[2+4]-CYCLOADDITION OF FLUOROOLEFINS AND FLUOROAZOMETHINES WITH 1,3-CYCLOHEXADIENE

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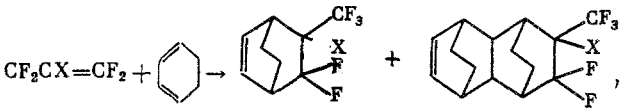
UDC 542.955:547.413.732:547.335.2:547.592.3

The [2+4]-cycloaddition of fluoroolefins and fluoroazomethines have been studied in extensive detail [1-3] but the reaction of these compounds with 1,3-cyclohexadiene (CHD) has not been investigated.

Terminal fluoroolefins react with CHD under vigorous conditions and pressure. Diadducts (III) and (IV) were obtained in addition to monoadducts (I) and (II).

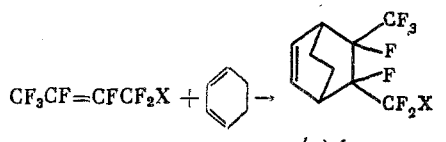


(I), (II) (III), (IV)

X = F(I), (III), CF_3(II), (IV).

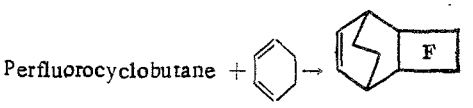
Terminal fluoroazomethines such as perfluoro-2-azapropene and perfluoro-2-azapentene do not react with CHD even under more vigorous conditions.

Internal fluoroolefins and fluoroazomethines react with CHD to give [2+4]-cycloadducts at 220-240°C under pressure.

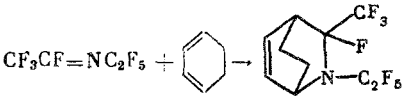


(V), (VI)

X = F(V), Cl(VI)

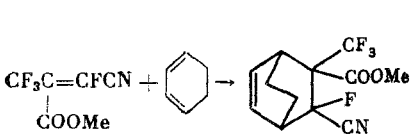


(VII)



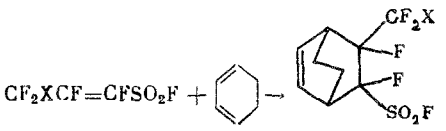
(VIII)

Functionally-substituted fluoroolefins, specifically, 2-methoxycarbonyltetrafluorocrotononitrile and 1-polyfluoroalkene-1-sulfonyl fluorides, react with CHD under relatively mild conditions at 50-80°C.



(IV) (IX)

X = F(X), Cl(XI).



(X), (XI)

A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 4, pp. 885-890, April, 1988. Original article submitted May 7, 1987.

0568-5230/88/3704-0765$12.50

TABLE 1. Reagent Charges and Yields of Compounds Synthesized

Compound	Reagent charge		Yield	
	dienophile, g (mole)	CHD, g (mole)	g	%
(I)	18,6 (0,124)	9,9 (0,124)	10,3	36,1
(II)	14,5 (0,073)	5,8 (0,073)	6,6	32,2
(III)	18,6 (0,124)	9,9 (0,124)	2,4	6,9
(IV)	14,5 (0,073)	5,8 (0,073)	1,4	5,4
(V)	12,2 (0,061)	4,9 (0,061)	7,3	42,7
(VI)	6,1 (0,028)	3,3 (0,028)	3,3	40,2
(VII)	14,0 (0,086)	6,8 (0,086)	8,3	40,0
(VIII)	13,8 (0,060)	4,8 (0,060)	6,5	28,5
(IX)	5,3 (0,027)	2,2 (0,027)	4,3	57,5
(X)	4,7 (0,022)	1,8 (0,022)	4,7	73,0
(XI)	7,1 (0,031)	2,5 (0,031)	7,7	80,0

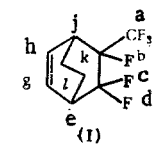
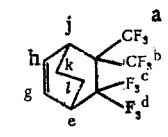
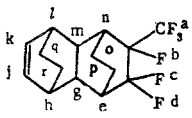
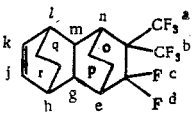
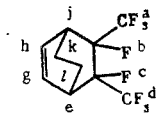
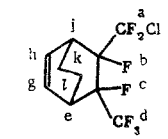
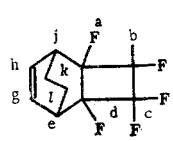
TABLE 2. Stereomer Ratio and Physicochemical Indices

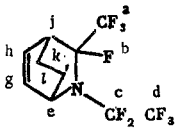
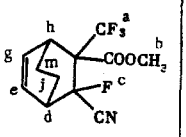
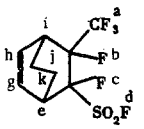
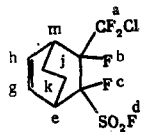
Compound	Stereomer ratio	Bp, °C (p, mm Hg)	d_4^{20}	n_D^{20}
(I)	1 : 1	54 (10)	1,3364	1,3912
(II)	1 : 1	65 (8)	1,3998	1,3959
(III)	3 : 2	100 (2)	1,1522	1,4770
(IV)	1 : 1	76 (1)	1,2419	1,4495
(V)	1,5 : 1	49 (4)	1,4483	1,3941
(VI)	1 : 1	63 (10)	1,4256	1,4121
(VII)	1 : 1	60 (2)	1,2724	1,4438
(VIII)	3 : 2	35 (3)	1,3925	1,3928
(IX)	1 : 1	94 (1)	1,2990	1,4093
(X)	3 : 2	82 (1)	1,4553	1,4128
(XI)	3 : 2	90 (1)	1,5694	1,4534

TABLE 3. Elemental Analysis Data of the Compounds Synthesized

Compound	Found/Calculated, %				Chemical formula
	C	H	F	Cl (N) (S)	
(I)	46,87 / 46,97	3,81 / 3,50	49,43 / 49,53		$C_9H_8F_6$
(II)	42,64 / 42,87	2,83 / 2,88	54,30 / 54,25		$C_{10}H_8F_8$
(III)	53,66 / 53,58	5,82 / 5,76	40,25 / 40,67		$C_{15}H_{16}F_6$
(IV)	53,12 / 53,34	4,43 / 4,48	42,20 / 42,18		$C_{16}H_{16}F_8$
(V)	42,77 / 42,87	2,89 / 2,83	54,15 / 54,25		$C_{10}H_8F_8$
(VI)	40,44 / 40,49	2,74 / 2,72	44,90 / 44,83	11,93 / 11,95	$C_{10}H_8F_7Cl$
(VII)	49,30 / 49,60	3,70 / 3,33	46,92 / 47,07		$C_{10}H_8F_6$
(VIII)	38,39 / 38,35	2,60 / 2,58	54,58 / 54,60	4,41 / 4,47 (N)	$C_{10}H_8F_9N$
(IX)	51,98 / 52,00	4,12 / 4,00	27,44 / 27,42	5,13 / 5,05 (N)	$C_{12}H_{11}F_4NO_2$
(X)	36,72 / 36,74	2,69 / 2,74	38,91 / 38,74	10,83 / 10,90 (S)	$C_9H_8F_6SO_2$
(XI)	34,81 / 34,80	2,52 / 2,60	30,59 / 30,58	11,38 / 11,41	$C_9H_8F_5ClSO_2$

TABLE 4. ^{1}H and ^{19}F NMR Spectral Parameters

Compound	^{1}H NMR δ, ppm		^{19}F NMR δ, ppm		Coupling constant, J, Hz	
 (I)	(d, j)	3,12 m 3,22 m	(a)	−3,6 d.d.d 2,2 d.d.d.	(a-b) (a-c) (a-b)	8,5 8,5 2,0
	(g, h)	5,84 m 6,24 m	(c, d)	22,5 m 26,2 m 30,7 m 37,8 m		
	(k, l)	1,86 m 1,96 m 2,01 m 2,21 m	(b)	91,7 m		
 (II)	(e, j)	3,27 m	(a, b)	−4,8 d.d.q −3,1 d.d.q.	(a-b) (a-c) (a-d) (b-c) (b-d)	7,3 26,1 16,9 3,0 4,7
	(g, h)	6,49 m				
	(k, l)	1,33 m 1,52 m 2,08 m 2,22 m	(c, d)	42,9 m 47,6 m		
 (III)	(n, e) (l, h)	2,87 m 3,19 m	(a)	−4,4 m 1,3 m	(a-b)	8,2
	(m, g)		(b, d)	25,8 m 30,1 m		
	(j, k)	5,47 m 6,22 m	(b)	93,4 m		
	(o, p) (q, r)	1,92 m 2,03 m 2,15 m				
 (IV)	(n, e) (l, h)	2,23 m 2,98	(a, b)	−5,3 m −2,8 m	(a−b)	7,1
	(m, g)		(c, d)	40,8 m 43,1 m		
	(j, k)	4,74 m 5,29 m				
	(o, p)	0,45 m				
	(q, r)	0,64 m 0,82 m 1,47 m				
 (V)	(j, e)	3,55 m	(a, d)	−3,0 d.d.q	(a-d)	4,9
	(h, g)	6,47 m	(b, c)	−4,1 m	(a-c)	16,6
	(l, k)	1,34 m 1,50 m 2,07 m 2,21 m		95,2 m 104,2 m	(a-d) (b-d)	7,8 25,4
 (VI)	(i, e)	3,26 m	(a)	−10,8 m	(a, c)	24,6
	(g, h)	6,00 m	(b, c)	82,0 m 95,2 m		
	(l, k)	1,33 m 1,51 m 2,07 m 2,21 m	(d)	−4,0 m		
 (VII)	(j, e)	3,08 m	(b, c)	33,5 m		
	(g, h)	5,85 m 6,45 m	(a, d)	48,5 m 98,3 m 100,4 m		
	(l, k)	1,91 m				

Compound	^{1}H NMR	^{19}F NMR	Coupling constant, J, Hz
	δ, ppm		
 (VIII)	(e, j) 3,63 m (g, h) 6,34 m 6,17 m (k, l) 1,53 m 1,78 m	(a) 4,8 d 6,8 d (b) 50,8 m 57,6 m (c) 13,6 q 14,8 q (d) −1,2 m −2,0 m	(a–b) 8,9
 (IX)	(d, h) 4,09 m 4,22 m 4,35 m (e, g) 5,65 m 5,83 m (b) 3,47 m 3,85 m (i, j) 1,19 m 1,81 m 1,99 m	(a) −14,3 d −18,3 d (c) 73,4 q 79,1 q	(a–c) 14,8 19,5
 (X)	(i, e) 3,51 m (g, h) 6,43 m (j, k) 1,55 m 2,04 m 2,20 m 2,50 m	(a) −3,6 m −5,2 m (b) 67,8 m 68,9 m (c) 71,3 m 73,4 m (d) −123,7 m −125,7 m	
 (XI)	(i, e) 3,52 m (g, h) 6,44 m (j, k) 1,53 m 2,02 m 2,19 m 2,47 m 2,50 m	(a) −21,3 m −19,5 d,d,d (b) 61,1 m 65,3 m (c) 74,0 m 79,5 m (d) −123,3 m −125,7 m	(a–b) 11,1 (a–d) 28,2 21,9 (a–d) 5,8 3,0

A functionally-substituted fluoroazomethine, namely, 1-cyanotetrafluoro-2-azapropene does not form a [2+4]-cycloadduct with CHD even under more vigorous conditions.

Products (I), (III), and (V)-(XI) are mixtures of endo- and exo-stereomers (diastereomers) as indicated by ^{19}F NMR spectroscopy.

EXPERIMENTAL

The ^{1}H and NMR spectra were taken on a Hitachi R-20 spectrometer at 60 MHz. The ^{19}F NMR spectra were taken on a Hitachi-20 spectrometer at 56.456 MHz. The chemical shifts (δ) are given in ppm relative to tetramethylsilane for the PMR spectra and CF_3CO_2H for the ^{19}F NMR spectrum in $CHCl_3$.

Reaction of Terminal Fluoroolefins with CHD (Typical Experiment) to give (I)-(IV). A solution of terminal fluoroolefin and CHD in 15 ml diethyl ether was heated in the presence of 0.1 g hydroquinone at 250-270°C in a steel autoclave for 28-30 h. Subsequent distillation gave fluorine-containing bicyclo[2.2.2]oct-2-enes (I) and (II) and tetracyclo[6.2.2.$2^{6,9}$.$0^{5,10}$]tetradeca-7-enes (III) and (IV).

Reaction of Internal Fluoroolefins and Fluoroazomethines with CHD (Typical Experiment) to give (V)-(VIII). A solution of internal fluoroolefin and fluoroazomethine and CHD in 15 ml diethyl ether was heated in the presence of 0.1 g hydroquinone in a steel autoclave 20-25 h. Subsequent distillation gave fluorine-containing bicyclo[2.2.2]oct-2-enes (V)-(VII) and 5-azabicyclo[2.2.2]oct-2-ene (VIII).

Reaction of 2-Methoxycarbonyltetrafluorocrotononitrile and 1-Polyfluoroalkene-1-sulfonyl Fluorides with CHD (Typical Experiment) to give (IX)-(XI). A solution of functionally-substituted fluoroolefin and CHD in 15 ml diethyl ether was heated at 50-80°C in a steel autoclave for 12-14 h. Subsequent distillation gave functionally-substituted fluorine-containing bicyclo[2.2.2]oce-2-enes (IX)-(XI).

The reagents charges and yields of the compounds synthesized are given in Table 1. The ratio of the stereomers in the products and the physicochemical indices are given in Table 2. The elemental analysis data are given in Table 3. The ^1H and ^{19}F NMR spectral data given in Table 4.

CONCLUSIONS

1. Terminal fluoroolefins and internal fluoroolefins and fluoroazomethines react with 1,3-cyclohexadiene at 220-270°C to give [2+4]-cycloadducts.

2. Methoxycarbonyltetrafluorocrotononitrile and 1-polyfluoroalkene-1-sulfonyl fluorides react with 1,3-dicyclohexadiene at 50-80°C.

LITERATURE CITED

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SYNTHESIS AND STRUCTURE OF 1-DIFLUORONITROACETYL-4-ARYLPIPERAZINES

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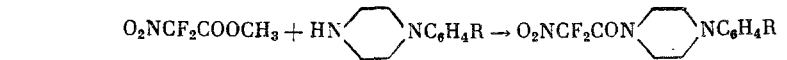
UDC 542.951.1:548.737:547.861.3

Piperazine and its derivatives are commonly used in verterinary and general medicine as effective antihelminthic and therapeutic drugs [1-3]. In a search for new physiologically active compounds, we synthesized a series of 1-difluoronitroacetyl-4-arylpiperazines (I)-(IV).

Products (I)-(IV) were obtained by the acylation of arylpiperazines by methyl difluoronitroacetate.



$R = H(I),\ p\text{-}F(II),\ p\text{-}CH_3(III),\ o\text{-}CH_3(IV)$

These products are stable crystalline compounds with good solubility in organic solvents. Their structure was established using IR, PMR, and ^{19}F NMR spectroscopy.

Product (II) was subjected to x-ray diffraction structural analysis. The molecular structure of (II) is shown in Fig. 1. The major bond angles are as follows: $O^1C^1C^4$ = 115.5 (5), $O^1C^1N^1$ = 125.7(6), $N^1C^1C^4$ = 118.8(5), $C^1N^1C^2$ = 126.7(5), $C^1N^1C^6$ = 118.3(5), $C^2N^1C^6$ = 113.9(5), $N^1C^2C^3$ = 110.4(5), $N^1C^6C^5$ = 111.9(6), $N^4C^3C^2$ = 111.8(6), $N^4C^5C^6$ = 110.7(6), and $C^3N^4C^5$ = 108.1(5)°. Selected torsion angles are: $N^1C^1C^4N^2$ = −170.2, $O^1C^1C^4N^2$ = 10.3, $O^1C^1N^1C^6$ = −9.7, $C^2N^1C^1C^4$ = 4.0, $C^3N^4C^7C^8$ = 57.1, and $C^5N^4C^7C^{12}$ = 2.5°. O^1, N^1, C^1, and C^4 are located in a plane; N^2, C^2, and C^6 are close to this plane. F^1 and F^2 extrude by about 1 Å in different directions from this plane, while the planar nitro group forms an angle of 84.7° with this plane. The bond length distribution in the $O^1{=}C^1{-}N^1$ fragment indicates π-delocalization of the double bond: $O^1{=}C^1{=}N^1$. Thus, hybridization of N^1 is close to trigonal planar; the extrusion of N^1 from the C^1, C^2, C^6 plane by 0.088(4) Å. The other nitrogen atom of the piperazine ring, N^4, is pyramidal; the extrusion of N^4 from C^3, C^5, C^7 plane

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Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 4, pp. 890-892, April, 1988. Original article submitted May 7, 1987.

0568-5230/88/3704-0769$12.50