IONIC HYDROGENATION OF BENZOFURANS

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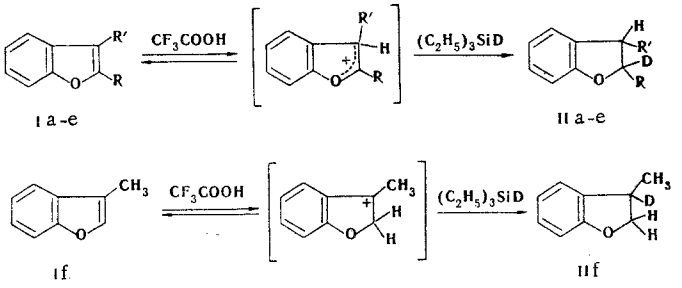
Benzofurans are arranged in the order 2-methylbenzofuran > 3-methylbenzofuran > benzofuran with respect to the case with which they undergo ionic hydrogenation. Benzofuran and 2-methylbenzofuran are protonated in the 3 position of the heterocyclic ring, whereas 3-methylbenzofuran is protonated in the 2 position. Individual monodeuterated 2,3-dihydrobenzofurans can be obtained in high yields by ionic hydrogenation.

It has been previously demonstrated [1-3] that heteroaromatic compounds readily undergo ionic hydrogenation.

The solution of the problem of the direction of initial attack of the proton in the ionic hydrogenation of alkylbenzofurans presents considerable difficulties. This is associated with the contradictory character of the calculated values [4-6] and the experimental data [7, 8] on the activity of the 2 and 3 positions of these molecules in electrophilic substitution reactions. In the present research triethyldeuterosilane and trifluoroacetic acid were used as the hydrogenating pair, and this made it possible to exclude the deuterium–hydrogen exchange that we previously observed when deuterotrifluoroacetic acid and triethylsilane were used [3].

Mass-spectrometric analysis of the products of ionic hydrogenation showed that they are exclusively monodeuterated 2,3-dihydrobenzofurans, the position of the deuterium in which, established from the PMR spectral data, completely confirmed the previously drawn conclusions regarding the direction of protonation of benzofurans [3]. The formation of monodeuterated 2,3-dihydrobenzofurans with a fixed position of the label during the ionic hydrogenation of benzofurans constitutes evidence for the absence of 1,2-hydride and methyl shifts in the intermediately formed carbonium ions. Ionic hydrogenation may thus serve as a preparative method for the synthesis of labeled 2,3-dihydrobenzofurans:



I, II a R = R′ = H; b R = D, R′ = H; c R = CH_3, R′ = H; d R = C_2H_5, R′ = H; e R = R′ = CH_3

2,2-Dideutero-2,3-dihydrobenzofuran was obtained by ionic hydrogenation of 2-deuterobenzofuran. In addition to the principal peak of ions with m/e 122, an ion peak with m/e 121, the formation of which can be represented as the result of fragmentation under the influence of electron impact of 2,2-dideutero-2,3-dihydrobenzofuran with elimination of a hydrogen radical, is present in the mass spectrum of this compound. The absence of an $[M - D]^+$ ion peak confirms the previously proposed fragmentation scheme [9], according to which the molecular ion of 2,3-dihydrobenzofuran loses a hydrogen radical from the 3 position.

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TABLE 1. Results of the Experiments on the Ionic Hydrogenation of Benzofurans (benzofuran to triethyldeuterosilane to trifluoroacetic acid ratio = 1 : 1.5 : 5, reaction time 3 h, 70°C)

2,3-Dihydrobenzofurans	Yield, %	Labeled compound, %	Proton chemical shifts, ppm*		
			H_2	H_3	alkyl group
IIa	81	98	4,25t	2,90d	—
IIb	80	94	—	2,90s	—
IIc	96	100	—	2,45d 2,90d	1,20s
IId	96	98	—	2,45d 2,90d	0,83t 1,50m
Ie	94	98	—	2,45m	1,10d
IIf	96	97	3,80d 4,35d	—	1,20s

*Abbreviations: s is singlet, d is doublet, t is triplet, and m is multiplet.

The relative rates of ionic hydrogenation of benzofuran and 3- and 2-methylbenzofurans by the triethylsilane–trifluoroacetic acid pair are, respectively, 1, 8, and 16; this is associated with the different contributions of the methyl group and the heteroatom to delocalization of the positive charge of the resulting carbonium ions.

2-Methyl-2,3-dihydrobenzofuran is formed in quantitative yield after 5 min in the hydrogenation of 2-methylbenzofuran at 70°, while the yields of hydrogenation products in the hydrogenation of 3-methylbenzofuran and benzofuran after the same time do not exceed 50 and 8%, respectively.

A mixture of cis and trans isomers of 2,3-dimethyl-2,3-dihydrobenzofuran in a ratio of 18 : 80 according to the results of gas–liquid chromatography (GLC) is formed in the ionic hydrogenation of 2,3-dimethylbenzofuran. The individual compounds were isolated by preparative GLC, and their structures were confirmed by their PMR spectra.

EXPERIMENTAL

Triethyldeuterosilane. This compound, with bp 107-108° and 100% deuterium content (according to mass spectrometry), was obtained in 64% yield by reduction of triethylchlorosilane with lithium aluminum deuteride.

2-Deuterobenzofuran. This compound, with bp 53-54° (10 mm) and 100% deuterium content, was obtained in 78% yield by deuterolysis of benzofuryllithium. The structure of the product was confirmed by its PMR spectrum (absence of the signal of an α-hydrogen atom and presence of a singlet of a β-hydrogen atom at 6.35 ppm with a relative intensity of one).

Ionic Hydrogenation of Benzofurans. Trifluoroacetic acid was added to a mixture of the appropriate benzofuran and triethysilane (the reagent ratio was 1 : 1.5 : 5, respectively). At the end of the reaction, the mixture was poured into water, and the aqueous mixture was neutralized with sodium carbonate and extracted with ether. The ether extract was dried with magnesium sulfate, the ether was removed by distillation, and the residue was vacuum distilled. The reaction products were analyzed by GLC with an LKhM-7A chromatograph with a thermal-conductivity detector; the column temperature was 150°, the column was 3 m long with a diameter of 0.4 mm, the support was Chromosorb W (60-80 mesh), the stationary phase was 15% polyethylene glycol with a molecular weight of 30,000, and the carrier gas was helium.

The mixture of isomers obtained by ionic hydrogenation of 2,3-dimethylbenzofuran was separated with a Varian M-705 preparative chromatograph with a flame-ionization detector. The column was 6 m long, the stationary phase was polyethylene glycol with a molecular weight of 20,000, the column temperature was 180°, and the carrier-gas (nitrogen) flow rate was 200 ml/min.

The PMR spectra were recorded without a solvent with a Varian T-60 spectrometer with hexamethyldisiloxane as the external standard. The mass spectra were recorded with an MKh-1303 spectrometer with a modified system for introduction of the substances directly into the ion source; the ionizing-electron energy was 50 eV, and the spectra were recorded at room temperature.

LITERATURE CITED

1. Z. N. Parnes, V. A. Budylin, E. Yu. Beilinson, and A. N. Kost, Zh. Organ. Khim., 8, 2564 (1972).
2. Z. N. Parnes, G. I. Bolesova, A. I. Belen'kii, and D. N. Kursanov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 1918 (1973).
3. É. A. Karakhanov, E. A. Dem'yanova, L. N. Borodina, and E. A. Viktorova, Dokl. Akad. Nauk SSSR, 214, 584 (1974).
4. L. Klasing, E. Pop, and N. Trinaistic, Tetrahedron, 28, 3465 (1972).
5. R. D. Brown and B. A. Coller, Austral. J. Chem., 12, 152 (1959).
6. R. Royer and J. Rem, Bull. Soc. Chim., France, 1029 (1970).
7. M. W. Farror and R. Levine, J. Amer. Chem. Soc., 72, 4433 (1950).
8. Q. M. Brooke, B. S. Furmis, and W. K. R. Musgrave, J. Chem. Soc., 580 (1968).
9. É. A. Karakhanov, S. V. Lysenko, V. V. Berentsveig, P. A. Sharbatyan, E. A. Viktorova, and A. P. Rudenko, Zh. Khim., 48, 2072 (1974).

MELDRUM'S ACID AND ITS ANALOGS

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2-Substituted or 2,2-disubstituted 4,6-dioxo-1,3-dioxanes, which are analogs of Meldrum's acid and were obtained by reaction of malonic acid with acetic anhydride and the appropriate carbonyl compound in the presence of sulfuric acid, exist in solution preferably in a single form according to the PMR and ^{13}C NMR spectral data. Fluctuation of the CH_2 group is not observed. The mass spectra are characteristic and are distinguished by splitting out of the carbonyl compound from the molecular ion or successive splitting out of CO_2 and ketene molecules. The Meldrum acid analogs do not affect plant growth but have a depressive effect on the central nervous system of animals and low toxicity.

The structure and reactivity of Meldrum's acid, i.e., 2,2-dimethyl-4,6-dioxo-1,3-dioxane (Ia), to which the 3,3-dimethyl-2-carboxy-β-propiolacetone structure had been assigned for a long time in view of its considerable acidity and the practical absence of enolization [1-3], up until now have given rise to misunderstandings, especially since the arylidene derivatives of Meldrum's acid and its analogs behave like neutral Lewis acids in that they readily add hydroxide ions [4]. The problem of the conformation of such structures is also in debate. Moreover, despite the accessibility of such models and their formal similarity to barbituric acid derivatives, the literature contains no information regarding the biological effect of Meldrum's acid and its analogs.

We have synthesized Meldrum's acid and some of its analogs (Ia-g) using the reaction of malonic acid with the appropriate carbonyl compound in the presence of acetic anhydride [1, 2, 5]. The yields are satisfactory when ketones of the aliphatic, alicyclic, or aliphatic-aromatic series are used in the reaction. Pronounced resinification was observed in the case of aliphatic aldehydes having an α-hydrogen atom, and we were unable to obtained the desired compound from cuminaldehyde.

The IR spectra of the synthesized compounds contain two intense absorption bands of ester carbonyl groups at 1740-1770 and 1780-1800 cm^{-1}. The UV spectra have pronounced absorption with maxima at

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