UDC 547.818.1
DOI: 10.52957/27821900_2021_04_77

COMPARATIVE QUANTUM-CHEMICAL ANALYSIS OF THE REACTIVITY OF 1-PHENILBUT-2-EN-3-TYON AND 2-(N-PIRROLIDINIL)PENT-2-EN-4-TYON AS HETERODIENS IN THE DIELS - ALDER REACTION

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Keywords:
unsaturated thiocarbonyl compounds, the Diels-Alder heteroreaction, thiopyranes synthesis, quantum-chemical modelling, AM1 method

We performed quantum-chemical AM1 modelling of the Diels-Alder heteroreaction of 1-phenylbut-2-ene-3-thione and 2-(N-pyrrolidinyl)pent-2-ene-4-thione with symmetrical dienophiles. We calculated the HOMO/LUMO energies of dienes and dienophiles as well as the activation energies of the corresponding reactions. The reaction has direct electron requirements. The principal possibility of the reaction of 2-(N-pyrrolidinyl)pent-2-ene-4-thione with electron-excessive dienophiles was outlined. Also we proved the significant difference in the reactivity of norbornene and cyclohexene dienophiles with α,β-unsaturated thiocarbonyl compounds.

Introduction

Compounds of the thiopyran group are insufficiently studied organic substances and are of interest in terms of synthetic organic chemistry. The development of the synthesis methods from available starting compounds is very important.

One of the most extensively studied methods for the synthesis of thiopyranes is their production by the Diels-Alder reaction from *α, β*-unsaturated thiocarbonyl compounds with various dienophiles [1-6] (Fig. 1):

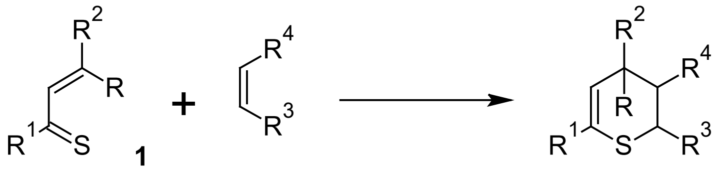


Fig. 1. Basic scheme for the synthesis of thiopyranes by the Diels-Alder reaction

The articles [1, 2] describe the Diels-Alder reactions of α, β-unsaturated thiocarbonyl compounds **1** (R = H; R^1, R^2 = Me, Ar). Both electron-abundant (norbornene, endic anhydride) and electron-deficient (maleic anhydride, maleimides) dienophiles react with these substrates.

However, for enaminothioketones 1**1** (R = $N(Alk)_2$; R^1, R^2 = H, Me, Ar) only reactions with electron-deficient dienophiles such as maleic anhydride [4], maleimides [5], croton and cinnamic aldehydes [7] are described. There are no references about attempts to introduce electron-abundant dienophiles into this reaction.

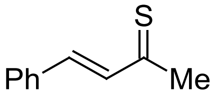
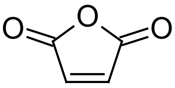
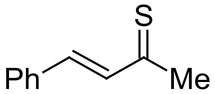
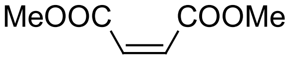
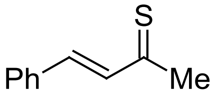
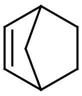
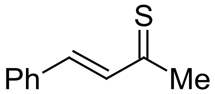
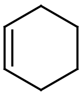
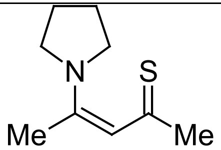
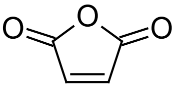
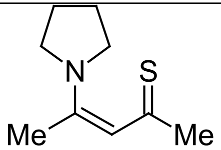
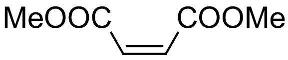
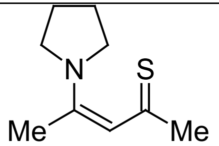
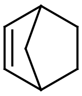
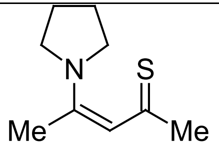
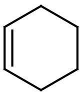
We performed quantum-chemical simulations of the Diels-Alder heteroreaction of 1-phenylbut-2-ene-3-thione (R = H; R^1 = Me; R^2 = Ph) and 2-(*N*-pyrrolidinyl)pent-2-ene-4-thione (R = N-pyrrolidinyl; R^1, R^2 = Me) with symmetrical dienophiles having both donor and acceptor substituents in order to evaluate the possibility of a Diels-Alder reaction of 2-(N-pyrrolidinyl)pent--2-ene-4-thione with electron-depleted dienophiles.

Results and Discussion

We applied the semiempirical AM1 method [8, 9] to model the molecules of all compounds and reaction pathways. This method has a sufficiently high degree of accuracy in geometry optimization with relatively low computer processing power requirements [10, 11]. The quantum chemical calculations were performed by the MOPAC 2016 software.

By the paper [12], the Diels-Alder reaction of 1,3-diphenylprop-2-ene-1-thione with unsymmetrical dienophiles are characterized by the energies of the boundary orbitals of the diene and dienophile. The results agree with the experimental data. In order to evaluate the possibility of the Diels-Alder reaction of 1-phenylbut-2-ene-3-thione and 2-(*N*-pyrrolidinyl)pent-2-ene-4-thione with different dienophiles we considered two similar reaction series for both dienes and calculated activation energies of each reaction as well as differences of LUMO dienophile and HOMO diene energies. The values obtained are shown in Table 1.

Table 1. Calculated activation energy E_a and energy difference between LUMO dienophile and HOMO diene ΔE

Diene	Dienophile	E_a, kJ/mol	ΔE, eV
		22.92	6.928
		56.87	7.949
		84.68	9.830
		107.1	9.874
		18.40	6.171
		58.42	7.192
		77.48	9.073
		100.3	9.117

By Table 1, the highest values of activation energies and differences of energies of LUMO dienophile and HOMO diene are observed in the cases of electron-deficient dienophiles (norbornene and cyclohexene), whereas for electron-deficient dienophiles (maleic anhydride and dimethyl maleate) the situation is the opposite. Also for both reaction series a symbiosis between activation energies and differences in the energies of the molecular boundary orbitals is evident. This indicates the electronic nature of the reaction.

According to the experimental data [2] the reaction of 1-phenylbut-2-ene-3-thione proceeds with 5-norbornen-2,3-dicarboxylic acid **2**, whereas no interaction occurs with 5-cyclohexene-2,3-dicarboxylic acid **3** (Fig. 2):

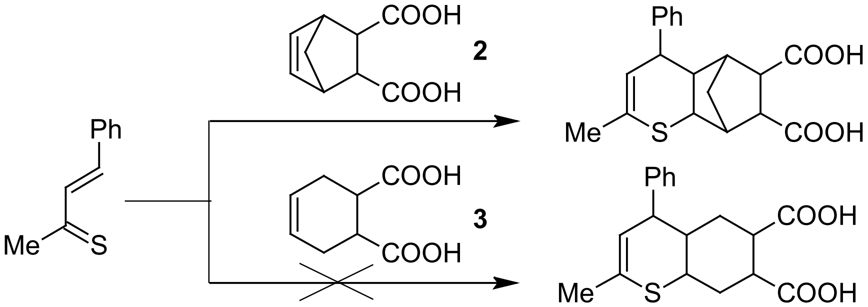


Fig. 2. Reactions of 1-phenylbut-2-ene-3-thione with 5-norbornen-2,3-dicarboxylic acid and 5-cyclohexen-2,3-dicarboxylic acid

The increased activation energies of the reactions of heterodienes with cyclohexene, as compared to those for norbornene, agree well with the experimental result. The slight disparity in the boundary orbital energy differences for cyclohexene and norbornene with 1-phenylbut-2-ene-3-thione do not explain the experimental data. It indicates on the influence of a steric factor which increases the transition state energy for the reaction with cyclohexene.

By the experimentally proved possibility of reactions of electron-deficient dienophiles and norbornene dienophiles with 1-phenylbut-2-ene-3-thione [2], we consider the theoretical possibility of analogous reactions with 2-(*N*-pyrrolidinyl)pent-ene-4-thione. We obtain similar energy characteristics of both dienes for corresponding diene-dienophile pairs.

Conclusions

The LUMO dienophile and HOMO diene activation energies and energy differences of the Diels-Alder reaction of symmetrical dienophiles with 1-phenylbut-2-ene-3-thione and 2-(*N*-pyrrolidinyl)pent-2-ene-4-thione obtained by AM1are electronic in nature. The obtained values show the theoretical possibility of reaction 2-(*N*-pyrrolidinyl)pent-2-ene-4-thione with electron-deficient dienophiles and dienophiles of the norbornene series. A significant difference in the reactivity of the dienophiles of the norbornene and cyclohexene series with *α,β*-unsaturated thiocarbonyl compounds seems to be due to the influence of the steric factor.

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Received 06.12.2021
Accepted 09.12.2021