[Contribution from the Chemical Laboratory of Iowa State College]

THE PREPARATION OF 5-BROMOFURFURAL AND SOME OF ITS DERIVATIVES

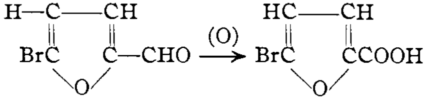
By Henry Gilman and George F. Wright

Received October 28, 1929 Published March 6, 1930

Introduction

One of the outstanding characteristics of aromatic compounds is the smooth and readily controlled substitution reactions which they undergo. Some heterocyclic types like furan, thiophene and pyrrole have physical, chemical and physiological properties which warrant their correlation with an aromatic compound like benzene.[1] For these reasons it is somewhat surprising that no bromofurfural is described in the literature, particularly because most of the reactions of furan have centered about the readily accessible and inexpensive furfural. Undoubtedly a chief reason for the difficulty in the preparation of bromofuran compounds is the great sensitiveness of the furan ring to halogens and halogen acids.

We have shown that it is possible to prepare 5-bromofurfural in relatively satisfactory yields by the direct bromination of furfural diacetate, the synthesis of which has been improved by recent directions of Gilman and Wright.[2] The position of the bromine atom in our bromofurfural was established by its oxidation to the known 5-bromofurfuroic acid.



There were prepared from 5-bromofurfural, in addition to the 5-bromofuroic acid, the oxime and diacetate.

Experimental Part

Several experiments, with variations, were carried out for the synthesis of 5-bromofurfural.

First, 198 g. (1.0 mole) of furfural diacetate, prepared in accordance with the directions of Gilman and Wright,[2] was dissolved in 400 cc. of carbon disulfide which had been dried by shaking with anhydrous calcium chloride. To this stirred solution contained in a one-liter, three-necked flask provided with a mechanical stirrer, condenser and separatory funnel, was added 320 g. (2 moles) of bromine.[3] The addition of bromine was effected in about a one-hour period and at room temperature. After refluxing over a water-bath for ten hours, the mixture was poured upon 100 g. of precipitated calcium carbonate contained in a two-liter steam distillation flask, and there allowed to react for about fifteen minutes. Then 125 cc. of water was added and steam was admitted

---

[1] Gilman and Pickens, This Journal, **47**, 245 (1925).

[2] Gilman and Wright, *Iowa State College J. of Science*, **4**, 35 (1929).

[3] The bromine was first dried by shaking with concentrated sulfuric acid and then distilled.

very *slowly* and *cautiously*. When the carbon disulfide had distilled over, the temperature of the condenser was raised to about 60–80° (by regulating the flow of cooling water), and the condensate was collected in a flask well cooled by water. The white solid obtained in this manner was redistilled with steam and yielded 41.5 g. or 23.7% of the theoretical amount of 5-bromofurfural which melted at 81.5–82°. When the quantity of bromine is increased under these conditions to 352 g. or 2.2 moles, the yield of bromofurfural is decreased considerably, and there also results, in a 4–5% yield, an as yet unidentified compound which melts at 134–135° when purified by steam distillation. This compound contains two atoms of bromine and gives a positive test with Tollens' reagent.

In a second preparation starting with 0.25 mole of furfural diacetate the bromine was added over a two-hour period during which the reaction mixture was kept at 10°. After stirring at this temperature for four hours, it was chilled to −15° and filtered. The filtrate was distilled under reduced pressure until most of the solvent was removed, and then the residue was carefully steam distilled to yield 12 g. or 27.3% of the bromofurfural melting at 81.5–82°. This method is, at present, preferred to the others.

Third, 49.5 g. (0.25 mole) of furfural diacetate in 100 cc. of chloroform was added to a chilled solution of a pyridine–bromine complex, prepared by adding 80 g. (0.5 mole) of bromine to 39.5 g. (0.5 mole) of pyridine in 100 cc. of carbon disulfide, to which was then added 100 cc. of chloroform. After allowing this mixture to stand for three days with occasional shaking, it was extracted with water and dilute acetic acid, and dried with anhydrous sodium sulfate. It was first distilled at 90–95° (8 mm.) and melted at 80°. Then on steam distillation, 15 g., or 34.1%, of the bromofurfural was obtained and this melted at 82°. Bromofurfural appears to be more stable than furfural, a not entirely unexpected phenomenon.

Anal. Calcd. for $C_5H_3O_2Br$: Br, 45.45. Found: Br, 45.97, 45.97.

In other experiments it was found that lower yields of the bromofurfural were obtained with smaller molecular proportions of bromine. The use of acetic anhydride as a solvent[4] at a temperature below 0°, also gave a lower yield of bromofurfural. With acetic anhydride as the solvent, some acetyl bromide and a smaller quantity of bromoacetyl bromide were detected.

Oxidation of 5-Bromofurfural.—The oxidation was effected in a 34% yield by adding aqueous potassium permanganate to 17.6 g. (0.1 mole) of bromofurfural suspended in water containing calcium hydroxide. The identity of the 5-bromofuroic acid was confirmed by a mixed melting point determination with the acid prepared in accordance with the method of Hill and Sanger.[5]

5-Bromofurfuraldoxime, $BrC_4H_2OCH{=}NOH$.—The oxime was prepared in the usual manner from the aldehyde, hydroxylamine hydrochloride and 10% sodium hydroxide. The yield (from 5 g. of the bromofurfural) was 75%. The oxime melts at 150–152°, and has a pleasant sweet taste.[6]

Anal. Calcd. for $C_5H_4O_2NBr$: Br, 42.10. Found: Br, 42.62.

5-Bromofurfural Diacetate, $BrC_4H_2OCH(OCOCH_3)_2$.—Forty-four g. (0.25 mole) of bromofurfural was refluxed for ten hours with 83.6 g. (0.82 mole) of acetic anhydride

---

[4] The acetic anhydride was used to stabilize the diacetate, a procedure now employed in this Laboratory for other substitution reactions of furan compounds. The diacetate is more conveniently and less expensively prepared than the diacetal of furfural.

[5] Hill and Sanger, *Ann.*, **232,** 46 (1885).

[6] See Gilman and Hewlett, *Iowa State College J. of Science,* **4,** 27 (1929), for a recent article on the correlation of sweet taste with constitution of some furan compounds.

and 9.6 g. (0.16 mole) of acetic acid. Distillation under reduced pressure yielded a low-boiling fraction, and a higher fraction distilling at 148–150° (11 mm.). The low-boiling fraction was refluxed for six hours with 75.5 g. (0.75 mole) of acetic anhydride and the mixture, after standing for several days, was distilled in a vacuum as before. The total yield of diacetate distilling at 128–130° (5–6 mm.) and melting at 51–52° was 60 g. or 87%. Hydrolysis with normal sulfuric acid gave 5-bromofurfural.

Anal. Calcd. for $C_9H_9O_5Br$: Br, 28.88. Found: Br, 29.02, 29.00.

Summary

The first bromofurfural, 5-bromofurfural, has been prepared by the direct bromination of furfural diacetate and characterized by a few appropriate derivatives.

AMES, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGICAL CHEMISTRY OF THE UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE]

THE PHENYLATION OF OLEIC ACID

BY E. G. SCHMIDT

RECEIVED OCTOBER 28, 1929 PUBLISHED MARCH 6, 1930

As a preliminary step in the study of the metabolism of certain fatty acids the introduction of various aromatic groups into the double bond of oleic acid has been investigated. Eijkman[1] as well as Marcusson[2] have studied the reaction between unsaturated fatty acids, benzene and anhydrous aluminum chloride with the production of phenyl-substituted saturated acids; however, if the double bond was in the α-position to the carboxyl group, phenylation did not take place. Marcusson drew attention to the fact that Poncio and Castaldi[3] found that these same acids had no iodine number and he pointed out the parallelism between unsaturated fatty acids which do not absorb iodine from Hubl's solution and non-reactivity with aromatic compounds in the presence of aluminum chloride. Nicolet and deMilt[4] noted that the derivatives of phenylstearic acid show little tendency to crystallize.

In the present work the reaction between benzene and oleic acid in the presence of anhydrous aluminum chloride has been studied with particular reference to the speed of the reaction and to the length of the reaction period as affecting the nature of the condensation products. The reaction proceeded with great speed and with a vigorous evolution of hydrogen chloride, and within less than five minutes it was practically completed, as determined by the drop in the iodine number and the neutralization equivalent. If the reaction was allowed to proceed for several hours, par-

[1] Eijkman, *Chem. Centr.*, II, 1100 (1908).

[2] Marcusson, *Z. angew. Chem.*, **33**, 231 (1920).

[3] Poncio and Castaldi, *Chem. Centr.*, II, 1154 (1912).

[4] Nicolet and deMilt, THIS JOURNAL, **49**, 1103 (1927).