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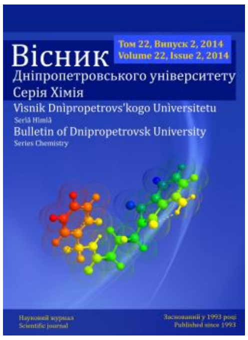

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THE QUANTUM-CHEMICAL INVESTIGATION OF *N*-CYCLIZATION REACTION MECHANISM FOR EPICHLOROHYDRIN AMINOLYSIS PRODUCTS

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Abstract

The mechanism of intramolecular cyclization for products of epichlorohydrin aminolysis by secondary amines has been investigated at *ab initio* level of theory. By comparative analysis of energetic characteristics, which obtained *in vacuo* as well as in acetonitrile solution with the trace quantities of water as an «active» solvation partner of reaction, it has been shown a decisive role of solvent, which occurs mainly at the expense of the polarizable effects for nonspecific solvation. Indeed, the addition to the substrate of one water molecule have decreased corresponding E_{ACT} values only 24.1 kJ/mol, while the appearance of acetonitrile surroundings have the same influence ~42.0 kJ/mol. The results of calculations are in good agreement with that data, which have been obtained for such type modeling previously.

Keywords: azetidinium chloride; nonspecific solvation; *ab initio* calculations.

КВАНТОВО-ХІМІЧНЕ ДОСЛІДЖЕННЯ МЕХАНІЗМУ РЕАКЦІЇ *N*-ЦИКЛІЗАЦІЇ ПРОДУКТІВ АМІНОЛІЗУ ЕПІХЛОРГІДРИНУ

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Анотація

Із застосуванням *ab initio* методів квантової хімії досліджено механізм внутрішньомолекулярної циклізації продуктів амінолізу епіхлоргідрину вторинними амінами. Порівняльний аналіз енергетичних характеристик, одержаних для газової фази та розчину ацетонітрилу, що містить слідові кількості води в ролі «активного» сольватаційного партнера реакції, свідчить про стабілізуючий вплив розчинника, переважно за рахунок поляризуючих ефектів неспецифічної сольватації. Так, додавання до субстрату однієї молекули води викликає зменшення відповідних величин $E_{\text{АКТ}}$ лише на 24.1 кДж/моль, тоді як поява ацетонітрильного оточення сприяє аналогічному впливу ~42.0 кДж/моль. Результати розрахунків добре узгоджуються з даними такого типу, одержаними раніше.

Ключові слова: азетидиній хлорид; неспецифічна сольватація; *ab initio* розрахунки.

КВАНТОВО-ХИМИЧЕСКОЕ ИССЛЕДОВАНИЕ МЕХАНИЗМА РЕАКЦИИ *N*-ЦИКЛИЗАЦИИ ПРОДУКТОВ АМИНОЛИЗА ЭПИХЛОРГИДРИНА

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Аннотация

С использованием *ab initio* методов квантовой химии исследован механизм внутримолекулярной циклизации продуктов аминолиза эпихлоргидрина вторичными аминами. Сравнительный анализ энергетических характеристик, полученных для газовой фазы и раствора ацетонитрила, содержащего следовые количества воды в роли «активного» сольватационного партнера реакции, свидетельствует о стабилизирующем влиянии растворителя, преимущественно за счет поляризующих эффектов неспецифической сольватации. Так, добавление к субстрату одной молекулы воды вызывает уменьшение соответствующих величин $E_{\text{АКТ}}$ только на 24.1 кДж/моль, тогда как появление ацетонитрильного окружения оказывает аналогичное влияние ~42.0 кДж/моль. Результаты расчетов хорошо согласуются с данными такого типа, полученными ранее.

Ключевые слова: азетидиний хлорид; неспецифическая сольватация; *ab initio* расчеты.

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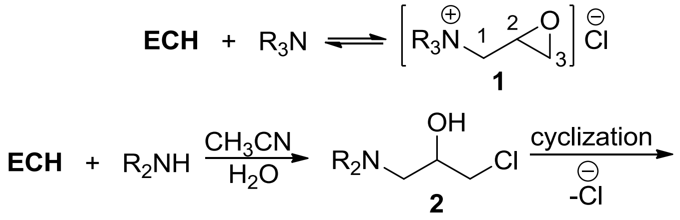
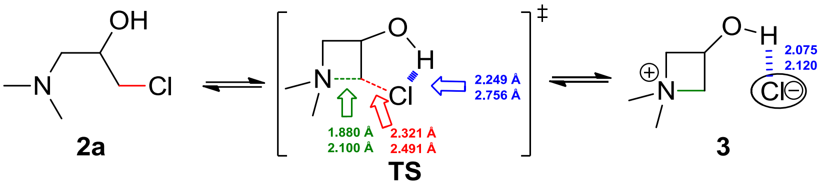


Scheme 1. Some reactions of ECH with tertiary and secondary amines (R = Alk)



Scheme 2. Mechanism of heterocyclization reaction for aminochlorohydrin (2a)

Introduction

Epichlorohydrin (ECH) has found wide usage in polymer chemistry because of its uniqueness in possessing both a labile chlorine and an oxirane group [1]. The authors' interest has been focused on the mechanisms of epichlorohydrin–amine reactions because of their importance in the chemical modifications of cellulose [2; 3]. Of particular interest are reactions catalyzed by tertiary and secondary amines (Scheme 1).

Tertiary amines react with ECH to form a glycidyl (2,3-epoxypropyl) ammonium salts (**1**) while the secondary one – to form the tertiary aminochlorohydrins (**2**), which give cyclic structures of the 3-hydroxy azetidinium salt type. Since these structures are fairly constrained they are also fairly reactive [4–6]. Compared to other nitrogen heterocycles such as aziridines, pyrolidines, or piperidines, the chemistry of azetidines is much less developed, probably because of their limited availability. The ring strain in these heterocycles makes them excellent candidates for nucleophilic ring-opening or ring-expansion reactions yielding higher ring systems or highly substituted acyclic amines [6].

The main purpose of this work is to investigate the mechanism of azetidinium salts formation under conditions of intramolecular cyclization reaction for products of ECH aminolysis by secondary amines. The influence of substrate structure as well as the specific and nonspecific solvation effects of medium on heterocyclization process has also been under our consideration.

Results and Discussion

I. The equilibrium state features for ring-closure and ring-opening reactions of azetidinium ion. For the first step of our investigation some features of equilibrium state for *N*-cyclization reaction have been considered at B3LYP/6-311++G(d,p) level of theory [7]. Some geometrical parameters for located structures of transition states (**TS**) as well as the corresponding values of activation barriers are shown in Scheme 2 and Tab. 1.

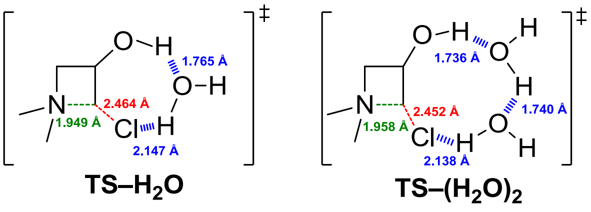
In the case of gas phase the full predominance of the reverse way of reaction is absolutely clear from the point of atomic charge compensation, which occurs under the absence of any polarizable effects for specific or nonspecific solvation. At the same time the full relaxation of geometry for all stationary points with CPCM model demonstrates another set of E_{ACT} values with some dominance for the forward conversation. These results are in good agreement with experimental data, which have been obtained for such type modeling previously [3].

Table 1

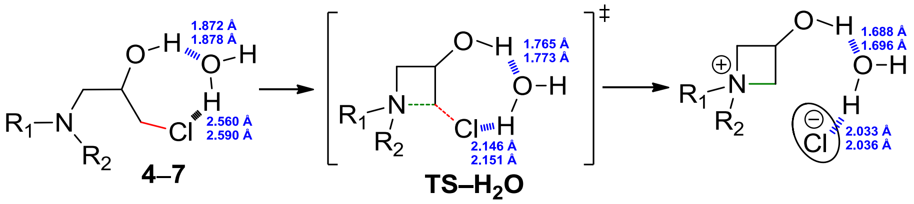
The activation barriers for ring-closure and ring-opening reactions of azetidinium ion *in vacuo* as well as in acetonitrile solution (*ε* = 36.6), calculated at B3LYP/6-311++G(d,p) level of theory

Levels of theory	E_{ACT}, kJ/mol	
	2a→3	**3→2a**
B3LYP/6-311++G(d,p)	118.8	10.1
CPCM-B3LYP/6-311++G(d,p)//B3LYP/6-311++G(d,p)	57.4	57.7
CPCM-B3LYP/6-311++G(d,p)	74.6	88.6

II. The effects of specific solvation. The total solvation effects with the details of the structure for the first solvation shells of the substrate have been investigated to continue our previous work.



Scheme 3. The structures of the first solvation shells with one and two water molecules



Scheme 4. Mechanism of heterocyclization reaction for aminochlorohydrins (4–7)

Table 2

The activation barriers as well as some geometrical parameters for transition states (TS–H_2O) of aminochlorohydrin's (4–7) intramolecular cyclization, calculated at B3LYP/6-311++G(d,p) and *CPCM*-B3LYP/6-311++G(d,p)//B3LYP/6-311++G(d,p) levels of theory

No's	R_1/R_2	Bond lengths, Å		Angles, deg		E_{ACT}, kJ/mol	
		N–C	C–Cl	NCCl	NCCC	*in vacuo*	in solution CH_3CN
4	Me/Me	1.949	2.464	176.2	21.4	94.7	51.5
5a	Me/Et	1.964	2.455	176.1	21.7	92.9	50.9
5b	Et/Me	1.961	2.451	176.1	21.0	90.1	48.0
6	Et/Et	1.975	2.442	176.1	20.8	87.4	46.2
7	Allyl/Allyl	1.959	2.459	176.3	21.2	94.9	53.3

There are two possible species in the case of water molecules, which are included in acetonitrile solution with trace quantities. The structures of transition states, which have been located at [**TS–H_2O**] and [**TS–$(H_2O)_2$**] theoretical models as well as some geometrical parameters for hydrogen bonds formed are shown in Scheme 3.

Calculated at B3LYP/6-311++G(d,p) level of theory activation barriers are 94.7 and 94.1 kJ/mol respectively, while the MP2/6-311++G(d,p)//B3LYP/6-311++G(d,p) [8; 9] theoretical approach indicates the reverse order of these values – 126.1 and 129.0 kJ/mol. Indeed, with addition of the first water molecule the E_{ACT} decreases on 24.1 kJ/mol (Tab. 1), while the appearance of the second water molecule have the same influence only 0.6 kJ/mol to compare with the previous model.

III. The concerted mechanism of heterocyclization. The full reaction pathway of intramolecular *N*-cyclization reaction, which occurs through the single S_N2-type transition state (**TS–H_2O**) has been investigated at DFT level of theory. Both the substrate structure and water molecule as an «active» solvation partner of reaction are included in our consideration. The results of calculations are represented below (Scheme 4, Tab. 2).

By comparison of calculated E_{ACT} values with one another it has been shown a decisive role of electron donating properties of R_1/R_2-groups, which are closely bonded with the attacking Nitrogen atom. As to the nonspecific solvation energies of cyclization, they are ~42.0 kJ/mol and have a great importance for these type reactions [10].

Computational Details

The quantum-chemical calculations have been carried out at B3LYP/6-311++G(d,p) and MP2/6-311++G(d,p)//B3LYP/6-311++G(d,p) levels of theory in Gaussian 03, Revision E.01 package of programs. The corresponding sets of vibrational frequencies were calculated for all stationary points. The main energetic characteristics of heterocyclization reactions have been established *in vacuo* as well as in acetonitrile solution with the aid of CPCM solvation model. Zero-point correction energies have also been included to final values of activation barriers.

Acknowledgment

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