Transetherification of difurazanyl ethers as a route to unsymmetrical derivatives of difurazanyl ether

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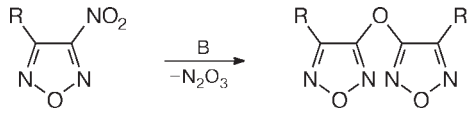
The reactions of 4,4′-dinitrodifurazanyl ether **1** with Na salts of hydroxyfurazans **2a—e** were studied. The nitrofurazanyl fragment is replaced by the more nucleophilic R-furazanyl group; the observed transetherification affords unsymmetrical derivatives of difurazanyl ether. The ratio of the rate constants for the successive reaction steps was determined.

Key work: furazans, difurazanyl ethers, hydroxyfurazans, transetherification.

Study of the behavior of 3-nitrofurazans (3-nitro-1,2,5-oxadiazoles) in the nucleophilic substitution revealed a number of interesting transformations of these compounds.[1,2] For example, it was shown that nitrofurazans containing electron-withdrawing substituents can be converted into the corresponding symmetrical derivatives of difurazanyl ether in the presence of salts with basic properties and weak nucleophiles (Scheme 1).[3—6]

Scheme 1



B is a base.

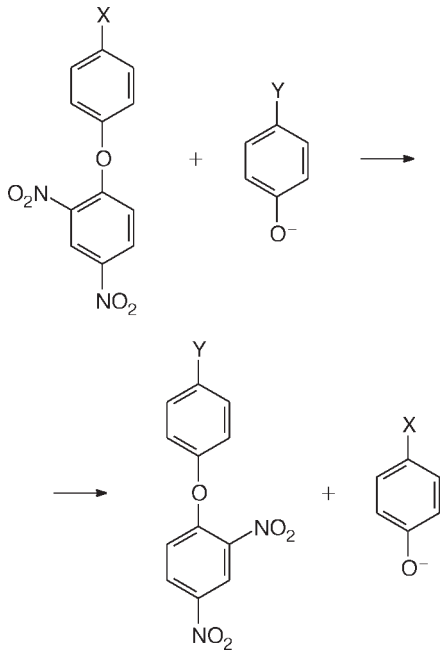
Meanwhile, only one unsymmetrical difurazanyl ether is known,[6] which is formed as a side product. The purpose of this work is to study the possibility of the synthesis of unsymmetrically substituted difurazanyl ethers.

Diphenyl ethers are known to undergo transetherification (Scheme 2)[7].

It was shown that aryloxy group with substituent X in the dinitro ether is displaced by the attacking aryloxy group with substituent Y in the case where the electron-releasing properties of Y are stronger than those of X. The attempts to carry out this reaction for an ether containing substituent X and a phenoxide with less electron-releasing substituent Y failed; the starting compounds were recovered unchanged.

To elucidate the possibility of performing a similar reaction in the furazan series (Scheme 3), we studied the reaction between 4,4′-dinitrodifurazanyl ether **1** [3] and the Na salt of 4-cyano-3-hydroxyfurazan **2a**,[8,9] which

Scheme 2



was expected to give unsymmetrical ether **3a** and the product of secondary transetherification, symmetrical ether **4** (Scheme 3).

Indeed, the reaction of ether **1** with salt **2a** in anhydrous acetonitrile at 50 °C afforded unsymmetrical ether **3a**. The GLC monitoring of the reaction showed that after 40 min, the reaction mixture contained approximately equal amounts of ethers **1** and **3a**. Note that 1 h after the beginning of the reaction, no symmetrical product **4** was detected, while after 2 h, the reaction mixture contained ~6% of this substance. Simultaneously,

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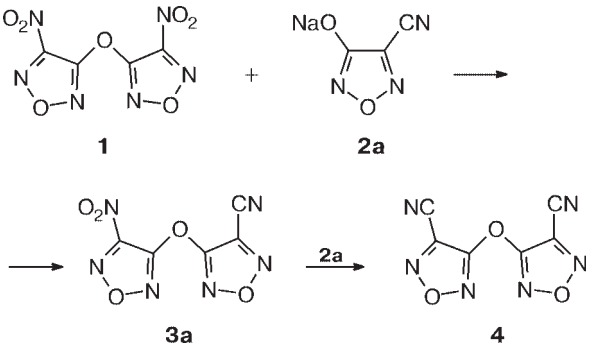
Scheme 3



14% of the starting ether **1** remained unchanged, and the proportion of the unsymmetrical product **3a** was 79%. The total yield of ethers in this reaction amounted to 99%.

The concentration profiles of compounds **1**, **3a**, and **4** are shown in Fig. 1. The curves are S-shaped, evidently, due to the fact that ether **1** was not added to the salt in one portion. Although the results cannot be regarded as a full-value kinetic experiment they still can be used to estimate qualitatively the ratio of the rate constants for the reaction steps. It can be seen from Scheme 3 that this process is a consecutive-parallel reaction. The ratio of the k_1 and k_2 constants for the first and second steps was determined by processing the data in terms of the equation[10]

$$N_1 = \frac{1}{k_2/k_1 - 1}\left[N_0 - N_0^{k_2/k_1}\right], \qquad (1)$$

where N_1 is the mole fraction of **3a**, N_0 is the mole fraction of **1**, k_1 and k_2 are the rate constants for the first and second steps, respectively. The results of the processing are shown in Fig. 2. This gave $k_2/k_1 = 0.05 \pm 0.02$.

When transetherification was carried out using hydroxyfurazan salts **2b—e**[11] containing substituents with

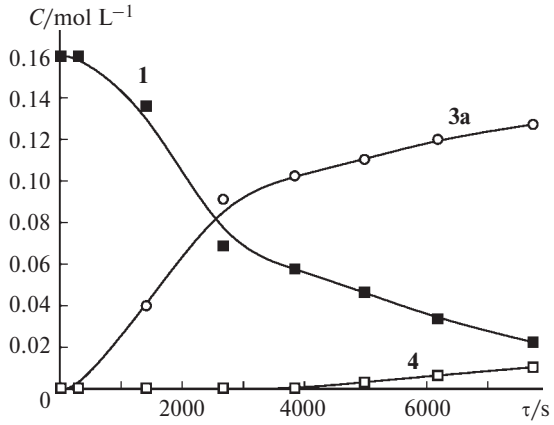


Fig. 1. Concentration profiles of the reaction components. The numbering of curves corresponds to the numbers of compounds in Scheme 3.

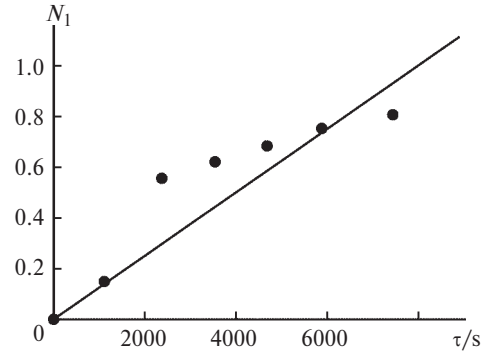
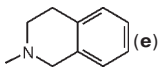


Fig. 2. Determination of the ratio of the rate constants for the first and second steps (see Scheme 3) from Eq. (1).[10]

stronger electron-releasing properties (Scheme 4), the formation of unsymmetrical ethers **2b—e** was completed as soon as after 5—15 min at 70—80 °C (according to TLC and GLC, the initial compound was absent from the reaction mixture). It is noteworthy that the process was not accompanied by secondary transetherification even when a twofold excess of salt **2b—e** was used and the reaction mixture was kept for 6 h.

Scheme 4

R = Me (**b**), NHMe (**c**), $N(CH_2CH_2)_2O$ (**d**),  (**e**)

The structures of the resulting difurazanyl ethers were confirmed by elemental analysis and by NMR, IR, and mass spectra (Tables 1 and 2). The presence of a narrow ($\Delta\nu_{1/2}$ = 8—15 Hz) singlet at about –40 ppm corresponding to the nitro-group nitrogen atom in the ^{14}N NMR spectrum is characteristic of all unsymmetrical ethers **3a—e**. The ^{13}C NMR spectra of ethers **3a—e** exhibit four signals due to the two furazan rings. The assignment of these signals presents no difficulties because the signal of carbon attached to the nitro group is appreciably broadened due to the ^{13}C—^{14}N coupling. The influence of the nitro group shows itself even two bonds away, giving rise to some broadening of the signal for C(2). The assignment is facilitated by the fact that the difference between the chemical shifts of the nitrofurazanyl carbon atoms $\Delta(\delta C(2) - \delta C(1))$ is fairly stable and varies from 2.3 to 3.2 ppm. The observed chemical shifts of the furazan-ring carbon atoms are in good agreement with the regularities that we elucidated previously.[11—13]

Table 1. Yields and characteristics of aymmetrical ethers **3a—e**

Compound	Yield (%)	M.p. /°C (solution)	Molecular formula	Mol. weight	Found / Calculated (%)			Mass spectrum, *m/z*
					C	H	N	
3a	75	49—50 (CCl_4)	$C_5N_6O_5$	224.09	26.67 26.80	—	37.56 37.50	224 $[M]^+$, 178 $[M - NO_2]^+$, 148 $[M - NO_2 - NO]^+$
3b	81	40—41 (hexane)	$C_5H_3N_5O_5$	213.11	28.32 28.18	1.36 1.42	33.01 32.86	213 $[M]^+$, 167 $[M - NO_2]^+$, 137 $[M - NO_2 - NO]^+$
3c	74	48.5—50 ($CHCl_3$)	$C_5H_4N_6O_5$	228.12	26.41 26.33	1.83 1.77	36.78 36.84	228 $[M]^+$
3d	69	84—85 ($CHCl_3$)	$C_8H_8N_6O_6$	284.19	33.89 33.81	2.85 2.84	29.50 29.57	284 $[M]^+$
3e	83	104—106 ($CHCl_3$)	$C_{13}H_{10}N_6O_5$	330.26	47.34 47.28	3.11 3.05	25.41 25.45	330 $[M]^+$

Table 2. Spectral characteristics of ethers **3a—e**

Compound	IR spectrum, ν/cm^{-1}	^{13}C NMR, δ						
		^{13}C NMR ($CDCl_3$)					^1H NMR	^{14}N NMR_{NO_2}
		C(1)	C(2)	C(3)	C(4)	Substituents		
3a	1595, 1570, 1500, 1490, 1400, 1350, 1230, 1195, 1035	153.8 151.2	156.1 153.9	162.2 160.8	128.9* 125.9	108.4* (C≡N); 104.4 (C≡N)		−38.6* −41.6
3b*	2990—2930, 1630, 1605, 1525, 1465, 1375, 1246, 1200	153.9	157.1	162.1	146.6	7.6 (Me)	2.25 (Me)	−37.8
3c	3408, 1624, 1608, 1564, 1544, 1360, 1256, 1192, 1040	151.4	154.4	152.6	149.2	30.7 (NMe)	3.01 (Me); 4.41 (NH)	−39.9
3d	2976, 2896, 2864, 1596, 1548, 1488, 1364, 1328, 1268, 1248, 1192, 1120	151.8	154.1	154.0	150.2	65.8 (CH_2O); 47.5 (CH_2N)	3.86 (CH_2O); 3.48 (CH_2N)	−40.1
3e	2952, 2904, 1592, 1586, 1544, 1488, 1464, 1440, 1424, 1388, 1356, 1328, 1296, 1248, 1232, 1192, 1032, 928	151.7	154.2	153.7	149.7	133.1 (C(11)); 131.8 (C(6)); 129.1 (C(10)); 128.5 (C(7)); 126.7 (C(8)); 126.2 (C(9)); 49.1 (C(5)); 45.0 (C(13)); 27.9 (C(12))	7.1 (Ar); 4.68 (C(5)); 3.84 (C(13)); 3.07 (C(12))	−39.9

* In acetone-d_6.

Thus, the possibility of transetherification in the series of dihetaryl ethers was demonstrated. This allowed the synthesis of a number of previously inaccessible unsymmetrical derivatives of difurazanyl ethers.

Experimental

Melting points were determined on a Koefler hot stage. ^1H, ^{13}C, and ^{14}N NMR spectra for natural abundances of isotopes were recorded on a Bruker AM-300 spectrometer operating at 300.13, 75.7, and 21.5 MHz, respectively. ^{14}N NMR chemical shifts are given in the δ scale and referred to external nitromethane; the $^1J_{^{15}N,^1H}$ values were measured using the INEPT technique. Mass spectra were recorded on Varian MAT CH-6 and Varian MAT CH-111 instruments (EI, 70 eV). IR spectra were measured on a Specord IR-75 spectrometer (KBr). GLC analysis was carried out on a Biochrom-2 chromatograph equipped by a flame ionization detector using an SE-54 capillary quartz column (25 m × 0.2 mm) and helium as the carrier gas. TLC on Silufol UV-254 plates was employed to monitor the reactions and to check the product purity (all the compounds fluoresce under UV light; the spots on chromatograms were visualized by spraying the TLC plates with a 5% solution of diphenylamine in hexane followed by irradiation with an UV lamp or heating; nitrofurazans appear as brown spots).

4,4′-Dinitrodifurazanyl ether (**1**) [4] and hydroxyfurazans[9,11] were prepared by procedures that we developed previously.

Synthesis of Na salts of hydroxyfurazans (2b—e) (general procedure). *Attention! Sodium salts of hydroxyfurazans explode*

on friction, impact, or fast heating, and K salts are even more dangerous to handle. These substances should be handled with special care. It is not recommended to prepare more than 100 mg of the salt in one operation. A 10% solution of sodium methoxide in methanol was added dropwise with stirring at ~20 °C to a solution of hydroxyfurazan (0.5 mmol) in anhydrous ether (15 mL). After addition of 3—5 drops of the methoxide, the precipitated crude product was filtered off. Further addition of the methoxide to the filtrate resulted in precipitation of a pure salt, which was filtered off and washed with ether and hexane at some intervals. It is noteworthy that the salt should be removed from the filter before hexane has evaporated (*otherwise, the risk of explosion is high!*) and transferred immediately into the flask where the next reaction will be performed. The product was dried to a constant weight and used for further transformations without additional purification. The yields of salts **2b—e** were 75—90%.

Reactions of dinitrodifurazanyl ether 1 with Na salts of hydroxyfurazans 2a—e (general procedure). A solution of ether **1** (1.5 mmol) in anhydrous acetonitrile (5 mL) was added dropwise to a stirred solution of salt **2a—e** (2 mmol) in the same solvent (10—15 mL) heated to 40 °C. The mixture was stirred until the initial compound was no longer detected (TLC, elution with CCl_4/CH_2Cl_2). The reaction mixture was diluted with CH_2Cl_2 (70 mL) and washed with water. The organic layer was dried with $MgSO_4$, filtered through a thin silica gel bed, and concentrated *in vacuo*. The crude product was recrystallized. In the case of compound **3a**, the product was isolated by column chromatography (SiO_2 60/100, elution with CH_2Cl_2/pentane, 1 : 1). The properties of the resulting compounds are presented in Tables 1 and 2. The spectroscopic and physicochemical properties of symmetrical ether **4** (m.p. 68—69 °C) corresponded to published data.[3]

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