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SHORT COMMUNICATIONS

Conformational Analysis of 4-Trifluoromethyl-1,3-dioxane

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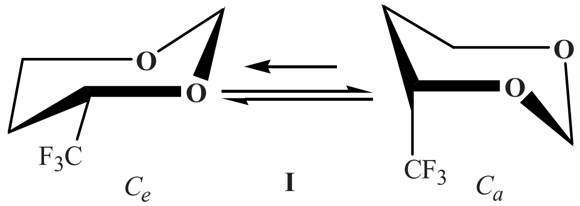
The interest to the structural investigation of 1,3-dioxanes, six-membered heteroanalogs of cyclohexane, originates from the features of their structure (the presence of two heteroatoms separated by sp^3-carbon atoms), from their valuable pharmacological properties, and also from the application to the fine organic synthesis [1–5]. In the last decade computer simulations play an important role in conformationsl studies of such compounds. It was shown in particular that the conformational isomerization of unsubstituted 1,3-dioxane and also of 2,2-, 4,4-, and 5,5-dimethyl-1,3-dioxanes occurred between two degenerate in energy invertomers of chair (*C* and *C**), and of 2-methyl-1,3-dioxane, between the conformers of equatorial and axial chair (C_e and C_a) along two materially equivalent paths [6–9].

This study is dedicated to the computer simulation of the paths of conformational isomerization of 4-trifluoromethyl-1,3-dioxane (**I**) by nonempirical quantum-chemical approximations RHF//STO-3G and 6-31G(*d,p*) in the framework of software HyperChem [10] under the conditions simulating the behavior of the molecules of this substance in the gas phase.

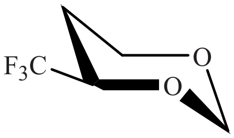
It follows from the data of ^{1}H NMR spectra of individual stereoisomers of 4-trifluoromethyl-5-methyl-1,3-dioxane that the molecules of 1,3-dioxane **I** exist at room temperature prevailingly in the conformation of equatorial *chair* (C_e) [11].



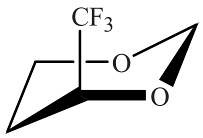
C_e **I** C_a

We revealed for the first time the general pattern of the conformational transformations and the character of the intermediate minima on the potential energy surface (PES) for the molecules of the compound in question.

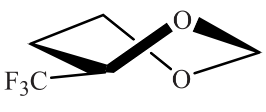
The general pattern suggests a multicomponent conformational equilibrium between the C_e and C_a forms



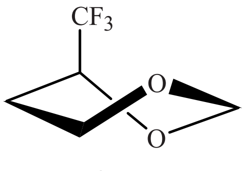
C_e



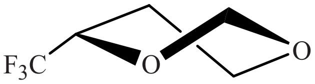
C_a



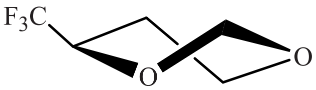
2,5-T_e



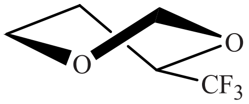
2,5-T_a



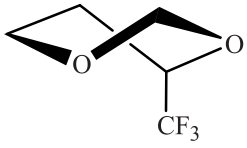
1,4-*T*(1)



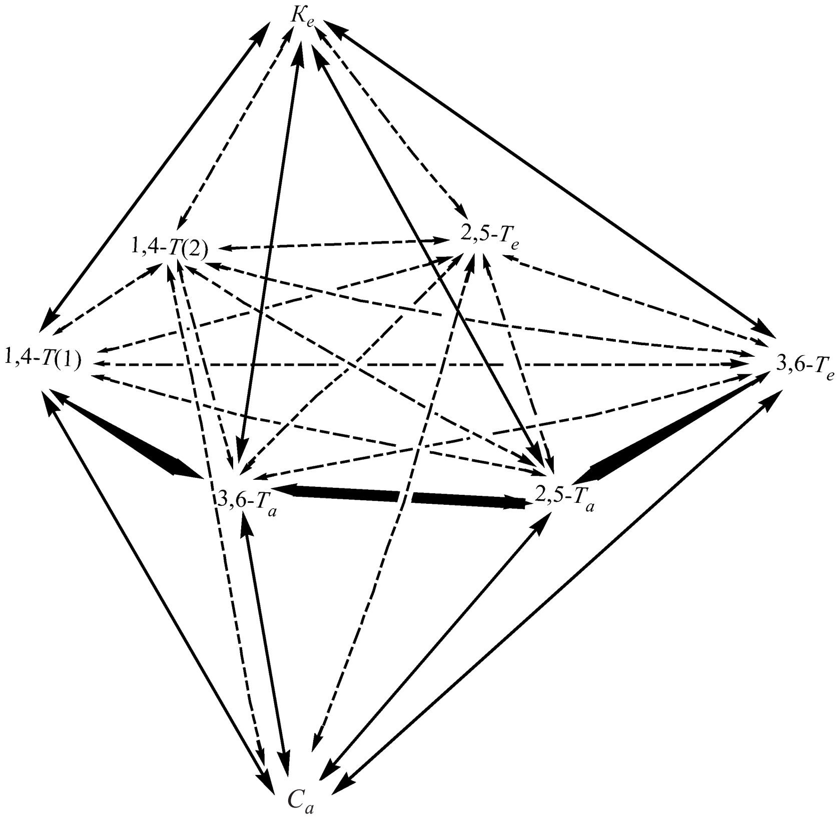
1,4-*T*(2)



3,6-T_e



3,6-T_a



Minima on PES of 4-trifluoromethyl-1,3-dioxane

Basises	Relative energy of conformers (kcal mol^{-1})[a]						
	C_a	1,4-T(1)	1,4-T(2)	2,5-T_e	2,5-T_a	3,6-T_e	3,6-T_a
STO-3G	1.9	4.8	5.0	4.2	6.2	4.5	5.8
6-31G(d,p)	2.1	5.5	4.7	4.0	5.8	4.8	6.0

[a] With respect to form C_e.

with a high extent of involvement of flexible forms 1,4-, 2,5-, and 3,6-T. It was established, that conformer C_e corresponded to the main minimum, and form C_a corresponded to the nearest local minimum (see the table). Further in the energy scale are located the flexible forms in different sequence depending on the calculation basis. The highest energy level corresponds to form 2,5-T_a (STO-3G) or 3,6-T_a [6-31G(d,p)]. Hence the conformers C_e and C_a undergo interconversion along six nonequivalent paths, and each flexible form can be involved simultaneously into seven conformational transformations.

The obtained scheme of the conformational isomerization of dioxane **I** resembles a spherical map describing the main conformations of six-membered rings in a polar coordinate system in dependence of folding parameters: the poles of the tentative sphere correspond to the chair conformers, and the flexible forms are situated on the equator [12–14]. Besides the data obtained show the more complex character of the potential energy surface of the compound under study than that of the unsubstituted 1,3-dioxane [7, 8] and 2-methyl-1,3-dioxane [9] due to the appearance of an additional number of flexible forms. This is caused by the general decrease in the symmetry of the heterocyclic ring owing to the presence of one substituent at the atom C^4.

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