SMILES REARRANGEMENT OF POLYFLUORO SUBSTITUTED 2-ACETYLAMINODIARYL ETHERS

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Polyfluoro substituted 2-acetylaminodiaryl ethers of the type $Ar_FOC_6H_4NHAc-o$ (II) that contain in the fluorinated ring an acceptor group, like analogs of the NH_2 group, undergo on heating in DMF the Smiles rearrangement accompanied by partial migration of the acetyl group and cyclization (in case of ethers (IIa, b)) to phenoxazine derivatives. In the case of heating in DMF, the rate constant of the rearrangement of diphenyl ether (IIa) is by an order of magnitude lower than the rate constant of the rearrangement of the rearrangement of its analog with an NH_2 group.

The most important factors that determine the possibility of carrying out a Smiles rearrangement are the degree of activation of the migrating aryl radical and the nucleophilicity of the attacking group. For diaryl ethers that contain a free amino group at the o-position, the rearrangement takes place only in case not less than two nitro groups are present in conjugate positions at the migrating ring [1-3]. Conversion of 2-acylaminodiaryl ethers without basic reagents proceeds considerably slower [4, 5].

Earlier we showed that polyfluorodiaryl ethers of the type $Ar_FOC_6H_4NH_2$ -o (I) that contain an acceptor group in the fluorinated ring, in contrast to 2,3,4,5,6-pentafluoro-2'aminodiphenyl ether, undergo in DMF conversion to the isomeric polyfluoro-2-hydroxydiarylamines [6]. In this investigation we have studied the possibility of carrying out the Smiles rearrangement of N-acetyl derivatives of ethers (I).

Polyfluoro-2-acetylaminodiaryl ethers (II), prepared by refluxing compounds of type (I) with AcCl in benzene, give on heating in DMF a mixture of the 2-hydroxy-N-acetyldiarylamine (III), its O-acetyl containing isomer (IV), and in the cases of starting compounds (Ia, b) also a phenoxazine derivative of type (V). The quantitative composition of the reaction mix-tures, determined by means of ¹⁹F NMR spectroscopy, is given in Table 1.



Scheme 1

 $\mathbf{R}=C-\mathbf{NO}_{2}\left(a\right),\quad C-CF_{3}\left(b\right),\quad \mathbf{N}\left(\,c\,\right).$

Formation of o-hydroxy substituted diarylamines in this process unambiguously points to realization of the Smiles rearrangement of starting ethers (II). The presence of compounds of type (IV) in the reaction mixtures is evidence of the fact that the rearrangement is accompanied by migration of the acetyl group from the nitrogen to the oxygen atom. An analogous conversion was found earlier in the nonfluorinated series [4, 5, 7]. The ratios of the amounts of isomeric compounds (III) and (IV) depends on the nature of group R. In the reaction mixture

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| - <u></u> | Reaction | conditions | Compositic | on of the re | eaction mixt | ure (by ¹⁹ F NMR), % |
|-----------|-----------|------------|------------|--------------|--------------|---------------------------------|
| Compound | т, °С | time, h | (11) | (III) | (IV) | (V) * |
| (IIa) | 100 90 | 4 | - 5 | 47 43 | 13 16 | 40 31 |
| (IIb) | 100 90 | 5 4 | 13 | 70 67 | 9 5 | 21 15 |
| (IIc) | 70 | 1 | - | 51 | 49 | - |

TABLE 1. Rearrangement of Polyfluorodiaryl Ethers (II)

*Phenoxazines (V) are described in [11].

obtained from ether (IIc) they are found in about equal proportions. Isomers (IIIc) and (IVc) were isolated in pure form and characterized by means of IR spectra and ¹⁹F NMR in THF.

Dissolving pure samples of (IIIc) and (IVc) in DMF leads to rapid (during the time of dissolving and recording the ¹⁹F NMR spectra) establishing of an equilibrium in which the ratio of the isomers is ~1:1. On the basis of literature data of analogs [8] it may be assumed that the observed N \neq O migration of the acetyl group takes place through an intermediate of a cyclic structure of type (VI).



We have shown that heating diarylamine (IIIa) in DMF at $100^{\circ}C$ does not lead to its conversion to phenoxazine (Va). When we adopt Scheme 2 for the rearrangement of diaryl ethers (II), which includes intermediate formation of spirocomplex (VII) and phenoxy anion (VIII) (cf. [1, 7, 9]), it may be assumed that the presence of compounds of type (V) in the reaction mixture is caused by cyclization of the latter.



Earlier we showed that lowering the acceptor power of group R in polyfluoro-2-aminodiaryl ethers (1) reduces the rate of their rearrangement [6]. It can be seen from the data of Table 1 that ether (IIb), which contains a CF_3 group at the fluorinated ring, reacts somewhat slower than the nitrosubstituted analog (IIa). At the same time the conversion temperature of compound (IIa) is abnormally low. To establish the cause of the increased reactivity of the latter and also to determine the influence of the N-acetyl group on the rate of the rearrangement, we have studied the kinetics of the conversion of ethers (IIa) and (IIc) in DMF. The degree of conversion of the starting compound was determined by means of the change of the integral of the signals of the fluorine atoms in the ¹⁹F NMR spectra in the course of time. The rate constants of the rearrangement of ether (IIa) in DMF at 90°C was calculated with the first-order equation

$$k_{\rm H} = \frac{1}{t} \ln \frac{C_0}{C} = \frac{1}{t} \ln \frac{H_0}{H}$$
(1)

in which H_0 is the initial integral of the signals of the fluorine atoms at positions 3 and 5 (or 2 and 6) in the spectrum of ether (IIa), H the integral of the same fluorine atoms in the spectrum at time t, and t the time in seconds.

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| Characteristics | |
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| Reaction Conditions, | |
| TABLE 2. | |

| | Reaction | conditions | | | Found | Calci | ulated, % | | | TD concettering | δ ¹⁹ F, ppm |
|----------|----------|------------|----------|--|------------------------------|---------------------|-----------------------|--------------|--|------------------------|--|
| Compound | T, °C | time, h | - Yield, | mp, ^o C (solvent) | C | Н | ţ. | N | Empirical formula | v, cm ⁻¹ | (rel. intensi- ties) |
| (IIa) | đq | - | 6 | 133-134 (benzene-petroleum | <u>48,49</u> <u>48,85</u> | 2,17 2,34 | $\frac{21,70}{22,08}$ | 7,85 8,14 | C14H8F4N2O4 | 1700 (CO) 3440 (NH) | 10,6, 16,1 (1:1) |
| (411) | * | | 38 | ether) 133-134 | 50,47 49,06 | <u>1,91</u> 2,19 | 35,91 36,22 | 3,61 3,82 | C ₁₅ H ₈ F7NO2 | 1700 (CO) 3440 (NH) | 10,1, 22,0, 107,4 (2:2:3) |
| (IIc) | * | - | 88 | (petroleum ether) 106-108 (benzene-petroleum | 52,17 52,01 | 2,59 2,68 | 24,99 25,32 | 9,23 9,33 | C ₁₃ II ₈ F ₄ N ₂ O ₂ | 1710 (CO) 3450 (NH) | 7,6, 73,2 (1:1) |
| (IIIa) | 20 | | 63 * | ether) 1/7-149 (benzene) | 48,60 48,85 | 2,35 | 22,09 22,08 | 7,90 8,14 | C ₁₄ H ₈ F ₄ N ₂ O ₄ | 1690 (CO) 3580 (OH) | $\begin{array}{c} 14,3; \ 21,8, \ 25,1 \\ 15,2, \ 21,2, \ 24,9 \\ (2:1:1) \end{array}$ |
| (qIII) | 110 | ო | 52 | 147-151 (benzene-petroleum ether) | <u>49,06</u> | 2,06 2,19 | 35,85 36,22 | 3,95 3,82 | C ₄₅ H ₈ F ₇ NO ₂ | 1700 (CO) 3580 (OH) | 20.5, 24.2, 107.2 20.6, 24.6, 107.6 † (3:1:3) |
| (IIIc) | 70 | | 14 | | | | | | C13118F4N2O2 # | 1700 (CO) 3580 (OH) | 20,2, 71,2 (1:1) |
| (IVc) | 02 | - | 42 | 78-80 (petroleum ether) | 52,11 52,01 | 2,80 | 25,30 25,32 | 9,18 9,33 | C ₁₃ H ₈ F ₄ N ₂ O ₂ | 1705 (CO) 3405 (NH) | 5,0, 68,5 (1:1) |

*We used 20% aqueous DMF. +In DMF. #m/z_{exp} 300.0496; m/z_{calc} 300.0522.

The lowering of the value of $k_{\rm H}$ (1.32·10⁻⁴ sec⁻¹) against the rate constant of the rearrangement of 4-nitro-2,3,5,6-tetrafluoro-2'-aminodiphenyl ether (Ia) in DMF at 90°C (12.2 × 10⁻⁴ sec⁻¹ [6]) complies with the data on the nature of the influence of the N-acetyl group on the rearrangement of o-aminodiphenyl ethers in the nonfluorinated series [4, 5].

Study of the kinetics of the conversion of compound (IIc) in DMF at 50°C showed that the value of the rate constants calculated with a first-order equation monotonically decrease in the course of time. The order of the reaction, determined with Eq. (2), proved to be 1.6.

$$n = \lg \frac{\omega_{0,2}}{\omega_{0,1}} / \lg \frac{C_{0,2}}{C_{0,1}} [10]$$
(2)

in which $\omega_{0,1}$ and $\omega_{0,2}$ are the initial reaction rates at initial concentrations $C_{0,1}$ and $C_{0,2}$.

The broken order of the reaction and the relative easiness of the rearrangement of ether (IIc) may be explained by the appearance of basic catalysis that consists of removal of a proton from the NHAc group in complex (VII) by the aza group of the pyridine ring. The structures of the compounds prepared in this investigation were determined on the basis of analytical and spectral data (see Table 2). In the ¹⁹F NMR spectra of diarylamines (IIIa) and (IIIb) the ortho fluorine atoms appear as two signals, which points to their nonequivalence. This may be caused by hindered rotation of the fluorinated aryl ring around the C_{ar}-N bond. In accordance with this is the fact that increasing the temperature to 70°C leads to coalescence of these signals at 23.8 ppm for ether (IIIa) and at 23.0 ppm for ether (IIIb).

Compounds (IVa) and (IVb) were not isolated from the reaction mixtures. The structures assigned to them are based upon comparison of IR and ¹⁹F NMR spectral data of mixtures of these compounds with the corresponding isomeric diarylamines (IIIa) and (IIIb) with the spectra of the same compounds (IIIa) and (IIIb). Thus, the IR spectra of compounds (IVa) and (IVb) contain bands at 1700 (CO) and 3440 cm⁻¹ (NH); the ¹⁹F NMR spectra (in DMF) of diarylamine (IVa) contains signals at 10.3 and 14.7 ppm with an intensity ratio of 1:1, and that of diarylamine (IVb) contains signals at 12.3, 19.0, and 108.7 ppm (2:2:3).

EXPERIMENTAL

The ¹⁹F NMR spectra were recorded on a Varian A 56/60 (56.4 MHz) spectrometer in THF. Temperature surveying was carried out on a Bruker HX-90 (84.6 MHz) spectrometer, and kinetic measurements on a Bruker WP-200 SY (188.28 MHz) spectrometer. Chemical shifts are reported in ppm from C_6F_6 . Molecular masses were determined on a Finnigan MAT 8200 instrument. IR spectra were taken on a UR-20 spectrometer from CHCl₃ solutions. As solvent we used DMF containing 0.3% of water, dried over molecular sieves NaA and NaX.

<u>Preparation of Polyfluoro-2-acetylaminodiaryl Ethers (II)</u>. One hundredth mole of polyfluoro-2-aminodiaryl ether (I) [6] and 0.012 mole of acetyl chloride were refluxed in 50 ml of dry benzene. The mixture was cooled to room temperature, poured out in water, and extracted with ether. The ethereal layer was extracted with water and dried over $CaCl_2$. The residue obtained after evaporation was washed with petroleum ether. Yield and charcteristics of prepared compounds (II) are listed in Table 2.

<u>Rearrangement of Polyfluoro-2-acetylaminodiaryl Ethers (II)</u>. A solution of 0.20 g of compound (II) in 5 ml of DMF was stirred under the conditions given in Table 1. The reaction mixture was poured out in water and extracted with ether. The residue obtained after evaporation of the ether was analyzed by means of ¹⁹F NMR spectroscopy (Table 1). Compounds (III) and (IVc), prepared under the conditions given in Table 2, were isolated by chromatography on plates with silica gel L 5/40 in $CHCl_3$.

<u>Heating of o-Hydroxydiarylamine (IIIa) in DMF</u>. A mixture of 0.10 g of compound (IIIa) and 0.25 ml of DMF was heated at 100°C for 3 h. According to ¹⁹F NMR spectral data, the reaction mixture contained diarylamines (IIIa) and (IVa) in the ratio of 74:26.

<u>Kinetic measurements</u> were carried out as described in [6]. The order of the conversion reaction of ether (IIa) was determined by keeping the latter in ampuls in amounts of 0.10 and 0.02 g in 0.25 ml of DMF. The difference in the calculated values of $k_{\rm H}$ at these concentrations is ~5%.

Ampuls containing 0.02 g of compounds (IIa) in 0.25 ml of DMF were stored in a thermostat at 90°C. Before recording the ¹⁹F NMR spectrum the ampuls were quickly cooled to -30°C and the recording was carried out at room temperature. The error in the determination of $k_{\rm H}$ (Ac) according to Eq. (1) is ~1.5%.

The order of the conversion reaction of ether (IIc) was determined at initial concentrations of 0.1, 0.5, and 1.0 mole/liter of the starting compound at 50°C according to Eq. (2). The values of $\omega_{0,1}$ and $\omega_{0,2}$ were determined graphically by means of the slope of the tangent lines drawn through the first points of the curves of the dependence of the concentration from the time.

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DIRECTED SYNTHESIS OF MACROCYCLIC PHENYLENE SULFIDES

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A method has been developed for the directed synthesis of macrocyclic phenylene sulfides with 4-8 phenylene sulfide fragments, by condensation of dihaloaromatic compounds of various types with sodium sulfide or dithiophenate. A combination of this method with high dilution techniques has afforded pure macrocycles in high yields, and the macrocycle with six phenylene sulfide fragments in yields as high as 73%.

Macrocyclic phenylene sulfides (MPS), first detected by mass spectrometry [1] in the low-molecular-weight products of the polycondensation of 1,4-dichlorobenzene with Na₂S, have so far received little attention. Cyclic tetra- and penta-1,4-phenylene sulfides were then isolated in the pure state [2]. These compounds are of interest as selective complexing agents and polymerizable monomers for the synthesis of polyphenylene sulfides. From the lowmolecular-weight fraction from the polycondensation of 1,4-dichlorobenzene with Na₂S, we isolated pure, crystalline hexa-, hepta-, and octa-1,4-MPS [3, 4], the main component of the macrocyclic fraction being the cyclic hexamer. The cyclic trimer, cyclo-(tris-1,3-phenyl sulfide), has been obtained from the polycondensation products of 1,3-dihalobenzene and Na₂S [5, 6]. The structures of these compounds were confirmed by spectral methods and x-ray diffraction analysis. The MPS have also been obtained by the thermal degradation of linear poly-1,4phenylene sulfide under high vacuum [7].

It is noteworthy that in all instances 1,4-disubstituted MPS are formed as multicomponent mixtures of oligo-homologs with from four to eight phenylene sulfide untis in the ring, which complicates their isolation in the pure state. The overall yield of the macrocyclic fraction in the polycondensation of 1,4-dichlorobenzene with Na₂S does not exceed 3% [1].

The present investigation was aimed at developing selective methods for the synthesis of MPS. The starting materials used for this purpose were the polynuclear α,ω -dihalodiaryl

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