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BROMINATION OF 2-ACETYL-5-METHYLFURAN

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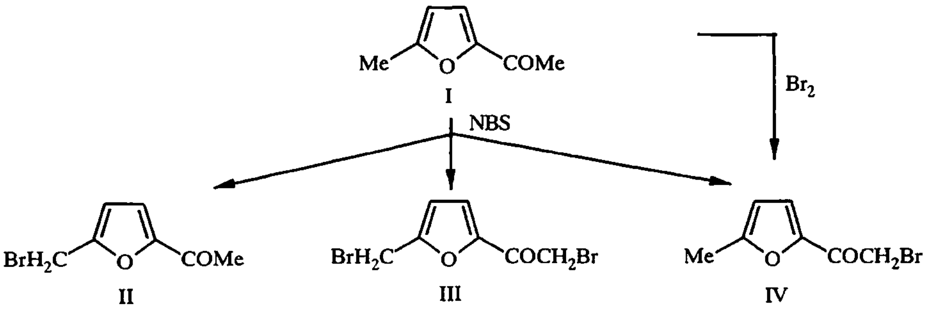
The bromination of 2-acetyl-5-methylfuran by bromine and N-bromosuccinimide was studied. The action of N-bromosuccinimide on 5-methyl-2-acetylfuran in various solvents leads to mixtures of an ω-bromo ketone, a 5-bromomethyl derivative, and 5-bromomethyl-ω-bromo ketone. The use of 2,2′-azobisisobutyronitrile as activator of the radical process does not make the reaction selective but promotes bromination at the methyl group of the ring. A selective method for the synthesis of 2-(bromoacetyl)-5-methylfuran by the bromination of 2-acetyl-5-methylfuran with bromine was developed.

The action of N-bromosuccinimide on silvan in carbon tetrachloride gives 2-bromomethylfuran [1], but 3-acetylfuran is not brominated at the ketone group [2]. It therefore seemed possible to obtain 2-acetyl-5-bromomethylfuran (II) by the action of the same reagent on 2-acetyl5-methylfuran (I). In practice, however, this reaction proved nonselective and led, according to TLC, LC, and the PMR spectra, to a mixture of products (II-IV) from bromination at the 5-methyl and acetyl groups.



The yield of the expected compound (II) amounted to only 17%, 2-(bromoacetyl)-5-bromomethylfuran (III) was formed in a somewhat smaller amount, while the main product was 2-(bromoacetyl)-5-methylfuran (IV). An attempt to make the reaction selective with a catalyst of radical processes (2,2′-azobisisobutyronitrile) only produced an increase in the fraction of the bromine derivatives (II, III) and a decrease in the fraction of the bromo ketone (IV).

If carbon tetrachloride was replaced by a mixture of acetic anhydride and a small amount of acetic acid, which has been used successfully for the selective bromination of 2-acetylthiophene at position 5 by the action of N-bromosuccinimide [3], the same compounds were obtained from the ketone (I) but with the monobromo derivatives (II, IV) in equal proportions and a small amount of the dibromo derivative (III).

The obtained mixtures of substances only keep comparatively well in solutions of organic solvents in the cold. During distillation of the solvent even at reduced pressure thick dark liquids that fume in air are formed. After a few days at room temperature they are converted into black solids. The obtained mixtures were analyzed by PMR a few hours after distillation of the solvent. The compositions of the bromination products in the various versions of the synthesis are given in Table 1, and the spectral characteristics of the individual compounds are given in Table 2.

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TABLE 1. The Bromination of the Ketone (I) by N-Bromosuccinimide.

Reaction conditions (solvent, time, temperature)	Reaction products, %			Amount of unreacted ketone, %
	II	III	IV	
CCl_4, 5 h, boiling	17	14	57	12
CCl_4, catalyst, 1 h, boiling	36	28	24	12
Ac_2O—AcOH, 1 h, 40°C	31	6	31	31

TABLE 2. The PMR Spectral Characteristics of 2-Acetyl-5-methylfuran (I) and its Bromine Derivatives (II-IV).

Compound	Chemical shifts, δ, ppm			*J*, Hz				
	3-H	4-H	other groups	3-H — 4-H	3-H — $C\underline{H}_3$	4-H — $C\underline{H}_3$	3-H — $C\underline{H}_2Br$	4-H — $C\underline{H}_2Br$
I	7,20 dd	6,28 dq	2,36 dd (5-$C\underline{H}_3$) 2,36 s ($COC\underline{H}_3$)	3,5	0,6	0,9	—	—
II	7,27 br. d	6,72 br. d	4,73 dd (5-$C\underline{H}_2Br$) 2,43 s ($COC\underline{H}_3$)	3,6	—	—	0,6	1,0
III	7,49 br. d	6,80 br. d	4,76 dd (5-$C\underline{H}_2Br$) 4,52 s ($COC\underline{H}_2Br$)	3,6	—	—	0,6	1,0
IV	7,43 dd	6,37 dq	2,40 dd (5-$C\underline{H}_3$) 4,52 s ($COC\underline{H}_2Br$)	3,5	0,6	0,9	—	—

The individual compounds were isolated from the mixtures for spectral analysis by high-performance liquid chromatography. The oily 5-bromomethyl derivatives (II, III) gradually darken in the light. Their boiling points were not determined on account of the small quantities. In contrast the bromo ketone (IV) was more stable. A sample, prepared by the action of bromine on the ketone (I) and purified by twofold crystallization, remained unchanged after storage in the dark for a year.

During the bromination of 2-acetyl-5-methylfuran with bromine in a 1:2.5 mixture of dioxane and ether high yields of 2-(bromoacetyl)-5-methylfuran (IV) were obtained. It can be concluded that bromosuccinimide brings about bromination of the methyl and acetyl groups of the initial molecule while bromine leads to selective synthesis of the corresponding bromoacetyl derivative.

EXPERIMENTAL

Thin-layer chromatography was carried out on Silufol UV-254 plates in the 3:1 benzene—ethyl acetate system. The mixtures were separated preparatively on a Du Pont 830 high-performance liquid chromatograph with a UV detector (λ 254 nm), 250x6.2 mm column, sorbent Zorbax-Sil, eluent 10% 2-propanol in hexane, 3.5 ml/min. The PMR spectra were recorded on a Bruker WH-90/DS instrument in hexadeuteroacetone with TMS as internal standard.

Reaction of 2-Acetyl-5-methylfuran (I) with N-Bromosuccinimide. A. To solution of 12.4 g (0.1 mol) of the ketone (I) in 100 ml of dry carbon tetrachloride we added 19.6 g (0.11 mol) of N-bromosuccinimide that had been recrystallized from water and dried over phosphorus pentoxide. The mixture was boiled for 5 h, the precipitated succinimide was filtered off, and the dark filtrate was purified with active charcoal and evaporated *in vacuo*; 20.2 g of a thick dark slightly fuming liquid were obtained, which we then submitted to chromatography and spectral analysis.

B. To solution of 6.2 g (0.05 mol) of the ketone (I) in 40 ml of carbon tetrachloride we added 0.05 g of 2,2′-azobisisobutyronitrile and then 8.9 g (0.05 mol) of purified N-bromosuccinimide. The mixture was boiled for 1 h until the N-bromosuccinimide precipitate had disappeared. The succinimide was filtered off and washed with 10 ml of carbon tetrachloride. The filtrate and the washing liquid were evaporated *in vacuo* and submitted to chromatographic and spectral analysis.

C. To solution of 12.4 g (0.1 mol) of the ketone (I) in mixture of 40 ml of acetic anhydride and 6 ml of acetic acid over 20 min we added in portions 19.6 g (0.11 mol) of purified N-bromosuccinimide. The reaction mixture was heated to 40°C and stirred at this temperature for 1 h, and the succinimide was filtered off. The filtrate was poured onto ice and neutralized with 40% sodium hydroxide and then with sodium bicarbonate until the release of carbon dioxide had ceased. The solution was extracted with 400 ml of ether. The extract was dried with magnesium sulfate, evaporated *in vacuo* (3 mm Hg), and analyzed by means of the PMR spectra.

2-(Bromoacetyl)-5-methylfuran (IV). To solution of 136.4 g (1.1 mol) of freshly distilled (65-68°C at 6 mm Hg) ketone (I) in a mixture of 200 ml of dioxane and 500 ml of ether at 20-25°C with vigorous stirring over 1 h we added 56 ml (1.1 mol) of bromine. The mixture was stirred for a further 20 min and poured onto 600 g of water with ice and 200 ml of ether. The upper layer was separated, washed with sodium bicarbonate solution, and dried with magnesium sulfate. The solvent was distilled *in vacuo*, and the brown crystalline residue was dried over phosphorus pentoxide in a vacuum desiccator. Bromo ketone (IV) (195 g, 87%; mp 50-55°C), containing a small amount of the initial ketone and dibromo ketone as impurity was obtained. The product formed colorless crystals; mp 65-65.5°C (from aqueous ethanol). Found %: C 41.09; H 3.47; Br 39.75. $C_7H_7BrO_2$. Calculated %: C 41.40; H 3.47; Br 39.36.

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