had been half neutralized with standard sodium hydroxide and by making use of the following expressions

$$[H^+] = K[HA/A^-] = K$$
$$pH = -\log K$$

All of the samples were compared at a concentration of 0.05 M in ethanol–water mixtures (50% by weight). A standard arrangement of a saturated calomel cell and hydrogen electrode was used.[6] The pH values of the hydroxyaldehydes were checked repeatedly by a calibrated glass electrode to within 0.05 unit on freshly prepared solutions.

Experimental

2-Hydroxy-1-naphthaldehyde was prepared by the action of chloroform and sodium hydroxide on β-naphthol.[7] The material was purified by formation of the bisulfite addition compound followed by decomposition and recrystallization from ethyl alcohol; yield 70%, m. p. 81–82°.

3-Hydroxy-2-naphthaldehyde was obtained from purified 2-hydroxy-3-naphthoic acid[8] by conversion to the acetyl derivative, formation of the acid chloride, reduction with hydrogen and palladium followed by saponification with dilute sodium hydroxide. The aldehyde after decomposition of the bisulfite addition product was recrystallized several times from ethanol and melted at 98–98.5°.

1-Hydroxy-2-naphthoic acid was prepared by a modification of Eller's method.[9] Sixty grams of α-naphthol was treated with the calculated quantity of sodium hydroxide and evaporated to complete dryness. The sodium salt was pulverized and immediately placed in a chilled bomb of one-liter capacity with a large excess of dry ice. The pressure of the closed bomb on standing rose to 450–500 lb./sq. in. (30–36 atm.). The temperature was raised slowly and at 130–135° the absorption of carbon dioxide was extremely rapid. Within an hour the pressure fell almost to zero. The contents of the bomb after cooling was added to a liter of water containing 75 g. of sodium carbonate and finally filtered. Careful acidification with hydrochloric acid yielded 72 g. or 92% of the desired acid which melted at 189–190°. Recrystallization raised the melting point to 190–191°.

1-Hydroxy-2-naphthaldehyde was prepared by the reduction of the corresponding acid with 3% sodium amalgam[10] in the presence of boric acid and sodium bisulfite. After decomposition of the solution with sulfuric acid the material was steam distilled and recrystallized from ethanol, m. p. 55°.[11]

Summary

The ionization constants of three isomeric hydroxynaphthaldehydes have been compared. These values indicate that the double bond in these naphthalene derivatives is largely between C_1 and C_2.

The acidity of the C_{2-3} disubstituted compound is attributed to valence isomers which contain a double bond between C_2 and C_3 thus giving rise to a vinylogous relation with formic acid.

These results are in full agreement with other physical measurements and quantum mechanical considerations.[12]

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[6] Davies, "Fundamentals of Physical Chemistry," P. Blakiston Sons and Co., 1932, p. 229.

[7] Fosse, *Bull. soc. chim.*, [3] **25**, 371 (1901).

[8] Boehm and Profft, *Arch. Pharm.*, **269**, 25 (1931).

[9] Eller, *Ann.*, **152**, 277 (1868).

[10] Weil and Ostermeier, *Ber.*, **54**, 3217 (1921).

[11] Boedecker and Volk, *Chem. Zentr.*, **107**, I, 883 (1936).

[12] Robertson, *J. Chem. Soc.*, 131 (1938).

MINNEAPOLIS, MINN. RECEIVED MARCH 14, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HOWARD UNIVERSITY]

The Alkylation of Oxymethylene Desoxybenzoin

BY A. H. BLATT

Oxymethylene ketones on treatment with an alcohol and hydrochloric acid have been reported either to yield an enol ether or to undergo hydrolysis with regeneration of the parent ketone from which the oxymethylene compound was prepared. Ether formation has been reported for oxymethylene camphor[1] and oxymethylene desoxybenzoin,[2] while oxymethylene acetone, acetophenone and menthone undergo hydrolysis[1] (pp. 385, 386). Quite recently, in the acid cleavage of a heterocyclic compound whose structure is not pertinent to the present discussion, we obtained a product which could only be formulated as the dimethylacetal of phenylbenzoylacetaldehyde (I, $R = CH_3$)—the acetal, that is, of the ketonic tautomer of oxymethylene desoxybenzoin. We were able to establish the structure of the acetal by synthesizing it, using the general method of acetal synthesis, from oxymethylene desoxybenzoin and methyl alcohol in the presence of hydrochloric acid. Similarly the ethyl and benzyl acetals (I, $R = C_2H_5$ and $CH_2C_6H_5$) were prepared from the corresponding alcohols. This selective acetal synthesis was in such striking contrast to all pre-

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[1] Bishop, Claisen and Sinclair, *Ann.*, **281**, 366, 383 (1894).

[2] (a) Jörissen, Dissertation, Basel, 1893; (b) Wislicenus and Ruthing, *Ann.*, **379**, 253 (1911).

viously reported work on oxymethylene ketones that a detailed study of the behavior of oxymethylene desoxybenzoin toward alkylating agents was undertaken.

$C_6H_5COCH(C_6H_5)CH(OR)_2$
I

$C_6H_5COC(C_6H_5){=}CHOCH_3$ $C_6H_5COCH(R)C_6H_5$
II III

A repetition of Jörissen's experiments in acid solution—saturating a methyl alcoholic solution of the ketone with hydrogen chloride and allowing it to stand for a day—furnished the same product which he obtained. An examination of this product, however, showed it to be desoxybenzoin. Repetition of Jörissen's experiments in alkaline solution—prolonged heating of a solution of the ketone in sodium methylate with methyl iodide—likewise furnished only desoxybenzoin. More gentle experimental conditions in the alkaline reactions gave the same results; the only product isolated was desoxybenzoin but presumably some of the methyl ether (II) and some methyldesoxybenzoin (III, $R = CH_3$) were present. The presence of the methyl ether is indicated by the fact that the residual oil, after separation of the desoxybenzoin and vacuum distillation, showed a small methoxyl content. The evidence for the presence of methyldesoxybenzoin is from analogy with the attempted alkaline alkylation of oxymethylene menthone which furnishes methylmenthone[3] and from the alkylation of oxymethylene desoxybenzoin with sodium methylate and benzyl chloride which furnishes benzyldesoxybenzoin (III, $R = CH_2C_6H_5$).

It seemed clear from the results so far described that the preparation of ethers of oxymethylene desoxybenzoin could be accomplished only in neutral solution. This proved to be the case for treatment with diazomethane furnished smoothly the hitherto unknown methyl ether (II). This methyl ether in alcoholic solution gives no immediate color with ferric chloride but the characteristic color given by oxymethylene desoxybenzoin and the reagent gradually develops on standing. If sodium acetate is added to the ferric chloride reagent no color develops. To this evidence that ether formation is reversible in an acidic medium should be added the fact that the methyl ether (II) is converted to the acetal (I, $R = CH_3$) by hydrochloric acid and methyl alcohol. Acetal formation likewise is in all probability reversible in the presence of acids for the ethyl acetal (I, $R = C_2H_5$) and the benzyl acetal (I, $R = CH_2C_6H_5$) are converted to the methyl acetal by hydrochloric acid and methyl alcohol.

The information in the preceding paragraph, together with that already available in the literature,[3] enables one to give the following general description of the behavior of oxymethylene ketones on treatment with alkylating agents in acidic or basic solution. An oxymethylene ketone on treatment with an acid or a base undergoes irreversible hydrolysis or alcoholysis. At the same time, in an acidic medium etherification which is definitely reversible and acetal formation which is probably reversible may take place. In alkaline solution in the presence of an alkyl halide, esterification may occur. This process, too, is reversible. These several reactions are shown in outline by the following equations using for convenience methyl alcohol and methyl iodide as typical reagents. The exact course which will be followed with a specific oxymethylene ketone, depending as it will upon experimental conditions and a series of rates and equilibria, cannot be foretold.

$$\begin{tikzcd}
\mathrm{RCOCH_2R' + HCO_2Na} & & \mathrm{RCOC(R'){=}CHOH} \arrow[ll, "\mathrm{NaOCH_3}", "\mathrm{CH_3OH}"'] \arrow[rr, "\mathrm{CH_3OH}", "\mathrm{HCl}"'] \arrow[d, leftrightarrow, shift right, "\mathrm{NaOCH_3\ CH_3I}"'] \arrow[d, leftrightarrow, shift left, "\mathrm{CH_3OH\ HCl}"] & & \mathrm{RCOCH_2R' + HCO_2CH_3} \\
 & & \mathrm{RCOC(R'){=}CHOCH_3} & \mathrm{RCOCH(R')CH(OCH_3)_2} \arrow[u, leftrightarrow, "\mathrm{CH_3OH\ HCl}"'] &
\end{tikzcd}$$

Experimental

The experiments made according to Jörissen's directions do not require a detailed description. Jörissen's procedures were followed exactly and the product, which corresponded with his description, was shown to be desoxybenzoin by mixed melting points with an authentic specimen of that ketone.

When 0.5 g. of oxymethylene desoxybenzoin was dissolved by warming in 5 cc. of methyl alcohol containing 5 drops of concentrated hydrochloric acid and then left overnight, the clear solution solidified when rubbed with a glass rod. The product filtered, washed and dried weighed 0.45 g. For analysis it was crystallized from methyl alcohol.

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.5; H, 6.7; OCH_2. 23.0. Found: C, 75.3; H, 6.9; OCH_3, 22.62.

Phenylbenzoylacetaldehyde dimethylacetal (I, $R = CH_3$) melts at 102–103° and can be distilled unchanged in high vacuum. It is sparingly soluble in and crystallizes

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[3] Ref. 1, page 369; Pechmann, *Ann.*, **273**, 164 (1893).

well from the common organic solvents. On prolonged heating with alcoholic aqueous sodium hydroxide it is hydrolyzed to desoxybenzoin. With phenylhydrazine in acetic acid it furnishes 1,4,5-triphenylpyrazole melting at 210–211° and identified by comparison with a sample prepared from oxymethylene desoxybenzoin.[4]

The ethyl acetal (I, R = C_2H_5) was obtained by warming 1.0 g. of oxymethylene desoxybenzoin with 9.5 cc. of ethyl alcohol and 0.5 cc. of concentrated hydrochloric acid until a clear solution resulted—about ten minutes. After twenty-four hours the reaction mixture was poured into water, extracted with ether and the ether extract washed with water and with 5% sodium hydroxide to remove oxymethylene desoxybenzoin. The residual oil left on evaporation of the ether was taken up in alcohol and this solution when chilled furnished the solid acetal. After crystallization from dilute ethyl alcohol the acetal melted at 68–69°.

Anal. Calcd. for $C_{19}H_{22}O_3$: OC_2H_5, 30.20. Found: OC_2H_5, 30.05.

The benzyl acetal (I, R = $CH_2C_6H_5$) was prepared in similar fashion from 1.0 g. of oxymethylene desoxybenzoin, 9.5 cc. of benzyl alcohol and 0.5 cc. of concentrated hydrochloric acid. The reaction mixture was poured, after twenty-four hours, into sufficient water to dissolve the excess benzyl alcohol and the aqueous layer was decanted from the oily product. The oil was taken up in ether and the ethereal solution was washed with water, 5% sodium hydroxide and saturated calcium chloride solutions, then dried. Evaporation of the ether left an oil which, when dissolved in alcohol and chilled, furnished the solid acetal. The product was crystallized from dilute ethyl alcohol and melted at 69–70°. Mixtures of the benzyl and ethyl acetals melt below 55°.

Anal. Calcd. for $C_{29}H_{26}O_3$: C, 82.5; H, 6.16. Found: C, 82.4; H, 6.5.

When 0.1 g. of the ethyl acetal (I, R = C_2H_5) was dissolved by warming in 1 cc. of methyl alcohol containing two drops of concentrated hydrochloric acid and left overnight, the reaction mixture solidified on chilling. The product, 0.05 g., was impure methyl acetal (I, R = CH_3) and on crystallization from methyl alcohol furnished the pure methyl acetal which was identified by a mixed melting point. In a parallel experiment starting with the benzyl acetal (I, R = $CH_2C_6H_5$) in which the reaction mixture was warmed for ninety minutes before leaving overnight, the crude reaction product was sufficiently pure so that recrystallization was not necessary in order to identify it as the methyl acetal.

When oxymethylene desoxybenzoin in sodium methylate solution was treated at room temperature for varying lengths of time with methyl iodide and with ethyl iodide and the reaction mixtures were worked up by pouring into water, extracting with ether and evaporating the ether after appropriate washing and drying, the product in each case was an oil. On chilling these oils small amounts of desoxybenzoin precipitated. This was removed by filtration and the filtrates were vacuum distilled (boiling range 150–160° at 4 mm.) but no solid products could be obtained. In a typical run with methyl iodide the distillate showed a methoxyl content of 2.3%. Using 2.2 g. of oxymethylene desoxybenzoin in 20 cc. of sodium methylate solution (0.48 g. of sodium) and 3.0 g. of benzyl chloride, 1.5 g. of benzyldesoxybenzoin (III, R = $CH_2C_6H_5$) melting at 123–124° was obtained. The sparingly soluble reaction product, which crystallized along with the sodium chloride during the course of the reaction, was identified by an analysis (calcd. for $C_{21}H_{18}O$: C, 88.11; H, 6.3. Found: C, 88.17; H, 6.4) and by a mixed melting point with a sample prepared by benzylating desoxybenzoin.[5]

Methylation of oxymethylene desoxybenzoin in chloroform solution by the addition of an ethereal solution of diazomethane took place quickly and smoothly. Evaporation of the solvents at room temperature left a mixture of the methyl ether (II) and unchanged oxymethylene desoxybenzoin which melted fairly sharply at 78–80°. This mixture could be separated by crystallization from dilute methyl alcohol or, better, by dissolving in ether and shaking with aqueous copper acetate to remove the oxymethylene compound. Crystallization from ether furnished the pure methyl ether (II) in long plates which melted at 130–131°.

Anal. Calcd. for $C_{16}H_{14}O_2$: OCH_3, 13.03. Found: OCH_3, 13.09.

The methyl ether (II) is converted to the acetal (I, R = CH_3) by methyl alcoholic hydrochloric acid. Thus when 12 mg. of the ether was dissolved by warming in 0.1 cc. of methyl alcohol containing concentrated hydrochloric acid (ten drops of acid in 5 cc. of alcohol) and left overnight, the reaction mixture solidified on chilling. Filtration and washing furnished 6 mg. of the acetal, identified by a mixed melting point. When one drop of ferric chloride solution (made from one drop of concentrated aqueous ferric chloride and 1 cc. of water) was added to 1 mg. of the methyl ether in 1 cc. of alcohol no color other than that of the reagent appeared. Within ten minutes, however, the solution developed a purple color and after six hours the color was indistinguishable from that of a solution of 1 mg. of oxymethylene desoxybenzoin in 1 cc. of alcohol to which a drop of the same reagent had been added. When a ferric chloride reagent made by adding 1 drop of concentrated aqueous ferric chloride solution to 2 cc. of 13% sodium acetate was added to an alcoholic solution of the methyl ether no color other than that of the reagent developed over a period of six hours.

Summary

Oxymethylene desoxybenzoin reacts with alcohols in the presence of hydrochloric acid to yield acetals derived from its aldehydic tautomer. More drastic treatment with hydrogen chloride brings about hydrolysis to desoxybenzoin. With alcoholates and alkyl halides, oxymethylene desoxybenzoin is hydrolyzed to desoxybenzoin but at the same time alkyl derivatives of desoxybenzoin and, probably, ethers of the oxymethylene ketone are formed. The substance reported in the literature as the methyl ether of oxymethylene

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[4] Reference 2a, p. 30; 2b, p. 257.

[5] Meyer and Oelkers, *Ber.*, **21**, 1300 (1888).

desoxybenzoin is in reality desoxybenzoin; the true methyl ether has been obtained by the action of diazomethane on the oxymethylene ketone. Certain of the reactions of the acetals and the methyl ether are described and a general outline of the behavior of oxymethylene ketones toward alkylating agents is presented.

WASHINGTON, D. C. RECEIVED JANUARY 26, 1938

[CONTRIBUTION FROM MELLON INSTITUTE OF INDUSTRIAL RESEARCH AND E. R. SQUIBB & SONS]

Halogeno-alkyl Glycosides. II. Dihalogeno-alkyl Derivatives

BY HAROLD W. COLES,[1] MARY L. DODDS[1] AND FRANK H. BERGEIM[2]

The preparation of various monohalogeno-alkyl glycosides has been described.[3] It was indicated in that paper that the ease of preparation was influenced by the stability of the acylhalogeno sugar, the type of halogenohydrin employed, and whether the bromo- or chlorohydrin was used. It seemed desirable to determine whether dihalogen compounds, such as glycerol dichlorohydrin or dibromohydrin, could be condensed with acylhalogeno sugars in the presence of silver carbonate.

A number of syntheses were carried out. It was found that the dihalogenohydrins condensed much less readily with acetobromoglucose or acetobromoxylose than did the monohalogenohydrins. The β-benzobromoglucose condensed with glycerol dichlorohydrin to form a white crystalline substance which, despite repeated recrystallizations, did not analyze correctly.

The condensations are described in the experimental part. The authors are indebted to Dr. George D. Beal, Assistant Director of Mellon Institute, for his advice during the progress of this work.

Experimental Part

Tetraacetyl-β-*d*-(dibromomethyl-methyl)-glucoside.—Six grams of β-acetobromoglucose, 7.2 g. of silver carbonate and 68.1 g. of glycerol α,γ-dibromohydrin were combined in a small Erlenmeyer flask. The evolution of carbon dioxide was slight. The flask was warmed very cautiously on the water-bath for several hours which increased the production of carbon dioxide. The flask was allowed to stand overnight at room temperature in complete darkness.

The silver salts were removed by filtration and washed with a very small amount of hot methanol. The condensation product was thrown out of solution by the addition of 50% methanol to the filtrate. The colorless needles formed slowly and crystallization was completed by immersion of the flask in ice water. The crystals were removed to a Büchner funnel where they were washed with cold 50% methanol. They were recrystallized from a minimum of hot methanol. The yield was very low. The crystals, which gave a strong Beilstein test for halogen, melted at 107.5°.[4]

Anal. Calcd. for $C_{17}H_{24}O_{10}Br_2$: Br, 29.16. Found: Br, 28.98.[5]

Tetraacetyl-β-*d*-(dichloromethyl-methyl)-glucoside.—The reaction between 13 g. of acetobromoglucose, 7.2 g. of silver carbonate and 20 g. of glycerol α,γ-dichlorohydrin was permitted to proceed overnight at room temperature in total darkness. The silver salts were removed and washed with a small amount of hot absolute alcohol. Considerable distilled water was added to the filtrate, which addition threw out a mobile oil. The supernatant liquid was decanted, and the oil washed several times with water.

The oil was taken up in a small amount of alcohol, and the solvent slowly removed by vacuum. Crystals started to form, and crystallization was completed by the addition of a small amount of water and chilling. The crystals were washed on a Büchner funnel with a cold alcohol-water mixture. The crystals were redissolved in a small amount of hot absolute alcohol, the solution filtered, and crystallization completed by strong chilling. The colorless crystals melted at 122–123°; yield 1 g.

Anal. Calcd. for $C_{17}H_{24}O_{10}Cl_2$: C, 44.44; H, 5.26. Found: C, 44.56; H, 5.29.

Triacetyl-β-*d*-(dibromomethyl-methyl)-xyloside.—This compound was obtained as the result of the reaction between 18.7 g. of glycerol α,γ-dibromohydrin, 5 g. of acetobromoxylose and 5 g. of silver carbonate. This mixture was allowed to stand at room temperature until all spontaneous bubbling ceased. The flask was warmed gently on the water-bath, which quickened the evolution of carbon dioxide, for one-half hour, and was then stored overnight.

The silver salts were removed and washed with a small amount of absolute alcohol. A large amount of distilled water was added to the alcohol filtrate, at which the condensation product and the excess dibromohydrin were thrown out. The supernatant liquid was removed by means of a separatory funnel. Enough alcohol was added to the dibromohydrin layer to take the dibromohydrin into solution, and the supernatant liquid decanted from the residual sirup. The sirup was washed several times with

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(1) Industrial Fellows, E. R. Squibb & Sons Industrial Fellowship, Mellon Institute.

(2) Research Laboratories, E. R. Squibb & Sons, Brooklyn, N. Y.

(3) Coles, Dodds and Bergeim, THIS JOURNAL, 60, 1020 (1938).

(4) Melting points are corrected for stem exposure.

(5) Micro-analyses by Saul Gottlieb, Columbia University.