REACTIONS OF AROMATIC AND HETEROAROMATIC COMPOUNDS BEARING ELECTRON-ACCEPTOR SUBSTITUENTS

XI.* SPECIFICITY OF THE BROMINATION OF THE COMPLEX OF ALUMINUM CHLORIDE WITH FURFURAL

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Complexing with aluminum chloride can change the specificity of the bromination of furfural in such a way that the major product becomes 4-bromofurfural. Consequently, as in the thiophene series, reinforcement of the electron-acceptor capacity of the carbonyl group by means of the complexing deactivates the free 5 position so much that the 4 position of the furan ring becomes the most active.

In a previous communication, we set forth the results of our study of the specificity of the isopropylation and acetylation of the complex of furfural with aluminum chloride. However, the results did not enable us to solve the problem of interest to us – the relative activity of the individual positions of the furan ring under conditions where the carbonyl compound reacts as a complex with a Lewis acid. The data presented below, which pertain to the bromination of such a complex, make it possible to at least qualitatively evaluate the relative capacity for substitution of the 4 and 5 positions of furfural in its complex with $AlCl_3$.

It is known that furfural is converted to 5-bromofurfural on bromination without a catalyst [2]. The bromination of furfural and 2-acetylfuran in excess aluminum chloride without a solvent gives the 4,5-dibromo-substituted compound as the major product, regardless of the amount of bromine used [3-5]. A composition of the product of bromination of furfural with a Br_2 to $AlCl_3$ to furfural molar ratio of 1.5 : 1.8 : 1, which differs somewhat from the composition indicated in [3, 5], was presented in a later brief note [6]. According to gas-liquid chromatography (GLC), the product formed under these conditions contains 58% 4,5-dibromofurfural, 28% 4-bromofurfural, and 14% 5-bromofurfural. Here one should note that some data presented in [6] remain unclear. The reason the authors specified using 1.5 moles of bromine per mole of furfural is obscure. Furthermore, the amount of 4-bromofurfural isolated (4.5%) deviates sharply from that detected by GLC (28%), and its melting point (28-29°) is substantially lower than that of a sample obtained in our laboratory [7] and by Robba and Zaluski [8] (54-55°).

We produced the experiment exactly under the same conditions that are described in [6] using GLC and PMR spectroscopy for the analysis of the mixture. We were unable to select the conditions for the chromatographic separation of the 4- and 5-bromofurfurals (the GLC conditions are not presented in [6]). The chromatograms contained peaks of the unchanged furfural, monobromofurfurals (together), 4,5-dibromofurfural, and the peak of an unidentified substance, emerging between the mono- and dibromides. The latter apparently corresponds to a small admixture of 5-chloro-4-bromofurfural which, as was recently shown [9], is formed under the reaction conditions from 4,5-dibromofurfural as a result of exchange of bromine by chlorine (from $AlCl_3$ [10]). After the furfural has been removed by distillation, the mixture of bromides can be readily analyzed by PMR spectroscopy. The data that we obtained (the ratio of 4,5-dibromide and

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*See [1] for communication X.

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4- and 5-monobromides is 75 : 20 : 5) differ from the results presented in [6], but there is no doubt that appreciable amounts of 4-bromofurfural are formed. This compound was also detected during a detailed study of the effect of the reaction conditions on the composition of the bromination products of furfural [9], but the data presented in this paper require refinement since 5-bromofurfural was not detected in the mixture formed. We note that GLC was used in [9] for the analysis under conditions that do not make it possible to separate the 4- and 5-bromo-substituted compounds, whereas we detected 5-bromofurfural in the mixture obtained under similar conditions by using PMR spectroscopy.

By using a method involving bromination in a solvent [11, 12], we were able to select the conditions under which the formation of the dibromide is considerably suppressed. Owing to this, the relative activity of the various positions during bromination of the complex of furfural with $AlCl_3$ can be judged from the composition of the product. In fact, when we used 1 mole of bromine per mole of aldehyde at 0° in chloroform, we obtained a mixture of 4- and 5-monobromofurfurals and 4,5-dibromofurfurals in a ratio of 65 : 20 : 15. Thus complexing with aluminum chloride changes the specificity of substitution of the furan ring in such a way that the 4 position of the ring becomes the most active position, although substitution in the 5 position cannot be completely suppressed.

This conclusion is in good agreement with the experimental data available for carbonyl compounds of the thiophene series [13] and also with the results of quantum-chemical calculations [14]. In this connection, it is interesting to note that complexing apparently deactivates the furan ring to a greater degree than is the case in the thiophene analogs. We drew this conclusion during a study of the acetylation of 2-acetylfuran and 2-methyl-5-acetylfuran [1], and it was confirmed in this study during an investigation of the bromination of furfural and 2-formylthiophene by the competitive reaction method.

It is apparent from the data presented above that the formation of 4,5-dibromofurfural as the chief product of the bromination, regardless of the amount of bromine used, does not attest to any "equalization" of the electron density in the 4 and 5 positions as a result of complexing with aluminum chloride. It can be assumed that the 4 position is the most active position under the complexing conditions, but the 4-bromofurfural formed is brominated more rapidly than the unsubstituted furfural and 5-bromofurfural, just as is observed in the bromination of 2-formylthiophene and 2-acetothienone in sulfuric acid [15]. Unfortunately, because of considerable resin formation, we could not give a quantitative evaluation for the differences in the reactivities of 4- and 5-bromofurfurals, but there is no doubt of an analogy in the behavior of carbonyl compounds of the furan and thiophene series under the conditions of complexing with $AlCl_3$.

EXPERIMENTAL

The chromatographic analyses were performed with an LKhM-8M chromatograph with a flame-ionization detector, nitrogen as the carrier gas, and the following columns: 1) a 4 × 2000 mm stainless steel column packed with 15% polyethylene glycol adipate on Chromosorb W, 175°, gas flow rate 55 ml/min; 2) a 4 × 3000 mm column with 5% SE-30 silicon elastomer on Chromaton N-AW, 140°, flow rate 40 ml/min.

The PMR spectra were recorded with an RS-60 spectrometer (Special Design Office of the Institute of Organic Chemistry, Academy of Sciences of the USSR) with hexamethyldisiloxane as the internal standard. The chemical shifts are presented on the δ scale relative to tetramethylsilane.

Authentic samples for GLC and PMR spectroscopy were obtained by known methods: 5-bromofurfural [2], 4-bromofurfural [7], and 4,5-dibromofurfural [16].

Bromination of Furfural in Excess $AlCl_3$ without a Solvent (see [6]). A 24 g (0.25 mole) sample of furfural was added with stirring and ice-water cooling to 60 g (0.45 mole) of anhydrous $AlCl_3$, and 19 ml (0.375 mole) of bromine was then added to the mixture without cooling. The mixture was allowed to stand overnight at 20°, after which it was poured over ice. The aqueous mixture was extracted with chloroform, and the extract was steam distilled. The distillate was extracted with chloroform, and the extract was dried with $MgSO_4$. Distillation gave the following fractions: a first fraction (5.2 g) with bp 65-110° (16 mm), a second fraction (2.6 g) with bp 112-120° (16 mm), and a third fraction (22.5 g) with bp 120-126° (16 mm). Fraction 1 was heated on a boiling-water bath for 1 h with 25 ml of 5% sodium sulfide solution, and the mixture was then steam distilled. The distillate was extracted with chloroform, and the extract was dried with $MgSO_4$ and distilled to give 1.9 g of a substance that crystallized in the receiver and had bp 93-113° (18 mm) and mp 52° (from heptane); a mixture with 4-bromofurfural melted at 52-53°. Fraction 2 was not investigated. Fraction 3 was 4,5-dibromofurfural with mp 37-37.2° (from heptane), which is in agreement with the data in [5].

The ratio of the bromides was determined by PMR spectroscopy of the undistilled mixture from which only the unchanged furfural had been removed (monitored by GLC). The calculation was made from the areas of the 7.06 ppm [3-H of all of the bromides (overlapped)], 6.49 ppm (4H in 5-bromofurfural), and 7.63 ppm (5-H in 4-bromofurfural) signals. The ratio of 4-bromo-, 5-bromo-, and 4,5-dibromofurfurals in the product obtained under the conditions presented above was ~20 : 5 : 75.

Bromination of Furfural with an Equimolar Amount of Bromine in Cooled Chloroform. A solution of 19.2 g (0.2 mole) of furfural in 120 ml of chloroform was added with stirring to 66.4 g (0.5 mole) of $AlCl_3$ while maintaining the temperature at ~0°. A 32 g (0.2 mole) sample of bromine was then added at the same temperature, and the mixture was stirred for 6 h and allowed to stand overnight without stirring at 0°. The mixture was poured over ice, and the aqueous mixture was extracted with chloroform. The extract was washed with water, sodium hyposulfite and sodium carbonate solutions, and water. It was then steam distilled, and the distillate was extracted with chloroform. The extract was dried with $MgSO_4$ and distilled to give the following fractions: a first fraction (5 g) with bp 66-79° (20 mm) (chiefly unchanged furfural); a second fraction (1.9 g) with bp 79-90° (20 mm) (which contained furfural, a mixture of monobromides, and traces of 4,5-dibromofurfural); and a third fraction (5.7 g) with bp 90-120° (20 mm) [which contained traces of furfural, considerable amounts of a mixture of monobromofurfurals, as well as 4,5-dibromofurfural and unidentified impurities (GLC)]. By means of GLC with an internal standard (4-bromo-2-formylthiophene), it was found that fraction 2 contains ~30% (by weight) monobromofurfurals, while fraction 3 contains ~60% (by weight) monobromofurfurals. The molar ratio of 4-bromo- and 5-bromo-, and 4,5-dibromofurfurals was found to be ~65 : 20 : 15 in fraction 3 by PMR spectroscopy.

Competitive Bromination of Furfural and 2-Formylthiophene in the Presence of Excess Aluminum Chloride. A 4 g (0.025 mole) sample of bromine was added to a solution obtained from 16.6 g (0.125 mole) of aluminum chloride, 2.4 g (0.025 mole) of furfural, and 2.8 g (0.025 mole) of 2-formylthiophene in 30 ml of chloroform, and the mixture was held at 20° for 24 h, after which it was poured over ice and worked up in the usual way to give ~5 g of a steam-distilled mixture of aldehydes boiling at 65-130° (20 mm) and containing furfural, 2-formylthiophene, monobromofurfurals, and 4-bromo-2-formylthiophene in a molar ratio of 1 : 0.35 : 0.25 : 2.0. The mixture also contained a very small amount of 4,5-dibromo-2-formylthiophene and scarcely any 4,5-dibromofurfural (according to GLC). Thus more than 70% of the bromine taken for the reaction was consumed in the bromination of 2-formylthiophene.

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