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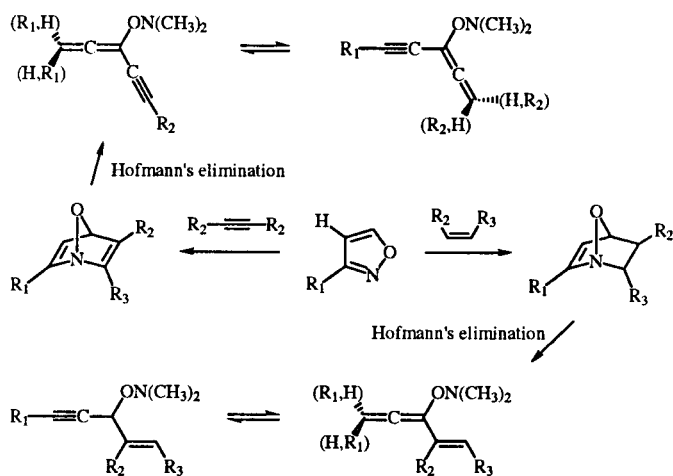
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The AM1 semiempirical and B3LYP density functional theory computational studies are undertaken with the target being to explore cycloaddition reactions with heterocycles that have two heteroatoms in the ring's 1 and 2 positions as an initial synthetic step in the preparation of allene's acetylene derivatives. Several qualitative computational approaches were used to evaluate the heterocycle reactivity, including two new approaches using electronic and bond order changes in transformation of the reactant pair into corresponding transition state structures. Finally, the reactivity was evaluated by computing activation barriers, and the feasibility of the proposed synthetic transformations was discussed.

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### Introduction.

From the synthetic chemist's point of view, heterocycles with two heteroatoms [1] in the 1 and 2 positions might be very useful as dienes for Diels-Alder reactions [2,3] because after the addition of a dienophile and ring opening, valuable unsaturated compounds could be synthesized. For instance, by adding alkene or alkyne derivatives to 1,2-oxadiazole, a new bicycloproduct with a bridged nitrogen can be formed. This compound can be subject to the Hofmann elimination, producing either an acetylenic conjugated allene or vinylallene derivatives (Scheme 1). A similar synthetic scheme can be outlined for the transformation of 1,2-thioazole, and 1,2-diazole into corresponding allenic derivatives.



Scheme 1. One possible synthetic route in the transformation of 1,2-oxadiazole into acetylene, or vinyl allenes.

The reactivity of five membered heterocycles [4] with two heteroatoms in the 1,2 position as dienes for Diels-Alder reactions is very low. In fact, there are not much experimental data in this area of research. It is believed that the main reason for their low reactivity is high heterocycle

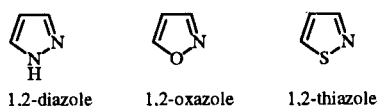
aromaticity; delocalization of molecular  $\pi$ -orbitals that should be part of the cycloaddition reaction. We would like to explore the reactivity of heterocycles with two heteroatoms in the 1,2 positions [5] as dienes for Diels-Alder reactions and to suggest necessary chemical transformations needed to make the heterocycles more reactive.

### Computational Methods.

All semiempirical calculations were performed on a DEC 7620 computer. Chem-3D Plus on a Macintosh IIfx was used as a graphical interface for drawing and visualizing all structures and for preparing input files for MOPAC [6]. In AM1, bond order is defined as the sum of the squares of the density matrix elements containing any two atoms. For instance, the C-C bond orders for ethane, ethylene, and acetylene are, by definition, 1, 2, and 3, respectively [6]. The transition state structures were localized, optimized, and verified as explained in our previous work [7]. All Density Functional Theory (DFT) computational studies were performed with B3LYP [8] and the 6-31G(d) [9] basis set as incorporated into the GAUSSIAN [10] computational package and will be regarded in this paper as DFT calculations.

### Results and Discussion.

Certainly, the most known theoretical explanation of cycloaddition reactions is the Woodward and Hoffmann selection rules [11]. According to these rules, the Diels-Alder reaction as  $\pi 2s + \pi 4s$  cycloaddition reaction is thermally permissible. Considering orbital symmetry, cycloaddition reactions between dienophiles and heterocycles, presented in Scheme 2, are thermally achievable reactions as well. This information does not actually suggest that the reaction with dienes presented in Scheme 2 is experimentally feasible. A theoretical approach that can give us slightly better insight as to the natures of these cycloaddition reactions is the comparison of the Frontier Molecular Orbital (FMO) energies of the diene and dienophile in the Diels-Alder reaction. This approach



Scheme 2. The heterocycles with two heteroatoms in the 1 and 2 positions considered in this study

requires relatively modest computational resources and time. Only relative reactivity of the series of reactions pairs can be obtained in such a way. There are two principles that are considered in the FMO approach: the energy difference between the Highest Occupied Molecular Orbital (HOMO) of one and the Lowest Unoccupied Molecular Orbital (LUMO) of the other, as well as maximal overlap between these two molecular orbitals. The pair of reactants that have the smallest energy gap between the HOMO and LUMO orbitals should be the most reactive. The regioselectivity is defined through maximum molecular orbital overlap between the reactants' HOMO-LUMO orbital. One combination that has higher molecular orbital overlap is likely occur over the other which has a smaller HOMO-LUMO overlap [12].

dienophiles. The FMO energy gaps between heterocycles from Scheme 2 and dienophiles (ethylene, acetylene, and cyclopropene) are presented in Table 1. According to these energy differences, the addition of acetylene to cyclopentadiene and 1,2-diazole is HOMO diene controlled or a "normal" Diels-Alder reaction. On the other hand, for the acetylene addition to both 1,2-oxazole and 1,2-thiazole, the smaller FMO energy gap was obtained with LUMO heterocycles and HOMO acetylene (Table 1), indicating that the reaction is LUMO diene (heterocycle) controlled cycloaddition reaction. If we now turn our attention to the more reactive dienophile, ethylene which has a LUMO energy that's substantially lower than acetylene, we can expect that the energy gap between reactants should be narrower. All cycloaddition reactions should now become HOMO diene (heterocycle) controlled. This is only partially true. In all cycloaddition reactions, the FMO energy gap between the reactant is smaller (Table 1), denoting that ethylene is indeed more reactive as a dienophile than acetylene, but addition to 1,2-oxazole and 1,2-thiazole is a LUMO diene (heterocycle) controlled cycloaddition reaction. Following the relative FMO energies, cyclopropene

Table 1

Frontier Molecular Orbital (FMO) Energy (eV) Gap Between the Heterocycles with Two Heteroatoms and Acetylene, Ethylene, and Cyclopropene Computed with the AM1 Semiempirical Method

| reactant     | HOMO    | LUMO   | A      | B      | C      | D      | E      | F      |
|--------------|---------|--------|--------|--------|--------|--------|--------|--------|
| acetylene    | -11.500 | 2.0532 |        |        |        |        |        |        |
| ethylene     | -10.551 | 1.438  |        |        |        |        |        |        |
| cyclopropene | -9.819  | 1.042  |        |        |        |        |        |        |
| CPD          | -9.079  | 0.482  | 11.132 | 11.982 | 10.517 | 11.033 | 10.121 | 10.301 |
| furan        | -9.317  | 0.723  | 11.370 | 12.223 | 10.755 | 11.274 | 10.359 | 10.542 |
| 1,2-diazole  | -9.706  | 0.955  | 11.759 | 12.455 | 11.144 | 11.506 | 10.748 | 10.774 |
| 1,2-oxazole  | -10.466 | 0.175  | 12.519 | 11.675 | 11.904 | 10.726 | 11.508 | 9.994  |
| 1,2-thiazole | -9.540  | -0.102 | 11.593 | 11.398 | 10.978 | 10.449 | 10.582 | 9.717  |

CPD = cyclopentadiene; A =  $LUMO_{\text{acetylene}} - HOMO_{\text{heterocycle}}$ ; B =  $LUMO_{\text{heterocycle}} - HOMO_{\text{acetylene}}$ ; C =  $LUMO_{\text{ethylene}} - HOMO_{\text{heterocycle}}$ ; D =  $LUMO_{\text{heterocycle}} - HOMO_{\text{ethylene}}$ ; E =  $LUMO_{\text{cyclopropene}} - HOMO_{\text{heterocycle}}$ ; F =  $LUMO_{\text{heterocycle}} - HOMO_{\text{cyclopropene}}$ .

It is well known that acetylene, ethylene, and cyclopropene add to cyclopentadiene in a synchronous cycloaddition mechanism with preservation of symmetry of the substituents on both the diene and dienophile [13]. We used these three cycloaddition reactions as models for cycloaddition reactions and compared them with similar cycloaddition reactions with heterocycles as dienes. These three reactions are perfect model systems because the addition of cyclopropene to cyclopentadiene occurs at room temperature, while for the addition of ethylene, an elevated temperature is necessary. For the addition of acetylene, more forceful reaction conditions such as the introduction of an acid catalyst are necessary. Therefore, with these three reactant pairs we can adjust the relative reactivity for aromatic heterocycles with the same

had the highest HOMO and lowest LUMO energy and therefore, should be more reactive as a dienophile than both acetylene and ethylene. Indeed, the computed FMO gaps were very low. The two energy gaps (one with LUMO and the other with HOMO orbitals of the heterocycle) for the 1,2-diazole-cyclopropene reactant pair were almost identical, indicating that both electron donating or electron withdrawing substituents on 1,2-diazole should facilitate the cycloaddition reaction. On the other hand, for both 1,2-oxazole and 1,2-thiazole reactant pairs with cyclopropene, the FMO energy gap clearly suggested that the reaction was LUMO diene (heterocycle) controlled. As a result of this, only electron-withdrawing substituents on the heterocyclic ring should facilitate a cycloaddition reaction (Table 1).

For the addition of ethylene to cyclopentadiene which is a LUMO dienophile controlled reaction, the AM1 computed FMO energy was 10.517 eV. As mentioned above, the reaction is experimentally feasible. One can then assume that for experimentally feasible reactions with the heterocycles, the FMO energy gap with certain dienophiles should be below 10.517 eV. It is obvious that the reactant pair 1,2-oxazole, and 1,2-thiazole with cyclopropene have lower FMO energy gaps than the experimentally feasible cyclopentadiene-ethylene reactant pair. Therefore, one can conclude that those two cycloaddition reaction should be able to be accomplished experimentally.

Another static approach that can give us the relative reactivity of heterocycles as dienes for Diels-Alder reactions is evaluation of their aromatic stability through the ring bond order uniformity. If, for a moment, we examine reactivity of the heterocycle on the basis of the FMO energy gap with cyclopropene as a dienophile, it is obvious that the most reactive heterocycle is 1,3-thiazole. It had a FMO energy gap of only 9.717 eV (Table 1). That finding is surprising, and as will be demonstrated later, it is contradictory to some other qualitative evaluations of the heterocycle reactivity.

This is a relatively simplistic approach that might be very useful when similar chemical systems are compared, but cyclopentadiene and heterocyclic compounds are quite different in regard to their physical and chemical properties. The majority of the differences come from the fact that heterocyclic compounds are aromatic while cyclopentadiene is not. Therefore, it is permissible to compare reactivity of these aromatic compounds with other aromatic compounds that we know can be easily engaged in cycloaddition reactions. It is well documented that furan and its derivatives react with cyclopropene under mild reaction conditions making cycloadduct products in high yield. Therefore, it is more appropriate to determine the reactivity of the heterocycle with heteroatoms in the 1,2 position by comparison of their physical properties with furan. One of properties that is directly reflected by aromatic character of the heterocycle ring is uniformity of the ring's bond order. It is based on the simple principle of

delocalization of the  $\pi$ -molecular orbitals in the ring system. With fully localized  $\pi$ -molecular orbitals, regardless of the atomic nature in of ring, the bond order (molecular orbital overlap) should be identical and their values should be somewhere between 1 and 2. The bond orders are computed as a reference to C-C bond order in ethane as one and C-C bond order in ethylene as two. Computed bond orders for cyclopentadiene, furan and the heterocycles with heteroatoms in the 1 and 2 positions are presented in Table 2. It is quite obvious that bond orders for cyclopentadiene are one and two, indicating very small delocalization between C(2)-(C3)-C(4)-C(5) atoms of the ring while C(1)-C(2) as well C(1)-C(5) bond orders are practically equal to one (Table 2). The sum of bond orders (SBO) for cyclopentadiene is 6.763 (Table 2). If we for a moment disregard that cyclopentadiene has one  $sp^3$  hybrid carbon atom, C(1), making perfect conjugation in the ring, impossible, in an ideal delocalized cyclic p-molecular orbital system all bond orders should be  $6.763/5 = 1.353$  (ABO). The sum of bond order deviation (BOD) is therefore a measure of how far the heterocyclic system is from an ideal aromatic ring system for a studied molecular ring (Table 2). In our case, the BOD for cyclopentadiene is 1.986, indicating strong localization of singlet and double ring bonds and its nonaromatic character.

Conversely, in furan, the O(1)-C(2) bond order is higher than one (1.10) and its BOD is substantially smaller than two, (1.290), showing that furan has some aromatic character. It forms an extra bond with oxygen's lone pair, which is delocalized through the furan ring. This further shows furan's higher stability in comparison with cyclopentadiene, the former having unclear localization of double and single bonds making it a poorer diene for Diels-Alder reactions than cyclopentadiene. Because we have defined reactivity of the five-membered cyclic dienes through sum of bond orders and knowing that furan undergoes cycloaddition reactions with cyclopropene we can assess the reactivity of heterocycles with heteroatoms in the 1,2-positions through evaluation of their sum of bond order deviation from an average bond order (aromaticity). Let us remember that the order of reactivity obtained from the reactants'

Table 2

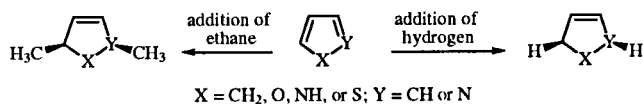
The Ring Bond Orders and Bond Order Deviation for Heterocycles with Two Heteroatoms Computed with the AM1 Semiempirical Method

|              | BO <sub>12</sub> | BO <sub>23</sub> | BO <sub>34</sub> | BO <sub>45</sub> | BO <sub>51</sub> | SBO   | ABO   | BOD   |
|--------------|------------------|------------------|------------------|------------------|------------------|-------|-------|-------|
| CPD          | 1.002            | 1.849            | 1.061            | 1.849            | 1.002            | 6.763 | 1.353 | 1.986 |
| furan        | 1.104            | 1.670            | 1.190            | 1.670            | 1.104            | 6.738 | 1.348 | 1.290 |
| 1,2-diazole  | 1.172            | 1.580            | 1.262            | 1.560            | 1.195            | 6.769 | 1.354 | 0.865 |
| 1,2-oxazole  | 1.108            | 1.702            | 1.156            | 1.689            | 1.101            | 6.756 | 1.351 | 1.377 |
| 1,2-thiazole | 1.176            | 1.640            | 1.205            | 1.629            | 1.178            | 6.828 | 1.366 | 1.076 |

CPD = cyclopentadiene; BO<sub>X,Y</sub> = bond order between atoms X and Y in the heterocycle ring; SBO = sum of ring bond orders; ABO = average bond order; BOD = sum of bond order deviation from the average ring bond order.

FMO energy differences is 1,2-thiazole, 1,2-oxazole, and 1,2-diazole (Table 1). Clearly, BOD for 1,2-diazole is very small (0.865), even smaller than furan, indicating its very high aromaticity. It was predicted that 1,2-diazole should have low reactivity, quite lower than, for instance, furan. 1,2-Thiazole also had a lower BOD (1.076) than furan but slightly higher than 1,2-diazole; therefore, it was also expected that this heterocycle should not be reactive as a diene for Diels-Alder reactions. Only 1,2-oxadiazole was expected to have comparable reactivity to furan in Diels-Alder reactions. As we have demonstrated, classical FMO can not be satisfactorily applied to heterocyclic aromatic compounds as is the case with nonaromatic dienes and dienophiles in Diels-Alder reactions.

As can be seen from Scheme 2, it is obvious that in the course of the cycloaddition reaction one C-N and one C-C bond should be formed. From both our experience in experimental (synthetic) and computational chemistry we know that for reactions that go through a concerted mechanism, carbon-heteroatom bond formation is energetically more demanding than carbon-carbon bond formation. Therefore the 1,2-oxazole might not be as reactive as furan as predicted on the basis of the sum of the bond order deviation from ideal bond order distribution (Table 2). This is due to the fact that in 1,2-oxazole, one energetically less favorite C-N bond formation is occurring. To better evaluate the effect of the C-N bond formation in heterocycles, we have performed an imaginary reaction of hydrogen and ethylene addition to the 2 and 5 ring positions. To effectively mimic the Diels-Alder reaction, two methyl groups in what was cyclopentadiene and furan were introduced in the cis positioned (Scheme 3). The heat for these imaginary reactions are presented in Table 2. For both hydrogen



Scheme 3. Imaginary reaction of hydrogen and ethane addition to unsaturated five-membered rings.

and ethylene addition to cyclopentadiene, the reaction is exothermic. Although for same reaction with furan, the heat of the reaction was exothermic, the exothermicity is noticeable smaller. For instance, for the ethylene addition to furan, exothermicity is by 12.8 kcal/mol smaller than in the case of imaginary ethane addition to cyclopentadiene. Of course, the majority of the energy difference comes from fact that the aromaticity of the furan ring was disrupted in the course of the imaginary addition reaction. Therefore, it is reasonable to expect that the reactivity of furan as a diene for the addition reaction is smaller when compared to cyclopentadiene.

In the case of imaginary hydrogen and ethane addition to five-membered heterocycles with heteroatoms in the 1,2 position coupled with disrupting the ring aromaticity, heteroatom-carbon bonds were formed. In the case of ethylene addition to 1,2-diazole, the reaction is by 8.3 kcal/mol endothermic, indicating that formation of the C-N bond should be around 45 kcal/mol less energetically favorable than the C-C bond formation (the value was obtained from the comparison of the heat of the reaction for ethane addition to furan and 1,2-diazole). This certainly is a high energy, and from this point of view, it is reasonable to expect that the majority of cycloaddition reactions with 1,2-diazole are not experimentally feasible. That, of course, might be changed if some strong activation substituents were placed on the heterocycle ring. Similar results were obtained for 1,2-thiazole as a diene (Table 3). The most reactive as predicted on the basis of the bond order distribution should be 1,2-oxazole which has a slightly higher BOD than furan (Table 3). Because the energetically unfavorable C-N bond is, in the course of the reaction, -35 kcal/mol in comparison with furan, it is also expected that 1,2-oxadiazole is not a suitable diene for the Diels-Alder reaction.

We trust that two very simple but resourceful approaches, BOD and heat of ethylene addition, give a qualitative picture of the heterocycle reactivity, defining them to be far less reactive than cyclopentadiene or even furan as dienes. Much better insight into a cycloaddition reaction with the heterocycles as dienes can be obtained by exploring structural,

Table 3  
The AM1 Computed Energies of Different Heterocycles with Two Heteroatoms

| Heterocycle     | HOF <sub>I</sub> | HOF <sub>II</sub> | HOF <sub>III</sub> | $\Delta E_I$ | $\Delta E_{II}$ |
|-----------------|------------------|-------------------|--------------------|--------------|-----------------|
| cyclopentadiene | 37.1             | 3.0               | -7.0               | -28.9        | -48.6           |
| furan           | 3.0              | -23.6             | -32.3              | -21.4        | -35.8           |
| 1,2-diazole     | 65.6             | 60.0              | 56.5               | -0.4         | 8.3             |
| 1,2-oxazole     | 42.9             | 25.1              | 25.0               | -12.6        | -0.5            |
| 1,2-thiazole    | 38.0             | 27.3              | 26.0               | -5.5         | 5.4             |

HOF<sub>I</sub> = heat of formation (kcal/mol) computed for aromatic heterocycle; HOF<sub>II</sub> = heat of formation (kcal/mol) computed for 2,5-dihydroaromatic heterocycle; HOF<sub>III</sub> = heat of formation (kcal/mol) computed for 2,5-dimethylaromatic heterocycle;  $\Delta E_I$  = energy of hydrogenation reaction;  $\Delta E_{II}$  = energy of imaginary reaction between heterocycle and ethylene; heat of formation for hydrogen is -5.2 kcal/mol; heat of formation for ethane is -17.4 kcal/mol.

electronic, as well as energetic properties of transition state structures. Optimization of transition state structures is nowadays becoming more or less a routine procedure. Transition state structure can be obtained for almost any chemical transformation [15]. The transition state structures for the acetylene, ethylene, and cyclopropene additions to cyclopentadiene are highly symmetric. They are for concerted mechanisms of cycloaddition reactions with synchronous formation of both C-C bonds as explained in many of our previous publications [5]. The cycloaddition reaction with heterocycles that have two heteroatoms in the 1,2 position as a diene has a concerted mechanism but the transition structure is for a highly unsynchronous reaction as demonstrated for the cyclopropene addition to 1,2-oxazole (Figure 1). As we have mentioned above (Table 1), the FMO energy gap between reactants in the cycloaddition reaction is not an appropriate qualitative approach to determine the reactivity of heterocyclic aromatic compounds as dienes for the Diels-Alder reaction. This approach selects that, as dienes, both 1,2-oxazole and 1,2-thiazole are more reactive for use in a Diels-Alder reaction than both cyclopentadiene and furan in reaction with cyclopropene. We have recently introduced

Frontier Molecular Orbital Energy Change (FMOEQ necessary for a reactant pair to adapt to reach their transition state structure. The selected energies for the reaction between cyclopropene and the heterocycles is presented in Table 4.

It is obvious that the reaction is a HOMO cyclopropene and LUMO heterocycle controlled cycloaddition reaction because their sum (A+D) is substantially smaller than the other frontier orbital combination, (B+C; Table 4). The furan FMOEC was only 1.084 eV while for heterocycles with heteroatoms in 1 and 2 position it was by three to four times higher. That clearly indicated that cycloaddition reactions with these heterocycles are far less feasible than for furan. Actually, the energy difference is so high that one can state that these reactions are not experimentally feasible.

The same principle of small electronic rearrangement in reactants to adapt the transition state structure can be applied for bond order uniformity change in the heterocycle moiety of the transition state structure (Table 5). To decrease the amount of data, only the bond order computed for the *endo* transition state structure with cyclopropene as a dienophile were reported, although the same conclusion can be drawn from the other dienophiles; as well. Again, we will only pre-

Table 4  
The AM1 Frontier Molecular Orbital (FMO) Energy (eV) Changes going from Reactants to the *endo* Transition State Structures with Heterocycles with Two Heteroatoms in the 1 and 2 Positions as Dienes in Reaction with Cyclopropene

| TS  | HOMO   | LUMO   | A     | B     | C     | D      | $\Sigma_1$ | $\Sigma_2$ |
|-----|--------|--------|-------|-------|-------|--------|------------|------------|
| I   | -8.893 | 0.565  | 0.926 | 0.424 | 1.488 | -0.158 | 1.084      | 1.912      |
| II  | 7.674  | -1.011 | 2.145 | 2.032 | 3.064 | -1.966 | 4.111      | 5.096      |
| III | -7.801 | -1.456 | 2.145 | 2.665 | 3.509 | -1.631 | 3.776      | 6.174      |
| IV  | -7.445 | -1.347 | 2.374 | 2.095 | 3.400 | -1.245 | 3.619      | 5.495      |

I = TS with furan; II = TS with 1,2-diazole; III = TS with 1,2-oxazole; V = 1,2-thiazole; a = for *exo* addition of cyclopropene; A = HOMO<sub>TS</sub> - HOMO<sub>cyclopropene</sub>; B = HOMO<sub>TS</sub> - HOMO<sub>heterocycle</sub>; C = LUMO<sub>cyclopropene</sub> - LUMO<sub>TS</sub>; D = LUMO<sub>TS</sub> - LUMO<sub>heterocycle</sub>;  $\Sigma_1 = |A| + |D|$ ;  $\Sigma_2 = |B| + |C|$ .

[16] a new approach for the evaluation of aromatic heterocycles in determination of their reactivity in Diels Alder reactions based on the Hammond postulate [17]. The postulate is based on the simple principle that the reactant pair that requires small structural, electronic and consequently energetic reorganization to reach its transition state, should be more reactive in comparison with others that require larger changes. We can demonstrate this principle by using the

Table 5  
Bond Orders and Bond Order Deviation of the Heterocycle Ring Going From Reactant to the Transition State Structure

| TS  | BOC <sub>12</sub> | BOC <sub>23</sub> | BOC <sub>34</sub> | BOC <sub>45</sub> | BOC <sub>51</sub> | SBOC  |
|-----|-------------------|-------------------|-------------------|-------------------|-------------------|-------|
| II  | -0.034            | -0.386            | 0.339             | -0.386            | -0.035            | 1.180 |
| III | -0.019            | -0.272            | 0.311             | -0.495            | -0.248            | 1.345 |
| IV  | -0.007            | -0.281            | 0.299             | -0.596            | -0.146            | 1.329 |
| V   | -0.172            | -0.492            | 0.300             | -0.267            | -0.009            | 1.240 |

I = TS with furan; II = TS with 1,2-diazole; III = TS with 1,2-oxazole; IV = 1,2-thiazole; BOC<sub>X-Y</sub> = bond order change for bonds between atoms X and Y in the heterocycle ring required to achieve transition state structures; SBOC = sum of the heterocycle bond order changes.

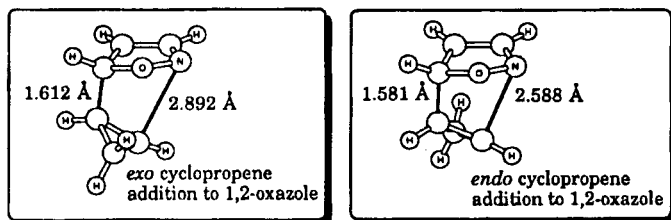


Figure 1. Transition state structures for cyclopropene addition to 1,2-oxazole

sent results for the *endo* cyclopropene addition to the aromatic. As one would expect, bond orders BO<sub>23</sub> and BO<sub>45</sub> were decreasing in the course of the reaction (negative bond orders). In a conventional bond order representation, it is a

Table 6

The AM1 and the DFT Computed Activation Barriers for the Acetylene, Ethylene, and Cyclopropene Additions to 1,2-Diazole, Oxadiazole and Thiazole

| reactant or reaction                    | HOF   | E           | $\Delta E_I$ | $\Delta E_{II}$ |
|---|-------|-------------|--------------|-----------------|
| acetylene + 1,2-diazole                 | 178.3 | -303.442657 | 57.9         | 48.2            |
| ethylene + 1,2-diazole                  | 133.0 | -304.704633 | 50.9         | 48.0            |
| <i>exo</i> cyclopropene + 1,2-diazole   | 183.2 | -342.752184 | 42.8         | 37.3            |
| <i>endo</i> cyclopropene + 1,2-diazole  | 183.0 | -342.754897 | 42.6         | 35.6            |
| acetylene + 1,2-oxazole                 | 148.3 | -323.281919 | 50.6         | 43.9            |
| ethylene + 1,2-oxazole                  | 102.8 | -324.546103 | 43.4         | 42.3            |
| <i>exo</i> cyclopropene + 1,2-oxazole   | 154.0 | -362.588141 | 36.3         | 35.1            |
| <i>endo</i> cyclopropene + 1,2-oxazole  | 153.4 | -362.593658 | 35.7         | 31.6            |
| acetylene + 1,2-thiazole                | 158.5 | -646.261924 | 65.7         | 63.8            |
| ethylene + 1,2-thiazole                 | 116.7 | -647.549554 | 62.2         | 47.4            |
| <i>exo</i> cyclopropene + 1,2-thiazole  | 170.6 | -685.594340 | 57.8         | 38.5            |
| <i>endo</i> cyclopropene + 1,2-thiazole | 164.6 | -685.575508 | 51.8         | 50.3            |

HOF = heat of formation computed by AM1; E total energy (a.u.) computed with DFT/AM1;  $\Delta E_I$  = activation barrier (kcal/mol) computed by AM1;  $\Delta E_{II}$  = activation barrier (kcal/mol) computed with the DFT method.

transformation of two double bonds of dienophiles into two single bonds. At the same time, two new single bonds and one new double bond ( $BO_{34}$ ) were formed. The minimal change of bond orders was again recorded for furan as a diene while all other heterocycles have higher numbers, reiterating that they are quite less reactive as dienes for Diels-Alder reactions. Therefore, all our qualitative studies suggest that heterocycles with two heteroatoms in the 1 and 2 positions do not react with dienophiles in a Diels-Alder type of cycloaddition reaction.

To finally confirm our qualitative studies, we have computed activation barriers for these reactions at both AM1 DFT theory levels (Table 6). Knowing that activation barriers for the addition of cyclopropene to furan computed at the DFT theory level were 18.7 and 18.4 kcal/mol [18] for an *endo* and *exo* cycloaddition reaction and providing that it is experimentally feasible, it becomes obvious that none of the cycloaddition reactions presented in Table 6 should be able to be accomplished experimentally. All activation barriers were around 40 kcal/mol or higher, with the exception of the cyclopropane addition to 1,2-oxazole.

## Conclusion.

Although the proposed synthetic procedure for preparation of valuable allene derivatives is very attractive, it cannot be accomplished due to an extraordinarily low reactivity of heterocycles with heteroatoms in 1 and 2 positions of the ring. The reaction is determined to be LUMO heterocycle controlled; thus, by adding strong electron withdrawing substituents the reaction barrier might decrease, but it is not reasonable to expect to bring it so low that the reaction becomes synthetically important. The classical approach to evaluate reactivity through reactants' frontier orbital gap cannot be applied to aromatic heterocycles and should be

avoided because it could produce false results. Our approach based on the heat of the ethane addition, as well as the heat of hydrogen addition to the aromatic ring creates a qualitative picture of the aromatic character of the heterocycle and its willingness to participate in cycloaddition reactions. The sum of bond order deviation, bond order changes and frontier molecular orbital energy change for transformation of reactants into corresponding transition state structure seems to be a much more reliable qualitative approach to determine the reactivity of heterocycles as dienes for Diels-Alder reactions. These results are in full agreement with computed activation barriers as well with the fact that there are no experimental results that employ these heterocycles as dienes for Diels-Alder reactions. Further theoretical studies that could reveal necessary structural changes heterocycles with two heteroatoms in the ring's 1 and 2 positions are needed in order to be able to realize the of viability the synthetic pathway outlined in Scheme 1.

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