Physical Chemistry

The Quantum-Chemical Modeling of Synthesis of some Phenylgycidates

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ABSTRACT. In the present paper we present geometrical and electronic characters of the intermediate products of the synthesis reaction of some phenylgycidates, such as heat of formation (ΔHf), the ionization potential (I), the dipole momentum (μ), the net atomic charge (qi) and the bond order (Pij), using quantum-chemical non-empirical density functional theory (DFT) and quantum-chemical semi-empirical AM1 methods. Epoxides are regarded as important synthons due to their versatile functionalities into the fine organic synthesis. For the production of safe drugs it is required such objects to be prepared from the particular enantiomers. Epoxides synthesis can be realized by the Darzen's reaction mechanism – the interaction of Ketones or Aldehydes with the α-halogen esters yielding the α, β-epoxy esters. The 3,4-dibenzyloxyphenyl and *tert*-butyl-2-chloracetate were chosen as an initial materials for *tert*-butyl-3-(3,4-dibenzyloxyphenyl)-oxirane-2-carboxylate synthesis. We calculated geometrical, energetic and electronic characteristics of the starting, intermediate and final states of the *tert*-butyl-3-(3,4-dibenzyloxyphenyl)-oxirane-2-carboxylate synthesis reaction using the density functional theory (DFT). Interaction of the 3,4-dimethoxybenzaldehyde and the methyl-2-chloracetate is one of the possibilities of the methyl-(3,4-dimethoxyphenyl)-oxirane-2-carboxylate synthesis. Geometrical, energetic and electronic characteristics of the starting, intermediate and the final states of methyl 3-(3,4- dimethoxyphenyl)-oxirane-2-carboxylate were calculated using the semi-empirical quantum-chemical (AM1) method. The quantum-chemical calculations revealed that *tert*-butyl-3-(3,4-dibenzyloxyphenyl)-oxirane-2-carboxylate synthesis reaction is exothermic while the 3-(3,4-dimethoxyphenyl)-oxirane-2-carboxylate synthesis reaction is endothermic. The activation energy is high in both cases. However, in convenient environment (temperature, pressure, pH) *tert*-butyl-3-(3,4-dibenzyloxyphenyl)-oxirane-2-carboxylate and 3-(3,4-dimethoxyphenyl)-oxirane-2-carboxylate synthesis reaction can be realized according to the considered scheme. © *2015 Bull. Georg. Natl. Acad. Sci.*

α, β-epoxy carbonyls are basic building blocks in organic synthesis, as these versatile functionalities are readily and stereoselectively transformed by ring opening into a variety of oxyfunctionalized compounds [1]. Esters of glycidic acid usually are prepared by base-promoted reaction of esters of a-
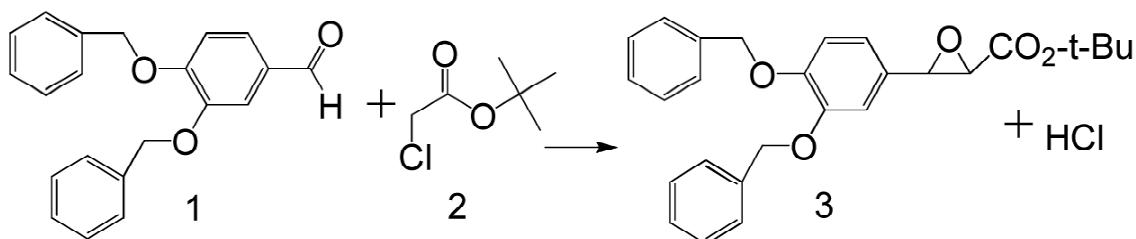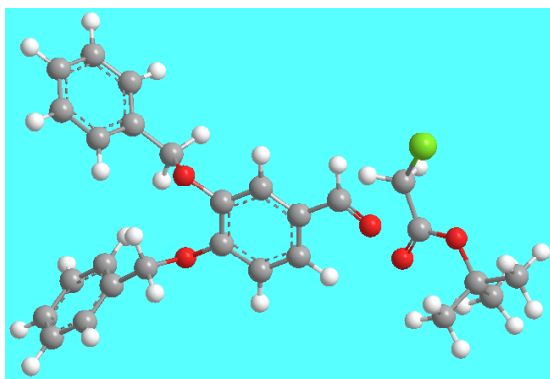
Scheme 1. Synthesis of *tert*-butyl-3-(3,4-dibenzyloxyphenyl)-oxirane-2-carboxylate (3) by reaction dibenzyloxybenzaldehyde (1) and *tert*-butyl-chloracetate (2).

halogeno acids with carbonyl compounds (Darzen's condensation) [2].

The goal of this work was modeling of Darzen's synthesis of glycidates using density functional theory (DFT) [3]. For the modeling of the synthesis of *tert*-butyl-3-(3,4-dibenzyloxyphenyl)-oxirane-2-carboxylate (3) by Darzen reaction dibenzyloxybenz-aldehyde (1) and *tert*-butyl-chloracetate (2) were taken as a starting materials (scheme 1). The geometrical, energetic and electronic possibilities of starting, intermediate and final states of Darzen reaction have been calculated. The 3D structures of starting and final compounds of reaction are shown on Figs. 1,2 respectively. The length between carbon atoms C_7 and C_{24} was taken on 1.0 Å larger than the length of the bond in final products (1.50 Å). The changing of the length $R_{C_7-C_{24}}$ between carbon atoms C_7 and C_{24} was changing by 0.05 Å interval. The dependence of the full energy of the system (ΔH) on the length $R_{C_7-C_{24}}$ between carbon atoms is given on Fig. 3. As it is evident from Fig. 3, the approaching of carbon atom C_7 to carbon atom C_{24} on the length of

$R_{C_7-C_{24}} = 2.00$ Å, energy of system is increased, bond order between C_7 and C_{24} is increased from 0.008 till 0.078. At the same time the bond orders between carbon atom C_7 and chlorine atom Cl_{33} ($P_{C-Cl} = 0.892-0.702$) and carbon atom C_{24} and hydrogen atom H_{62} ($P_{C-H} = 0.926-0.879$) are decreased. In the expected products take place formation of new bonds ($R_{C_7-C_{24}} = 0.008-0.078$; $P_{H_{63}-Cl_{33}} = 0.009-0.021$). A new compound *tert*-butyl-3-(3,4-dibenzyloxyphenyl)-oxirane-2-carboxylate (3) is obtained due to this reaction ($R_{C_7-C_{24}} = 0.947$). Hydrogen and chlorine atoms split out from carbon atom and interconnect by the formation of the hydrogen chloride ($P_{H_{62}-Cl_{33}} = 0.924$). The final state of the system is given on Fig. 2. According to diagram (Fig. 3.), the reaction of synthesis is exothermal ($\Delta\Delta H = -11,52751$ kJ/mol) and energy of activation is larger. However, under favorable experimental conditions (temperature, pressure, catalyst, pH) probability of the reaction according to the scheme 1 yielding *tert*-butyl-3-(3,4-dibenzyl-oxyphenyl)-oxirane-2-carboxylate (3) seems quite high.

Fig. 1. 3D structures of the starting compounds dibenzyloxybenzaldehyde (1) and *tert*-butyl-chloracetate (2).
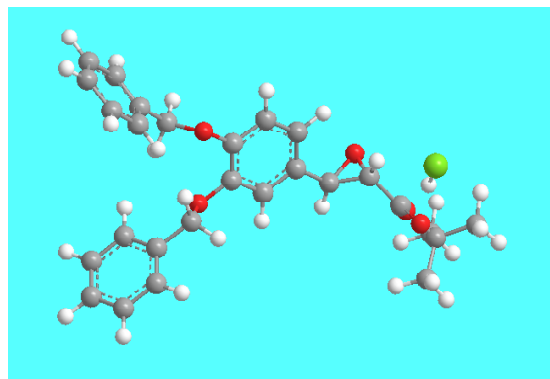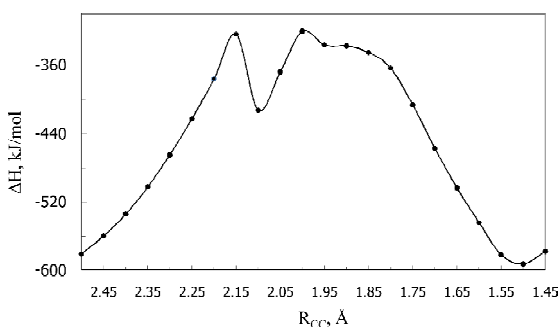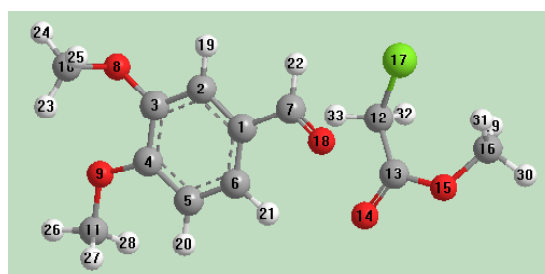

Fig. 2. The final state of the reacting substances.
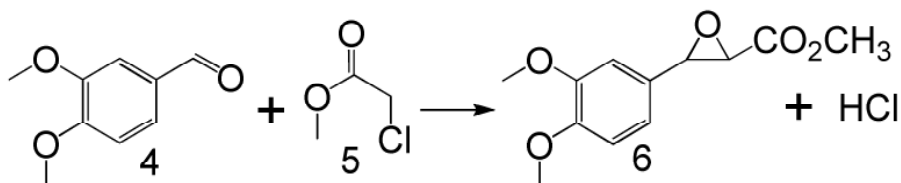
Scheme 2. Synthesis of methyl-(3,4-dimethoxyphenyl)-oxirane-2-carboxylate (6) by reaction ofdimethoxybenzaldehyde (4) and methylchloracetate (5).

For the modeling of the synthesis of methyl-(3,4-dimethoxyphenyl)-oxirane-2-carboxylate (4) by Darzen reaction, dimethoxybenzaldehyde (5) and methylchloracetate (6) were adopted as a starting materials (scheme 2). The geometrical, energetic and electronic possibilities of starting, intermediate and final states of this Darzen reaction was calculated by using semi-empirical quantum-chemical method AM1 [4]. The 3D structures of starting final compounds are shown on Figs. 4,5, respectively. The length between carbon atoms C_7 and C_{12} was taken on 1.0 Å larger than the length of the bond in final products (1.50 Å). The changing the length $R_{C_7-C_{12}}$ between carbon atoms C_7 and C_{12} occurs in the interval of 0.05 Å. The dependence of the full energy of the system (ΔH) on the length $R_{C_7-C_{12}}$ between carbon atoms is given on Fig. 6. As it is evident from Fig. 6, the approaching of carbon atom C_7 to carbon atom C_{12} on the length of $R_{C_7-C_{12}}$ = 2.05 Å, energy of the system is increased, bond order between C_7 and C_{12} is increased from 0.008 to 0.049. At the same time, bond order between carbon atom C_{12} and hydrogen atom H_{33} (P_{C-H} = 0.924-0.869) and car-

bon atom C_{12} and chlorine atom Cl_{17} (P_{C-Cl} = 0.977-0.970) decreased. In the expected products methyl 3-(3,4-dimethoxyphenyl)-oxirane-2-carboxylate involves the formation of new bonds ($P_{C_7-C_{12}}$ =0.007-0.048; $P_{Cl_{17}-H_{33}}$ =0.001-0.002). The structure of the intermediate state is given on Fig. 6. Between carbon atoms, C_7 and C_{12} on the length of 2.0 Å energy of the system is decreased, bond order between C_7 and C_{12} atoms reased till 0.061. At the same time it is decreased bond order between carbon atom C_{12} and hydrogen atom H_{33} and carbon atom C_{12} and chlorine atom Cl_{17} till 0.850 and 0.966, respectively. The decrease of energy continues till the length of $R_{C_7-C_{12}}$ =1.5 Å. At this time bond order between carbon atoms, C_7 and C_{12} reaches 0.944. However, the bond orders between carbon atom C_{12} and hydrogen H_{33} and chlorine Cl_{17} atoms are decreased till 0.00002 and 0.00099, respectively. Thus, a new compound methyl 3-(3,4-dimethoxyphenyl)-oxirane-2-carboxylate is obtained ($P_{C_7-C_{12}}$ =0.943). At the same time, hydrogen and chlorine atoms split out from carbon atoms and is interconnected by the formation of the hydrogen chloride ($P_{Cl_{17}-H_{33}}$ =0.890). The

Fig. 3. The difference of the system energy (DH) as a function of distance between the carbon atoms $R_{C_7-C_{24}}$.

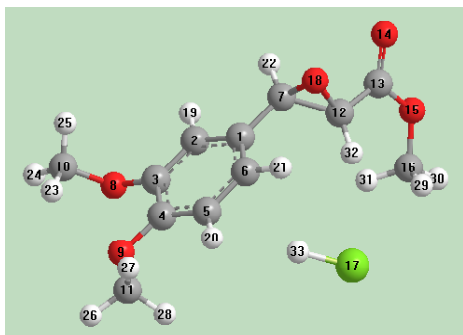

Fig. 4. The starting state of the reacting compounds.

Fig. 5. The final state of the reacting substances.

Fig. 6. The difference of the system energy (DH) as a function of $R_{C_7-C_{12}}$

final state of the system is given on Fig. 5. As it is evident from Fig. 6, the reaction is endothermal ($\Delta\Delta H$ = 6.64 kJ/mol) and energy of activation ($\Delta\Delta H^{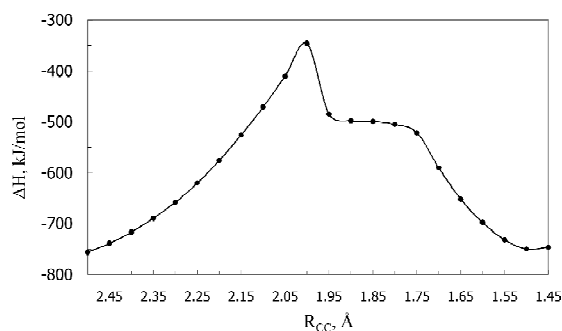\#}$ = 409.48 kJ/mol) is high. However, in favorable experi-mental conditions (temperature, pressure, catalyst, pH) probability of the reaction according to the scheme 2 yielding methyl 3-(3,4-dimethoxyphenyl)-oxirane-2-carboxylate seems high enough.

ფიზიკური ქიმია

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ეპოქსიდების სინთეზის რეაქციის სრული დახასიათებისათვის ჩატარებულ იქნა გათვლები სიმკვრივის ფუნქციონალის თეორიის მეთოდით (DFT) და ნახევრად-ემპირიული კვანტურ-ქიმიური მეთოდით (AM1). ქიმიური მრავალფუნქციურობის გამო ეპოქსიდები მიიჩნევა, როგორც მნიშვნელოვანი სინთონები ნატიფი ორგანული სინთეზისთვის. ეპოქსიდების სინთეზი შეიძლება განხორციელდეს ე.წ. დარზანის რეაქციის მექანიზმით - კეტონის ან ალდეჰიდის ურთიერთქმედებით α-ჰალოგენესტერთან α, β-ეპოქსი ესტერების წარმოქმნით. უსაფრთხო მედიკამენტების წარმოებისას აუცილებელია ასეთი ობიექტების მომზადებულ იქნეს ცალკეული ენანტიომერიდან. ტეტრა-ბუთილ 3-(3,4-დიბენზოქსიფენილ) ოქსირან-2-კარბოქსილატის სინთეზისთვის საწყის ნივთიერებად ავიღეთ 3,4-დიბენზოქსიფენილი და ტეტრა-ბუთილ 2-ქლორაცეტატი. სიმკვრივეთა ფუნქციონალის თეორიის (DFT) მეთოდის გამოყენებით გამოვითვალეთ ტეტრა-ბუთილ 3 –(3,4 დიბენზოქსიფენილ) ოქსირან-2 კარბოქსილატის სინთეზის რეაქციის საწყისი, გარდამავალი და საბოლოო მდგომარეობის გეომეტრიული, ენერგეტიკული და ელექტრონული მახასიათებლები. მეთილ 3 –(3,4 დიმეთოქსიფენილ) ოქსირან-2 კარბოქსილატის სინთეზის ერთ-ერთი შესაძლო

ვარიანტია 3,4-დიმეთოქსიფენილის და მეთილ 2-ქლორაცეტატის ურთიერთქმედება. ნახევრადემპირიული კვანტურ-ქიმიური მეთოდის (AM1) გამოყენებით გამოთვლილ იქნა მეთილ 3 –(3,4 დიმეთოქსიფენილ) ოქსირან-2 კარბოქსილატის სინთეზის რეაქციის საწყისი, გარდამავალი და საბოლოო მდგომარეობის გეომეტრიული, ენერგეტიკული და ელექტრონული მახასიათებლები. კვანტურ-ქიმიურმა გათვლებმა აჩვენა, რომ ტეტრა-ბუთილ 3-(3,4-დიბენზოქსიფენილ) ოქსირან-2-კარბოქსილატის სინთეზის რეაქცია ეგზოთერმულია და 3–(3,4 დიმეთოქსიფენილ)-ოქსირან-2 კარბოქსილატის სინთეზი ენდოთერმულია. აქტივაციის ენერგია კი ორივე შემთხვევაში მაღალია, მაგრამ ხელსაყრელი პირობების შექმნით (ტემპერატურა, წნევა, pH) ტეტრა-ბუთილ 3-(3,4-დიბენზოქსიფენილ) ოქსირან-2-კარბოქსილატის და 3–(3,4 დიმეთოქსიფენილ)-ოქსირან-2 კარბოქსილატის სინთეზი შეიძლება განხორციელდეს აღნიშნული სქემით.

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