FORMATION OF NITROXYL RADICALS CONTAINING FLUORINE β -ATOMS IN THE REACTION OF NITRONES WITH XENON DIFLUORIDE

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One of the possible ways of activating nitrones in nucleophilic addition reactions is the one-electron oxidation of them to cation radicals (CR) which on reacting with nucleophiles are capable of forming nitroxyl radicals (NR) [1, 2]. A cation radical mechanism is also considered as one of the probable paths for the formation of spin adducts from spin traps [3-5]. In this investigation we have studied the possibility of obtaining NR containing a fluorine β -atom by the reaction of different types of nitrones with XeF₂ in CH₂Cl₂. The choice of this system is governed, on the one hand, by its enabling CR to be generated [6] and, on the other, by its enabling a fluorine atom to be introduced into a multiple bond [7].

EXPERIMENTAL

We used Teflon ampuls in the EPR experiments; the concentration of the initial nitrones in methylene chloride was 10^{-2} M. After adding 1-2 crystals of XeF₂ to the ampul containing the nitrone solution the ampul was shaken and placed in the resonator of an RÉ-1306 EPR spectrometer. We used Fremy's salt to measure the g-factor ($a_N = 13.09$ Oe, g = 2.0057 [8]). The synthesis of the nitrones is described in [9-12]. In our study we used 5,5-diemthylpyrrolidine-N-oxide (DMPO) and 3,3,5,5-tetramethylpyrrolidine-N-oxide (TMPO) from the Sigma company. Methylene chloride was purified as described in [13].

<u>3-Nitroso-2,2,4,4-tetramethyl-5-phenyl-5-fluoroimidazolidine-1-oxide (IIIm)</u>. To a solution of 2.0 g of 1-nitroso-2,2,5,5-tetramethyl-4-phenyl-3-imidazoline-3-oxide (Im) in 50 ml of dry CH_2Cl_2 in a Teflon flask was added 1.0 g XeF₂ and the mixture stirred for 20 h at 20-25°C until the appearance of an intense crimson color. Half of the solvent was removed by blowing air through the reaction mixture and the solution chromatographed on a column containing silica gel (L100/160 from the Chemapol company), the product being eluted with $CHCl_3$. The colored solution was evaporated on a rotating evaporator, the residue dissolved in hexane and the solution filtered. After evaporating off the hexane a crimson-colored solid was obtained. Yield of (IIIm) 1.5 g (70%), mp 80-82°C (subl.). Found (%): C 58.9; H 6.4; F 7.5; N 15.8. Calculated for $C_{13}H_{17}FN_3O_2$ (%): C 58.6; H 6.4; F 7.1; N 15.8.

(IIIm) can be stored at -10° C for approximately 10 days. At ~20°C in air (IIIm) is converted into the original compound (Im) over the course of 1-3 days. The remaining NR containing fluorine β -atoms were not isolated, but their EPR spectra (Tables 1-3) were observed over the course of several hours and, in certain cases, over several days.

| | | - | - | | | | |
|--|--|---|--|--|--|---|--|
| NR | ^a N, 0e | ^𝔅 F, 0e | g-Factor | NR | ^a №.0e | a _₽ ,0e | g-Factor |
| (IIIa) (IIIb) (IIIc) (IIId) (IIIm) (IIIm) (IIIn) (IIIr) (IIIr) (IIIt) (IIIt) (IIIu) | $\begin{array}{c} 12.1\\ 12.1\\ 12.93\\ 12.79\\ 12.93\\ 12.55\\ 12.10\\ 12.65\\ 12.65\\ 12.93\\ 12.93\\ 12.65\\ \end{array}$ | 50.9 50.6 50.33 49.50 45.38 44.14 45.65 39.88 47.58 23.38 41.25 | 2,0070 2,0072 2,0073 2,0070 2,0071 2,0068 2,0073 2,0064 | (IV c) (IV e) (IVf) (IVg) (IVh) (IVi) (IVk) (IVk) (IVp) (IVs) | $\begin{array}{c} 13.06\\ 12.93\\ 12.38\\ 12.24\\ 12.38\\ 12.65\\ 12.65\\ 12.65\\ 12.65\\ 12.93\\ 12.79\\ 12.10\\ \end{array}$ | 50,46 50,73 46,48 44,83 45,51 48,13 49,50 47,03 47,03 47,71 47,85 | 2.0072 2.0068 2.0072 2.0073 2.0070 2.0073 2.0070 2.0069 2.0069 2.0068 2.0068 |

TABLE 1. Magnetic-Resonance Parameters of the Nitroxyl Radicals (III) and (IV)

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TABLE 2. Magnetic Resonance Parameters of NR (XV) and (XVI), NNR (XVIII) and INR* (XXI) and (XXII)

| Radical | ^a N, 0e | a _F ,0e | g-Factor | Radical | a _N .0e | a _F ,0e | g-Factor |
|------------------------------------|--|----------------------------------|---|---------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
| (XVa) (XVb) (XVIa) (XVIb) | $ \begin{array}{c c} 12.15\\ 11.96\\ 11.47\\ 12.54 \end{array} $ | 45.63 47.85 46.96 34,53 | $\begin{array}{c} 2.0064 \\ 2.0067 \\ 2.0069 \\ 2.0068 \end{array}$ | (XVI c) (XVIII) (XXI) (XXII) | 11,74 7.29 7.98 ** 8,25 *** | $34.09 \\ 22.14 \\ 32.45 \\ 16.50$ | 2.0065 2.0073 2.0067 2.0062 |

*INR is the iminonitroxyl radical.

 $**a_{\rm N}^3 = 3.99$ Oe.

 $***a_N^3 = 4.13$ Oe.

TABLE 3. Magnetic Resonance Parameters of $\beta,\beta-Difluoro-Substituted Nitroxyl Radicals$

| NR | ^a N,0e | ^a F∙0e | g-Factor | NR | a _N ,0e | a F , 0e | g- Factor |
|----------------------|-------------------------|-------------------------|------------------------------|-------------------|--------------------|-----------------|--------------------|
| (V) (VI) (XVe) | 11.83 12.38 11.00 | 20.21 22.41 25,03 | $2.0065 \\ 2.0067 \\ 2.0069$ | (XXIII) (XXIV) | 11.83 11,83 | 17.60 17,46 | $2,0064 \\ 2,0067$ |

DISCUSSION

At present there are data in the literature on several NR containing fluorine β -atoms obtained by the reaction of nitrones with AgF₂ [14-16] or in the photolysis of bis-(tri-fluoromethyl)peroxide in the presence of TMPO [17].

In Table 1 the magnetic resonance parameters (MRP) are presented of NR containing one fluorine β -atom (III) and (IV) which are formed from nitrones, derivatives of 1-nitroso-(I) and 1-nitro-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (II), in their reaction with xenon difluoride in CH₂Cl₂.

The EPR spectra of NR containing a fluorine β -atom (III), (IV) comprise a doublet of triplets characteristic of the case $a_N \ll a_F$. Furthermore, in the EPR spectrum of the NR (IIIa), which is formed initially from the aldonitrone (Ia), a hyperfine interaction (HFI) constant at the β -proton $a_H\beta$ = 4.68 Oe is observed. In the EPR spectrum of the deuterated analog of (IIIb) this additional HFI is absent.

While the value of the HFI constant a_N varies from 12 to 13 0e, the values of a_F depend strongly on the nature of the substituent R (Table 1). For the NR (IIIa-s) and (IVc-s) the value of the HFI constant a_F varies from 40 to 50 0e and is decreased on substitution by hetero-atoms in the same sequence as the values of a_H in the spin adducts formed from aldonitrones: C>S>O>F [15-17]. However, it should be noted that the range of variation in a_F is substantially greater (20-60 0e) than for a_H (4-20 0e) [14-17]. The presence of two asymmetrical C atoms in the NR (IVk) leads to the observation of two EPR spectra differing to some extent in the values of a_F and the g-factor belonging to the two diastereomers.

On treating the 4-phenyl-3-imidazoline-3-oxides (VII) and (VIII), which have an amino group in the 1 position, with XeF₂ the appearance of two groups of signals differing in the values of a_F is observed in the EPR spectra, which belong respectively to the NR (IX) (a_N = 12.65, a_F = 53.90 Oe, g = 2.0070), (X), (a_N = 12.65, a_F = 46.64 Oe, g = 2.0076) and (XI) (a_N = 12.65, a_F = 53.08 Oe, g = 2.0070), and (XII) (a_N = 12.65, a_F = 48.40 Oe, g = 2.0069).



EPR spectra having similar MRP are also observed on treating the N oxides (XIII) and N,N-dioxides of 2H-imidazole (XIV) with XeF_2 (Table 2). In the reaction of the compound (XIVa), which has two nonequivalent nitrone groups, with XeF_2 the formation is observed of the two NR (XIVa) and (XVIb) which differ markedly in the values of the HFI constants a_F . The MRP corresponding to them was assigned on the basis of a comparison with the MRP of the NR (XVIc) which is formed from the compound (XIVc) having two equivalent phenylnitrone groups (Table 2).



 $\begin{array}{l} R=C_6H_5, \ R^1=CH_3 \ (a); \ R=CH_3, \ R^1=C_6H_5 \ (b); \ R=C_6H_5, \ R^1=C_6H_5 \ (c); \ R=C_6H_5, \\ R^1=H \ (d); \ R=C_6H_5; \ R^1=F \ (e). \end{array}$

In the reaction of 4H-imidazole-1,3-dioxide (XVIIa) with XeF₂ the appearance is observed of an intense blue color typical of nitronylnitroxyl radicals (NNR). The EPR spectrum of the NNR (XVIII) is a doublet of partially overlapping quintets due to the HFI with the two magnetically equivalent nitrogen atoms and the F β -atom: $a_F \approx 1/3 a_F$ (Table 2). The EPR spectra of the iminonitroxyl radicals (INR) (XXI) and (XXII) formed in the reaction with XeF₂ of the 4H-imidazole N-oxides (XIX) and (XXa) differ substantially in the HFI constants a_F : a_F (XXI) \approx $2a_F$ (XXII). Nevertheless, even in the radical (XXII) having a fluorine atom remote from the nitroxyl group a fairly large value is observed for the constant a_F : $a_F = 2a_N^{-1} = 4a_N^{-3}$ (Table 2).



The data for the EPR spectra of NR having two fluorine β -atoms, which are the ultimate fluorine-containing radicals in the reaction of various derivatives containing the aldonitrone group with XeF₂ (1)-(3), are presented in Table 3. For the majority of cases the relationship $a_N < a_F < 2a_N$ is characteristic. The HFI constants a_N in these radicals are approximately 1 Oe lower than in NR having one F β -atom.

The NR containing fluorine β -atoms considered above may in principle serve as models of spin adducts of an α -fluoronitrone with various radicals.



The wide range of variation in the HFI constants a_F , as well as the high sensitivity of their values to various structural factors, makes the search promising for paths for the synthesis of α -fluoronitrones, potential spin traps.

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CONCLUSIONS

1. In the reaction of different types of nitrones with xenon difluoride in methylene chloride, nitroxyl radicals containing one or two fluorine β -atoms are formed.

2. A method is proposed for obtaining stable nitroxyl radicals containing fluorine β -atoms.

3. The values of the HFI constants a_F at the fluorine β -atom are very sensitive to various structural factors and vary over a wide range, from 20 to 60 Oe.

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