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QUANTUM-CHEMICAL STUDY OF THE REGIOSELECTIVITY OF THE DIELS-ALDER HETEROREACTION OF *α,β*-UNSATURATED THIOCARBONYL COMPOUNDS WITH UNSYMMETRICAL DIENOPHILES

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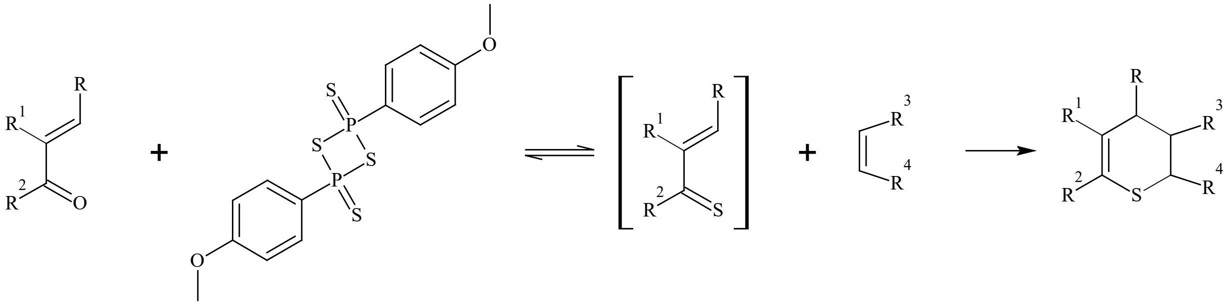
The study considers the quantum-chemical study of the Diels-Alder heteroreaction of various substituted 3,4-dihydro-2H-thiopyrans. We study the steric and electronic factors influencing the reaction of α,β-unsaturated thiocarbonyl compounds with unsymmetrical dienophiles. We used the methods AM1, B3LYP. The analysis of calculated data for asymmetric dienophiles shows that the regioselectivity of the reaction is subject to the electron factor and can be described by the reaction activation energies, energies and localisation parameters of the boundary orbitals. The calculations are confirmed by the experimental results.

Introduction

Thiopyranes are important compounds in terms of synthetic organic chemistry. They can be the starting compounds for the synthesis of various biologically active substances, pharmaceuticals. Thus, it is an urgent task to develop and improve methods of their production from available starting compounds.

One of the most promising is the Diels-Alder heteroreaction method of thiopyranes [1-3]. This reaction starting compounds are *α,β* unsaturated carbonyl compounds as diene and various dienophiles; Lavesson's reagent is used as sulphidising agent [4]:



This study contains the mathematical modelling of thiopyranes production in case of interaction of 1,3-diphenylprop-2-ene-1-one with styrene and acrylonitrile, and considers the factors influencing the regioselectivity of the reaction.

Study

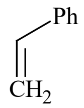
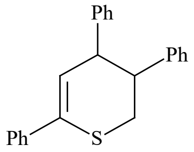
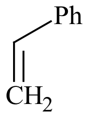
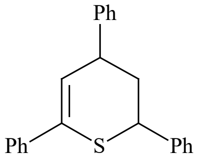
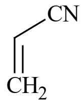
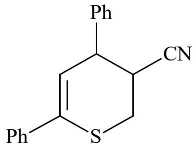
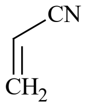
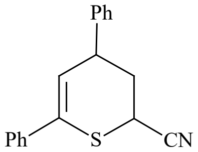
We use the semi-empirical AM1 method for quick calculating of the structures and reactions [5, 6]. In order to obtain fine results, we made calculations by B3LYP electron density functional method [7], which provides a high accuracy of geometry determination with relatively low computer requirements

The modern triple-exponential 3ζ (triple-zeta) basis def2-TZVP(-f) with polarisation functions [8, 9] was used for this purpose. It provides quite acceptable accuracy for calculating the geometry, energy and electronic parameters of organic molecules and reaction studies.

The semi-empirical quantum chemical calculations were made by the MOPAC 2016 software. The calculations by the electron density functional methods were made by the program Orca 4.0.1.2 [10].

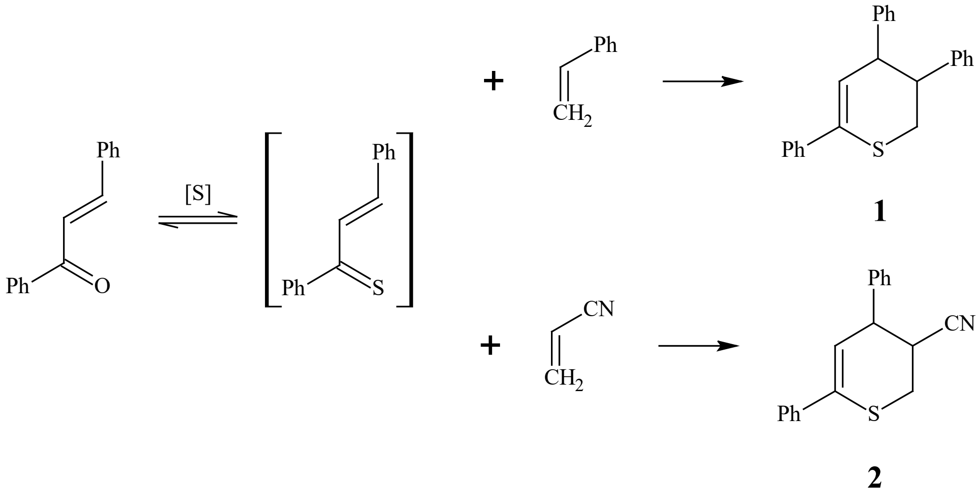
To assess the effect of the steric factor on the transition state structure, the product and transition state structures of both accession variants were calculated for asymmetric dienophiles (Table 1).

Table 1. Bond lengths in the regioisomers of some thiopyranes and their transition states of formation (B3LYP method)

Dienophile	Thiopiran	Thiopiran		Transition state	
		R_{C-S}, Å	R_{C-C}, Å	R_{C-S}, Å	R_{C-C}, Å
		1.83	1.56	2.20	2.48
		1.85	1.54	2.60	2.13
		1.83	1.56	2.21	2.44
		1.85	1.54	2.47	2.17

By the table, the transition states have increased interatomic distance on the bulk substituent side of the dienophile, irrespective of the direction of its addition. It correlates with the steric effect. So, we can note the influence of the steric factor on the geometry of the transition state in such reactions. The influence of the steric factor on the geometry is neutralising, judging by the minimal differences in the lengths of the corresponding bonds.

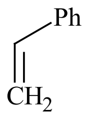
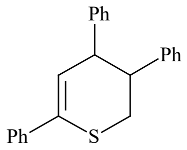
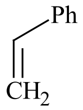
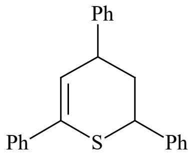
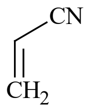
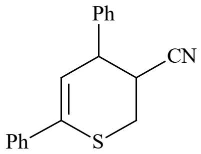
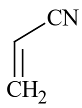
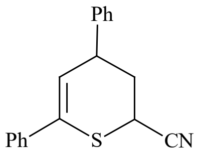
However, according to experimental data [1], only one regioisomer (compounds 1 and 2) is formed by the reactions:



The experimentally observed regioselectivity is not correlated with the influence of the steric factor described above. We suppose reaction is governed by an electron factor.

Table 2 shows the calculated activation energies for the reaction of various regioisomers of the cycloaddition of thiochalcon to styrene and acrylonitrile.

Table 2. Calculated activation energies for the reaction of various regioisomers of cycloaddition of thiochalcon to styrene and acrylonitrile (B3LYP method)

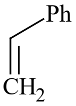
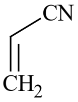
Dienophile	Thiopiran	E_a, kJ
		65.10
		79.59
		55.89
		75.70

By the table, for styrene and acrylonitrile the calculated activation energies are lower exactly for the experimentally obtained products. It is energetically efficient to attach a dienophile to a diene. Its unsubstituted carbon atom forms a bond with the sulphur atom of the thiochalcon.

Probably, it is the influence of HOMO (highest occupied molecular orbital). It is localising on the sulphur atom, which provides the nucleophilic properties of sulphur. For a dienophile containing an electron acceptor group, the electrophilic properties are characteristic of the beta-carbon atom.

The squares of the coefficients of the p_z orbital wave function of HOMO at the reaction centres in diene and LUMO (lowest unoccupied molecular orbital) in dienophile were calculated. Thus, the HOMO energy of the thiochalcon is -8.508 eV, C^2p_z HOMO at the sulphur atom is 0.862 eV, and at the carbon atom 0.011 eV. HOMO for diene C^2p_z by Table 3.

Table 3. Calculated LUMO energies of some asymmetric dienophiles and squares of wave function coefficients on α- and β-carbon atoms (AM1 method)

Dienophile	E_{LOMO}, eV	C^2p_z α-carbon atom	C^2p_z β-carbon atom
	0.019	0.089	0.202
	-0.050	0.305	0.466

By the table, the beta-carbon atom makes up the largest fraction of the LUMO of the dienophiles, giving rise to its high electrophilicity with the alpha-carbon atom. Thus, the most reactive for nucleophilic sulphur atom of the thiochalcon is the highly electrophilic beta-carbon atom of the asymmetric dienophile. This explains the observed regioselectivity of such reactions.

Conclusions

The analysis of the AM1 and B3LYP methods for the Diels-Alder heteroreaction of the synthesis of 3,4-dihydro-2*H*-thiopyrans from unsymmetrical dienophiles and *α,β*-unsaturated thiocarbonyl compounds shows the regioselectivity of the reaction corresponds to the calculated activation energy, depends on the electronic factor and characterized by the orbital localization energies and parameters. The results agree with the experimentally observed regioselectivity of the reaction.

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