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1,3-Dipolar cycloaddition of azomethine ylide with ethene and 2-butene: a computational study

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Abstract—B3LYP/6-311 + G(d,p) has been used to calculate the relative energies and geometrical parameters of the respective reactants, transition states, and cycloadducts from the cycloadditions of azomethine ylide and ethene, (*Z*)-2-butene, and (*E*)-2-butene. The half-chair (envelope) transition state structures are consistent with a synchronous concerted cycloaddition mechanism.

The cycloaddition of 1,3-dipoles to alkenic and alkynic dipolarophiles is one of the most widely used routes to the construction of a variety of five-membered heterocyclic systems.[1–3] The conformational behavior, structures, and chemistry of nitrogen-containing five-membered rings have attracted considerable interest from experimentalists and theoreticians for many years. Although there are numerous experimental studies on the cycloaddition of 1,3-dipoles to alkenes, there are only fragmentary computational studies on azomethine ylide (**1a** $C_{2v'}\mu = 1.30$ D; $[\mathbf{1b}]^{\dagger}$ $C_{s'}\mu = 5.21$ D, 1079i cm^{-1}, Fig. 1). The resonance stabilized planar form **1a** is 33.4 kcal/mol lower in energy than $[\mathbf{1b}]^{\dagger}$.[4]

This B3LYP/6-311 + G(d,p) computational study[5,6] of the reactions of azomethine ylide (**1**) with ethene, (*Z*)-2-butene, and (*E*)-2-butene, to form the respective azacyclopentanes (pyrrolidines) **2a** (N–H$_{ax}$) and **2b** (N–H$_{eq}$),[7] *cis*-3,4-dimethylazacyclopentane **3a** (N–H$_{ax\,trans}$), **3b** (N–H$_{ax\,cis}$), and **3c** (N–H$_{eq}$), and *trans*-3,4-dimethylazacyclopentane **4a** (N–H$_{ax}$) and *trans*-3,4-dimethylazacyclopentane **4b** (N–H$_{eq}$) was undertaken in order to examine the cycloaddition mechanism as well as to determine the influence of methyl substituents in the dipolarophiles on the structures and relative energies of the transition states (Figs. 2 and 3). Substituents are known to influence the mechanisms, reactivity, and regioselectivity of cycloaddition reactions and concerted 1,3-dipolar cycloadditions are expected to be stereoselective with regard to the dipoles and dipolarophiles.

The azacyclopentanes **2a**, **2b**, **3a**, and **3c** have the half-chair conformations (four atoms coplanar) and azacyclopentanes **3b**, **4a**, and **4b** have distorted half-chair

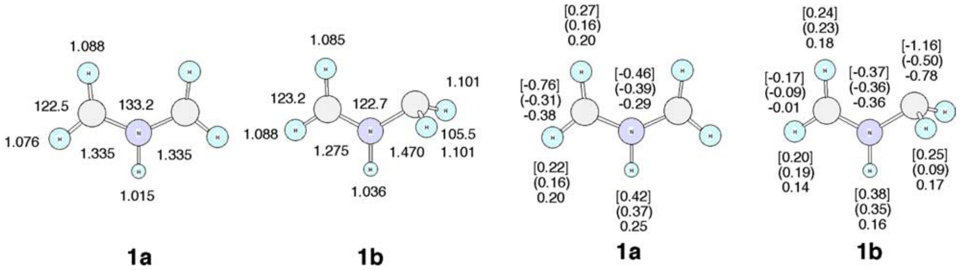

Figure 1. B3LYP/6-311 + G(d,p) geometrical parameters and MP2/6-31G(d) atomic charges [electrostatic, (Mulliken), [Natural] for azomethine ylide (**1a**,**b**).

Keywords: Azacyclopentane; Cycloaddition; Pyrrolidine; Transition state structure.

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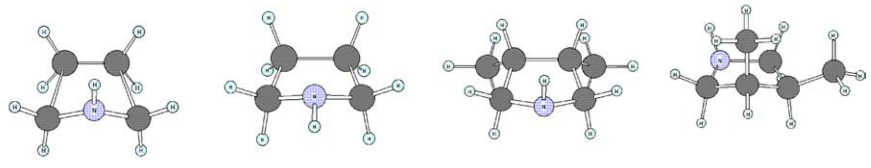
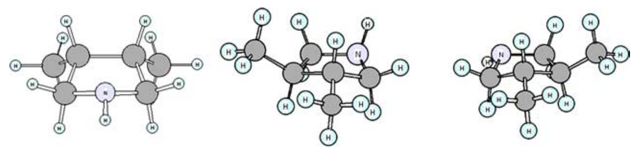


2a **2b** **3a** **3b**

Figure 2. Azacyclopentanes **2a** and **2b** and 3,4-dimethylazacyclopentanes **3a** and **3b**.



3c **4a** **4b**

Figure 3. 3,4-Dimethylazacyclopentanes **3c**, **4a**, and **4b**.

structures. Azacyclopentane **2b** (τC2–C3–C4–C5 = 1°) is 0.19 kcal/mol more stable than **2a** (τC2–C3–C4–C5 = 0°).[7] 3,4-Dimethylazacyclopentane **3c** (τC2–C3–C4–C5 = 0°) is 0.15 and 0.18 kcal/mol, respectively, more stable than **3a** (C_s, τC2–C3–C4–C5 = 0°) and **3b** (C_1, τC2–N1–C5–C4 = 9°, C5–N1–C2–C3 = 39°). 3,4-Dimethylazacyclopentane **4a** (τC2–N1–C5–C4 = 9°, τC5–N1–C2–C3 = −30°) is 1.73 and 0.20 kcal/mol, respectively, more stable than **3c** and **4b** (τC2–N1–C5–C4 = 33°, C5–N1–C2–C3 = −12°).

The transition state structures shown in Figure 4 are consistent with a concerted $\pi_s^4 + \pi_s^2$ cycloaddition mechanism. Intrinsic reaction path (IRC)[8] calculations have been used to connect the transition structures with their respective reactants and products. Transition state **TS 1** (308i cm^{-1}) is 3.89 and 63.0 kcal/mol, respectively, higher in energy than the reactants and the product (**2a**). The equal N–C2 and N–C5 bonds and the equal C2–C3 and C4–C5 bonds in transition state **TS 1** are consistent with a synchronous concerted cycloaddition mechanism. Transition state **TS 2** (359i cm^{-1}) is 9.38 and 62.8 kcal/mol, respectively, higher in energy than the reactants and the product (**3a**). Transition state **TS 3** (357i cm^{-1}) is 10.14 and 63.5 kcal/mol, respectively, higher in energy than the reactants and the product (**3b**) and transition state **TS 4** (350i cm^{-1}) is 9.75 and 63.6 kcal/mol, respectively, higher in energy than the reactants and the product (**4a**).

In contrast to the concerted 1,3-dipolar $\pi_s^4 + \pi_s^2$ cycloaddition of azomethine ylide (**1**) with ethene, the anionic [3+2] cycloaddition of the 2-azaallyl anion with ethene involves a two-step pathway.[9]

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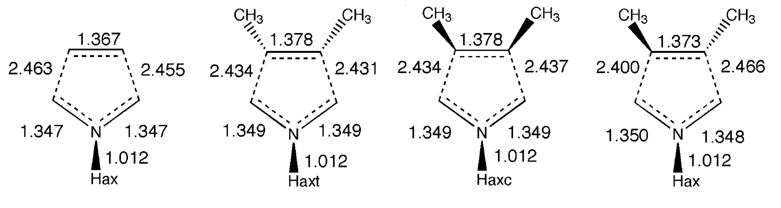

TS 1 **TS 2** **TS 3** **TS 4**

Figure 4. Transition state structures **TS 1**, **TS 2**, **TS 3**, and **TS 4**.

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