New fluorinated isoxazolidines

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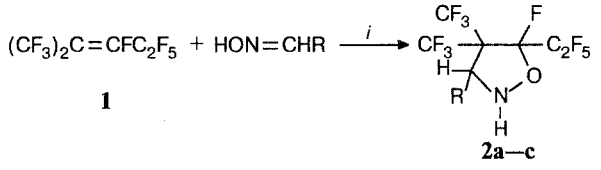
A simple procedure for the synthesis of fluorinated isoxazolidines from perfluoro-2-methylpent-2-ene and aliphatic aldoximes is described.

Key words: isoxazolidines, synthesis; perfluoro-2-methylpent-2-ene, aldoximes.

In this work the reactions of perfluoro-2-methylpent-2-ene (**1**) with aldoximes as *O*-nucleophiles have been thoroughly investigated. As in the case of alcohols,[1] an olefin reacts with oximes only in the presence of a base.

The reaction of equimolar amounts of olefin **1**, an aldoxime, and Et_3N (catalyst) affords isoxazolidines (**2a—c**) in moderate yields.



R = Me(**a**, 52%); Et (**b**, 43%); Pr (**c**, 37%)

i. NEt_3, 0 °C, diglyme

Benzaldoxime does not form the corresponding isoxazolidine (**2d**, R = Ph).

One can assume that the oxime anion attacks the C atom of the multiple bond in olefin **1** (Scheme 1).

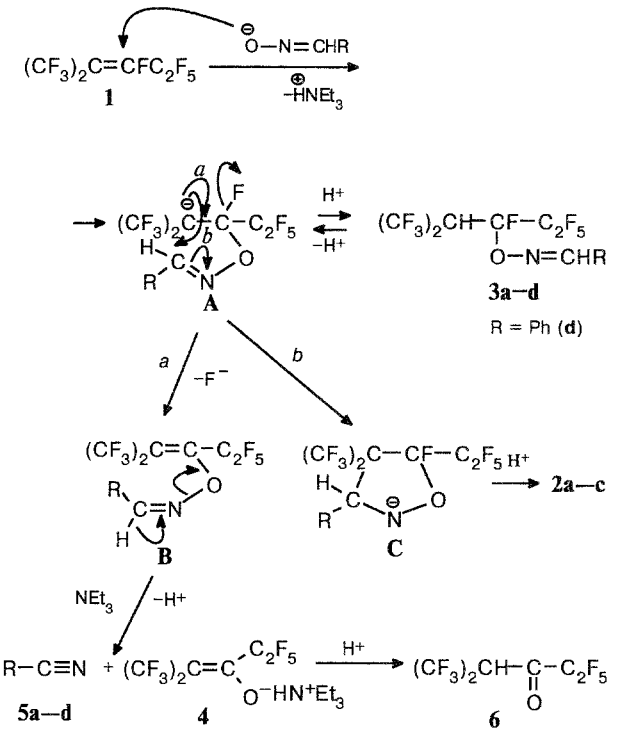
Carbanion **A** is formed by the attack of the *O*-nucleophile, and either attaches a proton to form a type **3** adduct, or eliminates F^- to give unsaturated *O*-alkoxime (**B**) (path *a*), or is transformed to the anion of isoxazolidine (**C**) as a result of intramolecular addition* to the C=N bond (path *b*).

Apparently, compound **B** formed *via* path *a* is unstable and decomposes giving triethylammonium enolate (**4**) and nitrile (**5**).

When catalytic amounts of base are used, along with the major reaction products **2**, **4**, and **5**, adducts **3** are also found; the latter are totally dehydrofluorinated if the amount of base is increased to equimolar.

Treatment of the reaction mixture with 15 % HCl transforms enolate **4** to volatile 2-hydroperfluoro-2-methylpentanone-3 (**6**), and nitriles **5a—c** are transferred to the aqueous phase. Thus, isoxazolidine **2a—c** can be easily isolated by distillation.

Scheme 1



In the case of benzaldoxime only adduct **3d** was isolated in moderate yield, *i.e.*, the cyclization reaction (path *b*) does not proceed at all. The presence of enolate **4** and benzonitrile **5d** in the reaction mixture (and ketone **6** after treatment of the reaction mixture with 15 % HCl), was confirmed by ^{19}F NMR spectroscopy, chromatography, and GC—mass spectrometry.

The structures of the new isoxazolidines **2a—c** were determined unequivocally by spectral methods. Thus, in

*It is known that perfluorinated carbanions are able to add to activated multiple bonds.[2]

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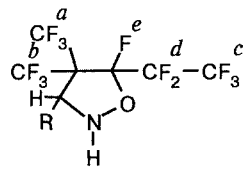
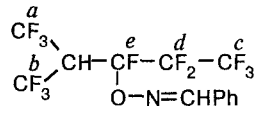
Table 1. ^{19}F NMR data for compounds **2a—c** and **3d**



2a—c



3d

Compound	Isomer	δ, ppm					*J*/ Hz
		a	*в*	*c*	*d*	*e*	
2a	*trans*	−16.8	−12.5	2.8	41.0(A) 44.6(B)	37.4	11(*a*—*b*); 31(*a*—*e*); 11(*a*—B); 17(*b*—B); 5(*b*—*e*); 32(*b*—A); 17(*c*—*e*); 10(*e*—A); 288(A—B)
	cis	−18.1	−15.4	2.5	43.1(A) 45.3(B)	24.9	27(*b*—A); 9(*e*—A); 282(A—B); 15(*c*—*e*)
2b	*trans*	−16.9	−12.6	3.0	41.2(A) 44.5(B)	37.5	11(*a*—*b*); 30.5(*a*—*e*); 10.8(*a*—B); 16.9(*b*—B); 4.8(*b*—*e*); 31.8(*b*—A); 17(*c*—*e*); 9.8(*e*—A); 290(A—B)
	cis	−18.0	−15.5	2.6	43.1(A) 45.3(B)	24.8	29(*b*—A); 9(*e*—A); 282(A—B); 16(*c*—*e*)
2c	*trans*	−17.1	−12.5	3.1	41.5(A) 44.3(B)	37.3	290(A—B); 10.5(*a*—*b*); 31(*a*—*e*); 11(*a*—B); 17(*b*—B); 5(*b*—*e*); 32(*b*—A); 16.9(*c*—*e*); 10(*e*—A)
	cis	−18.1	−15.7	2.7	43.1(A) 45.3(B)	24.8	283(A—B); 16(*c*—*e*); 28(*b*—A); 9(*e*—A)
3d	—	−17.4	−16.9	2.2	42.8(A) 44.5(B)	35.2	288(A—B); 11.4(*c*—*e*)

Table 2. Mass spectral data for isoxazolidines **2a—c** (EI, 70 eV)

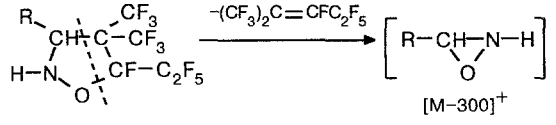
Compound	Molecular mass	R	Isomer	I_{rel}(%), *m/z*								
				M^+	$[M-R]^+$ 344	$C_2F_5^+$ 119	CF_3^+ 69	$[M-300]^+$	256	Other ions 43	42	41
2a	359	Me	*trans*	8.9	13.9	15.9	21.7	100	4.9	13.9	23.1	2.2
			cis	6.1	2.1	10.5	17.0	100	1.7	14.6	21.3	2.1
2b	373	Et	*trans*	6.1	100	22.5	20.7	24.6	14.9	—	—	2.7
			cis	3.0	21.3	20.1	32.7	100	6.3	—	5.2	5.3
2c	387	Pr	*trans*	4.6	100	21.1	18.7	18.6	11.3	18.8	4.0	8.5
			cis	9.1	59.3	26.2	31.5	100	12.7	47.0	7.1	14.2

the ^{19}F NMR spectra (Table 1) two sets of signals are present (*trans*- and *cis*-isomers, the ratio of which varies slightly depending on the substituent R). The chemical shifts and coupling constants are in accordance with the structures proposed. The fluorine atoms of the CF_2 group located near the chiral center give an AB spin system with J_{A-B} 290 Hz in the ^{19}F NMR spectra. In the ^1H NMR spectra two signals with equal intensity in the 6.2—6.5 ppm (NH) and 4.2—4.5 ppm (CH) regions are present along with the characteristic signals of alkyl radicals.

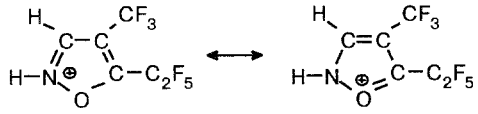
Using GC—MS the mass spectra of the *cis*- and *trans*-isomers of isoxazolidines (Table 2) were obtained. In the spectra of all of these compounds peaks of the molecular ions M^+ and of $[M-R]^+$, CF_3^+, and $C_2F_5^+$ are present.

The intensity of the $[M-R]^+$ peak is higher for *trans*-isomers and increases as the volume of the radical R increases: 13.9% (Me) and 100% (Et and Pr).

The most intense peaks in the MS of the *cis*-isomers are the peaks of $[M-300]^+$ ions, apparently formed by cleavage of the isoxazolidine molecule to afford "perfluoroalkenyl" and "oxime" fragments.



In all of the spectra the peak m/z 256 (5—15 %) is also present, indicating the elimination of the substituents R, CF_3, and F from the molecule. This ion might have the following structure:



Experimental

The ^{19}F and ^1H NMR spectra were obtained with a Bruker WP-200 spectrometer (188.4 and 200 MHz, respectively) relative to external standards (CF_3COOH and tetramethylsilane), and the mass spectra were measured with a VGMS 70—70e GC—MS instrument.

Reaction of perfluoro-2-methylpent-2-ene (1) with aldoximes (general procedure). Anhydrous Et_3N (10 g, 0.1 mol) was added dropwise with stirring at 0 °C to a mixture of perfluoro-2-methylpent-2-ene (**1**) (15 g, 0.05 mol), aldoxime (0.05 mol) and anhydrous diglyme (20 mL). After 1 h, the reaction mixture was washed with 15 % HCl (2 portions) and water, and dried over $MgSO_4$. Oxazolidines **2a—c** were isolated by distillation.

5-Fluoro-3-methyl-5-pentafluoroethyl-4,4-di(trifluoromethyl)-1,2-oxazolidine (2a), yield 52%, b.p. 52—55 °C (10 Torr). ^1H NMR ($CDCl_3$, δ, ppm, *J*/ Hz): 1.5 (d, 3 H, J = 6); 4.0 and 4.4 (*trans*- and *cis*-, 1 H, CH); 6.2 (br.s, 1 H, NH). Found (%): C, 27.03; H, 1.43; F, 62.79. $C_8H_5F_{12}NO$. Calculated (%): C, 26.74; H, 1.39; F, 63.51.

3-Ethyl-5-fluoro-5-pentafluoroethyl-4,4-di(trifluoromethyl)-1,2-oxazolidine (2b), yield 43%, b.p. 59—62 °C (12 Torr). ^1H NMR ($CDCl_3$, δ, ppm, *J*/Hz): 1.1 (t, 3 H, CH_3 J = 7); 1.6 and 2.0 (AB spin system, 2 H, CH_2); 3.9 and 4.4 (*trans*- and *cis*-, 1 H, CH); 6.3 (br.s, 1 H, NH). Found (%): C, 29.13; H, 1.97; F, 61.01. $C_9H_7F_{12}NO$. Calculated (%): C, 28.95; H, 1.88; F, 61.13.

5-Fluoro-5-pentafluoroethyl-4,4-di(trifluoromethyl)-3-propyl-1,2-oxazolidine (2c), yield 37%, b.p. 73—76 °C (10 Torr). ^1H NMR ($CDCl_3$, δ, ppm, *J*/ Hz): 1.0 (t, 3 H, CH_3, J = 7); 1.6 (m. 2 H, CH_2); 1.6 and 2.0 (AB spin system, 2 H, CH_2); 3.9 and 4.4 (*trans*- and *cis*-, 1 H, CH); 6.3 (br.s, 1 H, NH). Found (%): C, 31.15; H, 2.29; F, 59.12. $C_{10}H_9F_{12}NO$. Calculated (%): C, 31.01; H, 2.33; F, 58.91.

Reaction of perfluoro-2-methylpent-2-ene (1) with benzaldoxime. The reaction of compound (**1**) (15 g, 0.05 mol), benzaldoxime (6 g, 0.05 mol), and Et_3N (5 g, 0.05 mol) in anhydrous diglyme (20 mL) was carried out as described above for the synthesis of **2a,b**. Distillation gave 6.9 g (33%) of *O*-[3-(2-trifluoromethyl-1,1,1,3,4,5,5,5-nonafluoro)pentyl]benzaldoxime (**3d**), b.p. 110—112 °C (10 Torr). ^1H NMR ($CDCl_3$, δ, ppm, *J*/ Hz): 4.6 (d.hept, 1 H, $CH(CF_3)_2$, J = 4 and 8); 7.1—7.4 (m, 5 H, Ph); 8.0 (s, 1 H, CH=N). Found (%): C, 37.18; H, 1.63; F, 54.66. $C_{13}H_7F_{12}NO$. Calculated (%): C, 37.05; H, 1.66; F, 54.16.

References

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