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# ASYMMETRIC NITROGEN—35†

## STRUCTURE AND PROPERTIES OF 1(S)-α-CARBOXYETHYL-3, 3-BIS(TRIFLUOROMETHYL)DIAZIRIDINE AND ITS DERIVATIVES

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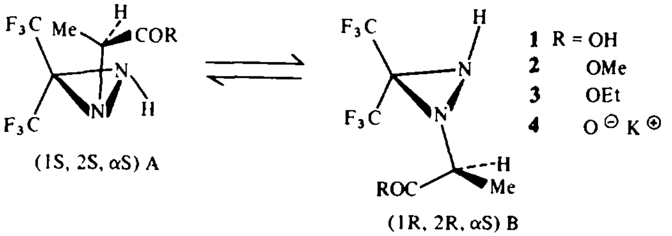
**Abstract**—A second-kind asymmetric transformation involving N-atom inversion has been observed at 20° for 1(S) - α - carboxyethyl - 3,3 - bis(trifluoromethyl)diaziridine **1** and its methyl ester **2**. X-Ray data for the diastereomer (1S, 2S, α-S), **1A** (which is thermodynamically preferred in the crystalline phase), $^1$H NMR spectra of ethyl ester 3-$^{15}$N(1) and 3-$^{15}$N(2), CD spectra of **1A,B**, **2A,B**, potassium salt **4A,B**, and semiempirical calculations (MINDO/3 and INDO) for **1A**, show that the stereospecificity of crystallization of the diastereomer A is due to the higher energy of the crystal lattice of the diastereomer (1R, 2R, α-*S*), **1B** because of hindered charge compensation as well as to the hindrance by the $CF_3$ groups to intermolecular H-bonds. According to semiempirical calculations, the stability of 3,3 - bis(trifluoromethyl) - diaziridines (TFD) to the action of electrophiles is due to the lowering of the n- and w-orbital energies and depolarization of the C–N bonds due to hyperconjugation and the inductive effect of the $CF_3$-groups. The steric effect of these groups is the reason of the low configurational stability of TFD compared with the 3,3-dimethyl analogues.

1 - Alkyl - 3,3 - bis(trifluoromethyl)diaziridines (TFD) differ from 3,3-dialkyl analogues by a higher thermal and chemical stability[2] as well as lower configurational stability.[2–4] In particular, diastereomers A and B are rapidly epimerized in the melt (at 90° for **1** and 55° for **2**) and in solution (at 25.5° for **1–4**); in the case of **2** the content of the dominant diastereomer in the equilibrium mixture increases with solvent polarity.[2]



Scheme 1.

Crystallization of the melt or removal of the solvent from the solutions of **1** and **2** at 20°, leads to a complete asymmetric transformation. In the crystalline state **1** and **2** exist only as one polar diastereomer.[2]

In this work we have carried out X-ray and quantum-chemical investigations of **1** and studied the CD spectra of **1**, **2**, **4** and the $^1$H NMR spectra of 3-$^{15}$N with a view to finding out the reasons of stereospecificity of crystallization and the observed different in the chemical and stereochemical behavior of TFD and 3,3 - dialkyl - diaziridines.

The absolute configuration of N-atoms of the less polar diastereomer **1A** has been established in the coordinates of the α-carbon chiral center C(4) of the known (S)-configuration (Fig. 1). The same (1S, 2S)-absolute configuration is typical of the N-atoms of the diastereomers **2**, **3** and **4** which are less thermodynamically stable in solution, since they have been found to have a chemical relation to **1A**.[2]

In the crystalline state, **1A** has a conformation of the N-substituent in which the H-atom, the smallest substituent at C(4), is eclipsed by the diaziridine ring. In accordance with the MINDO/3 calculation, such a conformation in 1 ($A_1$) (Scheme 2) has an energy minimum (Fig. 2). Another local minimum on the curve of the potential energy of rotation about the N(1)–C(4) bond corresponds to a conformation similar to $A_2$ (Scheme 2). However, the latter minimum is, apparently, a spurious one since it presupposes a covalently bonded chain

$$\mathrm{C(6)}\overset{1.11\,\text{Å}}{\text{———}}\mathrm{H(5)}\overset{1.10\,\text{Å}}{\text{———}}\mathrm{F(4)}.$$

Conformation $A_3$ (Fig. 2, Scheme 2) is the most destabilized one the considerable steric and dipole–dipole repulsion between the polar COOH-group and the diaziridine ring. Molecular energy minimization at every calculated point of the potential curve was carried out only in function of the angle of rotation of the COOH-group relative the C(4)–C(5) bond (*θ* in Fig. 2). Therefore, the energies of conformations $A_2$, $A_3$ has, apparently, been overestimated. Indeed, optimization of only the valence angles at the N(1) atom at the energy maximum point

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†Part 34, see Ref. 1.

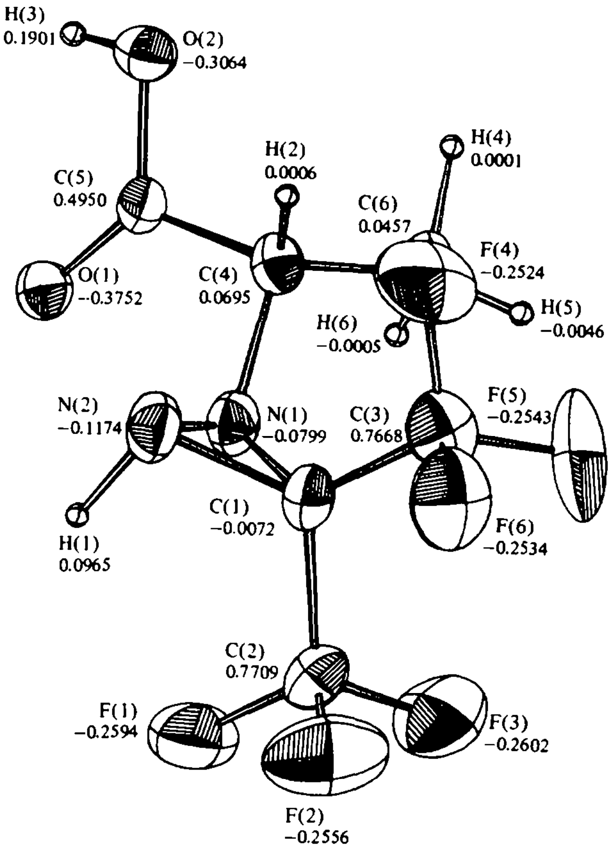
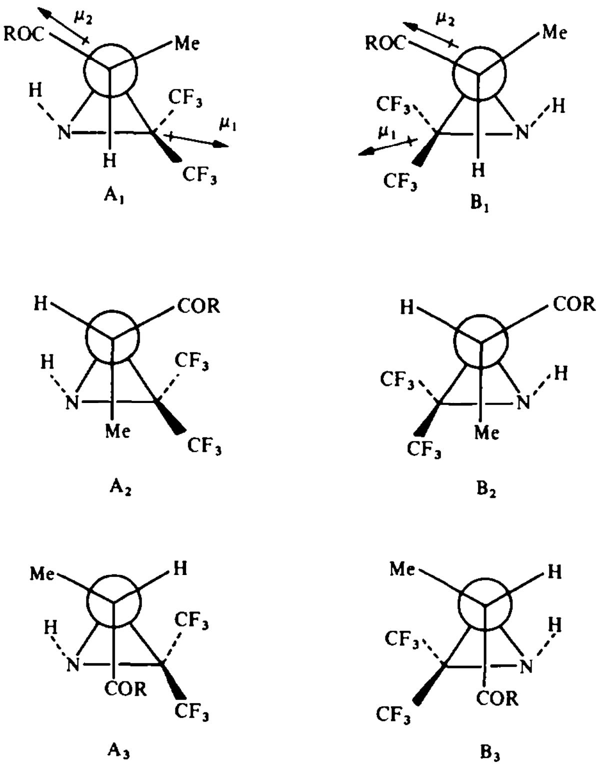


Fig. 1. The molecule **1A** with 30%-probabilistic thermal osillation ellipsoids for atoms other than hydrogen atoms. The atomic charges indicated have been calculated by the INDO procedure.



Scheme 2.

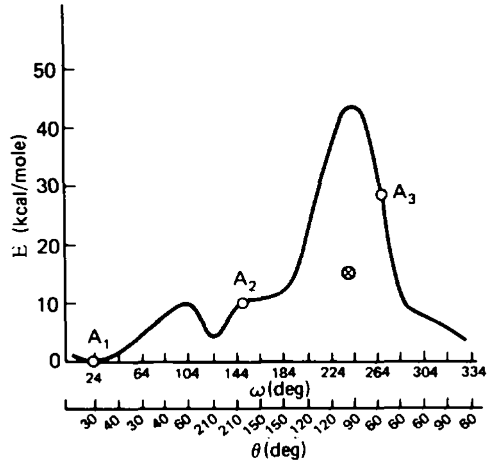


Fig. 2. Potential energy of **1A** molecules as function of the torsional angle ω/C(1)–N(1)–C(4)–H(2)/ calculated by the MINDO/3 procedure with minimization with respect to θ /N(1)–C(4)–C(5)–O(1)/. The cross symbol marks the optimum valence angles at N(1) when ω = 244°, θ = 90°.

for the case of eclipsed C(4)–C(5) and N(1)–C(1) bonds reduced this maximum to 19 kcal $mol^{-1}$. One may assume nonetheless, that the theoretical curve gives qualitatively correct estimates of the relative energies of the conformations $A_1$, $A_2$, $A_3$.

Hence, the populations of the above conformations are determined by the nonbonding interaction between the substituents at C(4) and diaziridine ring. Accordingly for diastereomer B the conformation with the eclipsed H and diaziridine ring, i.e. conformation $B_1$, must also be the most populated one (Scheme 2). Here, in contrast to $A_1$, it is the polar COOH group which comes closest to the $C(CF_3)_2$ fragment. Since in accordance with the INDO calculation the charge distribution in **1** is such (Fig. 1) that the dipole moment of the 3,3-bis(trifluoromethyl)-substituted diaziridine cycle ($\mu_1$) is directed towards the $CF_3$-groups, diastereomer $A_1$ is less polar than $B_1$.

Hence, it is clear why the equilibrium content of diastereomer **2B** increases with solvent polarity.[2]

In order to investigate the conformations in diastereomeric TFD in solution we have recorded the $^1H$ NMR spectra of isotope - labelled 3-$^{15}N(1)$, 3-$^{15}N(2)$ and the CD spectra of **1**, **2**, **4**.

Diaziridine 3-$^{15}N(1)$ was obtained according to Scheme 3.[2]

In the $^1H$ NMR spectrum of the equilibrium mixture of 3-$^{15}N(1)$ A, B in $CDCl_3$, the splitting on the nucleus of $^{15}N$ is observed only for the Me-group protons, with $^3J_{^{15}N,^1H} = 3.65$ Hz for both diastereomers A and B, which corresponds to $^3J_{^{14}N,^1H} = 2.46$ Hz. Using the calculated relationship between $^3J_{^{14}N,^1H}$ and the dihedral angle N–C–C–H (φ) for ethyl amine,[5] one may assume that the contribution of rotamers $A_2$, $B_2$, which correspond to the S-conformation of ethyl amine with $^3J_{^{14}N,^1H} = 0.61$ Hz, is very small.

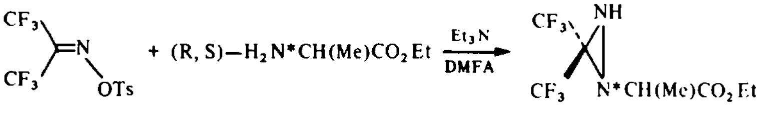
The absence of geminal coupling $^2J_{^{15}N,^1H}$ of the methine proton in both diastereomers A and B is confirmed by comparison of the $\Delta\nu_{1/2}$ of the mean line of the quintuplet CH 3-$^{15}N(1)$ (3.0 Hz) and 3-$^{14}N(1)$ (3.2 Hz). Such a situation with $^2J_{^{15}N,^1H} = 0$ is fairly described by the conformation $A_1$, $B_1$ involving a transorientation of the lone pair (LP) N(1) and the C–H bond.[5] For the rotamers $A_3$, $B_3$ one may expect the same value of $^3J_{^{15}N,^1H}$ as for $A_1$, $B_1$. However, for $A_3$, $B_3$, the constant $^2J_{^{15}N,^1H} = -3.8 \pm 1.3$ Hz must correspond to the dihedral angle LP–N–C–H of 60 ± 5°,[5] which is not supported by experimental data.

Thus the equal values of $^3J_{^{15}N,^1H}$and the absence of $^2J_{^{15}N,^1H}$ in the diastereomers 3-$^{15}N(1)$–A, B testify to the fact that it is the conformation with a trans-orientation of lone pair and the C–H bond and the same dihedral angle N(1)–C(4)–C(6)–H(i), i.e. $A_1$, $B_1$, which is the most populated one in solution.

The coupling constant $^3J_{^{15}N,^1H}$ is transferred via carbon and the heteroatoms, N-atom for example.[6] Therefore, in order to obtain more information about the populations of the rotamers $A_{1-3}$ and $B_{1-3}$ we have synthisized diaziridine 3-$^{15}N(2)$ (Scheme 4).

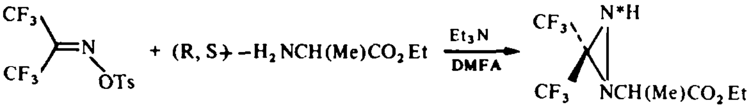
However only the direct constant $^1J_{^{15}N,^1H}$ (60.7 Hz for A and 56.3 Hz for B) is observed in the $^1H$ NMR spectrum of the equilibrium mixture of 3-$^{15}N(2)$—A, B. As it is in the case of 3-$^{15}N(1)$, the $\Delta\nu_{1/2}$ of the mean line of the quintuplet of the methine proton 3-$^{15}N(2)$ (3.37 Hz) practically coincides with the $\Delta\nu_{1/2}$ of CH of the unlabelled sample **3**, which indicated the absence of $^2J_{^{15}N,^1H}$ in 3-$^{15}N(2)$.

For diaziridines the configuration with a trans orientation of N-substituents and lone pairs is preferable,[7] therefore, one may assume that the spin–spin coupling of $^{15}N$–$^1H$ is not communicated through the N-atom of the diaziridine ring. The constant $^3J_{^{15}N,^1H}$ in the $^{15}N$–N–C–H chain is observed for N-nitroso-compounds[6] where the N–N– bond is partly double.



3-$^{15}N(1)$

Scheme 3.



3-$^{15}N$ (2)

Scheme 4.

In the CD spectrum of the acid **1A** in MeOH one observes only one absorption band at 214.5 nm which shifts towards the shorter wavelengths (203.7 nm) for the carboxylate anion **4A** (Fig. 3). Among the (S) - α - alanine derivatives, (S) - α - trimethylammoniumpropionic acid chloride is the closest analogue of **1A** as far as chiroptical properties are concerned. The CD spectrum of this compound is also characterized by only one positive Cotton effect (CE) for the n-π* transition at 213 nm which undergoes a hypsochromic shift towards 205 nm for the carboxylate-anion chromophore in betaine, $Me_3\overset{+}{N}CH(Me)CO_2^-$.[8]

The picture is quite similar in the case of diastereomer **1B**: the positive CE of the acid at 212.5 nm (the branch) shifts to 200 nm in the spectrum of potassium salt **4B** (Fig. 3).

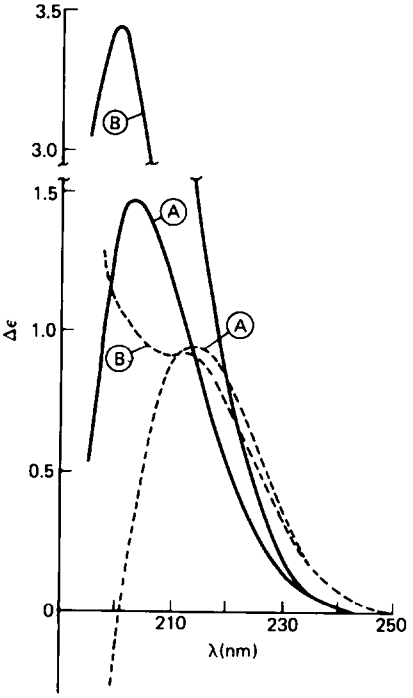
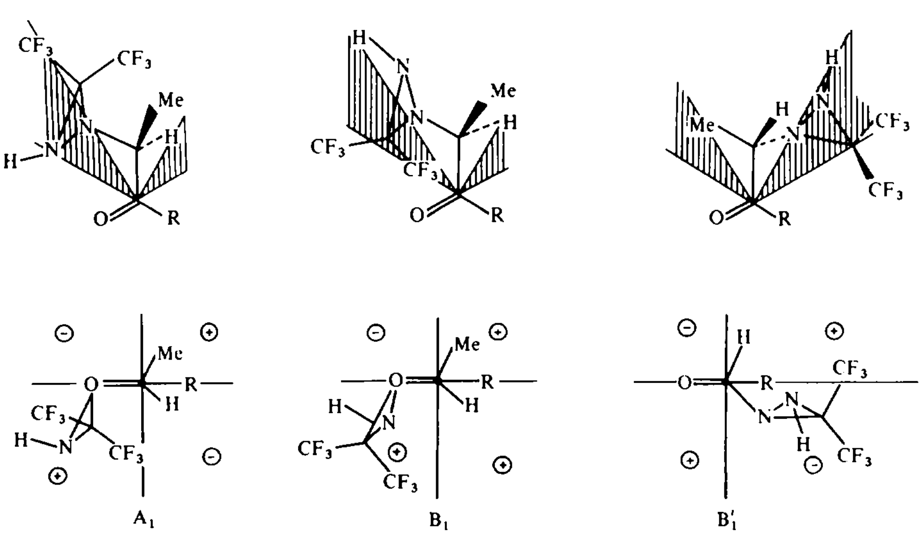


Fig. 3. The CD spectra of the acid **1A, B** in MeOH (——) and the potassium salt **4A, B** in $H_2O$ (——).

The absolute configuration of (S)-α-trimethylammoniumpropionic acid is related to the sign of CE on the assumption of the conformation relative to the C–CO bond with the N-atom lying in the nodal plane of the π-system of carboxyl group.[8] In the solid phase, the α-heteroatom N(1) of the acid **1A**, like that of (S) - α - alanine[9] only deviates slightly from the carboxy group plane. The conformation about the C–CO bond with a synperiplanar orientation of the heteroatom and the C=O bond is also preferred in solution for all α - hetero - substituted carboxylic acids[10,11] and their esters.[11-13] In accordance with the analysis of the molecular models of diastereomers **1A,B** in terms of the sector rule,[11] the rotamers $A_1$ and $B_1$ are the most congruous to the observed positive positive CE of the n-π* transition of carboxyl group with a synperiplanar orientation of N(1) (Scheme 5).

This conclusion apparently holds true for the ester **2** as well, in the spectra of both diastereomers of which in MeOH one observes an intensive positive CE near 210 nm (band 1) and a minor negative CE at 245.5 nm (band 2) (Fig. 4). The same absorption bands are typical of (S) - α - alanine ester.[12,13]

Interpretations of band 2 in the CD spectra of the amino acids have been ambiguous, it has been suggested that the intensity of this band depends on the nucleophilic properties of N-atom, and the band has been attributed to the $n_N$-$\pi^*_{CO}$ charge transfer.[12] On the basis of low-temperature measurements the band has been attributed to the $n_0$–$\pi^*_{CO}$ transition in the conformer with a synperiplanar orientation of the α-alkyl group and the C=O bond.[13] The CD data for **2A,B** confirms the conformational origin of band 2, since the lowering of the energy of non-bonding orbitals of N-atoms as a result of their inclusion in the three-member cycle with strongly electronegative $CF_3$-groups (*vide infra*) and the unfavorable orientation of the $n_N$- and $\pi^*_{CO}$-orbitals preclude the intramolecular $n_N$– $\pi^*_{CO}$ charge transfer in α - carboxy - substituted TFD. The higher intensity of band 2 of **2B** in heptane may be attributed to an increased population of the rotamer $2A_1$ whose polarity is lower than that of $2B_1$ due to trans-orientation of the C–N and C=O bonds (Scheme 5).



Scheme 5.

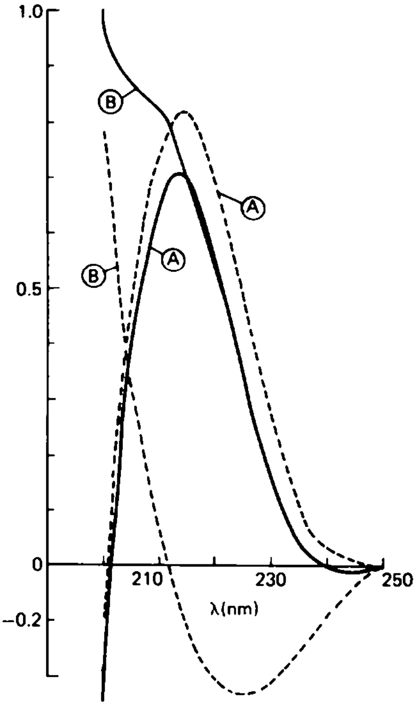


Fig. 4. The CD spectra of the ester **2A, B** in heptane (——) and MeOH (——).

In the solid state, the strong H-bonds of the COOH-group O(1)... O(2) – 2.698(6) Å combine the **1A** molecules into trimers (Fig. 5). The contact O(1)... N(2) 3.18 Å and O(1)... H(1) 2.38 Å is either a weak H-bond or a strong van der Waals interaction. All the other inter-molecular contacts do not exceed the sum of the van der Waals atomic radii.

The complete asymmetric A + B→A conversion accompanying crystallization of **1** and **2** means that the crystal lattice energy of A is much smaller than that of B and A + B.[2] The reason, apparently, lies in the following. If we assume that, as in the case of A, the conformation occuring in a hypothetical crystal B is $B_1$ with a synperiplanar orientation of the C–N and C=O bonds, then in the crystal structure of the either **2B** the formation of intermolecular H-bonds involves approach of at least two electro-negative groups CO and $CF_3$ and in the case of the acid **1B** of two of the groups CO and $CF_3$, OH and $CF_3$ (Scheme 6).

Such approach must increase the crystal lattice energy, since charge compensation in the crystal by an opposite charge will be hindered. It cannot be ruled out, besides, that the screening of COR by the cis-$CF_3$-group in diastereomer B hinders crystallization by preventing formation of the intermolecular H-bonds, whereas in the diastereomer A the COR group is sterically more accessible.

According to the CNDO[7] and *ab initio*[14] calculations, the inversion of diaziridines occurs via a monoplanar transition state.

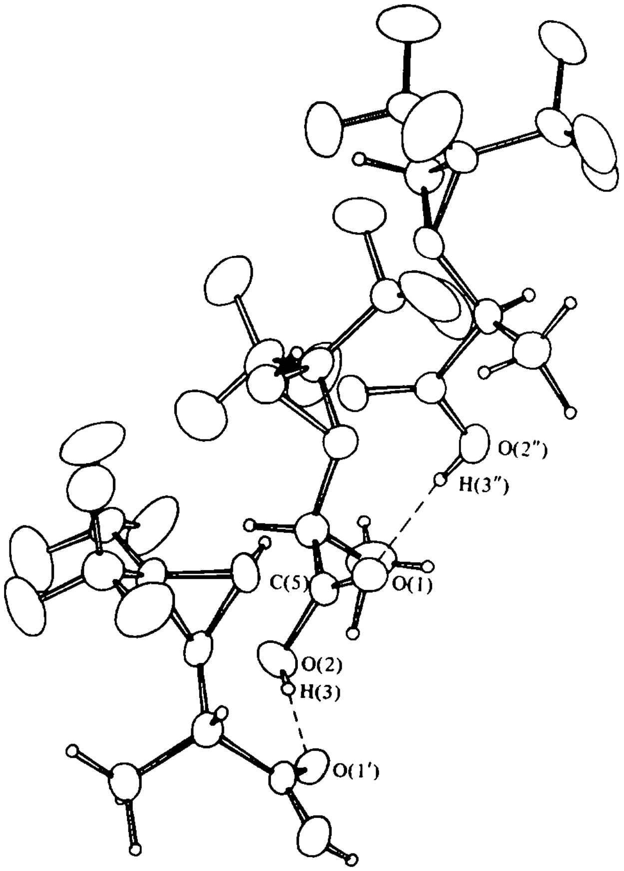
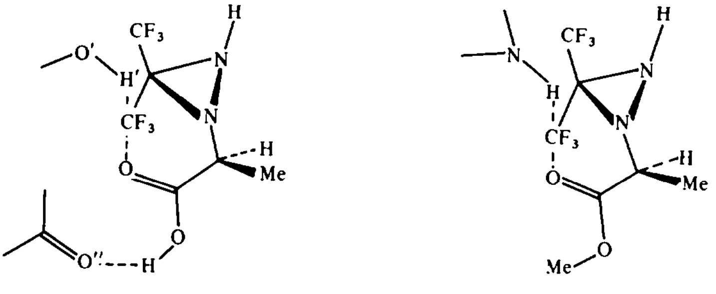
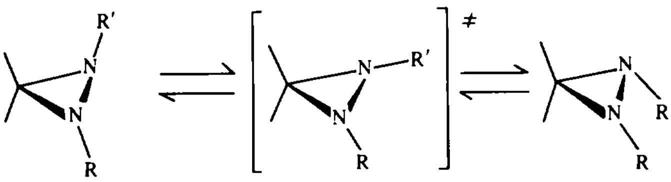


Fig. 5. The trimer **1A** which constitutes the crystalline structure.



**1B** **2B**

Scheme 6.



Scheme 7.

It has been shown earlier that the inversion barrier of TFD varies in function of the substituent at N(1).[2] Therefore, it is the inversion of N(1) which is the limiting stage of TFD topomerization. Mean $\varDelta G^{\ddagger}$ values found from epimerization kinetics of diastereomers **1A, 5, 6**; the $\varDelta G^{\ddagger}$ values for **5, 6** have been calculated for 25.5° under assumption of $\varDelta S^{\ddagger} = 0$. Compared with the earlier-studied 3,3-pentamethylendiaziridine **5**[15] ($\varDelta G^{\ddagger}_{25.5^\circ} = 28.1$ kcal mol$^{-1}$,[3] and diaziridine - 3,3 - dicarboxylic acid amide **6** ($\Delta G^{\ddagger}_{25.5^\circ} = 27.3$ kcal mol$^{-1}$),[16] which are more configurationally stable, the N(1) pyramide in the diaziridine **1A** ($\Delta G^{\ddagger}_{25.5^\circ} = 22.5$ kcal mol$^{-1}$)[2] is considerably flattened (Scheme 9), which is indicative of a relationship between the structural parameters of the N-pyramid and inversion energy parameters.

Further, in **1A** the C(1)–N(1) bond is shorter and the N(1)–N(2) bond is longer than in **5** or **6** (Scheme 9).

The reason of the structural, chemical and stereochemical peculiarities of TFD lies, apparently, with the electronic and steric effects of the $CF_3$-groups.

The replacement of H atoms in the methyl group by the most electronegative F atoms results in a sharp increase of the accepting ability of this group and the C–$CF_3$ bond.[17] Therefore, one may hypothesize the following three strongest donor-acceptor interaction in TFD: $n_{-}-\pi^{*}_{C(CF_3)_2}$, $n_{+}-\sigma^{*}_{C(CF_3)_2}$ and $w_2 - \pi^{y*}_{CF_3}$ (Scheme 8) which, together with the induction effect of the $CF_3$-groups, cause electron redistribution in the diaziridine ring, lowering of the n- and w-orbital levels and, consequently, a variation of the structural parameters and reactivity of TFD.

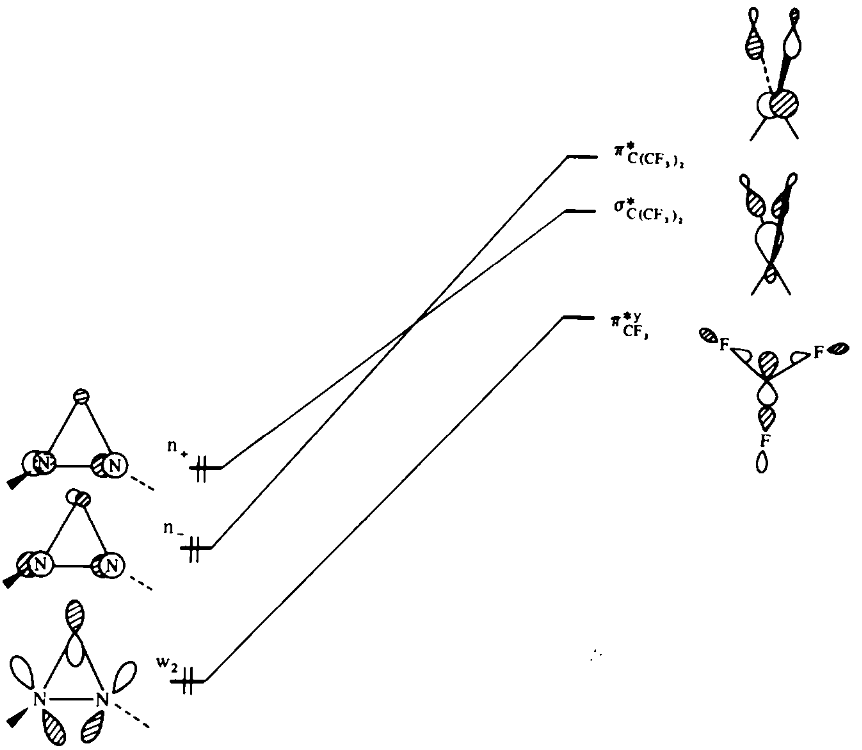
Indeed, according to the INDO calculation, the levels of the n- and w-MO of the diaziridine ring are smaller by 1.53, 1.63 and 0.79 eV in diaziridine **1A** compared with the model 3,3-dimethyl analog **7**. The same geometry as for **5** was used for calculation (Scheme 9).

The considerable contribution of the induction effect of the $CF_3$-groups follows from the fact that the population of the C(1) atom in **1A** (4.0071) is the higher than that of the corresponding atom in **7** (3.7561). The lower orbital population of N(1) and N(2) (5.0799 and 5.1174) in **1A** (in **7** the populations are 5.1665 and 5.2022, respectively) is due both to the induction effect and the hyperconjugation involving the nonbonding orbitals $n_{+}-\sigma^{*}_{C(CF_3)_2}$ and $n_{-}-\pi^{*}_{C(CF_3)_2}$. The relative positions of the levels of the unperturbed MO of the diaziridine fragment have been assumed the same as in ref. 18.

On the basis of the structural parameters and the calculation results it may be concluded that the $n_{-}-\pi^{*}_{C(CF_3)_2}$-hyperconjugation is the one which is predominantly realized. Assuming that the unperturbed antisymmetric nonbonding $n_{-}$-orbital is localized predominantly on N(1) and the symmetric $n_{+}$-orbital on N(2).

The interaction of the n-orbital with the group antibonding $\pi^{*}_{C(CF_3)_2}$-orbital elongates the N–N– bond (decrease of bonding) and shortens the C–N bond (decrease of antibonding) (Scheme 8), which is really observed in the **1A** molecule (Table 2, Scheme 9), whereas the $n_{+}-\sigma^{*}_{C(CF_3)_2}$-interaction should decrease the antibonding between N(1) and N(2) and, accordingly, render it shorter. The $n_{-}-\pi^{*}_{C(CF_3)_2}$-hyperconjugation steps up the order of the N(1)–C(1) bond (the Viberg index for the $p_Z$-orbital, $V_{N(1)p_Z-C(1)} =$ 0.014: in the case of **7**, $V_{N(1)p_Z-C(1)} = 0.009$), since the $n_{-}$-orbital is localized on N(1) and steps down the order of the antiperiplanar C(1)–C(3) bond as compared with the synperiplanar C(1)–C(2) bond in relation to the lone pair of N(1) ($V_{p_Z}$ are 0.211 and 0.248, respectively). Since the group $\pi^{*}_{C(CF_3)_2}$-orbital is made up of the $p_Y$-orbitals localized on C(2) and C(3), the $n_{-}-\pi^{*}_{C(CF_3)_2}$ electron transfer manifests itself also in the increase of the population of the $p_Y$-orbital of C(3) (0.7641) over C(2) (0.7379).

The Viberg index for the $p_Z$-orbital of N(2) on which $n_{+}$ is localized with C(1) in TFD **1A** is the same as in **7**–0.009, which indicates that the contribution of the $n_{+}-\sigma^{*}_{C(CF_3)_2}$ is small.



Scheme 8.

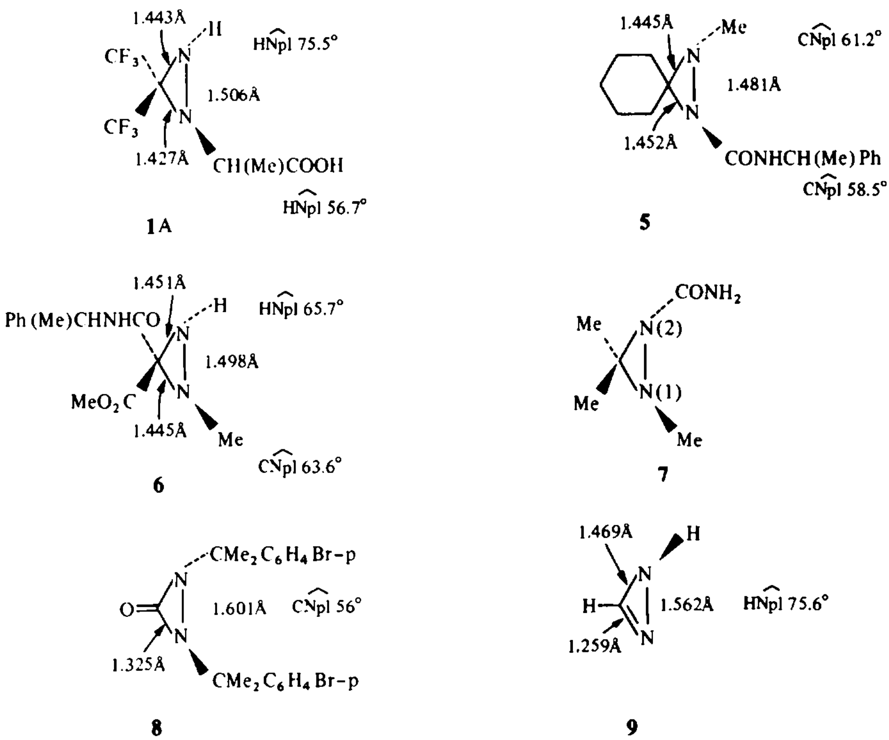
As a result of the $n_- - \pi^*_{C(CF_3)_2}$-hyperconjugation, the diaziridine ring becomes partly antiaromatic which manifests itself, apart from elongation of the N–N bond, in the increased pyramidality of N(2). There are structure data for diaziridines **6**, **8**[19] that carry a substituent at the C atom which reduce the levels of the antibonding orbitals localized on this atom. From analysis of these data one can perceive the tendency for shortening of the C–N bond and elongation of the N–N– bond in proportion with the increasing antiaromaticity of the ring in the series **5** < **6** < **1A** < **8** < **9** (Scheme 9). The extreme case of an antiaromatic ring is the hypothetical 1H-diaziridine **9**.[20] Elongation of the N–N bond in diaziridinone **8** may be, alternatively due to donation of the n-orbital of O-atom to the antibonding orbital of the cycle and distortion of the valence angle at C=O, as it had been assumed for cyclopropanone.[21]

The increase of pyramidality of N(2) must result, apart from reduction of the level of the n-orbital, in an increase of the N(2) inversion barrier and, consequently, in that the inversion of NH will be the limiting stage of the topomerization of N-monosubstituted TFD (*vide supra*). This is, however, contrary to the experimental facts.[2] It follows hence that any relationship between the structural parameters of the N pyramide and the inversion energy parameters can exist only in the class of ligands bonded to N via an identical atom.

The elongation of the N–N bond and depolarization of the C–N bond are responsible for the relative ease of nucleophilic opening of the diaziridine ring at the N–N bond at the action of an alkali on 1 - α - carbmethoxymethyl - 3,3 - bis(trifluoromethyl) diaziridine.[2]

Under the effect of the electronegative group X at the α - C - atom of the substituent, the inversion barrier of N is lowered due to the stabilizing $n - \sigma^*_{CX}$ or $n - \pi^*_{CX}$ interaction which is enhanced in the planar transition state of inversion.[22] However, in the case of TFD an increase of the $n - \sigma^*_{C(CF_3)_2}$ and $n - \pi^*_{C(CF_3)_2}$ interaction should lead to an increase of ring antiaromaticity and, accordingly, destabilization of the transition state of inversion. According to INDO calculation, the Viberg index of the N(1)–C(1) bond is not increased in transition from the pyramidal to a planar state ($V_{N(1)pz-C(1)} = 0.013$). One may assume, therefore, that the inversion barrier reduction in TFD flattening of the N(1) pyramide are largely due to the steric effect of the $CF_3$-groups.[4]

The calculation of contacts has been based on the molecular geometries derived by the X-ray analysis, except the position of the H-atoms. Analysis of the intramolecular contacts in **1A**, **5** and the model compound **1A** (exocyclic valence angles at N(1) are assumed to be the same as in **5**) shows that only in **1A** are there contacts that are 0.35 Å shorter than the sum of the van der Waals atomic radii: N(2)···· H(2) 2.25, F(4)···· H(2) 2.13, F(4)···· C(4) 2.74, C(3)···· C(4) 3.03, F(5)···· H(5) 2.22 Å. The van der Waals radii of the atoms are: $R_0 = 1.3$, $R_N = 1.5$, $R_C = 1.7$ Å; $R_H = 1.07$ Å according to the adopted H-atom geometry.[23] In the real **1A** the respective contacts are 2.51, 2.22, 2.88, 3.11 and 3.35 Å. In **5** only two shortened intramolecular contacts have been observed: one between the C-atom of the Me–N group and the cis - α - C - atom of the cyclohexane ring (2.99 Å) and the other between the H-atoms of the corresponding carbons (1.96 Å). The assumption of steric hindrances in **1A** is further corroborated



Scheme 9.

by the considerable increase of the valence angle C(1)N(1)C(4)–122.1° as compared with N(2)N(1)C(4)–113.2°, as well as by the largest exocyclic angle at C(1), N(1)C(1)C(3)–126.7°.

It may be assumed that the interaction between the $w_2$-orbital of the diaziridine ring and the antibonding $\pi^{Y*}$-orbitals of the $CF_3$-groups (Scheme 8) contributes to the elongation of the N–N bond (decrease of bonding) and shortening of the C–$CF_3$ bonds by 0.012 and 0.028 Å, compared with the C–$CF_3$ bonds in triazoline[24] and isoxazolidines.[25] The larger deviation of the cis - $CF_3$ - group from the cycle plane relative to the substituent at N(1) (*vide supra*), which is due to steric repulsion, is compensated for by the greater shortening of the C(1)–C(3) bond compared with C(1)–C(2). The lengths of the C(2)–F(1) and C(3)–F(4) bonds which must be the most sensitive to the $w_2$–$\pi^{Y*}$-interaction are not seen to increase

The induction effect of the $CF_3$-groups and the above mentioned hyperconjugation phenomena reduce the acceptor capacity of the C–N bonds by causing depolarization and the donor capacity of the N–N-fragment in TFD. This tends to hinder both the electrophile ($E^+$) attack on the lone pairs of N and the subsequent rearrangement involving electron pair transfer from the n-orbital of N to the antibonding orbital of the C–N bond.

Thus the higher thermal and chemical stability of TFD is largely due to the electronic effect of the $CF_3$-groups and the lower configurational stability to steric factors. The reason of the stereospecific nature of crystallization of diastereomer A in its versions 1 and 2 resides in the steric and dipole–dipole intramolecular interaction of the $CF_3$- and RCO-groups.

## EXPERIMENTAL

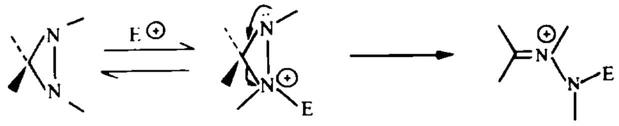
$^1H$ NMR spectra were taken by means of an NT-360WB "Nicolet" spectrometer; the CD spectra by means of a J-20A JASCO spectropolarimeter. X-Ray data have been deposited with the Cambridge Crystallographic Data Centre.

The preparation and characteristics of (S) - 1 - α - carboxyethyl - 3,3 - bis(trifluoromethyl)diaziridine derivatives **1**–**4** are described elsewhere.[2]

$^{15}N(1)$ - (R, S) - 1 - α - *Carbethoxyethyl* - 3,3 - *bis(trifluoromethyl)diaziridine* **3** was obtained according to the procedure of ref. 2 form 1.09 g (3.2 mmol) of O-tosyloxime hexafluoracetone and 0.45 g (3.8 mmol) of ethyl ester of $^{15}N$ - (R, S) - α - alanine with a yield of 65%.

$^1H$ NMR spectra ($CDCl_3$), δ, ppm: (A) 1.44 (dd, MeCH, $^3J_{MeCH}$ 7.0 Hz, $^3J_{^{15}N,^1H}$ 3.65 Hz), 1.30 (t, $MeCH_2$, J 7.0 Hz) 3.46 (q., CH), 4.22 and 4.25 ($OCH_AH_B$, $J_{AB}$ 11 Hz), 3.44 (NH); (B) 1.53 (dd, MeCH), 1.27 (t. $MeCH_2$) 3.48 (q., CH), 4.20 and 4.23 ($OCH_AH_B$, $J_{AB}$ 10 Hz), 3.21 (NH).

*Hexafluoracetone* $^{15}N$ *- O - tosyloxime*. A soln of 3.00 g (0.02 mol) of hexafluoracetone and 1.05 g (0.015 mol) of $^{15}N$-hydroxylamine hydrochloride in 10 ml of abs pyridine was kept for 2 h in a sealed tube at 20° and for 8 h at 100°. After cooling to *ca* – 5°, the tube was opened and a soln of 3.82 g (0.02 mol) of TsCl in 12 ml of abs pyridine was added dropwise. After agitation for 10 h at 0° the reaction mixture



Scheme 10.

was added to 100 ml of 10% HCl, the residue was separated, dried *in vacuo* and recrystallized from 30 ml of hexane. Obtained 2.10 g (42%) of product with m.p. 89–90° (m.p. 89–90°).[2]

$^{15}$N(2) - (R, S) - 1 - *a* - Carbethoxyethyl - 3,3 - bis(trifluoromethyl)diaziridine **3** was obtained according to ref. 2 with a yield of 63% from 1.01 g (3.0 mmol) of $^{15}$N - O - tosyloxime hexafluoracetone and 0.41 g (3.5 mmol) of (R, S) - α - alanine ethyl ester.

$^1$H NMR spectra ($CDCl_3$), δ, ppm: (A) 1.45 (d., $\underline{\text{Me}}\text{CH}$, $^3J_{MeCH}$ 7.2 Hz), 1.31 (t., $\underline{\text{Me}}\text{CH}_2$, J 7.0 Hz), 3.47 (q., $\overline{\text{CH}}$), 4.23 (q., $OCH_2$), 3.46 (d. $\overline{\text{NH}}$, $^1J_{^{15}N,^1H}$ 60.70 Hz); (B) 1.56 (d., $\underline{\text{Me}}\text{CH}$), 1.29 (t., $MeCH_2$), 3.49 (q., CH), 4.23 (q., $CH_2$), 3.19 (d., NH, $^1J_{^{15}N,^1H}$ 56.3 Hz).

### *CD spectra*

Diastereomers **1A**, **2A**, **4A** recorded at 20° immediately after dissolution of the samples. After keeping the solutions for 24 h at 20°, the spectra of equilibrium mixture were recorded. The CD spectrum of the diastereomer B was obtained by subtracting the spectrum of A from that of the equilibrium mixture, with allowance for the diastereomer ratio in the mixture as measured by $^{19}$F and $^1$H NMR spectroscopy.[2]

*Acid* **1** (MeOH), $\lambda_{max}$ nm (Δε):(A) 214.5 (0.949), (B) 212.5 (0.920). Ester **2**, $\lambda_{max}$ nm (Δε): MeOH, (A) 213.5 (0.704), (B) (0.824); heptane, (A) 214.5 (0.822), (B) 225 (−0.230). *Potassium salt* **4** ($H_2O$), $\lambda_{max}$ nm (Δε): (A), 203.7 (1.476), (B) 200 (3.451).

### *X-Ray analysis of* **1A**

M.p. 86–86.5°, elementary cell $a = b = 10.023(3)$, $c = 8.363(2)$ Å, $\gamma = 120°$, the spatial group $P3_1$, $M = 252, 112$, $V = 727.6$, $d_{calc} = 1.73$ g/cm$^3$. The intensities of 632 reflexes with $I \geqslant 2\sigma$ (I) have been measured using a DAR–UM diffractometer. Absorption was not allowed for ($\mu_{CuK_\alpha} = 8.2$ cm$^{-1}$). The structures were identified by "manual" computations using the ROENTGEN-75 program.[26] The coordinate reflexes were selected in according to ref. 27. The H-atoms have been localized on the basis of the differential syntheses. More accurate results were obtained by applying the least-squares method in the full-matrix anisotropic (atoms F, O, N, C) and isotropic (H atoms) approximation up to $R = 0.040$. The picture of the molecule was obtained using the ELLIDS program.[28]

### *Quantum-chemical calculations*

Carried out using the VIKING program,[29] the electronics structure was determined by the INDO methos and rotation barriers by MINDO/3. Number of operations, 200, convergence criterion 0.0001. Molecular geometry was determined by the X-ray diffraction analysis. The geometry of H atoms was borrowed from ref. 30: ∠CCH = 110.0°, C–H 1.11 Å and from ref. 28 ∠COH = 110.2°, O–H 1.01 Å; assumed ∠NCH = 109.5°, ∠XCH = 109.5°.

In calculations of **1A** with a planar configuration of N(1) the valence angle N(2)N(1)C(1) has not been changed. The exocyclic valence angles at N(1) have been taken in the same ratio as for the pyramidal N(1).

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