[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

Studies on the Willgerodt Reaction. V. An Anomalous Synthesis of Dithioöxalodimorpholide[1]

BY FREEMAN H. MCMILLAN AND JOHN A. KING[2]

In our work on the Willgerodt reaction it has been noted that whenever a compound of the type $RC(CH_3)=CH_2$ is subjected to the morpholine modification of the reaction a certain amount of cleavage at the double bond occurs, as evidenced by the isolation from the hydrolyzed reaction mixture of not only the expected acid $RCH(CH_3)COOH$ but also the degraded acid RCH_2COOH. In each case the originally formed thiomorpholide mixture contains a small amount of a high-melting, sparingly soluble crystalline material. The characterization, proof of structure and possible mode of formation of this material constitute the subject matter of the present paper.

Rupture of a carbon chain during the Willgerodt reaction has been observed by several workers.[3] In our own Laboratory, using the sulfur and morpholine procedure for the reaction, cleavage at the double bond has been observed with commercial diisobutylene, which contains approximately 80% 2,4,4-trimethylpentene-1,[4] with α-methylstyrene, and with α,*p*-dimethylstyrene, and in each case the same high-melting by-product was obtained. In addition the same material was similarly obtained from β-phenethyl mercaptan and from di-β-phenethyl disulfide, when less sulfur was used.

This colorless crystalline neutral compound of the empirical formula C_5H_8NOS was insoluble in most solvents and was resistant to all but drastic hydrolysis. The action of refluxing 70% (by weight) sulfuric acid on the material yielded sulfur and morpholine, but comparison with an authentic sample showed that the substance was not thioformylmorpholine. Hydrolysis with 25% alcoholic potassium hydroxide gave oxalic acid.

Although the isolation of both morpholine and oxalic acid as hydrolysis products of the high-melting compound was strong evidence for its identity as dithioöxalodimorpholide, the final proof of its identity was afforded by comparison of it with an authentic sample of dithioöxalodimorpholide which was prepared by an unequivocal method.

The exact mode of formation of this material from $RC(CH_3)=CH_2$ has not been ascertained. It has been suggested[5] that cleavage during the Willgerodt reaction occurs by 2,3-scission of a 1,4-diradical. In the present cases one of the initially formed cleavage products would be thioformaldehyde, liberated in its diradical form, $*CH_2\text{-}S*$. Whether this is oxidatively coupled to dithioglyoxal, whether it first reacts with morpholine, or whether it is first oxidized to dithioformic acid is as yet unknown. Because trithioformaldehyde,[6] when treated with sulfur and morpholine under reflux conditions remained unchanged and was recovered almost quantitatively, it seems apparent that the trimer does not revert to the monomeric (reactive) state under the conditions of the reaction.

Experimental[7,8]

Dithioöxalodimorpholide, $(C_5H_8NOS)_x$ (from Willgerodt Reaction).—A mixture of commercial di-*i*-butylene[9] (54.5 g., 0.50 mole), sulfur (40.0 g., 1.25 moles) and morpholine (87 g., 1.00 mole) was refluxed under an air condenser[10] for thirty hours. During the reflux period crystals were observed forming in the flask. The cooled reaction mixture was diluted with water (300 cc.) and the solid material was removed by filtration and washed first with water and then with 10 cc. of cold benzene. The dry colorless crystals weighed 13.0 g. and melted at 226–230°. After two recrystallizations from absolute alcohol[11] the material melted constantly at 253–254° and weighed 9.0 g. (13.8% yield).

Anal. Calcd. for $(C_5H_8NOS)_x$: C, 46.16; H, 6.15; N, 10.77; S, 24.61. Found: C, 46.20; H, 6.18; N, 10.46; S, 24.28.

By a similar procedure, using a two-hour reflux period, α-methylstyrene and α,*p*-dimethylstyrene each gave about a 5% yield of the same material. Similarly, equimolar amounts of morpholine, sulfur and β-phenethyl mercaptan, or di-β-phenethyl disulfide, gave small yields of the same material after a two-hour reflux period.

The material was soluble in concentrated sulfuric acid from which it was precipitated unchanged on dilution with water. It was resistant to refluxing with concentrated hydrochloric acid, 50% aqueous potassium hydroxide or 50% (by weight) sulfuric acid.

Acid Hydrolysis of $(C_5H_8NOS)_x$.—A mixture of $(C_5H_8NOS)_x$ (1.3 g.) and 70% (by weight) sulfuric acid (15 g.) was refluxed six hours. After the hydrolysate had cooled a globule of sulfur was removed, the solution was made alkaline with dilute sodium hydroxide, and extracted three times with equal volumes of ether. Removal of the solvent from the combined ethereal extract left a small amount

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[1] For the preceding paper of this series see King and McMillan, THIS JOURNAL, **68**, 2335 (1946).

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[3] (a) Willgerodt, *Ber.*, **21**, 534 (1888); (b) Willgerodt and Merk, *J. prakt. Chem.*, [2] **80**, 192 (1909); (c) Arnold, Schultz and Klug, THIS JOURNAL, **66**, 1606 (1944); (d) Arnold and Rondestvedt, *ibid.*, **67**, 1265 (1945); (e) Carmack and DeTar, *ibid.*, **68**, 2029 (1946); (f) Pattison and Carmack, *ibid.*, **68**, 2033 (1946).

[4] (a) McCubbin and Adkins, THIS JOURNAL, **52**, 2547 (1930); (b) Tongberg, Pickens, Fenske and Whitmore, *ibid.*, **54**, 3706 (1932); (c) Whitmore and Church, *ibid.*, **54**, 3710 (1932).

[5] King and McMillan, THIS JOURNAL, **68**, 632 (1946).

[6] Baumann, *Ber.*, **23**, 67 (1890).

[7] Melting points are uncorrected.

[8] All analytical determinations were carried out under the direction of Mr. Morris E. Auerbach in the Analytical Laboratories of this Institute.

[9] Purchased from Standard Alcohol Company.

[10] If a water-cooled condenser is used it will become plugged with the sublimate of morpholinium sulfide and bisulfide.

[11] It was subsequently learned that recrystallization from benzene is more convenient because a more moderate volume of solvent is necessary.

of residual liquid which was taken up in absolute alcohol. Addition to this solution of 5 cc. of a saturated alcoholic solution of picric acid gave a yellow precipitate (m. p. 130–134°) which, after two recrystallizations from absolute alcohol, melted at 147–148°, undepressed when mixed with an authentic sample of morpholine picrate.[12]

Thioformylmorpholine.[13]—A solution of formylmorpholine[14] (34.5 g., 0.30 mole) in benzene (500 cc.) was rapidly stirred as phosphorus pentasulfide (133 g., 0.60 mole) was added portionwise during fifteen minutes. The mixture warmed spontaneously to about 45°. Stirring was continued for one hour and the mixture was allowed to stand at room temperature for two days. The mixture was heated to boiling and filtered hot, the benzene removed under vacuum from the filtrate, and the residue leached with 50 cc. of boiling absolute alcohol. The chilled alcoholic filtrate, on standing overnight, deposited colorless crystals (9.0 g., 23% yield, m. p. 65–68°) which melted at 67.5–68.5° after recrystallization first from ethanol and then from Skellysolve C.

Anal. Calcd. for C_5H_9NOS: N, 10.69; S, 24.43. Found: N, 10.49; S, 24.75.

Alkaline Hydrolysis of $(C_5H_8NOS)_x$.—A mixture of $(C_5H_8NOS)_x$ (1.3 g.) and alcoholic potassium hydroxide (7 g. of potassium hydroxide in 21 g. of absolute alcohol) was refluxed three hours and then diluted with an equal volume of water. A slight amount of suspended material was removed by filtration, the filtrate was chilled, and then acidified with hydrochloric acid. The acidic solution was extracted five times with 50-cc. portions of ether, the solvent removed from the combined extract and the residue stirred well with water (5 cc.). This mixture was filtered and the filtrate allowed to evaporate spontaneously, yielding colorless crystals, m. p. 98–100°, undepressed when mixed with an authentic sample of oxalic acid dihydrate.

Oxalodimorpholide.—A mixture of morpholine (89 g., 1.00 mole) and ethyl oxalate (73 g., 0.50 mole) was placed in a 1-liter round-bottomed flask fitted with a six-inch helices-packed column topped by a still head and downward condenser. The mixture was slowly distilled, the alcohol of reaction being removed as it was formed (only about two-thirds of the theoretical amount was obtained). The still-residue crystallized on cooling and was pressed out on a filter and washed with Skellysolve B. The dry material (m. p. 169–175°) weighed 60 g. (53% yield) and melted at 184–185° after two recrystallizations from acetone.

Anal. Calcd. for $C_{10}H_{16}N_2O_4$: C, 52.63; H, 7.01; N, 12.28. Found: C, 52.69; H, 6.97; N, 12.31.

Dithioöxalodimorpholide (from Oxalodimorpholide).—A finely ground mixture of oxalodimorpholide (5.7 g., 0.025 mole) and phosphorus pentasulfide (3.4 g., 0.021 mole) was placed in a 50-cc. round-bottomed flask containing a thermometer whose bulb was in the solid mixture. The flask was heated in an oil-bath to 110°, at which temperature a vigorous reaction started and the internal temperature rose rapidly to 250°. The flask was cooled and its cinder-like contents were ground in a mortar and then leached with 1500 cc. of boiling absolute alcohol. The chilled alcoholic filtrate deposited colorless crystals (1.4 g., 22% yield, m. p. 249–250.5°) which after recrystallization from benzene melted at 252–253°, undepressed when mixed with a sample of the material obtained from diisobutylene.

Treatment of oxalodimorpholide with phosphorus pentasulfide and potassium sulfide in xylene[15] failed to give the desired product.

Summary

When the morpholine modification of the Willgerodt reaction is applied to compounds of the type $RC(CH_3)=CH_2$ there is obtained as a cleavage product a small amount of material of the empirical formula C_5H_8NOS. Degradative hydrolyses and an independent synthesis have shown that this material is dithioöxalodimorpholide.

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[12] Sand, *Ber.*, **34**, 2909 (1901).

[13] This procedure is based on the preparation of thioformylpiperidine described by Willstätter and Wirth, *Ber.*, **42**, 1921 (1909).

[14] Medard, *Bull. soc. chim.*, [5] **3**, 1343 (1936).

[15] A fairly general method used by Kindler, *Ann.*, **431**, 187 (1923), for the conversion of amides to thioamides.

RENSSELAER, N. Y. RECEIVED DECEMBER 26, 1946

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. LXXXIII. Synthesis of 3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone[1]

BY HERBERT E. FISHER AND HAROLD HIBBERT

In previous reviews on the structure of lignin[2,3,4] the opinion has been expressed that native lignin is derived, essentially, from a very reactive progenitor, β-oxyconiferyl alcohol, R—CH=C(OH)—CH_2OH, this product being the enol form of a keto alcohol, R—CH_2—CO—CH_2OH (R = 4-hydroxy-3-methoxyphenyl).

The veratryl analog has been synthesized,[5] and after ethanolysis was found to yield the two benzoin ethyl ethers, R′—$CHOC_2H_5$—CO—CH_3 and R′—CO—$CHOC_2H_5$—CH_3 (R′ = 3,4-dimethoxyphenyl). Considerable evidence has been obtained recently[5,6,7] that the parent benzoins II and III may be formed from the veratryl analog of oxyconiferyl alcohol, I, by the following series of reactions

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[1] Based, in part, on a thesis submitted by H. E. Fisher to the Faculty of Graduate Studies and Research, McGill University, in partial fulfilment of the requirements for the degree of Doctor of Philosophy, October, 1943. The preliminary part of this investigation was carried out at the Pulp and Paper Research Institute, McGill University, Montreal. Numerous modifications and improvements resulted from a more extended research carried out by one of us (H. F.) in the Department of Chemistry, University of British Columbia, with funds generously supplied by the senior author (H. H.). The untimely death of the latter interrupted our collaboration before completion of the manuscript for publication.

[2] Hibbert, *Paper Trade J.*, **113**, No. 4, 35 (1941).

[3] Hibbert, *Ann. Rev. Biochem.*, **11**, 183 (1942).

[4] Eastham, Fisher, Kulka and Hibbert, THIS JOURNAL, **66**, 26 (1944).

[5] Fisher, Kulka and Hibbert, *ibid.*, **66**, 598 (1944).

[6] Mitchell and Hibbert, *ibid.*, **66**, 602 (1944).

[7] Gardner and Hibbert, *ibid.*, **66**, 607 (1944).