FLUORINE-CONTAINING AZOLES.

3.* REACTION OF IMIDAZOLES AND PERIMIDINES WITH PERFLUOROALKENES

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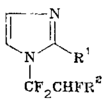
UDC 547.785.5'221:542.97:543.422'51

Trifluorochloroethylene, tetrafluoroethylene, hexafluoropropylene, and α,β,β-trifluorostyrene add to imidazole, 2-alkylbenzimidazoles, and perimidines in the presence of aqueous solutions of potassium hydroxide or fluoride to give the corresponding N-fluoroalkylazoles.

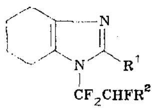
A well-known method for the preparation of N-trifluorochloroethyl-, N-tetrafluoroethyl-, and N-hexafluoropropylazoles is the catalytic (in the presence of potassium metal) [2] or noncatalytic [3, 4] addition of fluoroolefins to azoles under pressure and at temperatures above 100°C.

Recently one of us [5] showed that in the case of carbazole tetrafluoroethylene and hexafluoropropylene readily add to the NH group even at room temperature and normal pressure if the reaction is carried out in diglyme in the presence of a 30-40% aqueous solution of potassium hydroxide in an equimolar amount with respect to carbazole. The aim of the present research consisted in the extension of this method to other NH heterocycles. In addition to tetrafluoroethylene and hexafluoropropylene we also studied the possibility of the addition of trifluorochloroethylene and α,β,β-trifluorostyrene to azoles.

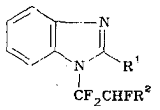
We established that all of the investigated fluoroolefins add to imidazoles and perimidines to give the corresponding N-fluoroalkyl derivatives (I-IV):



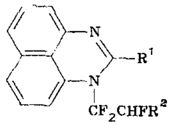
Ia-d



IIa,b



III a-m



IVa-c

I—IV a $R^1=H$, $R^2=F$; b $R^1=H$, $R^2=CF_3$; I, III, IV c $R^1=H$, $R^2=C_6H_5$; I, III d $R^1=H$, $R^2=Cl$; III e $R^1=CH_3$, $R^2=F$; f $R^1=CH_3$, $R^2=CF_3$; g $R^1=CH_3$, $R^2=C_6H_5$; h $R^1=CH_3$, $R^2=Cl$; i $R^1=C_2H_5$, $R^2=F$; j $R^1=C_2H_5$, $R^2=CF_3$; k $R^1=C_3H_7$, $R^2=F$; l $R^1=C_3H_7$, $R^2=CF_3$; m $R^1=CF_3$, $R^2=CF_3$

In the case of hexafluoropropylene the addition to all of the investigated azoles proceeds even without a catalyst. The addition of the other perfluoroolefins requires the use of a catalyst. Judging from the reaction times and the yields of the desired products the ease with which the process occurs depends to a great degree on the type of catalyst (Table 1). Potassium fluoride has a milder catalyzing effect than potassium hydroxide. This is manifested in the inability of KF to catalyze the addition of the less active tetrafluoroethylene and in an increase in the reaction times by factors of 2-70 for the remaining fluoroolefins. In addition, the mildness of the catalytic action of KF has a favorable effect on the addition of the more reactive hexafluoropropylene to heterocycles, for which the yields of N-hexafluoropropylazoles are increased by 26-78% as compared with the process catalyzed by potassium hydroxide and by 8-55% as compared with the noncatalytic process.

The rate of absorption of the fluoroolefin and the yield of the reaction product are often contradictory as criteria of the extent of the reaction: Frequently, the faster the reaction, the lower the yield of N-fluoroalkyl derivative and the poorer its quality.

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*See [1] for communication 2.

State Scientific-Research and Planning Institute of the Chlorine Industry, Borislav 293760. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 524-528, April, 1984. Original article submitted September 17, 1983.

0009-3122/84/2004-0426$08.50

TABLE 1. Parameters of the Addition of Fluoroolefins to Azoles

Compound	Fluoroolefin absorption time, h			Yield, %		
	with KOH	with KF	without catalyst	with KOH	with KF	without catalyst
Ia	11,5	—*	—	89	—	—
Ib	0,5	0,9	2,2	8,5	86,5	60
Ic	8,0	22	34	71	60	46
Id	1,0	4,5	27	86	81	79
IIa	23	—	—	63	—	—
IIb	1,5	5,0	9	29	65	50
IIIa	20	—	—	71	—	—
IIIb	0,6	2	4,5	27	65	57
IIIc	12	80	—	83	40	—
IIId	1,2	55	20	89	72	2
IIIe	26	—	—	97	—	—
IIIf	1,0	4,0	10	66	80	60
IIIg	19	120	—	66	39	—
IIIh	1,3	89	—	90	62	—
IIIi	48	—	—	86	—	—
IIIj	0,8	4	13	62	78	51
IIIk	37	—	—	80	—	—
IIIl	1,0	5	17	56	69	48
IIIm	0,5	2	15	55	57	3
IVa	3,0	—	—	3	—	—
IVb	0,5	3	10	Resinification	44	5
IVc	4	—	—	52	—	—

*The dash means that the reaction does not occur even on contact with the perfluoroolefin for 150 h.

Nevertheless, we will be inclined to estimate the ease of addition from the rate of absorption of the fluoroolefin. On the basis of this the parameters of the activities of the investigated azoles with respect to fluoroalkenes decrease in the order imidazole > benzimidazole > tetrahydrobenzimidazole.

Similarly, with respect to their activities with respect to azoles the fluoroolefins can be arranged in the following order, which is in agreement with their relative electrophilicities [6]: $CF_2{=}CF{-}CF_3 > CF_2{=}CF{-}Cl > CF_2{=}CF{-}Ph > CF_2{=}CF_2$.

It might be expected that in the catalytic reaction the activity of the heteroring would be higher, the higher the nucleophilicity of the corresponding N anion. The latter should increase as the acidity of the N—H bond decreases. In fact, 2-trifluoromethylbenzimidazole, which has significant NH acidity, does not react with tetrafluoroethylene. In addition, imidazole, the anion of which should be more active than the anion of benzimidazole, undergoes perfluoroalkylation considerably more actively than benzimidazole. However, the logic of this reasoning is violated by the behavior of tetrahydrobenzimidazole. The NH acidity of this compound should be lower than the NH acidities of imidazole and benzimidazole, and the anion of this compound should consequently be the most active. However, tetrahydrobenzimidazole undergoes addition with greater difficulty than imidazole and benzimidazole. The activity of the heterocycle in the addition of fluoroolefins is evidently determined by the combination of a number of factors: the relative NH acidity of the heteroring, i.e., the ease of formation of an N anion, the nucleophilicity of the N anion, steric factors, etc.

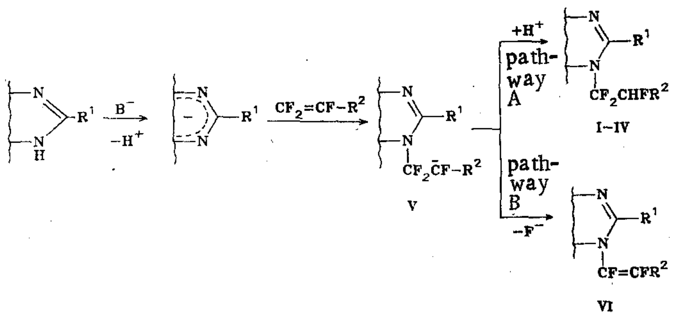
It is difficult for us to estimate the activities of perimidines in the addition reaction, since the process is accompanied by considerable resinification, and the yields of N-fluoroalkylperimidines are low. This can be explained by the extreme sensitivity of the N anion of perimidine to oxidation [7], including oxidation by air oxygen, and also by the instability of the reaction products under the conditions of the synthesis (the latter was confirmed experimentally).

The role of the catalysts used probably reduces to ionization of the N—H bond and the formation of the N anion of the heterocycle. It should be noted that the catalytic addition of the fluoroalkene to the azole proceeds in a two-phase system: aqueous potassium hydroxide or fluoride—acetone. The water, inasmuch as it is an additional source of hydrogen ions, promotes the fastest stabilization of intermediate carbanion V (pathway A).

TABLE 2. Characteristics of the Synthesized Ia-d, IIa, b, IIIa-m, and IVa-c

Compound	bp, °C (mm)	mp, °C	n_D^{20}	Found, %		Empirical formula	Calc., %	
				F	N		F	N
Ia	47—49 (12)	—	1,3944	45,5	16,5	$C_5H_4F_4N_2$	45,2	16,7
Ib	72—74 (14)	—	1,3763	52,0	12,9	$C_6H_4F_6N_2$	52,3	12,8
Ic	124—126 (2)	—	1,5289	25,4	12,7	$C_{11}H_9F_3N_2$	25,5	12,4
Id	115—117 (75)	—	1,4320	—	—	—	—	—
IIa	93—95 (5)	—	1,4513	34,0	12,9	$C_9H_{10}F_4N_2$	34,2	12,6
IIb	109—110 (5)	—	1,4322	52,1	10,2	$C_{10}H_{10}F_6N_2$	51,9	10,3
IIIa	77—78 (2)	29—30	—	34,9	12,5	$C_9H_6F_4N_2$	34,8	12,8
IIIb	97—98 (2)	68—69	—	40,0	10,1	$C_{10}H_6F_6N_2$	40,4	9,9
IIIc	180—182 (2)	—	1,5918	20,3	10,4	$C_{15}H_{11}F_3N_2$	20,6	10,1
IIId	108—109 (2)	—	1,5219	—	—	—	—	—
IIIe	99—101 (2)	74—75	—	32,2	12,2	$C_{10}H_8F_4N_2$	32,7	12,0
IIIf	80—82 (2)	64—66	—	40,1	10,2	$C_{11}H_8F_6N_2$	40,4	9,8
IIIg	183—185 (2)	77—78	—	19,9	9,6	$C_{16}H_{13}F_3N_2$	19,6	9,7
IIIh	112—114 (2)	56—57	—	—	—	—	—	—
IIIi	132—134 (2)	61—62	—	31,1	11,6	$C_{11}H_{10}F_4N_2$	30,9	11,4
IIIj	95—96 (2)	—	1,4759	38,3	9,7	$C_{12}H_{10}F_6N_2$	38,5	9,5
IIIk	117—118 (2)	—	1,4975	29,4	10,7	$C_{12}H_{12}F_4N_2$	29,2	10,8
IIIl	114—116 (3)	—	1,4741	36,8	9,0	$C_{13}H_{12}F_6N_2$	37,0	9,1
IIIm	59—60 (2)	—	1,4342	51,1	8,4	$C_{11}H_5F_9N_2$	50,8	8,3
IVa	—	65*	—	28,6	10,2	$C_{13}H_8F_4N_2$	28,3	10,4
IVb	—	119	—	35,7	9,1	$C_{14}H_8F_6N_2$	35,8	8,8
IVc	195—196 (2)	96	—	17,2	8,9	$C_{19}H_{13}F_3N_2$	17,5	8,6

*By sublimation at 140°C (2 mm).



In the addition of trifluorochloroethylene, α,β,β-trifluorostyrene, and hexafluoropropylene one observes the formation of, in addition to N-fluoroalkylazoles, a certain amount of N-fluoroalkenylazoles VI, the IR spectra of which contains a strong absorption band at 1700-1760 cm^{-1}, which is characteristic for a fluorinated double bond [8]. Unfortunately, we were unable to isolate these compounds preparatively because their physicochemical properties are similar to those of N-fluoroalkylazoles. Purification to remove the unsaturated products was carried out by bromination of the mixtures of fluorinated azoles in light at 60-80°C with subsequent separation of the bromo derivatives.

As in the case of the reaction of secondary alkylamines with perfluoroalkenes [9], elimination of a fluoride ion from carbanion V (pathway B) [10] is probably the reason for the formation of N-fluoroalkenylazoles. We established that the formation of VI via splitting out of a molecule of HF from the N-fluoroalkylazoles does not occur under the reaction conditions.

The structures of the synthesized compounds were confirmed by the results of elementary analysis (Table 2) and data from the IR, PMR, and mass spectra (Tables 3 and 4). In the IR spectra of I-IV the frequency of the absorption of the C—H bond is found at 3065-3140 cm^{-1}; this was confirmed experimentally by deuterium and was in agreement with the literature data [11]. Absorption bands that are characteristic for the C=C and C=N bonds of the heterocyclic molecule are present in the spectra of I-III, and an intense doublet that characterizes N-substituted perimidines is observed in the spectra of IV. A series of bands that is characteristic for polyfluoroalkyl substituents is present in the spectra of all of the compounds at 1110-1290 cm^{-1}. The proton of the tetrafluoroethyl grouping gives a triplet in the PMR spectra, and the hexafluoropropyl grouping gives a multiplet at 5.3-6.2 ppm. The mass-spectroscopic characteristics of some N-polyfluoroalkylazoles are presented in Table 4.

TABLE 3. Spectral Characteristics of the Synthesized Compounds

Compound	IR spectrum, cm^{-1}		PMR spectrum, δ, ppm (J, Hz)
	νC—H*	νC=C/C=N	
Ia	3135	1640, 1600, 1490	6,04 (t, CHF_2, 54)
Ib	3140	1640, 1600, 1490	5,25 (m, CHF)
Ic	3135	1602, 1585, 1486	5,62 (m, CHF)
Id	3140	1630, 1590, 1482'	
IIa	3115	1600, 1490	6,37 (t, CHF_2, 54)
IIb	3120	1603, 1490	
IIIa	3138	1610, 1595, 1510	6,15 (t, CHF_2, 54)
IIIb	3100	1610, 1595, 1510	5,32 (m, CHF)
IIIc	3070	1614, 1590, 1500	5,80 (m, CHF)
IIId	3100	1615, 1590, 1510	
IIIe	3075	1614, 1590, 1545	6,12 (t, CHF_2, 54)
IIIf	3075	1612, 1590, 1545	
IIIg	3080	1620, 1590, 1550	
IIIh	3100	1610, 1595, 1505	
IIIi	3070	1612, 1590, 1540	6,02 (t, CHF_2, 54)
IIIj	3075	1610, 1590, 1540	
IIIk	3075	1610, 1590, 1540	
IIIl	3070	1612, 1590, 1543	
IIIm	3080	1610, 1590, 1540	5,25 (m CHF)
IVa	3070	1630, 1595	
IVb	3060	1635, 1595	5,55 (m CHF)
IVc	3080	1630, 1590	

*Fluoroalkyl group.

TABLE 4. Mass Spectra of Ia, IIIb, j, k, m, and IVb*

Compound	m/z^+ values (relative intensities of the peaks, %) †
Ia	**168** (72,9), 167 (15,1), 166 (27,1), 149 (100), 146 (19,1), 145 (28,8), 140 (28,8), 117 (26,5), 90 (44,9)
IIIb	**268** (93,7), 168 (10,1), 167 (100), 147 (29,9), 140 (19,9), 95 (27,1), 90 (15,8), 69 (20,8), 63 (10,3)
IIIi	**246** (100), 245 (44,9), 196 (13,2), 175 (12,1), 146 (27,3), 145 (90,3), 144 (14,4), 143 (8,7), 95 (16,5)
IIIj	**296** (100), 295 (20,4), 195 (19,1), 146 (46,8), 145 (70,2), 95 (14,0), 69 (10,7)
IIIm	**336** (66,7), 316 (11,6), 235 (57,5), 186 (100), 167 (10,0), 166 (22,6), 140 (19,5), 95 (20,7), 90 (14,3), 69 (22,4), 57 (14,0)
IVb	318 (20,3), 269 (35,7), 268 (100,0), 267 (13,7), 258 (19,5)

*As in Russian original. The compounds in the heading do not match the compounds in the table.

†The peaks of the ions with intensities >10% are presented. The mass numbers of the molecular ions are printed in boldface.

EXPERIMENTAL

The IR spectra of solutions of the compounds in CCl_4 were recorded with a UR-20 spectrometer. The PMR spectra of 0.04 mole/liter solutions of the compounds in CCl_4 or CF_3COOH were obtained with Tesla BS-467 (60 MHz) and Tesla BS-487 (80 MHz) spectrometers with hexamethyldisiloxane as the internal standard. The mass spectra were recorded with a Jm-01-JC-2 mass spectrometer with direct introduction of the samples into the ion source at an ionization energy of 75 eV.* The course of the reactions and the purity of the compounds were monitored by means of thin-layer chromatography (TLC) (activity IV aluminum oxide and Silufol UV-254) in chloroform.

N-Tetrafluoroethylazoles (Ia, IIa, IIIa, e, i, k, and IVa†). A 5% excess (with respect to the theoretical amount) of trifluorochloroethylene was bubbled at 25-30°C into a well-stirred two-phase system consisting of 0.1 mole of the azole in 80 ml of acetone and 0.1 mole of potassium hydroxide in 10 ml of water, after which the organic layer was separated, the solvent was removed by distillation, and the reaction product was distilled.

N-Trifluorochloroethyl- (Id, IIId, h) and N-Hexafluoropropylazoles (Ib, IIb, IIIb, f, j, l, m, IVb). A 5% excess (with respect to the theoretical amount) of trifluorochloroethylene or hexafluoropropylene was bubbled with vigorous stirring into a mixture consisting

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*We thank N. A. Klyuev for his assistance in recording the mass spectra.

†The synthesis of IVa-c was carried out in a stream of argon.

of 0.1 mole of the azole, 80 ml of acetone, 0.1 mole of potassium hydroxide or fluoride, and 10 ml of water, after which the organic layer was dried with calcium chloride, and the solvent was removed by distillation. The residue, which was a mixture of N-polyfluoroalkylazoles and N-polyfluoroalkenylazoles, was distilled, and the distillate was illuminated and treated with bromine at 60-80°C until it had a persistent yellow color. The desired products were distilled *in vacuo*.

N-Hexafluoropropylazoles (Ib, IIb, IIIb, f, j, *l*, IVb). A 0.1-mole sample of the azole was dissolved in 80 ml of acetone, 10 ml of water was added, and a 5% excess of hexafluoropropylene was passed through the mixture. The solvent was evaporated, and the residue was distilled. The distillate was illuminated and treated with bromine at 60-80°C until it had a persistent yellow color. The N-hexafluoropropylazoles were separated from the bromination products by distillation.

N-α,α,β-Trifluoro-β-phenylethylazoles (Ic, IIIc, g, IVc). A 0.1-mole sample of the azole was dissolved in 80 ml of acetone, a solution of 0.1 mole of potassium hydroxide or fluoride in 10 ml of water and 0.1 mole of α,β,β-trifluorostyrene were added, and the mixture was stirred vigorously at 30-50°C. The resulting mixture of N-fluoroalkyl and N-fluoroalkenyl derivatives was distilled *in vacuo*, the distillate was dissolved in 15 ml of CCl_4, and the solution was illuminated with stirring and treated with bromine at 30-40°C until it had a persistent yellow color. The solvent was removed by distillation, and the N-fluoroalkyl derivative was distilled *in vacuo*.

LITERATURE CITED

1. V. G. Poludenko, O. B. Didinskaya, and A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 4, 520 (1984).
2. D. C. England, L. R. Melby, M. A. Dietrich, and R. V. Lindsey, J. Am. Chem. Soc., 82, 5116 (1960).
3. W. Ried and H. Lohwasser, Ann. Chem., 699, 88 (1966).
4. V. I. Troitskaya, V. I. Rudyk, É. B. Lifshits, and L. M. Yagupol'skii, Zh. Org. Khim., 9, 1054 (1973).
5. V. G. Poludnenko and A. L. Bel'ferman, Khim. Geterotsikl. Soedin., No. 1, 118 (1980).
6. R. D. Chambers and R. G. Mobbs, Advances in Fluorine Chemistry, Vols. III and IV, Butterworths, London.
7. A. F. Pozharskii and I. S. Kashparov, Khim. Geterotsikl. Soedin., No. 1, 111 (1970).
8. V. I. Troitskaya, V. I. Rudyk, E. V. Konovalov, and L. M. Yagupol'skii, Zh. Org. Khim., 10, 1524 (1974).
9. I. L. Knunyants, L. S. German, and B. A. Dyatkin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 11, 1355 (1956).
10. I. L. Knunyants, A. I. Shchekotikhin, and A. V. Fokin, Izv. Akad. Nauk SSSR, Ser. Khim., 282 (1953).
11. J. H. Simons (editor), Fluorine Chemistry, Vol. 2, Academic Press, New York.