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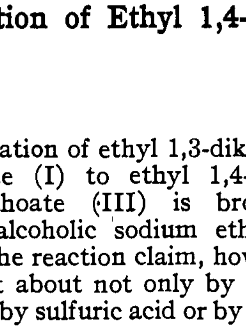
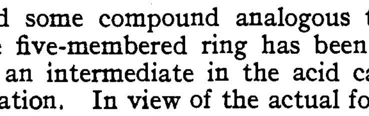
The Cyclization of Ethyl 1,4-Dihydroxy-2-naphthoate to 1,4-Dihydroxy-2,3-benzofluorenone

BY C. F. KOELSCH

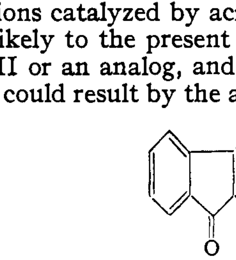
The isomerization of ethyl 1,3-diketo-2-phenylindene-2-acetate (I) to ethyl 1,4-dihydroxy-3-phenyl-2-naphthoate (III) is brought about smoothly by alcoholic sodium ethoxide.[1] The discoverers of the reaction claim, however, that it can be brought about not only by this basic reagent, but also by sulfuric acid or by zinc chloride. Now II is almost certainly an intermediate when the transformation is effected with sodium ethoxide, and some compound analogous to it, in which the five-membered ring has been opened would be an intermediate in the acid catalyzed transformation. In view of the actual formation of many 2,2-disubstituted-1,3-indandiones in reactions catalyzed by acidic reagents,[2] it appeared unlikely to the present author that cleavage of I to II or an analog, and cyclization of, *e. g.*, II to III could result by the action of an acidic reagent.



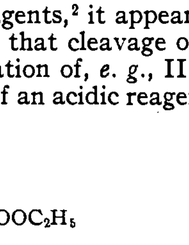
I



II



III



IV

In agreement with these considerations, attempts in this laboratory to carry out the isomerization using sulfuric acid have given no III, but only water soluble non-crystalline products. A further argument against the formation of III by sulfuric acid is found in the experiments described in the present paper. It is shown that III, formed from I by the action of sodium ethoxide, is not stable to sulfuric acid, but is cyclized by this reagent, forming IV.

Experimental

1,4-Dihydroxy-2,3-benzofluorenone (IV).—A mixture of 15.5 g. of III[1] and 40 ml. of concd. sulfuric acid was heated for three minutes on a boiling water-bath. The solution was then cooled, and water was added dropwise. The IV so precipitated (13 g., 98%) was nearly pure; from acetic acid it formed fine orange needles, m. p. 254°.[3]

Anal. Calcd. for $C_{17}H_{10}O_3$: C, 77.9; H, 3.8. Found: C, 77.6; H, 4.2.

The hydroquinone (IV) gave a deep red-violet solution in aqueous sodium hydroxide or sodium carbonate. It was oxidized to a black crystalline substance, apparently a quinhydrone, by silver oxide or mercuric oxide and by nitric acid in acetic acid. Bromine in acetic acid converted it into **9-keto-2,3-benzofluorene-1,4-quinone**, permanganate colored needles from acetic acid, m. p. 235–238°.

Anal. Calcd. for $C_{17}H_8O_3$: C, 78.5; H, 3.0. Found: C, 78.4; H, 3.3.

When this quinone was boiled with alcoholic potassium hydroxide, it was reduced nearly quantitatively to IV; the same transformation was brought about by aqueous alkali, but the yield was poor.

When the hydroquinone (IV) was boiled for a few minutes with acetic anhydride containing potassium acetate, it was converted quantitatively into its **diacetate**, bright yellow needles from acetic acid, m. p. 243–244°.

Anal. Calcd. for $C_{21}H_{14}O_5$: C, 72.8; H, 4.0. Found: C, 72.4; H, 4.2.

When a solution of IV in sodium hydroxide was shaken with methyl sulfate, or when dilute sodium hydroxide was added dropwise to a stirred mixture of methyl sulfate and IV, there was obtained a difficultly soluble orange sodium salt in nearly quantitative yield. Acidification of this salt

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[1] Rădulescu and Gheorgiu, *Ber.*, **60**, 186 (1927).

[2] Freund and Fleischer, *Ann.*, **414**, 1 (1917).

[3] Melting points are corrected.

furnished a monomethyl ether, presumably **1-hydroxy-4-methoxy-2,3-benzofluorenone**, pale yellow needles from acetic acid, m. p. 151–152°.

Anal. Calcd. for $C_{18}H_{12}O_3$: C, 78.3; H, 4.3. Found: C, 77.9; H, 4.6.

The monomethyl ether was converted into its silver salt, an orange-red insoluble substance, and a suspension of this in methanol containing excess methyl iodide was boiled for one hour. The resulting **1,4-dimethoxy-2,3-benzofluorenone** formed bright yellow needles from ethanol, m. p. 171–172°.

Anal. Calcd. for $C_{19}H_{14}O_3$: C, 78.6; H, 4.8. Found: C, 78.3; H, 4.6.

When the monomethyl ether was boiled for a few minutes with acetic anhydride containing potassium acetate, it yielded **1-acetoxy-4-methoxy-2,3-benzofluorenone**, bright yellow needles from acetic acid, m. p. 163–164°.

Anal. Calcd. for $C_{20}H_{14}O_4$: C, 75.4; H, 4.4. Found: C, 75.5; H, 4.6.

To show that the cyclization did not involve the hydroxyl groups of III, the dimethyl ether obtained from the cyclization product was also synthesized from ethyl 1,4-dimethoxy-3-phenyl-2-naphthoate. An excess of 10% sodium hydroxide was added dropwise to a warm alcoholic solution of 2 g. of methyl sulfate and 1 g. of III. Water and ether were then added, the ether was removed, and the resulting oil was warmed at 60° for ten minutes with 10 ml. of concd. sulfuric acid. Water was added, and the solid product was triturated with dilute sodium hydroxide. The alkali-insoluble part separated from alcohol in the form of yellow needles (0.5 g.) that melted at 171–172° alone or mixed with the dimethyl ether described above. The alkali-soluble substance, orange plates from acetic acid (*ca.* 50 mg.), m. p. 214–215°, was presumably **4-hydroxy-1-methoxy-2,3-benzofluorenone.** Its solution in aqueous alkali was blue-violet.

Anal. Calcd. for $C_{18}H_{12}O_3$: C, 78.3; H, 4.3. Found: C, 77.9, 78.3; H, 4.5, 4.7.

Summary

Contrary to a result previously claimed, the conversion of ethyl 1,3-diketo-2-phenylindene-2-acetate into ethyl 1,4-dihydroxy-3-phenylnaphthoate was not brought about by sulfuric acid. Indeed, the substituted naphthoic ester is not stable to sulfuric acid, but is converted by this reagent into 1,4-dihydroxy-2,3-benzofluorenone.

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[CONTRIBUTION FROM THE COLLEGE OF PHARMACY AND THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF TEXAS]

Some Naphthenyl Sulfanilamides

BY J. RICHARD STOCKTON AND H. L. LOCHTE

Although hundreds of sulfanilamide derivatives have been synthesized, relatively few alicyclic acyl derivatives have been prepared.[1] Since a number of naphthenic acids had been investigated in connection with other researches, the preparation of N¹- and N⁴-acylsulfanilamides from some of these acids was undertaken. Thus from campholic acid have been prepared N⁴-campholylsulfanilamide, N⁴-acetyl-N¹-campholylsulfanilamide and N¹-campholylsulfanilamide. Analogous compounds were obtained from cyclopentanecarboxylic acid and from 2,2,6-trimethylcyclohexanecarboxylic acid.

Experimental

The Acids.—Cyclopentanecarboxylic acid was prepared by a series of reactions starting with adipic acid as follows. Cyclopentanone was obtained by fusion of adipic acid with barium hydroxide.[2] Hydrogenation of cyclopentanone by the method of Adkins, Homer and Cramer[3] but with Raney nickel as catalyst gave the alcohol. Cyclopentanol was converted to the chloride by treating the alcohol (1) with dry hydrogen chloride at 110°[4] or (2) with zinc chloride and concentrated hydrochloric acid[5] and most satisfactorily by (3) refluxing one mole of hydrochloric acid with 0.5 mole of cyclopentanol for six hours; the latter method gave a 59% yield. Yarnall and Wallace,[6] using a hydrochloric acid–calcium chloride method, reported a yield of 46%. Cyclopentanecarboxylic acid was prepared from the chloride by the Grignard reaction.[7,8] Since this gave a yield of only 20%, the Grignard reaction was repeated with the bromide,[9] and a yield of 87% was obtained. The superiority of the bromide for this reaction was unexpected since Gilman and Zoellner[7] found cyclohexyl chloride preferable to the bromide for making cyclohexanecarboxylic acid.

Campholic acid was prepared by the fusion of *d*-camphor with dry potassium hydroxide in a steel bomb.[10,11]

2,2,6-Trimethylcyclohexanecarboxylic acid was isolated from California petroleum and identified in this Laboratory.[12]

The acyl halides were prepared by treating the acids with about 1.3 equivalents of thionyl chloride and—after allowing effervescence to cease or after permitting the mixture to stand overnight—heating in a bath at 70 to 80° for two hours. The products were fractionated at reduced pressures.

N⁴-Acetyl-N¹-naphthenylsulfanilamides.—The derivative of cyclopentanecarboxylic acid was prepared by condensation of the acyl chloride with N⁴-acetylsulfanilamide[13] in dry pyridine.[1] However, the treatment of N⁴-acetylsulfanilamide in dry pyridine with the acid chloride of campholic acid or of 2,2,6-trimethylcyclohexanecarboxylic acid resulted in either case in the formation of large amounts of an amorphous, brittle, tan solid (insoluble in water, acid or alkali, soluble in acetone) but only small quantities of the desired derivatives. These latter reactions were endothermic, requiring continuous heating to maintain the desired temperature of 100–110°, whereas the condensation of acyl chlorides with N⁴-acetylsulfanilamide in anhydrous pyridine is typically an exothermic process. Longer periods of heating produced no observable improvement. Attempts to condense 2,2,6-trimethylcyclohexanecarbonyl chloride with N¹-potassium-N⁴-acetylsulfanilamide[14] suspended in boiling pyridine[1] produced a deeply colored, vis-

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[1] Crossley, Northey and Hultquist, THIS JOURNAL, **61**, 2950 (1939).

[2] "Organic Syntheses," Coll. Vol. I, p. 187.

[3] Adkins, Homer and Cramer, THIS JOURNAL, **52**, 4349 (1930).

[4] Zelinsky, *Ber.*, **41**, 2627 (1908).

[5] "Organic Syntheses," Coll. Vol. I, p. 137.

[6] Yarnall and Wallace, *J. Org. Chem.*, **4**, 284 (1939).

[7] Gilman and Zoellner, THIS JOURNAL, **53**, 1945 (1931).

[8] "Organic Syntheses," Coll. Vol. I, p. 353.

[9] "Organic Syntheses," Vol. XIX, p. 88 (1939).

[10] Williamson, Thesis, University of Texas, June, 1941.

[11] Rupe and Kloppenburg, *Helv. Chim. Acta*, **2**, 363 (1919).

[12] Shive, Horeczy, Wash and Lochte, THIS JOURNAL, **64**, 385 (1942).

[13] "Organic Syntheses," Coll. Vol. I, p. 8.

[14] Miller, Rock and Moore, THIS JOURNAL, **61**, 1198 (1939).