ALKYLATION OF FURAN, THIOPHENE, AND PYRROLE WITH FURFURYL ALCOHOL IN THE PRESENCE OF THE STRONGLY ACIDIC AMBERLYST 15 SULFO CATION-EXCHANGE RESIN

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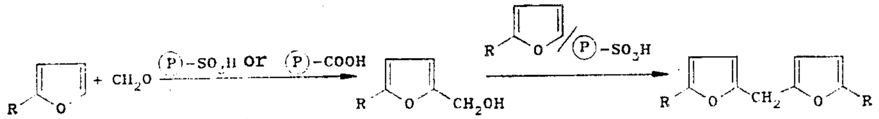
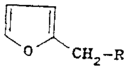
The corresponding 2-furylhetarylmethanes were obtained by the reaction of furan, thiophene, or pyrrole with furfuryl alcohol in the presence of the strongly acidic Amberlyst 15 cation-exchange resin in the H^+ form. The alkylation of furan and thiophene takes place regiospecifically in the 2 position, whereas 2-furyl-2-pyrrolyl- and 2-furyl-3-pyrrolylmethane in a ratio of 6.2:1 are formed in the case of pyrrole.

In an investigation of the hydroxymethylation of furan and silvan (α-methylfuran) in the presence of acidic catalysts (various cation-exchange resins in the H^+ form) [1] it was observed that weakly acidic (Amberlite IRC-50 with a carboxy function) and strongly acidic (Amberlyst 15 and Dowex 50W × 4 with an SO_3H function) cation-exchange resins protonate formaldehyde and catalyze the formation of the corresponding alcohols; in addition, strongly acidic cation-exchange resins (in contrast to the weakly acidic resin) protonate the furylcarbinols formed, as a result of which the hydroxymethylation products are converted to di(2-furyl)-methanes:



Ia R=H; b R=CH$_3$ I a,b

The present research was devoted to a study of the reactions of furfuryl alcohol (Ia) with furan, thiophene, and pyrrole in the presence of the strongly acidic* Amberlyst 15 sulfo cation-exchange resin in the H^+ form in order to obtain the corresponding 2-furylhetarylmethanes II-IV.



II-IV

II R=2-furyl III R=2-thienyl IV a R=2-pyrrolyl b R=3-pyrrolyl

The use of an ion-exchange resin in the H^+ form as an acidic catalyst in processes with the participation of acidophobic heterocyclic compounds makes it possible to decrease resinification and increase the yields of desired products as compared with traditional catalysts (dissolved acids) [1, 3].

The literature contains very little data on the synthesis and properties of di(hetaryl) methanes II-IV. While the potential areas of application of these substances are extremely diverse [4-6], the methods used to obtain them are primarily multistep processes and laborious, and the yields are low.

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*From the results of [2], the Hammett acidity function H_0 for Amberlyst 15 suspended in water is equal to −2.15 to −2.18, which corresponds to 35 to 38% aqueous H_2SO_4.

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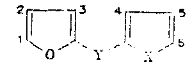
TABLE 1. Reaction of Furfuryl Alcohol (Ia) with Heterocycles in the Presence of Amberlyst 15 Sulfo Cation-Exchange Resin

Substrate	Molar ratio Ia:substrate:H^+	Reaction temp., °C	Reaction time, h	Alcohol Ia concn., % (according to GLC)	Reaction products (yield, %, according to GLC)
Furan	1 : 2 : 0,05	25	5	70	II (65), V (1 ... 2)
Thiophene	1 : 3 : 0,2	25	15	100	III (47), VI (22)
Pyrrole	1 : 3 : 0,2	100	28	90	IVa (62), IVb (~10), VI (6)

TABLE 2. Characteristics of the Synthesized Compounds



Compound	X	Y	bp, °C/mm (lit.)	PMR spectrum	
				Chemical shift, δ, ppm	Assignment of signals according to data in
II	O	CH_2	82/15 (79 ... 81/12 [8])	3,98 (H_Y), 6,04 (3-H, 4-H), 6,27 (2-H, 5-H), 7,29 (1-H, 6-H)	[15]
VI	O	CH_2OCH_2	65 ... 67/1	4,48 (H_Y), 6,33 (2-H, 3-H, 4-H, 5-H), 7,40 (1-H, 6-H)	[16]
III	S	CH_2	60/1 (73 ... 74/3,5 [9])	4,15 (H_Y), 6,09 (3-H), 6,30 (2-H), 6,89 (4-H), 6,95 (5-H), 7,14 (6-H), 7,31 (1-H)	[16]
IVa	NH	CH_2	70 ... 80/1*	3,97 (H_Y), 5,95 ... 6,35 (2-H, 3-H, 4-H, 5-H), 6,68 (6-H), 7,31 (1-H), 8,04 (br., NH)	[10, 16]

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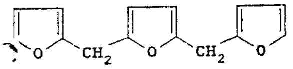
*In a mixture with isomer IVb.

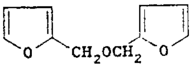
Thus di(2-furyl)methane (II) was obtained in 14% yield in the reaction of furan with formalin in the presence of 48% HF [7]. Compound II was synthesized in 1.7% yield via the same reaction but in the case of catalysis with 20% HCl. If alcohol Ia and furan are used as the starting compounds, the yield of II is 15% [8]. Furylthienylmethane III was obtained in 45-53% yield by metallation of thiophene with butyllithium and subsequent reaction with 2-chloromethylfuran [9]. 2-Furyl-2-pyrrolylmethane (IVa) was synthesized by reduction of 2-furyl 2-pyrrolyl ketone with lithium aluminum hydride or sodium borohydride in 40% and 75% yields, respectively) [6, 10].

We studied the reaction of alcohol Ia with furan, thiophene, and pyrrole in the presence of the strongly acidic Amberlyst 15 sulfo cation-exchange resin (exchange capacity 4.6 mg-eq H^+/g) and the effect on these processes of the reagent ratio [in the Ia interval: substrate:H^+ = 1:1-5:0.05-0.5 (moles)], the temperature (25-100°C), and the reaction time. The trend of the reactions was monitored by GLC and chromatographic mass spectrometry. The optimal conditions and the yields of the products of the investigated alkylation reactions are presented in Table 1.

The principal product of the reaction of furan with alcohol Ia in the presence of Amberlyst 15 resin is difuryl-methane II (m/z 148, M^+). The mass spectrum of this compound that we obtained coincides with that described in [11, 12] (there are inaccuracies in the spectrum of II in [13]).

The use of excess furan with respect to alcohol Ia slows down resinification; an increase in the amount of catalyst and raising the temperature above the indicated temperatures promote polymerization. An increase in the reaction time leads to the development of significant amounts of the product of subsequent transformation of difurylmethane II, viz., 2,5-di(2-furyl)furan (V) (m/z 228, M^+), which was identified from the coincidence of its mass spectrum with the described spectrum of V [11].


V


VI

The reactivity of thiophene in the reaction with alcohol Ia under the investigated conditions is lower than that of furan. The principal reaction product is furylthienylmethane III (m/z 164, M^+); the mass spectrum obtained coincides with that presented in a catalog [11]. In addition, significant amounts of difuryl ether (VI) (identified from the complete coincidence of the mass spectrum with the known spectrum [11]) are formed.

Experiments showed that an increased temperature is necessary for the alkylation of pyrrole with alcohol Ia in the presence of the sulfo cation-exchange resin. Two isomeric 2-furylpyrrolylmethanes IV (m/z 147, M^+) are observed in the reaction products. With respect to the assembly and relative intensities of the peaks the mass spectra of these substances that we obtained differ considerably from the spectrum of 1-furfurylpyrrole [14]: C-alkylation products — 2-furyl-2-pyrrolylmethane (IVa) and 2-furyl-3-pyrrolylmethane (IVb) (the mass spectra of these compounds have not been described in the literature) — and a small amount of difuryl ether (VI) (Table 1) are formed in the investigated reaction.

The PMR spectrum of II (Table 2) coincides completely with the spectrum presented in [15]. The spectra of III and VI have not been described in the literature; we assigned the signals in accordance with the data in [16]. We also obtained the PMR spectrum of individual furylpyrrolylmethane IVa, which basically coincides with the spectrum presented for this compound in [10]; some refinements in the assignment of the 1-H and 6-H signals in accordance with [6] were made. Since the yield of IVb is low in the alkylation of pyrrole, we were unable to isolate it in the individual state, and the PMR spectrum was obtained only in a mixture with isomer IVa. The signal of the protons of the methylene group of isomer IVb is observed at stronger field than in the case of isomer IVa (this is in agreement with the data in [16]), while the chemical shifts of the aromatic protons of the two compounds are extremely close to one another.

Thus the alkylation of furan and thiophene with alcohol Ia in the presence of Amberlyst 15 resin takes place regiospecifically in the 2 position of these heterocycles, while pyrrole is alkylated to a small degree also in the 3 position. In the alkylation of heterocycles with tert-butanol in the presence of the same cation-exchange resin [3, 17] substitution in the 3 position is characteristic for pyrrole more than for other heterocycles. In the case of thiophene a mixture of 2- and 3-tert-butylthiophene is formed, but alkylation in the α position of the heterocycles predominates in all cases.

As indicated in Table 1, considerable amounts of VI are formed along with thienylfurylmethane III in the reaction of alcohol Ia with thiophene. In the alkylation of furan this compound virtually is not formed, whereas in the case of pyrrole its yield is low (the formation of ether VI does not occur in the case of contact of alcohol Ia with the cation-exchange resin). An additional experiment showed that ether VI is formed in the reaction of the previously obtained individual dihetarylmethane III with alcohol Ia in the presence of Amberlyst 15 cation-exchange resin. It might be assumed that diarylmethane III, by blocking or modifying a certain part of the centers of the cation-exchange resin, promotes intermolecular dehydration of alcohol Ia, which leads to ether VI. Recent investigations [18] provide evidence that there are H^+ centers with different strengths and accessibilities in sulfo cation-exchange resins.

Similar processes evidently also occur in the alkylation of pyrrole but to a lesser extent.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in deuterochloroform were recorded with a Bruker WH-90/DS spectrometer with tetramethylsilane (TMS) as the internal standard. Chromatographic mass-spectrometric analysis of the reaction mixtures was carried out with a Kratos MS-25 chromatograph with an ionizing-electron energy of 70 eV. Analysis by GLC was carried out with a Chrom-4 chromatograph with a flame-ionization detector; the column was glass (1.2 m by 0.3 cm), the sorbent was 5% OV-17 on Chromosorb W-HP (80-100 mesh), the carrier gas was helium (60 ml/min), and the temperature was 150-180°C.

Additional purification of the vacuum-fractionated alkylation products was carried out by preparative GLC with a Pye—Unicam 105 chromatograph; the column dimensions were 2.1 m by 0.7 cm, the sorbent was 10% SE-30 on Chromaton N AW-DMCS (0.43-0.60 mm), and the temperature was 200°C. The Amberlyst 15 cation-exchange resin (exchange capacity 4.6 mg-eq H^+/g), furan, thiophene, and pyrrole (Fluka products) were used without additional purification. The furfuryl alcohol was fractionated in vacuo prior to use.

Di(2-furyl)methane (II). A mixture of 1.2 ml of alcohol Ia, 2 ml of furan, and 0.15 g of Amberlyst 15 cation-exchange resin was stirred for 5 h at 25°C, after which the reaction mass was removed from the catalyst by filtration. The catalyst was washed on the filter with ethanol, the combined filtrate was evaporated with a rotary evaporator, and the residue was fractionated in vacuo (Table 2). In order to obtain its PMR spectrum II was additionally purified by preparative GLC.

2-Furyl-2-thienylmethane (III) and Difuryl Ether (VI). These compounds were similarly obtained from 1 ml of alcohol Ia and 3 ml of thiophene in the presence of 0.5 g of Amberlyst 15 resin. The reaction conditions, constants, and yields of products are given in Tables 1 and 2.

2-Furyl-2-pyrrolylmethane (IVa) and 2-Furyl-3-pyrrolyl-methane (IVb). These compounds were obtained in the form of a mixture from 1 ml of alcohol Ia and 2.4 ml of pyrrole in the presence of 0.5 g of Amberlyst cation-exchange resin. The reaction conditions, constants, and yields of products (according to GLC) are presented in Tables 1 and 2. The mass spectra of IVa and IVb (the peaks with relative intensities > 10% are presented), m/z: IVa: 147 (M^+, 100), 118 (55), 91 (20), 80 (20), 67 (20); IVb: 147 (M^+, 100), 118 (75), 91 (25), 80 (15), 67 (20). Individual isomer IVa was isolated from the mixture of isomers IVa and IVb by preparative GLC. Individual isomer IVb could not be isolated because of its small amount. PMR spectrum (in a mixture with IVa): 3.87 (s, 2H, CH_2), 6.0-7.3 ppm (m, 6H).

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