylacetophenone with Acetic Anhydride and Pyridine.—Two grams of the compound was heated at the refluxing temperature for twelve hours with 4 cc. of pyridine and 16 cc. of acetic anhydride. The reaction mixture was worked in the usual fashion; yield, 1.5 g. of the acetate (IX); m. p. 133–135°; the pure compound melted at 138.5–140°.

Synthesis of Di-o-tolylcarbinol.—A solution of o-tolylmagnesium bromide was prepared from 171 g. of o-bromotoluene, 24 g. of magnesium and 250 cc. of ether. To this solution was added 33.4 g. of ethyl formate. The solution was refluxed and stirred for seven hours before it was cooled and decomposed with hydrochloric acid and ice. It was necessary to add 250 cc. of benzene to the mixture in order to dissolve all the organic matter. The organic layer was separated, dried over calcium chloride and evaporated; yield, 70 g. (73%); m. p. 115–119°[9].

Synthesis of Di-o-tolylchloromethane.—The di-o-tolylcarbinol was converted, without further purification, into

di-o-tolylchloromethane by the method of Reid[10]; yield, 94%.

Synthesis of Di-o-tolylacetonitrile.—A mixture of 23.1 g. of di-o-tolylchloromethane, 10.7 g. of cuprous cyanide and 20 cc. of dry pyridine was heated for twenty-four hours at 200–215°. Ground glass equipment, protected from moisture by a calcium chloride tube, was used. The dark mass was cooled and poured into dilute aqueous ammonia. The organic matter was extracted with ether. It was necessary to remove some dark solid material by filtration. The ethereal solution was washed successively with dilute ammonia, water, dilute hydrochloric acid and finally with water. The solution was dried with calcium chloride and evaporated to dryness. The residue was recrystallized from 95% ethanol; m. p. 107–109°; yield, 12 g. (54%). The pure compound, recrystallized from 95% ethanol, melted at 114–115°.

Anal. Calcd. for $C_{16}H_{15}N$: C, 86.83; H, 6.83. Found: C, 87.17; H, 6.91.

Synthesis of ω,ω-Di-o-tolylacetophenone.—A solution of phenylmagnesium bromide, made from 14.1 g. of bromobenzene, 1.94 g. of magnesium and 35 cc. of ether, was added to a well-stirred solution of 4.5 g. of di-o-tolylacetonitrile in 75 cc. of ether. The solution was stirred and refluxed for twenty-four hours, after which it was cooled and decomposed with hydrochloric acid and ice. The organic layer was separated and discarded. The aqueous layer was digested on a steam-bath for two hours. Cooling to room temperature produced an oil which soon solidified; yield, 4 g.; m. p. 100–102°. Recrystallized from methanol, the product melted at 104–106° alone or mixed with other samples of (VIII).

Summary

Dioxolones, acetone derivatives of α-hydroxy acids, react with t-butylmagnesium chloride to yield the corresponding α-isopropoxy acids. The reaction is a hydrogenolysis of the dioxolane ring and appears to be new in type.

(9) Boyd and Hatt, *J. Chem. Soc.*, 898 (1927).

(10) Reid, This Journal, **61**, 3238 (1939).