

Nonempirical Study on the Potential Energy Surface of 5-Methyl-1,3-dioxane

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Abstract—Quantum-chemical study on the potential energy surface of 5-methyl-1,3-dioxane at the nonempirical RHF//STO-3G, RHF//3-21G, RHF//6-31G(*d*), RHF//6-31G(*d,p*), and MP2//6-31G(*d,p*) levels of theory revealed two energy-equivalent paths of conformational transformation of the equatorial and axial *chair* conformers. Potential barriers to these processes were estimated. The ΔG° value for the methyl substituent on C⁵ in 1,3-dioxane ring, determined on the basis of the experimental (NMR) and calculated vicinal ¹H–¹H coupling constants, was very consistent with published data.

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Interest in structural studies on 1,3-dioxanes is related to both specificity of their structure and their application as reagents in fine organic synthesis [1–4]. We previously showed [5–9] that the global minimum on the potential energy surface (PES) of unsubstituted 1,3-dioxane, as well as of 2-methyl- and 4,4-dimethyl-1,3-dioxanes, corresponds to *chair* (C) or equatorial *chair* (*C_{eq}*) conformer. Local minima were occupied by axial *chair* (*C_{ax}*), 1,4-*twist* (1,4-T), and 2,5-*twist* (2,5-T) conformers, whereas *half-chair*, *sofa*, and unsymmetrical *boat* conformers were characterized by maximal energies. In the present work we studied conformational transformation of 5-methyl-1,3-dioxane (**I**) in terms of nonempirical RHF//STO-3G, RHF//3-21G, RHF//6-31G(*d*), RHF//6-31G(*d,p*), and MP2//6-31G(*d,p*) approximations using HyperChem software [10].

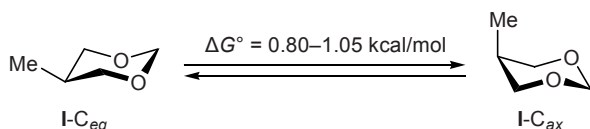
According to the ¹H NMR data, the conformational equilibrium of compound **I** at room temperature is displaced toward the equatorial *chair* conformer (*C_{eq}*) with a relatively small free conformational energy of the methyl substituent (ΔG°) [2] (Scheme 1). We have revealed the general pattern of conformational trans-

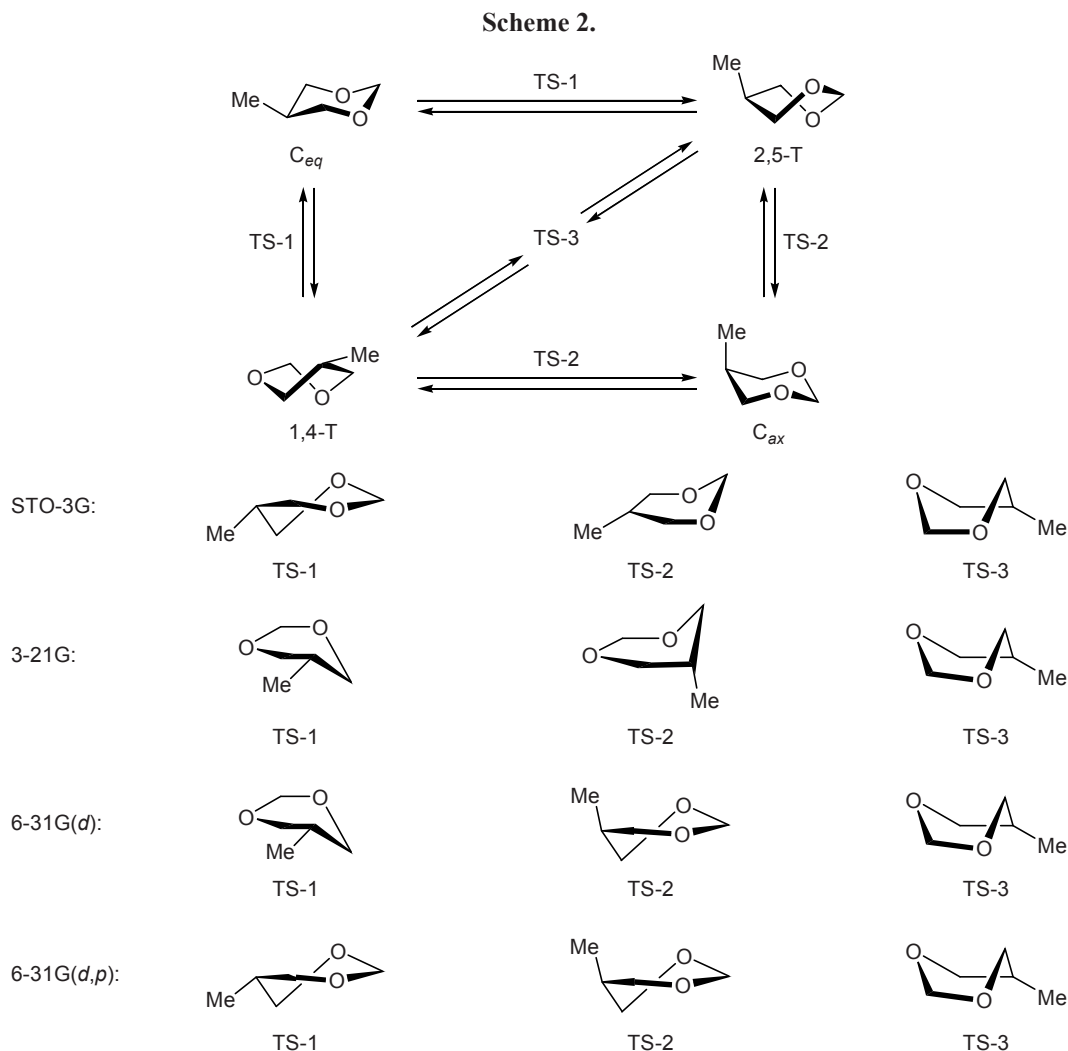
formations and intermediate minima and maxima on the potential energy surface of dioxane **I**. The calculations showed two paths of the transformation *C_{eq}* → *C_{ax}* (Scheme 2), which were analogous to those found for unsubstituted 1,3-dioxane and its 2-methyl- and 4,4-dimethyl-substituted derivatives [6–9]. In all cases, except for the 3-21G calculation data, the global minimum on the PES corresponded to *C_{eq}*. In terms of the MP2//6-31G(*d,p*) approximation, structures *C_{eq}* and *C_{ax}* have almost similar energies (Table 1). In all cases, the deepest minimum on the PES was occupied by 1,4-T conformer.

The structures corresponding to maxima or transition states (TS) depended on the basis set used. However, regardless of the latter, conformer *C_{eq}* is formed from 1,4-T or is converted into 2,5-T through transition state TS-1, whereas conformer *C_{ax}* can be formed from 1,4-T or 2,5-T through transition state TS-2. Intermediate structures 1,4-T and 2,5-T are converted into each other through TS-3. The global maximum on the PES (except for the STO-3G calculations) corresponds to TS-2. Thus, the conformational transformation paths *C_{eq}* → 2,5-T → *C_{ax}* and *C_{eq}* → 1,4-T → *C_{ax}* are equivalent in energy.

The results of studying the PES of compound **I** show that its conformational behavior may be described fairly appropriately as binary equilibrium be-

Scheme 1.





tween conformers C_{eq} and C_{ax} , which correspond to the global minimum and next to it. It is also known that the experimental Gibbs conformational energy of the methyl group on C^5 in 1,3-dioxanes, determined by different methods, ranges from 0.80 to 1.05 kcal/mol [2]. Therefore, it was interesting to estimate ΔG° of dioxane **I** on the basis of experimental coupling constants ${}^3J_{AX}$ and ${}^3J_{BX}$ (determined from the ${}^1\text{H}$ NMR spectra) and calculated coupling constants J_{Aax} , J_{Bax} , J_{Aeq} , and J_{Beq} for conformers C_{eq} and C_{ax} whose fractions in the equilibrium mixture are N and $1 - N$, respectively [11]:

$${}^3J_{AX} + {}^3J_{BX} = N(J_{Aax} + J_{Bax}) + (1 - N)(J_{Aeq} + J_{Beq}).$$

Using the value of N calculated from the above equation, ΔG° may be found using the formula

$$\Delta G^\circ = -RT \ln[N/(1 - N)].$$

The theoretical values of J_{Aax} , J_{Bax} , J_{Aeq} , and J_{Beq} can be calculated using the modified Karplus equation on the basis of the calculated torsion angles φ for the interacting protons [12]:

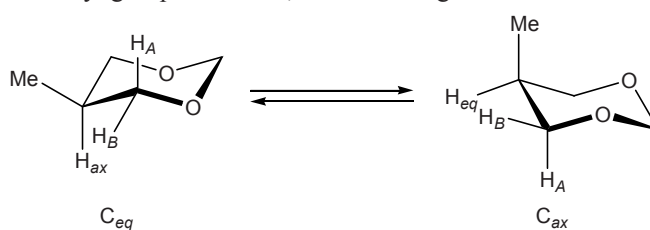
$${}^3J_{\text{HH}} = P_1 \cos^2 \varphi + P_2 \cos \varphi + P_3 + \sum \Delta\chi_i [P_4 + P_5 \cos^2(\xi_i \varphi + P_6 |\Delta\chi_i|)].$$

Here, $\Delta\chi_i$ is the difference in the electronegativities of substituents in the corresponding ethane fragment and hydrogen atom [13]; ξ_i takes a value of -1 or 1 , depending on the orientation of substituents at the carbon atoms in the ethane fragment; and P_1 – P_6 are parameters depending on the degree of substitution in the ethane fragment.

The calculated values of ΔG° (Table 2) are fairly consistent with published data. On the other hand, such agreement may be accidental. The main disadvantage of the used approach was that the theoretical vicinal

Table 1. Energy parameters of conformational transformations of 5-methyl-1,3-dioxane (**I**)

Method	Energy minima ΔE , kcal/mol				Energy maxima ΔE^\ddagger , kcal/mol		
	C_{eq}	C_{ax}	2,5-T	1,4-T	TS-1	TS-2	TS-3
RHF							
STO-3G	0	0.5	4.6	5.0	10.1	9.7	5.3
3-21G	0.5	0	4.1	5.2	8.4	8.6	5.2
6-31G(<i>d</i>)	0	0.6	4.6	5.8	9.3	10.3	6.2
6-31G(<i>d,p</i>)	0	0.7	4.7	5.9	9.3	10.4	6.2
MP2	0	0.04	4.9	6.4	11.0	11.6	7.0
6-31G(<i>d,p</i>)							

Table 2. Estimation of ΔG° of the methyl group on C^5 in 1,3-dioxane ring

Basis set (RHF)	Torsion angles, deg				Coupling constants, Hz				N	$-\Delta G^\circ$, kcal/mol
	φ_{Aax}	φ_{Bax}	φ_{Aeq}	φ_{Beq}	J_{Aax}	J_{Bax}	J_{Aeq}	J_{Beq}		
STO-3G	173.2	54.4	48.3	70.6	11.7	5.0	3.4	2.7	0.84	0.98
3-21G	176.8	55.8	53.3	68.4	11.6	4.6	2.7	2.8	0.89	1.24
6-31G(<i>d,p</i>) ^a	174.5	54.7	48.3	71.8	11.7	4.9	3.4	2.5	0.85	1.03
Experimental data [2]	${}^3J_{AX} = 10.5$, ${}^3J_{BX} = 4.5$ Hz [14]									0.80–1.05

^a The geometric parameters of conformers C_{eq} and C_{ax} in terms of the RHF//6-31G(*d*) approximation were similar to those found by RHF//6-31G(*d,p*) calculations.

coupling constants were calculated on the basis of torsion angles φ found by geometry optimization of isolated molecule, while the experimental coupling constants were found from the ${}^1\text{H}$ NMR spectrum recorded for solution. Differences in the solvation of conformers could strongly affect parameters of conformational equilibria, as well as geometric parameters of the conformers involved therein [15]. Thus exhaustive solution of the problem requires appropriate theoretical conformational analysis of a compound in the presence of particular solvent.

Our results indicate higher conformational mobility of 5-methyl-1,3-dioxane molecules as compared to 2-methyl-substituted analog [8] due to weaker spatial interactions of the axial methyl group on C^5 with the hydrocarbon ring fragment.

EXPERIMENTAL

5-Methyl-1,3-dioxane (**I**) was reported previously [16]; its ${}^1\text{H}$ NMR spectrum was given in [14]. The interconversion barriers were determined using HyperChem Transition State procedure [10]. Stationary points on the potential energy surface were identified as maxima if the corresponding Hesse matrix contained one negative eigenvalue. The suitability of the used calculation methods for determination of Gibbs conformational energies of substituents in 1,3-dioxanes was discussed in detail in [17]. Electronegativity values taken from [13] were used in the calculation of ${}^1\text{H}$ – ${}^1\text{H}$ coupling constants. The parameters P_1 – P_6 for trisubstituted ethane fragment had the following values [12]: $P_1 = 13.22$, $P_2 = -0.99$, $P_3 = 0$,

$P_4 = 0.87$, $P_5 = -2.46$, $P_6 = 19.9^\circ$. The ΔG° value was determined assuming the temperature 298 K.

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