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STEREOSPECIFICITY OF SPIN-SPIN COUPLING CONSTANTS (SSCC) OF ^{1}H, ^{15}N, AND ^{19}F NUCLEI IN SUBSTITUTED 2,2-BIS(TRIFLUOROMETHYL)AZIRIDINES*

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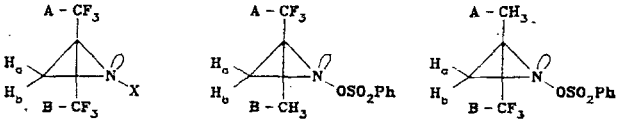
1-Chloro-, 3-methyl-, 1-chloro-3-cyano-, 1-carbomethoxymethoxy-3-methyl-, and 1-carboxymethoxy-3-methyl-2,2-bis(trifluoromethyl)aziridines were synthesized for the first time. Criteria for distinguishing cis- and trans-3-substituted and 1,3-disubstituted 2,2-bis(trifluoromethyl)aziridines from the parameters of the ^{1}H, ^{13}C, and ^{19}F NMR spectra were found.

Stereospecificity of the spin-spin coupling constants (SSCC) of the ring protons is observed in series of configurationally stable 2-methyl-2-trifluoromethyl- and 2,2-bis(trifluoromethyl)aziridines. Thus the long-range trans-SSCC with respect to the nuclei of CF_3 and CH_3 substituents ($^{4}J^{trans}$) is always greater for the H_a proton, which is cis-oriented relative to the unshared electron pair (UEP) of the ring N atom [2, 3]:



$^{4}J^{trans}_{B\text{-}CF_3H_a} > {}^{4}J^{trans}_{A\text{-}CF_3H_b}$ and $^{4}J^{trans}_{B\text{-}MeH_a} > {}^{4}J^{trans}_{A\text{-}MeH_b}$

It has been shown by theoretical calculations and experimental studies that the geminal SSCC of the N nucleus of the aziridine ring $^{2}J_{NH}$ is always greater with the cis proton with respect to the UEP of the N atom and amounts to ~10.5 Hz, while with the trans proton it does not exceed 1 Hz or is not observed at all [4].

For other aziridine derivatives it has been established that, regardless of the type of substituent in the ring, the vicinal SSCC of the ring protons $^{3}J^{cis}$ in the cis position relative to the UEP of the N atom is 1-2 Hz smaller than for the trans protons [5].

*Communication 64 from the series "Asymmetric nitrogen." See [1] for communication 63.

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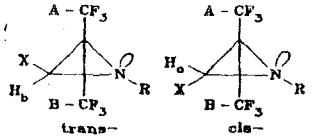
TABLE 1. Parameters of the ^1H and ^{19}F NMR Spectra of Aziridines I–VIII and XV–XVII



Compound	R	X	Solvent	Isomer	T, °C	^1H, δ, ppm			J, Hz			^{19}F, δ, ppm		$^4J_{FF}$, Hz
						H_a	H_b	other groups	B-CF_3H_a	A-CF_3H_b	other groups	A-CF_3	B-CF_3	
I*	H	H	$C_6D_5CD_3$	—	25	1,62	1,62	0,84 (NH)	—	—	9,9 (H_aNH H_bNH)	6,75	7,35	—
					−40	1,48	1,27	1,1 (NH)	1,7	1,2	8,8 (H_aNH) 10,6 (H_bNH)	6,67	7,66	6,6
II	Cl	H	C_6D_6	—	25	1,85	1,92	—	2,2	0,9	4,2 (H_aH_b)	8,3	15,57	7,7
III*	H	CN	$CDCl_3$	Mixture	25	3,21	3,21	2,95 (NH)	—	—	9,0 (CHNH)	7,78	11,08	6,8
			$C_6D_5CD_3$	Mixture	25	1,90	1,90	1,3 (NH)	—	—	10,0 (CHNH)	6,98	10,18	6,8
				cis	−40	1,70	—	1,33 (NH)	0,7	—	8,7 (H_aNH)	6,29	11,59	6,6
				trans	−40	—	1,53	1,1 (NH)	—	1,3	10,3 (H_bNH)	7,59	9,68	7,0
IV	Cl	CN	$CDCl_3$	cis	25	3,60	—	—	1,0	—	—	8,68	19,10	8,1
				trans	25	—	3,63	—	—	0,7	—	11,89	15,81	7,7
V	H	Me	$C_6D_5CD_3$	cis	25	2,06	—	0,88 (Me)	—	—	—	6,89	15,04	—
					−30	1,93	—	0,77 (Me) 0,8 (NH)	2,8	—	1,3 (B-CF_3Me) 7,3 (H_aNH) 5,9 (H_aMe)	6,72	15,74	6,8
				trans	25	—	2,17	1,09 (Me)	—	—	—	7,48	13,39	
					−30	—	2,13	1,05 (Me) 0,9 (NH)	—	1,1	10,3 (H_bNH) 5,9 (H_bMe) 1,5 (A-CF_3Me)	7,87	13,59	7,2
VI	OCH_2COOMe	Me	^1H in $CDCl_3$ ^{19}F in CD_3OD	cis	25	2,72	—	1,62 (MeC) 3,74 (MeO) 4,36 4,46 (CH_2)	1,7	—	6,4 (H_aMe) 1,7 (B-CF_3Me) 16,6 (^2J, CH_2)	6,77	19,62	8,4
				trans	25	—	3,23	1,35 (MeC) 3,75 (MeO) 4,33 4,43 (CH_2)		1,2	1,2 (A-CF_3Me) 6,4 (H_bMe) 16,6 (^2J, CH_2)	13,24	15,19	7,6
VII	OCH_2COOH	Me	Same	cis	25	2,75	—	1,62 (MeC) 4,42 4,52 (CH_2)	1,7	—	1,7 (B-CF_3Me) 6,4 (H_aMe) 17,1 (^2J, CH_2)	6,82	19,62	8,3
				trans	25	—	3,24	1,35 (MeC) 4,40 4,50 (CH_2)		1,2	1,2 (A-CF_3Me) 6,4 (H_bMe) 17,1 (^2J, CH_2)	13,24	15,19	7,6
VIII	OTs	Me	Same	cis	25	2,87	—	1,66 (MeC) 2,42 (Me Ts) 7,18—7,66 ($-C_6H_4-$)	1,7	—	1,7 (B-CF_3Me) 6,8 (H_aMe) 8,3 (HH arom.)	8,37	21,08	8,5
				trans	25	—	3,34	1,34 (MeC) 2,48 (Me Ts) 7,4—7,8 ($-C_6H_4-$)	—	1,2	1,2 (A-CF_3Me) 6,6 (H_bMe) 8,3 (HH,arom.)	15,07	16,34	7,6
XV [7]	Me	H	CH_2Cl_2	—	−40	2,11	2,36	2,61 (Me)	2,7	0	2,0 ($MeCF_3$)	4,40	15,0	7,0
XVI [7]	Br	H	^1H in CCl_4 ^{19}F in $PhNO_2$	—	25	2,50	2,56	—	2,2	0,6	—	10,0	15,9	7,5
XVII** [7]	F	H	$PhNO_2$	—	25	2,99	3,46	—	2,4	0,8	$^4J_{B\text{-}CF_3NF} = 46$ $^4J_{A\text{-}CF_3NF} < 6$	6,9	15,9	7,0

*The $\Delta G^{\neq}$ values for inversion of the N atom were found from the coalescence of the ^{19}F signals of the diastereotopic CF_3 groups for aziridines I and III; the $\Delta G^{\neq}$ values were 15.2 and 13.1 kcal/mole, respectively, i.e., they were of the same order of magnitude as the value for 1-methyl-2,2-bis(trifluoromethyl)aziridine ($\Delta G^{\neq}$ = 13.6 kcal/mole [7]).

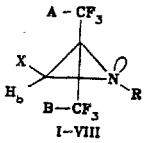
**In contrast to the conclusions in [7], $J^{trans}_{HFN} < J^{cis}_{HFN}$, and thus for aziridine XVII $^3J_{H_bFN}$ = 40 Hz, and $^3J_{H_aFN}$ = 29 Hz.

TABLE 2. Spin-Spin Coupling Constants (SSCC) with the Participation of the ^{15}N Nucleus ($J_{X^{15}N}$, Hz) in Aziridines IIIa, XIII, and XIV

Compound (solvent)	X	Isomer cis	Isomer trans	Compound (solvent)	X	Isomer cis	Isomer trans
IIIa ($C_6D_5CD_3$)	NH	66,4*	67,4*		*A*-CF_3	6,7	
	H_a (H_b)	8,6*	(0)*		*B*-CF_3	0	
	B-CF_3	2,2	1,0	XIV (C_6D_6)	H_c	0	9,5
	A-CF_3	0	2,0		H_a	11,5	0
XIII ($CDCl_3$)	H_a	10,5			H_b	9,5	0
	H_b	1,0			CH_3	1,2	3,2
	A-CF_3	2,2			CH_3	0	6,1
	B-CF_3	0			$C_{(2)}$	13,45	11,0
	$C(CF_3)_2$	12,1			$C_{(3)}$	12,2	12,2
	CH_2	11,6					

*The indicated SSCC have the same values in $CDCl_3$.

In the present research we studied the possibility of the use of the examined criteria to determine the configurations of substituted 2,2-bis(trifluoromethyl)aziridines. For this, we synthesized I-VIII, which are known to have a high barrier to inversion of the N atom and also invert rapidly (on the NMR time scale), for investigation at low temperatures:



I-VIII

I R=X=H; II R=Cl, X=H; III R=H, X=CN; IV R=Cl, X=CN; V R=H, X=Me; VI R=OCH_2COOMe, X=Me; VII R=OCH_2COOH, X=Me; VIII R=OTs, X=Me

Nonequivalence of the protons and CF_3 groups is observed from the ^1H and ^{19}F NMR spectra of aziridine I (Table 1) under conditions of slow inversion of N at −40°C. The signals of the H_a and H_b protons were assigned on the basis of the relationship of the vicinal SSCC $^3J^{cis}_{HCNH} > {}^3J^{trans}_{HCNH}$ known for aziridines [4, 6]; the relationship $^4J^{trans}_{B\text{-}CF_3H_a} > {}^4J^{trans}_{A\text{-}CF_3H_b}$ examined above is observed in this case.

It should be noted that spin-spin coupling with the NH proton is usually not observed for N-unsubstituted aziridines because of rapid exchange catalyzed by traces of water. The determination of the corresponding SSCC requires thorough drying of the samples [4, 7]. However, exchange of the NH proton does not occur in aziridine I even in CD_3OD and is realized only when CD_3COOD is added to this solution. This slowing down of NH exchange, which is unusual for aziridines, can be explained by a decrease in the basicity of the N atom due to two electronegative CF_3 groups.

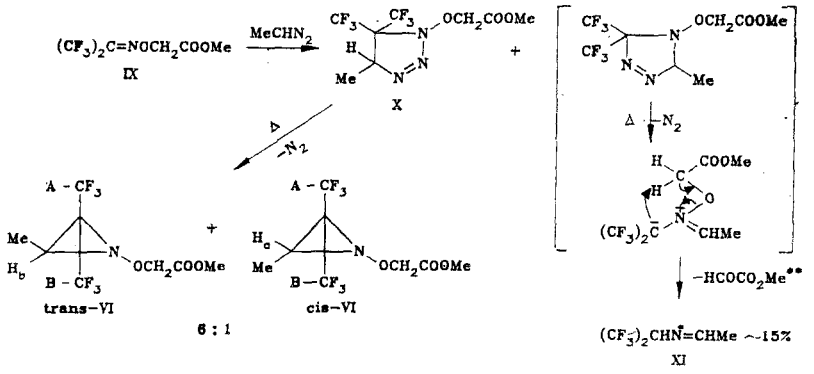
Chlorination of I with N-chlorosuccinimide or tert-BuOCl gave 2,2-bis(trifluoromethyl)-1-chloroaziridine (II), which, with respect to the NMR spectral parameters, is similar to 1-sulfonyloxy derivatives [2, 3]. The signals in its spectra (Table 1) were therefore also assigned on the basis of the relationship $^4J^{trans}_{B\text{-}CF_3H_a} > {}^4J^{trans}_{A\text{-}CF_3H_b}$.

Preferred trans orientation of the substituents, which is due to minimization of the nonbonded interaction, is observed in 1,2-disubstituted aziridines [8]. Because of the low conformational energy of the CN group, in 1-substituted 2-cyanoaziridines the population of the cis form increases substantially, but the trans isomer predominates nevertheless [9, 10]. In the case of 2,2-bis(trifluoromethyl)-3-cyanoaziridine (III) [11] in the equilibrium observed from the ^1H and ^{19}F NMR spectra the predominant (~3:1) isomer was therefore assigned to the trans form. The trans invertomer of III is characterized by large $^3J_{HCNH}$ and $^4J_{CF_3H}$ values as compared with the cis-aziridine (Table 1), i.e., the $^3J^{cis}_{HCNH} > {}^3J^{trans}_{HCNH}$ relationship is retained, while the above-examined regularity in the change in $^4J^{trans}_{CF_3H}$ is violated. To obtain additional information we therefore synthesized aziridine IIIa, which contains the ^{15}N isotope in the ring.

According to the calculated dependence of $^2J_{NH}$ on the angle between the bisector of angle CNC of aziridine and the NH bond [4], the maximum SSCC value should be observed for cis-aziridine III (cis orientation of H_a and the UEP of the N atom). According to the aziridine IIIa at −40°C in $CDCl_3$ and in $C_6D_5CD_3$, $^2J_{NH}$ = 8.6 Hz for the minor isomer, while $^2J_{NH}$ = 0 Hz for the predominant isomer (Table 2). Thus only the relationship between the $^4J_{CF_3H}$ SSCC is violated for aziridine IIIa.

From aziridine III by the action of tert-BuOCl (or N-chlorosuccinimide) we obtained the configurationally stable 1-chloroaziridine IV in the form of a mixture of cis and trans isomers in a ratio of ~1:10, which does not change in the case of heating for 2.5 h at 100°C. In contrast to aziridine III, $^4J^{trans}_{A-CF_3H_b}$ is smaller for the predominant trans isomer of IV than $^4J^{trans}_{B-CF_3H_a}$ for the cis isomer of IV, although the difference is only 0.3 Hz (Table 1). Thus a disparity in the relationship of the $^4J_{CF_3H}$ constants is observed only in the case of N-unsubstituted 3-cyanoaziridine III. One might have assumed that this is generally characteristic for 3-substituted 2,2-bis(trifluoromethyl)aziridines with an NH group. To verify this hypothesis, by cleavage of 1-carbomethoxymethoxy-3-methyl-2,2-bis(trifluoromethyl)aziridine (VI), we synthesized 3-methyl-2,2-bis(trifluoromethyl)aziridine (V). Aziridine VI was obtained by the action of diazoethane on the corresponding hexafluoroacetone oxime derivative IX [12] with subsequent decomposition of the resulting triazoline X. As compared with the 4-unsubstituted analog [12], triazoline X is less stable and undergoes spontaneous decomposition at 20°C with the formation of a mixture of cis- and trans-aziridines VI [13, 14], which differ with respect to their ^{19}F, ^1H, and ^{13}C NMR spectra (Tables 1 and 3).

The reaction of oxime IX with diazoethane gave, in addition to aziridine VI and triazoline X, aldimine XI (a mixture of cis and trans isomers in a ratio of ~1:6*), which is evidently formed through a regioisomeric adduct with diazoethane:



Aziridine VI was cleaved by the action of KOH in CD_3OD; the course of the reaction was monitored from the ^1H and ^{19}F NMR spectra. It was established that saponification of the ester group occurs along with deprotonation of the methylene group and the formation of aziridine V, and a mixture of salts XII is obtained.

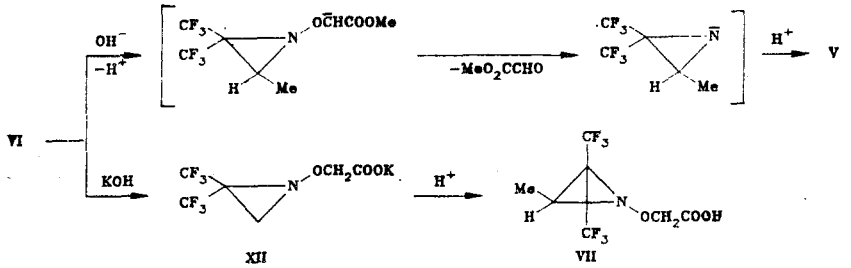
For the isolation of aziridine V it was removed from the reaction mixture by distillation in vacuo along with the solvent into a cooled trap, the condensate was diluted with water, and the heavier aziridine V was separated. The residual potassium salt XII was converted to cis- and trans-acids VII without further purification by the action of Dowex 50w × 12 ion-exchange resin in the H^+ form in $MeOH/H_2O$. An appreciable difference in the reactivities of the diastereomers of VI is not observed under the indicated conditions, as evidenced by the invariability of the ratio of the cis and trans isomers in the starting aziridine and in reaction products XII and VII.

*The trans isomer of XI was described in [15]; we obtained aldimine XI in the form of two isomers in an attempt to synthesize aziridine V by the reaction of diazoethane with hexafluoroacetone imine (see [3] and the experimental section).
**Methyl glyoxalate was not isolated.

TABLE 3. ^{13}C NMR Spectra of Aziridine VI in C_6D_6 (δ, ppm; J, Hz)

Observed group	cis-VI			trans-VI		
	δ	$^1J_{CH}$* (J_{CF})	$^3J_{CH}$ ($^3J_{CF}$)	δ	$^1J_{CH}$* (J_{CF})	$^3J_{CH}$ ($^3J_{CF}$)
MeCH	5,4	130,62 (^4J=3,7)	—	10,62	129,39	—
CHMe	43,76	171	(3,66)	45,72	170,9	(3,6)
$C(CF_3)_2$	46,77	(^2J=33,98)		49,71	(^2J=34,18)	
A-CF_3**	122,72	(^1J=277,93)	3,66	122,08	(^1J=278,32)	2,44
B-CF_3**	121,96	(^1J=277,93)	2,44	121,83	(^1J=278,32)	4,88
CH_2O	70,95	145,26	—	70,95	145,26	—
		147,71	—		147,7	—
MeO	51,98	147,71	—	51,28	146,48	—
C=O	169,2			169,4		

*For the cis and trans isomers $^2J_{CH}$ = 6.1 Hz.
**The assignment of the A-CF_3 and B-CF_3 signals in the ^{13}C NMR spectrum was made on the basis of the Karplus dependence: $^3J_{CCCH}$ is greater for a dihedral angle of 0° than for 120°.

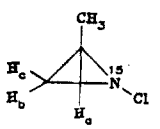


Signals of cis and trans isomers in a ratio of ~1:3 are observed in the ^1H and ^{19}F NMR spectra of aziridine V on cooling. A smaller $^3J_{HCNH}$ SSCC and a larger $^4J^{trans}_{CH_3H}$ SSCC than in the case of the trans isomer are observed for cis-aziridine V (Table 1), i.e., the above-examined relationships between these constants are valid for 3-methyl-substituted NH-aziridine V. The violation of the relationship between the $^4J_{CF_3H}$ SSCC in aziridine III can therefore be explained by the disturbing effect of the electronegative substituent (CN) in the 3 position. In this connection the halving of the $^4J_{B\text{-}CF_3H_a}$ constant on passing from chloroaziridine II to 3-cyano-substituted compound IV should be noted (Table 1). The examined stereospecific relationships between the ^1H and ^{19}F SSCC are also retained for aziridines VI-VIII.

The criterion of the stereospecificity of the SSCC with the CF_3 groups is not extended to the ^{13}C nucleus. Thus in the ^{13}C NMR spectrum of aziridine VI a $^4J_{CF}$ SSCC is observed only for the cis isomer (Table 3).

In conformity with [4], for 1-tosyloxy-2,2-bis(trifluoromethyl)aziridine-^{15}N (XIII) we observed $^2J_{H_a{}^{15}N}$ = 10.5 Hz and $^2J_{H_b{}^{15}N}$ = 1 Hz, as well as stereospecific long-range SSCC $^3J_{F^{15}N}$ and $^2J_{C^{15}N}$, which are greater in absolute value for CF_3 groups cis-oriented relative to the USP of the N atom (Table 2).

Similar regularities in the change in the $^1H^{15}N$ and $^{13}C^{15}N$ SSCC are observed for aziridinecarboxylic acid esters [16] and for the cis and trans isomers of 2-methyl-1-chloroaziridine-^{15}N (XIV) (Table 2).

In the case of trans-3-cyanoaziridine IIIa  we also observed a larger $^3J_{F^{15}N}$ value for the CF_3 group cis-oriented relative to the UEP of the N atom as compared with trans-CF_3. However, the relationship between these SSCC is reversed for the cis isomer of IIIa (Table 2). Thus a second incidence of exclusion from the general regularities of the SSCC is observed for aziridine IIIa.

In the light of these data the assignment of the H_a and H_b protons of 2,2-bis(trifluoromethyl)aziridines that was presented in [7] should be changed; the SSCC values obtained after this are given in Table 1 (XV-XVII).

It should be noted that for the stereoisomeric 3-substituted 2,2-bis(trifluoromethyl)-aziridines a significantly greater difference in the ^{19}F chemical shifts of the CF_3 groups is observed for the cis isomers as compared with the trans isomers. In addition, for N-unsubstituted trans-3-substituted 2,2-bis(trifluoromethyl)aziridines the SSCC of the geminal CF_3 groups are much greater than for the cis isomers ($^4J_{FF}^{trans} > {}^4J_{FF}^{cis}$), while the pattern is reversed for 1,3-disubstituted derivatives: $^4J_{FF}^{cis} > {}^4J_{FF}^{trans}$. These data can be used to assign the configurations. The investigated compounds are also characterized by the surprising closeness of the ^{13}C shifts of the CF_3 groups, which differ markedly with respect to their ^{19}F shifts (see Tables 1 and 3, as well as [3, 17, 18]). This can be explained by the buffer effect of the F atoms. A similar pattern was previously observed for other systems (for example, see [19]).

EXPERIMENTAL

The NMR spectra were recorded with Bruker WM-400 (^1H, 400.13 MHz; ^{13}C, 100.62 MHz) and WP-80-SY (^{19}F, 75.39 MHz) spectrometers with CF_3COOH as the external standard.

2,2-Bis(trifluoromethyl)aziridine (I). This compound was obtained by the methods in [12, 20].

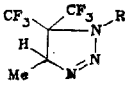
2,2-Bis(trifluoromethyl-1-chloroaziridine (II). A 0.45-g (3.3 mmole) sample of N-chlorosuccinimide was added to 0.3 g (1.6 mmole) of 2,2-bis(trifluoromethyl)aziridine (I) in 1.5 ml of $CDCl_3$. After 12 h, the volatile products were recondensed in vacuo (1 mm) in a cooled (to −70°C) trap. According to the ^1H and ^{19}F NMR spectra, the condensate contained, in addition to the solvent, only aziridine II (Table 1). Because of its high volatility the product distilled along with the solvent, and its boiling point therefore could not be determined. ^{13}C NMR spectrum ($CDCl_3$): 120.7 and 120.9 (CF_3, $^1J_{CF}$ = 279.54 Hz), 46.92 ($C(CF_3)_2$, $^2J_{CF}$ = 36.62 Hz), 40.14 ppm (CH_2, $^1J_{CH}$ = 175.8 and 181.9 Hz).

2,2-Bis(trifluoromethyl)-3-cyano-1-aziridine-^{15}N (IIIa). This compound was obtained by the method in [11]. A 60-mg (1.22 mmole) sample of powdered NaCN was added to 220 mg (0.63 mmole) of 1-tosyloxy-2,2-bis(trifluoromethyl)aziridine-^{15}N (XIII) [3, 17] in 2.5 ml of dry DMSO, after which the mixture was stirred for 0.5 h and then maintained for 12 h at 20°C. It was then poured into 25 ml of cold (below 10°C) water, and the aqueous mixture was extracted with ether (three 20-ml portions). The extract was washed with cold water (three 10-ml portions) until the wash water was neutral, dried for 1 h over $MgSO_4$, and evaporated in vacuo to give 90 mg (77%) of aziridine IIIa, which had mp 36°C after sublimation. The parameters of the NMR spectra are presented in Table 2.

2,2-Bis(trifluoromethyl)-1-chloro-3-cyanoaziridine (IV). A) A 0.1-g (5 mmole) sample (a known excess) of tert-BuOCl was added at 20°C to a solution of 40 mg (0.2 mmole) of aziridine III in 0.7 ml of $CDCl_3$. After 12 h, the volatile products were evaporated in vacuo (100 mm). According to the NMR spectra, the residue [16 mg (35%)] — a crystalline product — was a mixture of cis- and trans-aziridines IV in a ratio of ~1:10 (Table 1). The isomer ratio did not change when a solution of aziridines IV in $CDCl_3$ was heated for 2.5 h at 100°C (sealed ampul). Under the influence of Et_3N chloroaziridine IV undergoes complete dechlorination to starting aziridine III. Two drops of dry Et_3N were added to an ampul containing 16 mg of IV. After 24 h, only aziridine III and small amounts of impurities were recorded in the ^{19}F NMR spectra.

B) A 0.5-g (3.7 mmole) sample of N-chlorosuccinimide was added to 0.12 g (0.6 mmole) of aziridine III in 1 ml of $CDCl_3$. After 24 h, a mixture of aziridines III and IV in a ratio of ~1:1 was recorded in the ^1H NMR spectrum of the reaction mass.

4-Methyl-1-methoxycarbonylmethoxy-5,5-bis(trifluoromethyl)-Δ^2-1,2,3-triazoline (X). A 3.5-g (1.4 mmole) sample of imine IX [12] was treated at 20°C with excess diazoethane in ether. After 2-3 days, the volatile substances were evaporated in vacuo (25 mm) in a cooled (to −70°C) trap. The viscous residue was characterized from the NMR spectra as triazoline X containing a small amount of aziridine VI. The spectrum of the triazoline is given in Table 4.

TABLE 4. Parameters of the ^1H and ^{19}F NMR Spectra of Triazolines  in $CDCl_3$

Compound	R	δ, ppm				J, Hz			
		CH_3 (dq)	CH (qq)	CF_3 (q)	other groups	CF_3CF_3	CH_3CF_3*	CH_3CH	CF_3CH*
X	MeO_2CCH_2O	1,7	4,71	9,82 and 14,98 br	3,79 (3H,s, CH_3O), 4,67 (2H, br s CH_2O)	9,3	2,4	7,3	1,7
XVIII	H	1,63	4,66	6,37 and 8,21 br	6,22 (1H, br s NH)	9,3	1,9	7,5	1,2
	TsO [3]	1,72	4,76	10,3 and 14,7 br	2,44 (3H, s, CH_3), 7,36 : 7,85 (4H,m, arom.	9,4	2,2	7,5	1,7

*A constant of spin-spin coupling with the weak-field CF_3 group is observed; the constants were found from the ^1H NMR spectra.

The ether was removed from the condensate by distillation, and the residue was fractionated with a high-fractionating column to give 0.5 g (16%) of aldimine XI with bp 75-78°C and n_D^{20} 1.3402. The NMR spectra of solutions in $CDCl_3$ were recorded. ^1H spectrum of trans-aldimine XI: 2.14 (3H, d, J = 4.88 Hz, CH_3), 3.98 (1H, sept, $^3J_{HF}$ = 6.59 Hz, CH), 7.95 (broad q, =CH); ^{19}F spectrum: 7.53 (dd, $^3J_{HF}$ = 6.59 Hz, $^5J_{FH}$ = 0.98 Hz). ^1H spectrum of cis-aldimine XI: 2.17 (3H, d, J = 2.75 Hz, CH_3), 3.74 (1H, sept, $^3J_{HF}$ = 6.59 Hz, CH), 9.75 (q, =CH); ^{19}F spectrum: 4.46 (d, $^4J_{FF}$ = 6.6 Hz). When the signals of the methyl groups at 2.14 and 2.17 ppm were suppressed, the signals of the ethylidene protons (CH=) were transformed into singlets; the peak at 7.95 ppm was broadened more than the peak at 9.75 ppm.

3-Methyl-1-methoxycarbonylmethoxy-2,2-bis(trifluoromethyl)aziridine (VI). A 2.5-g sample of triazoline X was distilled with careful heating to give 2.1 g (92%) of aziridine VI with bp 58°C (8 mm Hg), 42-45°C (2 mm Hg), and 32-34°C (1 mm Hg) and n_D^{20} 1.3751. Found: C 34.18; H 3.41%. $C_8H_9F_6NO_3$. Calculated: C 34.18; H 3.23%.

Alkaline Hydrolysis of Aziridine VI. A solution of 0.3 g (5.3 mmole) of KOH in 1.5 ml of CD_3OD was added at 0°C to 1.2 g (4.27 mmole) of a mixture of the cis and trans isomers of aziridine VI (~1:6) in 1.2 ml of CD_3OD. The mixture warmed up to 40°C. After 24 h, the volatile compounds were removed by distillation into a cooled (to −70°C) trap. The residue [0.59 g (38.5%)] was a solid product, which was characterized from the NMR spectra as a mixture of cis-trans-isomeric salts XII. ^{19}F NMR spectrum ($CDCl_3/CD_3OD$): 7.48 (q) and 20.14 ppm (q, $^4J_{FF}$ = 8.1 Hz, CF_3 in cis-XII), 13.81 (q) and 15.8 ppm (q, $^4J_{FF}$ = 7.4 Hz, CF_3 in trans-XII).

1-Carboxymethoxy-3-methyl-2,2-bis(trifluoromethyl)aziridine (VII). A 0.5-g (1.6 mmole) sample of salt XII was dissolved without additional purification in a mixture of 10 ml of MeOH and 1 ml of water, and the solution was treated with 1 g of Dowex 50W×12 ion-exchange resin in the H^+ form. After 12 h, the mixture was filtered and evaporated in vacuo, and the product was extracted from the residue with hot hexane to give 0.2 g (46%) of a semicrystalline mixture of cis- and trans-aziridines VII. Found: C 31.55; H 2.47%. $C_7H_7F_6NO_3$. Calculated: C 31.48; H 2.64%.

3-Methyl-2,2-bis(trifluoromethyl)aziridine (V). The condensate collected in the trap in the alkaline hydrolysis of aziridine VI was shaken with a fivefold volume of water, after which the heavier aziridine was separated, dried with Na_2SO_4, and recondensed rapidly over CaH_2 in vacuo to give 0.2 g (20%) of aziridine V with bp 88°C (in a capillary). According to the NMR spectral data, the product was virtually free of impurities.*

*2,2-Bis(trifluoromethyl)aziridine (I), which was the principal reaction product in [12], was similarly isolated from the methanol solution.

cis-3-Methyl-1-tosyloxy-2,2-bis(trifluoromethyl)aziridine (VIII). This compound was obtained by decomposition of the corresponding triazoline* by the method in [3] in a mixture with the trans isomer; cis/trans ~1:6. ^{13}C NMR spectrum ($CDCl_3$): 120.1 (A-CF_3, $^1J_{CF}$ = 278.3 Hz), 120.1 (B-CF_3, $^1J_{CF}$ = 279.5 Hz), 21.6 and 129-146.2 (Ts), 45.49 (**C**$(CF_3)_2$, $^2J_{CF}$ = 36.6 Hz), 36.34 ppm (CH_2).

1-Tosyloxy-2,2-bis(trifluoromethyl)aziridine-^{15}N (XIII). This compound was obtained by the methods in [3] and [17] from hexafluoroacetone-^{15}N N-tosyloxime [21].

2-Methyl-1-chloroaziridine-^{15}N (XIV). This compound was synthesized from 2-methylaziridine-^{15}N under the influence of NaOCl by the method in [22] in the form of a mixture of cis and trans isomers in a ratio of ~1:1.3. 2-Methylaziridine-^{15}N was prepared by the method in [23] from amino-2-propyl-^{15}N sulfate. The action of a fivefold excess of KOH on 80 g (0.6 mole) of $(^{15}NH_4)_2SO_4$ (71% ^{15}N) in 130 ml of water gave 19 g (87%) of $^{15}NH_3$, which was dissolved in 20 ml of water at −5°C. A 12-g (0.2 mole) sample of propylene oxide was added dropwise to it, after which the mixture was stirred for 12 h at −5°C and then maintained for 48 h at 8-10°C. Evaporation and distillation gave 3.9 g (25%) of 1-amino-2-propanol-^{15}N with bp 62-65°C (12 mm Hg), to which 4 ml of water and a solution of 4.5 ml of H_2SO_4 in 2 ml of water were then added successively dropwise at 0°C. The mixture was maintained for 2 h at 20°C, the water was removed by distillation at 45-60°C (30 mm Hg), and the residue was evacuated at 15 mm Hg until the reaction mixture began to crystallize (~2 h). The cooled salt was pulverized and washed with absolute MeOH until the wash MeOH was almost neutral to give 6.5 g (73%) of 1-amino-2-propyl-^{15}N with mp 252-255°C, which was placed in a distilling flask and treated with 50 ml of 30% NaOH solution. The product was removed by distillation with water to bp 102°C, and the cold distillate was treated with 5 g of KOH. The aqueous layer was discarded, and the amine was dried over KOH and distilled successively over KOH and sodium metal to give 1.54 g (71%) of 2-methylaziridine-^{15}N with bp 66-68°C. According to the ^1H and ^{13}C NMR spectroscopic data, the ^{15}N enrichment was 71%. The NMR spectra of aziridine XIV were recorded in C_6D_6. ^{13}C spectrum of the cis isomer of XIV: 14.42 (Me, $^1J_{CH}$ = 128.2 Hz), 37.2 ($C_{(2)}$ $^1J_{CH}$ = 170.9 Hz), 42.15 ppm ($C_{(3)}$, $^1J_{CH}$ = 168.5 and 173.3 Hz); ^1H spectrum: 1.07 (3H, d, ^3J = 5.86 Hz, CH_3), 1.63 (H_a, $^3J_{ab}$ = 6.84 Hz), 1.8 (H_b, $^2J_{bc}$ = 2.93 Hz), 1.29 (H_c, $^3J_{ac}$ = 6.35 Hz). ^{13}C spectrum of the trans isomer of XIV 17.19 (Me, $^1J_{CH}$ = 127 Hz), 43.34 ($C_{(2)}$, $^1J_{CH}$ = 170.9 Hz), 42.85 ppm ($C_{(3)}$, $^1J_{CH}$ = 169.6 and 173.3 Hz); ^1H spectrum: 0.72 (3H, d, ^3J = 5.86 Hz, CH_3), 1.92 (H_a, J_{ab} = 7.81 Hz), 1.73 (H_b, J_{bc} = 2.93 Hz), 1.39 (H_c, $^3J_{ac}$ = 5.62 Hz).

Reaction of Hexafluoroacetone Imine with Diazoethane. A 3.5-g (~20 mmole) sample of hexafluoroacetone imine was treated with excess diazoethane in ether at −25°C, after which the mixture was maintained for 1 h at −15°C and evaporated in vacuo to a volume of ~4 ml. The residue without heating was recondensed in vacuo (35 mm Hg) in a cooled (to −70°C) trap. The residual liquid [0.2 g (4.2%)] was characterized by the NMR spectra as 4-methyl-5,5-bis(trifluoromethyl)-Δ^2-1,2,3-triazoline (XVIII) (Table 4). Aziridine V ($CDCl_3$ in the presence of acids) was detected in the ^{19}F NMR spectra in the decomposition of triazoline XVIII by photolysis or by the action of acids ($Et_2O \cdot BF_3$ or CF_3COOH): 7.86 (q) and 14.59 ppm (broad q, CF_3, $^4J_{FF}$ = 7.32 Hz). However, according to the ^1H NMR spectrum, difficult-to-identify impurities were present in the preparation.

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*In addition to the triazoline, we obtained hexafluoroisopropylacetamide which is evidently formed from the regioisomeric adduct of diazoethane relative to the C=N bond. The NMR spectra were obtained in $CDCl_3$. ^1H spectrum: 2.13 (3H, s, CH_3), 5.34 (1H, doublet of septets, $^3J_{FH}$ = 7.3 Hz, CH), 6.4 ppm (1H, broad d, $^3J_{CHNH}$ = 12 Hz, NH); ^{19}F spectrum: 6.67 ppm (dq, $^4J_{FF}$ = 7.0 Hz).

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INDOLE DERIVATIVES.

131.* THE BASICITY OF 5- AND 6-AMINOINDOLES

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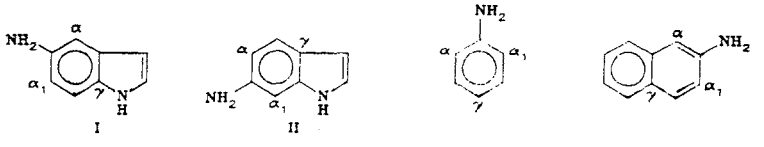
UDC 547.754:541.132:543.422.25

The pK_a values for the 5- and 6-aminoindoles were determined from potentiometric titration curves and from ^{13}C NMR data on the total change of the chemical shifts of the carbon atom signals on protonation of the amino group. The pK_a values obtained (5.99 and 5.53) were higher than those of aniline (3.92) or β-naphthylamine (3.39).

A number of different methods of synthesizing the 5- and 6-aminoindoles (I and II) have been reported [2-8] and a recent review describes methods of synthesizing compound I [9]. However, there is little information in the literature on the properties of these compounds and, in particular, there is no data on their basicity.



I II

*For Communication 130, see [1].

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