ACTION OF BROMINE AND TERT-BUTYL CHLORIDE ON METHYL-2-FURYL KETONE IN THE PRESENCE OF EXCESS ALUMINUM CHLORIDE

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One of us and Vol'kenshtein [1] showed that the Pearsoh-Pope method [2] of blocking the side chain of aromatic ketones with aluminum chloride makes it possible to change the bromination of 2-acetothienone in such a way that there is substitution in the ring with the formation of mainly 4-bromo-2-acetothienone. It seemed interesting to determine how methyl-2-furyl ketone (MFK) would react under similar conditions, as this compound is brominated in the side chain without catalyst [3] or in the presence of a very small amount. It is known [4-7] that in the halogenation of furan derivatives with an electronegative substituent in position 2, the predominant role is played by the α -orienting effect of the ring oxygen, which is apparently stronger than the effect of the heteroatom in thiophene. For example, the bromination of furfural yields only 5-bromofurfural [4], while 2-thiophenealdehyde forms a mixture of the 4- and 5-isomers [8], though with a predominance of the latter. Nonetheless, according to Pearson (see above) the direction of the reaction in the bromination of MFK was more difficult to determine.

It was also advantageous to determine how MFK would react with an alkyl halide under conditions when this ketone is present in the form of a complex with aluminum chloride. In this connection, it should be pointed out that the Friedel-Crafts alkylation of furfural with isopropyl chloride forms 4-isopropylfurfural [9] while tertbutyl enters position 5 of the nucleus to form 5-tert-butylfurfural [10].

The results we obtained may be summarized as follows: In the action of bromine on MFK at room temperature in the presence of 3 moles of aluminum chloride without solvent, the furan ring is attacked, but, in contrast to the case of 2-acetothienone, the reaction with MFK could not be stopped at the formation of a monobromo derivative. It was only with a low temperature and a short experiment that it was possible to isolate a small amount of the monobromo derivative, methyl-5-bromo-2-furyl ketone, together with methyl 4,4-dibromo-2-furyl ketone (I), which forms the bulk of the product from the reaction of bromine with MFK at room temperature. The yield of the latter was increased from 34 to 62% if the molar ratio of bromine and MFK was 2:1.

The structure of (I) was demonstrated by oxidation to known 4,5-dibromo-2-furancarboxylic acid (II), which was identical with (II) obtained by direct bromination of 2-furancarboxylic acid [7]:



Of the three methods of oxidizing (I), namely, with $K_3Fe(CN)_6$ [11], $KMnO_4$ [3] or NaOCI [12], the last method was found to be the best; the acid yield was then 84%.

By the action of tert-butyl chloride on MFK in the presence of excess aluminum chloride we obtained methyl tert-butyl-2-furyl ketone (III). It was found to be identical in the melting points of the semicarbazone and 2,4-dinitrophenylhydrazone with the product we obtained by acetylation of tert-butylfuran (IV), which in its turn was synthesized by Gilman's method [13] by tert-butylation of methyl 2-furancarboxylic acid (V), hydrolysis of (VI), and decarboxylation of the 5-tert-butyl-2-furancarboxylic acid (VII) formed. If, as Gilman considered, we assume that this route leads to (IV), then our ketone, which was formed by the action of tert-butyl chloride on MFK, should be assigned structure (III). On oxidation with NaOC1 [12] this ketone gives (VII), described by the investigator mentioned.



EXPERIMENTAL

Bromination of MFK. Over a period of 1.5 hr, 24.7 g of MFK was added to 89.7 g of AlCl₃ at 0-10° and then 27.7 ml of dry bromine was added to the complex dropwise at 20-25° over a period of 2 hr and the mixture left at 24-25° for 14 hr and then poured onto a mixture of ice and 10 ml of HCl. The oil liberated was extracted with ether and the extract washed with sodium carbonate and hyposulfite solutions and water, dried over MgSO₄, and vacuum distilled. Two distillations yielded 37.3 g of (I) (yield 62%) with b.p. 98-110° (4 mm) and m.p. 54.5-55.5° from ligroin. Found: C 27.06; 26.96; H 1.73; 1.67; Br 58.75; 59.01%. C₆H₄Br₂O₂. Calculated: C 26.90; H 1.51; Br 59.66%. The oxime had m.p. 148-149° (with decomposition, from alcohol). Found: N 5.54; 5.30%.C₆H₅Br₂NO₂. Calculated: N 5.21%. We also isolated two bromides in amounts of 1.5 g and 0.75 g and the first of these was not investigated further, while the second, which had m.p. 92-92.3° (from alcohol) was found to have the elementary composition: C₆H₃Br₃O₂.

 $\frac{4,5-\text{Dibromo-2-furancarboxylic acid (II).}}{168-168.5^{\circ} (\text{from water}); \text{ the yield was } 84.2^{\%}.} \text{ Literature data [14]: m.p. 168-168.5^{\circ}. Found: C 22.21; 22.54; H 0.64; 0.74; Br 59.14; 59.33^{\%}. C_5H_2B_{I2}O_3. Calculated: C 22.25; H 0.75; Br 59.22^{\%}.}$

Bromination of MFK at low temperature. To 74.5 g of AlCl₃ at 0-5° was added 20.5 g of MFK over a period of an hour and then 10.5 ml of bromine over a period of 1.5 hr at -5 to -6°. After being stirred for 40 min at 21°, the mixture was treated as in the first experiment. Two vacuum distillations yielded 1.45 g (4% yield) of methyl 5-bromo-2-furyl ketone with b.p. 73-75° (4 mm) and m.p. 94-95° (from ligroin). Found: C 38.26; 38.42; H 2.70; 2.77%. C₆H₅BrO₂. Calculated: C 28.12; H 2.67%. The oxime had m.p. 78-79° (from aqueous alcohol). Literature data [15]: the ketone has m.p. 94-95° and the oxime m.p. 79.5°. We also obtained 7.2 g (14% yield) of (I) with b.p. 98-110° (4 mm) and m.p. 54-55°.

Methyl 5-tert-butyl-2-furyl ketone (III). To 19.6 g of AlCl₃ at 5° was added 5.4 g of MFK over a period of 40 min and then 4.5 g of $t-C_4H_9Cl$ dropwise at 10-15°; the mixture was left at 25° for 21 hr, heated at 30-40° for 2 hr, and treated as described above. Two distillations yielded 3.9 g (48% yield) of (III) with b.p. 78.5° (4 mm) and b.p. 125-126° (10 mm); n_D^{20} 1.4920; Found: C 71.71; 71.85; H 8.55; 8.47%. C₁₀H₁₄O₂. Calculated: C 72.26; H 8.49%. The semicarbazone had m.p. 200-201° (with decomposition, from alcohol, in a sealed tube). Found: N 18.43; 18.67%. C₁₁H₁₇N₃O₂. Calculated: N 18.82%. The 2,4-dinitrophenylhydrazone had m.p. 219° (from ethylacetate-alcohol). Found: N 15.96; 16.15%. C₁₆H₂₀N₄O₅. Calculated: N 16.08%. In addition, we obtained 0.3 g of a substance which was not investigated.

5-Tert-butyl-2-furancarboxylic acid (VII). Oxidation [12] of 1.2 g of (III) yielded 0.7 g (54% yield) of (VII) with m.p. 104-105° (from aqueous alcohol). It did not depress the melting point of (VII) obtained by hydrolysis of (VI). Literature data [13]: m.p. 104-105°. Acetylation of 5-tert-butylfuran. From 4.8 g of (IV) and 8.2 g of acetic anhydride in the presence of 3.2 g of ZnCl₂ [16] we obtained 3.9 g (~61% yield) of (III) with h.p. 125-126° (10 mm); n_D^{20} 1.4921. The semicarbazone (m.p. 200-201°) and 2,4-dinitrophenylhydrazone (m.p. 219-220°) did not depress the melting points of the samples described above.

SUMMARY

Methyl 2-furyl ketone is brominated in the nucleus in the presence of 3 moles of aluminum chloride without solvent.

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