Summary

Four new esters of levulinic acid have been prepared and characterized by some of their physical properties. Evidence has been presented to show that these esters decompose at their boiling points near atmospheric pressure.

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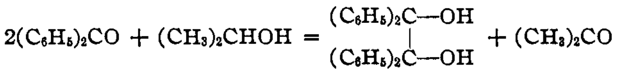
The Photochemical Reduction of Ketones to Hydrols

BY W. E. BACHMANN

It has recently[1] been shown that a small amount of sodium alcoholate can effect the decomposition of a large amount of benzopinacol into a mixture of benzohydrol and benzophenone. It occurred to us that through this reaction it should be possible to obtain hydrols by photochemical reduction of ketones. From the classical work of Ciamician and Silber[2] it is known that if an alcoholic solution of benzophenone is exposed to sunlight, the benzophenone is reduced to benzopinacol at the expense of the alcohol, which is oxidized to aldehyde. Cohen[3] showed that a number of substituted ketones can be reduced to pinacols in the same manner and he found that a variety of primary and secondary alcohols can be used as reducing agents. It appeared that if a small amount of sodium alcoholate was present in the alcoholic solution of the ketone which was exposed to sunlight, a combination of the two reactions would take place: (1) reduction of the ketone to pinacol and (2) decomposition of the pinacol into hydrol and ketone. The ketone that is regenerated in the second reaction would go through the series of reactions until the hydrol was the sole product.

Actually, we found that if a small amount of sodium alcoholate is present in the alcoholic solution, the reduction proceeds exactly as expected; no pinacol is obtained; instead, the hydrol is formed in nearly quantitative yield. For the reaction we employed isopropyl alcohol in preference to ethyl alcohol because the reduction with this alcohol is more rapid and the oxidation product, acetone, is not affected by alkali so readily as is acetaldehyde. The reactions that take place are expressed in the following formulation



$$2(C_6H_5)_2CO + (CH_3)_2CHOH = \begin{array}{c}(C_6H_5)_2C{-}OH\\ |\\ (C_6H_5)_2C{-}OH\end{array} + (CH_3)_2CO \qquad (1)$$

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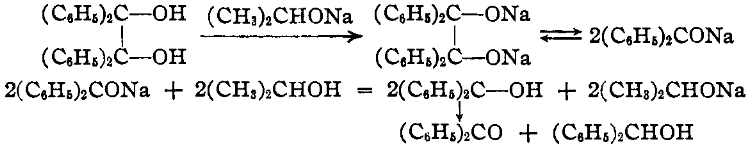
[1] Bachmann, THIS JOURNAL, **55**, 355 (1933).

[2] Ciamician and Silber, *Ber.*, **33**, 2911 (1900).

[3] Cohen, *Rec. trav. chim.*, **39**, 242 (1920).



$$\begin{array}{l} (C_6H_5)_2C{-}OH \\ \quad | \\ (C_6H_5)_2C{-}OH \end{array} \xrightarrow{(CH_3)_2CHONa} \begin{array}{l} (C_6H_5)_2C{-}ONa \\ \quad | \\ (C_6H_5)_2C{-}ONa \end{array} \rightleftharpoons 2(C_6H_5)_2CONa \qquad (2a)$$

$$2(C_6H_5)_2CONa + 2(CH_3)_2CHOH = 2(C_6H_5)_2C{-}OH + 2(CH_3)_2CHONa \qquad (2b)$$

$$\downarrow$$

$$(C_6H_5)_2CO + (C_6H_5)_2CHOH \qquad (2c)$$

As fast as the pinacol is formed by the photochemical reaction (Equation 1) it reacts with the sodium alcoholate and gives sodium pinacolate[4] (Equation 2a). The sodium ketyl radicals[5] produced by dissociation of the sodium pinacolate react with isopropyl alcohol or with pinacol (Equation 2b); one molecule of the ketyl is converted to hydrol as another goes to ketone (2c). The ketone and sodium alcoholate which are regenerated go through the series of reactions until all of the ketone has been converted to hydrol.

In support of this mechanism may be cited the fact that a solution of benzophenone in isopropyl alcohol containing sodium isopropylate becomes greenish-blue on exposure to sunlight, the greenish-blue color being characteristic of the sodium ketyl radical. If the flask containing the colored solution is protected from sunlight, the greenish-blue color disappears, an indication that the reaction represented in Equation 2b is taking place. Renewed exposure to sunlight restores the color. Finally, if this mechanism is correct, then the greenish-blue color should disappear completely when all of the ketone has been reduced. Such is the case. After several days of exposure, the solution becomes colorless and remains so. Indeed, this proved to be a convenient visual indication that the reaction was at an end.

Further support for this mechanism was furnished by a comparison of the rate of reduction of benzophenone to benzohydrol with the rate of reduction to benzopinacol. Since the decomposition of the pinacol by sodium alcoholate is very rapid, the rate of reduction to hydrol should be nearly the same as the rate of pinacol formation. Experiment showed that the rates of reduction are practically equal; under nearly identical conditions of exposure, a 93% yield of benzohydrol was obtained when sodium alcoholate was present in the time that a 97% yield of benzopinacol was formed in absence of sodium alcoholate.

Not only benzophenone but a number of other ketones can be reduced to hydrols. In every case the alcoholic solutions of the ketones become colored on exposure to sunlight and this color disappears after several days of exposure. The yields of hydrols varied from 80–95%. Cohen found that Michler's ketone, phenyl α-naphthyl ketone, fluorenone and 4-phenylbenzophenone were not reduced to pinacols on exposing alcoholic solutions of the ketones. In agreement with our view that the pinacols are the

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[4] For an alternate mechanism of the decomposition of pinacol see Ref. 1.

[5] Compare Cohen [*Rec. trav. chim.*, **38**, 113 (1919)], who considers that pinacols, or more likely diphenylhydroxymethyl radicals, $(C_6H_5)_2COH$, are intermediate products in the reduction of ketones to hydrols by alkaline reducing agents.

initial products in the reduction to hydrol, it was found that Michler's ketone and phenyl α-naphthyl ketone are not reduced to hydrols; in fact, most of the ketone can be recovered unchanged after prolonged exposure. In like manner, fluorenone is not reduced in the manner of benzophenone; however, the ketone does not remain unaffected but undergoes a reaction which is not a photochemical process. To our surprise 4-phenylbenzophenone was reduced nearly quantitatively to 4-phenylbenzohydrol. According to our mechanism the ketone should give pinacol when an alcoholic solution without sodium alcoholate is exposed. Actually we found that in isopropyl solution the ketone is reduced to the pinacol, 4,4′-diphenylbenzopinacol.

Experimental

Photochemical Reduction of Ketones to Hydrols.—Three grams of benzophenone was added to a solution of sodium isopropylate which had been prepared from 0.03 g. of sodium and 30 cc. of anhydrous isopropyl alcohol in a 30-cc. test-tube. The tube was corked and exposed to direct sunlight. Almost immediately the solution assumed a greenish-blue color. This color disappeared when the solution was exposed to air or when it was protected from sunlight. After four days the solution was colorless in bright sunlight, indicating that the reaction was at an end. The solution was poured into an evaporating dish and was diluted with an equal volume of acidified water. On evaporation the benzohydrol crystallized out; it was filtered off, dried and recrystallized from petroleum ether; yield, 2.98 g. (98%). Experiments in which ethyl alcohol was used were not successful because of the reactions undergone by the acetaldehyde.

In one experiment 25 g. of benzophenone in a 150-cc. Pyrex flask was dissolved in 125 cc. of isopropyl alcohol with which 0.25 g. of sodium had reacted. After one week of exposure 20 g. of benzohydrol was obtained. When the reaction was carried out in a long tube the reaction was complete in three days.

A comparison of the rate of reduction to hydrol with the rate of reduction to pinacol was made by exposing two tubes of the same size side by side; one tube contained sodium alcoholate, the other did not. After four days the one tube gave a 93% yield of benzohydrol and the other gave a 97% yield of benzopinacol.

In Table I are given the results obtained by reducing a number of ketones; in each case 3.0 g. of ketone was reduced in the same manner as described for benzophenone. The crude hydrol was recrystallized from a mixture of benzene and petroleum ether; the yields given in the table are based on recrystallized product.

The reaction between fluorenone, isopropyl alcohol and sodium isopropylate is not a photochemical process since the same products result when the mixture is kept in a dark place; heat and not light is the chief factor in hastening the reaction. It is well known that ketones are reduced to hydrols when the ketone is heated for a long time with an alcoholic solution of sodium hydroxide but it is not recognized that the reaction occurs at room temperature with a small amount of sodium alcoholate as it does with fluorenone. We have found that the reaction takes place with benzophenone to a considerable extent under the influence of heat. Five grams of benzophenone was added to a solution of sodium alcoholate prepared from 0.06 g. (10%) of sodium and 20 cc. of isopropyl alcohol and the mixture was refluxed for fifteen hours on a steam-bath; hydrolysis gave 3.92 g. (78%) of benzohydrol. The reaction is best explained by the following formulation which shows that a small amount of sodium alcoholate should be sufficient for reduction

$$(C_6H_5)_2CO + (CH_3)_2CHONa \longrightarrow (C_6H_5)_2CHONa + (CH_3)_2CO \qquad (3)$$

$$(C_6H_5)_2CHONa + (CH_3)_2CHOH \rightleftharpoons (C_6H_5)_2CHOH + (CH_3)_2CHONa \qquad (4)$$

TABLE I

PHOTOCHEMICAL REDUCTION OF KETONES TO HYDROLS

Ketone	Color during reduction	Time of exposure, days	Hydrol yield, %
Benzophenone	Greenish-blue	4	98
4-Methylbenzophenone	Greenish-blue	6	95
4,4′-Dimethylbenzophenone	Blue	6	90
4-Methoxybenzophenone	Greenish-blue	6	90
4-Chloro-4′-methylbenzophenone[a]	Blue	7	80
4-Phenylbenzophenone[b]	Green	7	95
4-Chlorobenzophenone	Green	7	80
Michler's ketone[c]	None	33	00
Phenyl α-naphthyl ketone[d]	None	15	00
Fluorenone[e]	......	7	..

[a] The yields of halogen-substituted hydrols are lower because some of the halogen is removed in the reaction. This is especially true when the halogen is in the ortho position; the corresponding hydrols cannot be prepared conveniently by this method.

[b] Although Cohen reported that this ketone is not reduced to the pinacol in ethyl alcohol solution, we find that the reduction took place when a suspension of the ketone in isopropyl alcohol was exposed to sunlight. The pinacol was recrystallized from a mixture of acetone and chloroform and was obtained in the form of colorless needles which melted at 198° and which proved to be identical with the pinacol produced by reduction of the ketone by a mixture of magnesium and magnesium iodide [Gomberg and Bachmann, THIS JOURNAL, **49**, 236 (1927)].

[c] After thirty-three days of exposure, 80% of the ketone was recovered; some decomposition products were present.

[d] A 70% yield of pure ketone was recovered.

[e] Three tubes containing isopropyl alcohol solutions of fluorenone were exposed simultaneously. One tube contained no sodium alcoholate; another tube had sodium alcoholate in it; the third tube contained sodium alcoholate but the tube was wrapped in a black cloth. The tube that contained no sodium alcoholate remained unchanged; after twenty-two days of exposure the fluorenone was recovered entirely unaffected. Both tubes containing sodium alcoholate became dark-brown and nearly black in color; after six days the solution was light-brown. Hydrolysis gave a 44% yield of fluorenol from the uncovered tube and a 56% yield from the covered tube. Prolonged exposure gave fluorenone and other products. Practically the same results were obtained from a solution which was kept in the dark for the same length of time.

A study is being made of the action of this reducing mixture on other ketones and on other types of compounds. In order to determine whether any benzohydrol is formed by this reaction by the heat received during exposure to sunlight, two tubes were exposed side by side, one of which was wrapped in a black cloth. In the time that the uncovered tube gave a 93% yield of benzohydrol, only 10% of the ketone in the covered tube was affected. The products presented in Table I represent, therefore, the results of photochemical reduction nearly entirely.

Preparation of Benzopinacol by Photochemical Reduction of Benzophenone.—We have confirmed the excellent work of Cohen,[6] who obtained a quantitative yield of benzopinacol by exposing 10 g. of benzophenone in 16 cc. of isopropyl alcohol. From the standpoint of preparation we find it more convenient to use a larger amount of alcohol and have prepared benzopinacol by the procedure which follows. A solution of 50 g. of

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[6] Cohen, *Rec. trav. chim.*, **39**, 245 (1920).

benzophenone in 450 cc. of isopropyl alcohol contained in a 500-cc. round-bottomed Pyrex flask is supported in an inverted position on a tripod and exposed to direct sunlight. After three hours crystals of benzopinacol are present. After one week 45 g. of benzopinacol is filtered off. To the filtrate is added a further 50 g. of ketone and the solution is again exposed to sunlight. This procedure was repeated until 300 g. of pinacol was obtained.

In one experiment a solution of 400 g. of benzophenone in 400 cc. of isopropyl alcohol and 400 cc. of benzene was exposed. After one month a quantitative yield of pinacol was obtained. The disadvantage of using benzene lies in the fact that the pinacol crystallizes with benzene of crystallization in the form of a compact mass which is difficult to remove from the flask.

Summary

Benzophenone and certain substituted benzophenones are reduced nearly quantitatively to hydrols when solutions of the ketones and a small amount of sodium isopropylate in isopropyl alcohol are exposed to sunlight.

The mechanism of the reaction has been elucidated. The ketone is reduced initially to the corresponding pinacol by a photochemical reaction; the pinacol is then converted to a mixture of ketone and hydrol by the action of the sodium alcoholate and alcohol; the ketone that is regenerated in this manner goes through the series of reactions again.

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Researches on Nitrogenous Glycosides. II. The Synthesis of Glycosido Ureides[1]

BY KATHERINE M. HARING AND TREAT B. JOHNSON

The present investigation[2] was undertaken in order to develop a general method for the preparation of glycosido ureides of the hydantoic acid and hydantoin types. Glycosidohydantoins and their reduced forms, the unknown glycosidoimidazoles, are of interest because of their structural relationship to the natural purine nucleosides. In addition, it was believed that a study of such nitrogenous glycosides would be of biochemical importance in relation to the problem of the structure of naturally occurring protein-carbohydrate complexes.

The interest in the latter field has recently received an added stimulus in the discovery that carbohydrate units form integral parts of the proteins of blood serum[3] and egg white,[4] which were formerly considered simple

[1] Constructed from a dissertation presented by Katherine M. Haring to the Faculty of the Graduate School of Yale University in June, 1932, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] The research described was supported in part by a grant from the Therapeutic Research Committee of the American Medical Association for 1930–1931 and 1931–1932.

[3] Rimington, *Biochem. J.*, **23**, 430 (1929); **25**, 1062 (1931).

[4] Levene and Mori, *J. Biol. Chem.*, **84**, 49 (1929).