Quantum chemical study of 5,5-dimethyl-1,3-dioxane isomerization to 2,2-dimethyl-3-methoxypropanal, - the general reaction scheme

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Abstract. The results of quantum chemical simulation by B3PW91 method in the 6-31G(d,p) basis for formation of 2,2-dimethyl-3-methoxypropanal from 5,5-dimethyl-1,3-dioxane in the presence of proton are given. The proposed reaction scheme involves protonation of the parent molecule - formation of the oxonium ion, breaking of C─O bond with receipt of alkoxycarbenium ion, rearrangement of the alkoxycarbenium ion by two successive 1,3-displacement or 1,5 displacement of positive charge, deprotonation of the oxycarbenium ion with formation of the reaction product. Data on the structure and energy characteristics of molecular products, ions, and transition states are obtained not only for the states characterized minimum Gibbs energy ($G_{298}$, $\Delta G_{298}$, $\Delta G_{\neq 298}$), but also for possible conformers and transitions between them. Based on the calculations, an energy diagram is drawn up in accordance with the general reaction scheme.

Comparison of the estimated activation barriers ($\Delta G_{\neq 298}$) for implementation of the reaction in two stages (1,3-migrations) and one-stage 1,5-migration showed that they are comparable in size, the difference is about 2 kcal/mol. Since conversion of 5,5-dimethyl-1,3-dioxane to 2,2-dimethyl-3-methoxypropanal is an endothermal reaction with heat absorption of 3.4 kcal/mol, it can be assumed that in real conditions transformation of ions as per the reaction coordinate will include both two-stage and one-stage conversion of alkoxycarbenium ion to the oxycarbenium ion.

1. Introduction

Some examples of isomerization of 1,3-dioxanes in the presence of acid catalysts are known [1,2]. 1,3-Dioxanes with substituents at C(4) form tetrahydropyranols, which are easily transformed into dihydropyrans [3]. Presence of substituents at C(5) provides for isomerization of 3-methoxypropanal. Rearrangement occurs at an elevated temperature in the presence of pumice or silica gel, which have the properties of weak acids [4-6].

It should be noted that there is no experimental data on the possibility of rearranging in liquid phase 5,5-disubstituted 1,3-dioxanes into the corresponding alkoxycarbenions in the liquid phase. On the other hand, it is known that acyclic acetals are converted to alkoxycarbenium ions as a result of the carbenium center displacement [7-9].

\[
\text{CH}_2(O\text{CH}_2\text{R})_2 + \text{H}^+ \rightarrow \text{CH}_2\text{=O} + \text{OCH}_2\text{R} \rightarrow \text{CH}_3\text{=O} + \text{CHR}.
\]

The study of the behavior of 1,3-dioxanes that do not contain substituents at C(2) in superacid media showed that the first stage of the reaction includes formation of cyclic oxonium ion, which
converts into alkoxycarbenium ions with temperature increase [10]. The structure of these ions [11,12] suggests the possibility of the reaction center displacement to form a new alkoxycarbenium ion.

Quantum chemical calculations of non-substituted, 2-methyl-, 5-methyl- and 2,5-dimethyl-1,3-dioxanes indicate this possibility, since the activation energy of the limiting stage is 21.7-33.1 kcal/mol [13]. On the other hand, it has been experimentally shown that in the presence of zeolites, the reaction products formation is associated with ion hydrogenation, isomerization, splitting, and their combinations. 3-Methoxypropanols are present in small quantities among the reaction products (at temperatures of 400-440°C) [14]. It is possible that the relatively high temperatures and mobility of the hydrogen atom at C(5) are the reasons for low selectivity of the transformations directions.

To investigate the possibility of 5,5-dimethyl-1,3-dioxane isomerization to 2,2-dimethylmethoxypropanal appears to be interesting.

2. Materials and methods

The calculations were performed using the PC GAMESS FireFly 8.2.0 software [13].

The geometry of molecules, transition states and all possible ion conformations is optimized using the density functional method [16] (B3PW91/6- 31+G(d,p)). This method is applicable for calculating the states with closed and open shells and conveys well the geometric parameters of 1,3-dioxanes [17]. Identification of stationary points on PPE surface was carried out by the Hessian analysis. The Gibbs energy (G298) values at a temperature of 298.15 K are determined.

3. Results

Transition of 5,5-dimethyl-1,3-dioxane (1) to 2,2-dimethyl-3-methoxypropanal (2) involves several stages:

– protonation of molecule 1 to form oxonium ion 3;
– dissociation of the C─O bond in the oxonium ion, which leads to formation of alkoxycarbenium ion 4;
– migration of the carbenium center in ion 4, which can proceed in two directions - either two successive 1,3-migrations (formation of ion 5 and its transition to ion 6), or formation of ion 6 in one stage, i.e. 1,5-migration of the positive charge.

Deprotonation of ion 6 leads to the reaction product - molecule 2 (figure 1).

We evaluated the energy characteristics of ions (3, 4, 5 and 6), and transition states between conformers (TS3, TS4, TS5 and TS6) ions and transition energies between ion isomers (TS3-4, TS4-5, TS5-6 and TS4-6).

The structure of ions 3, 4, 5 and 6 makes it possible to form conformers due to inversion of the cycle and axial and equatorial orientation of the bond O─H⁺ (ion 3) or the rotation of fragments in ions 4, 5 and 6:

![Figure 1. Transformation of 5,5-dimethyl-1,3-dioxane to 2,2-dimethyl-3-methoxypropanal.](image-url)
Figure 2. Possible variants of formation of 4, 5 и 6 ion conformers.

Ions 3 formed by protonation of molecule 1 are structurally as chair and twist conformations with axial or equatorial orientation of the bond OH+ . In addition, it is possible to assume the possibility of implementation of other conformations of ion 3. However, it is known that such ions have high energies [18-21], so the ion in boat-like conformations have not yet been analyzed.

Analysis of energy transitions between ions 3 indicates the possibility of all isomers, activation barriers are 6.8-13.6 kcal/mol (table 1). The difference in the energy of the formed 3 ions is 4.3 kcal/mol, and the transition states of TS3 are about 6.8 kcal/mol. It can be assumed that when the reaction is implemented in real conditions, the formation of all 3 ions is possible.

Transformation of oxonium ions 3 to alkoxycarbenium ions 4 involves the С─О bond rupture. This reaction stage proceeds with heat absorption, the thermal effect is about 10 kcal/mol, and the energy of transition states equals from 8.2 to 29.3 kcal/mol (table 1).

Table 1. Energy characteristics* of ions (G298, 3, 4, 5, 6) of transition states between conformers (∆G≠298, TS3, TS4, TS5, TS6) of ions and transition energies between ion isomers (∆G≠298, TS3→4, TS4→5, TS5→6, TS4→6) - min and max values are given.

| Ion, reaction | Number of localized isomers | G298, kcal/mol | Number of localized transition states | ∆G≠298, kcal/mol |
|---------------|-----------------------------|----------------|-------------------------------------|-----------------|
|               |                             | G298, kcal/mol | min  | max  | min  | max  |
| 3→4          | 4                            | -242432.7      | -242428.4 | 6    | 6.8  | 13.6 |
| 4→5          | 10                           | -242421.5      | -242414.0 | 14   | 17.0 | 29.9 |
| 5→6          | 10                           | -242436.3      | -242424.6 | 10   | 3.9  | 17.5 |
| 4→6          | 8                            | -242432.7      | -242424.6 | 7    | 3.8  | 6.90 |

*when calculating ∆G≠298, the energy of ion 3 in the chair-like conformation with the axial orientation of the proton is assumed (G298= -242432.7 kcal/mol) as the initial (zero) level

Analysis of the geometric characteristics of ions 4 shows that their formation is associated with different spatial locations of CH3─CHO+ and CH3OH fragments due to their rotation C(4)─C(5) and C(5)─C(6), as well as fragments of CH2O+ and OH due to rotation around bonds O(1)─C(6) and O(3)─C(4) (figure 3). Following the calculation results, 10 conformations of ion 4 and 14 transition states between them were realized. The energies of 4 ions formation vary quite substantially from 17.0 to 29.9 kcal/mol, while the difference in ion energies is less than 7.5 kcal/mol.

Rearrangement of ions 4 into ions 5 requires high energy costs from 20.8 to 45.0 kcal/mol, which allows us to consider this reaction stage as limiting.

Scanning of the PPE when changing the dihedral angle C(7)─C(5)─C(6)─O(1), consideration of the –O(3)H bond rotation possibility, consideration of the C(2)H3 fragment cis- and trans- orientation possibility were performed to search for stable conformations of ion 5. Ten (10) conformations of ion 5 are localized, which have energies from -242436.3 to -242424.6 kcal/mol, the Gibbs energy difference equals 11.7 kcal/mol (figure 4), and the energy barrier of ions 5 isomerization varies from...
3.9 to 17.5 kcal/mol. This reaction stage proceeds both with the release and absorption of heat (depending on the ions 5 energy), the thermal effect varies from -3.6 to 8.2 kcal/mol.

Transition between groups of 5 and 6 ions is possible through transition states TS5-6 with penetration of the barrier from 6.7 to 19.6 kcal/mol, the endothermal effect reaches 8.1 kcal/mol.

The transformation of ions 4 → 5 → 6 represents two successive rearrangements leading to 1,3-displacements of the carbenium center. An alternative option of ion 6 formation consists in direct isomerization of ion 4 to ion 6, i.e. 1.5-rearrangement. Calculation of energy parameters of the rearrangement shows that its implementation occurs through barriers of 18.8 kcal/mol, which correspond to two transition states (table 1).

Figure 3. Gibbs energy diagram ($\Delta G_{298}^\circ$, $\Delta G_{298}^\neq$) of assumed ion transformations during isomerization of 5,5-dimethyl-1,3-dioxane to 2,2-dimethyl-3-methoxypropanal (the initial (zero) level is taken to be the energy of oxonium ion 3 in the chair-like conformation with axial orientation of the proton ($G_{298}^\neq=-242432.7$ kcal/mol): - min and max values of ion energy $\Delta G_{298}^\circ$,  $\Delta G_{298}^\neq$ - the ranges of change of values $\Delta G_{298}^\neq$.

General nature of energy characteristics (figure 3) of isomerization of 5,5-dimethyl-1,3-dioxane into 2,2-dimethyl-3-methoxypropanal enables us to determine that one of the isomers of ion 5 (-242436.3 kcal/mol) is the most stable of the formed ones.

Comparison of activation energies during the transition of ion 4 to ion 6 in two stages (4 → 5 → 6) or in one stage (4 → 6) shows that the direct transformation of ion 4 to ion 6 occurs with lower energy costs. However, the difference in the energies of two and one-stage transitions is not great, it is only 2.2 kcal/mol. In this regard, it can be assumed that in real conditions the isomerization of 5,5-dimethyl-1,3-dioxane to 2,2-dimethyl-3-methoxypropanal can occur with implementation of the ion rearrangement mechanism both in two or in one stage.

It should be noted that isomerization of 5,5-dimethyl-1,3-dioxane to 2,2-dimethyl-3-
methoxypropanal is an endothermal reaction with a thermal effect of 3.4 kcal/mol, so the reaction can only occur when heated.

4. Summary
The results obtained by quantum chemical simulation of 5,5-dimethyl-1,3-dioxane (1) isomerization into 2,2-dimethyl-3-methoxypropanal (2) (figure 1) show that the proposed mechanism makes it possible to implement the reaction at elevated temperatures, since the reaction is endothermal. \( \Delta G_{298} \) of the transition from molecule 1 to molecule 2 is 3.4 kcal/mol. The minimum activation energy required for transformation of the initial substance into the reaction product is about 19-21 kcal/mol. This predetermines that oxonium ions in various conformations and alkoxycarbenium ions with positive charge localization on ion fragments O(1) → C(6) and O(3) → C(4) can be formed on the reaction path.

Comparison of the energies of two proposed options of isomerization of the alkoxycarbenium ion 4 to ion 6 shows that two successive 1,3-transitions and 1,5- transition (4 → 5 → 6 and 4 → 6 reactions, respectively) are comparable in activation energy, approximately 20 ± 1 kcal/mol.

Thus, it can be assumed that not only solid acid catalysts, but also Brønsted acids can be effective for converting 5,5-dimethyl-1,3-dioxanes to 2,2-dimethyl-3-methoxypropanals.

References

[1] Bogatsky A B, Garkovik N L 1968 Advances in 1,3-dioxane chemistry Russian Chemical Reviews 37(4) 581-607
[2] Apyok J, Bartok M, Karahanov R A, Shuikin N I 1969 Chemical properties of 1,3-dioxanes Russian Chemical Reviews 38(1) 72-115
[3] Gevorkyan A A, Sahakyan L A, Tokmadzhyan G G, Kosyan S M, Kazaryan, P I 1975 Recyclization of 1,3-dioxanes to tetrahydropyrans. Chemistry of Heterocyclic Compounds 11 1573-1574
[4] Rondestved C S Jr 1962 Catalytic Isomerization of m-Dioxanes to p-Alkoxyaldehydes. III. Reaction Mechanism and byproducts J. Am. ChemSoc. 84(17) 3319-3326
[5] Rondestved C S Jr, Mantell G J 1960 New Rearrangement: Catalytic Isomerization of m-Dioxanes to p-Alkoxy Aldehydes J. Am. Chem. Soc. 82(24) 6419-6420
[6] Rondestved C S Jr, Mantell G J 1962 A New Rearrangement Catalytic Isomerization of m-Dioxanes to p-Alkoxy Aldehydes. II. Scope and Limitations J. Am. Chem. Soc 84(17) 3307-3319
[7] Ola G A 1975 Carbocations and electrophilic reactions Russian Chemical Reviews 44(5) 793-867
[8] Akhmatdinov R T, Kantor E A, Imashev U B, Yasman Y B, Rakhmankulov D L 1981 Formation and conversion of cations derived from 1,1-dialkoxyalkanes in fluorosulfonic acid Journal of Organic Chemistry 17(4) 718-723
[9] Akhmatdinov R T 1981 Products and the mechanism of liquid-phase acid-catalyzed transformations of acetals (Ufa: Ufa State Petroleum Technical University)
[10] Borichevsky A I, Golub N M, Matusevich LV 2004 Study of the mechanism of the first stage of acid hydrolysis of symmetrically substituted 1,3-dioxanes by quantum-chemical methods. Bulletin of Brest University, Series of Natural Sciences 2(40) 50–56
[11] Borichevsky A I 2013 Study of the first stage of acid hydrolysis of 1,3-dioxanes. In N. S. Step (Ed.) Mendeleev Readings 2013: collection of articles. scientific. Art. interuniversity scientific method. Conf. (Brest: BrSU) pp 7-11
[12] Nikitina A P 2010 Conversions of 5-methyl-, 2-methyl- and 2,5-dimethyl-1,3-dioxanes on acid catalysts. Dissertation of Candidate of Chemical Sciences (Ufa: Ufa State Petroleum Technical University)
[13] http://classic.chem.msu.su/gran/gamess/index.html
[14] Khursan S L 2005 Quantum mechanics and quantum chemistry: Lecture notes (Ufa: BSU)
[15] Syrylbaeva R R, Vakulin I V, Talipov R F 2010 The use of combined calculation methods in the study of organic compounds Journal of Structural Chemistry 51(2) 225-230
[16] Mamleev A Kh, Gunderova L N, Galeev R V, Shapkin A A, Faizullin M G 2007 Structure and Spectra of 1,3-Dioxanes Journal of Structural Chemistry 48(3) 456-461
[17] Alabugin I V 2000 Steroelectronic Interactions in Cyclohexane, 1,3-Dioxane,1,3-Oxathiane, and 1,3-Dithiane: W-Effect, σ_C-X→σ_C-H interactions, anomeric effects. What Is Really Important? J.Org. Chem. 65(13) 3910-3919
[18] Kuramshina A E, Mazitova E G, Kuznetsov V V 2006 Conformational analysis of 1,3-dioxane and its oxonium ion Modern high technologies 2 80-82
[19] Mazitova E G, Kuznetsov V V 2003 Analysis of the potential energy surface of the oxonium ion formed during protonation of 1,3-dioxane Information and computing technologies in solving fundamental and applied scientific problems: Proceedings of the electronic conference Retrieved from http://www.ivtn.ru.
[20] Mazitova E G, Kuramshina A E, Kuznetsov V V 2004 Analysis of the potential energy surface of 1,3-dioxane and its protonated form. Journal of Organic Chemistry 40(4) 615-616
[21] Kuramshina A E, Bochkor S A, Kuznetsov V V 2008 Stable conformers of the oxonium ion of 2-methyl-1,3-dioxane Modern high technologies 2 147-149