Cycloaddition of *o*-benzyne to benzene and the inner phase of a hemicarcerand

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Becke3LYP/6-31G* calculations predict a small energy of concert for the Diels–Alder reaction of *o*-benzyne with benzene, and force-field calculations indicate that steric interactions and transannular strain are responsible for the regiospecificity of the Diels–Alder reaction between *o*-benzyne and its host hemicarcerand.

In a previous communication, Warmuth reported the Diels–Alder (DA) reaction of an *o*-benzyne guest with an aromatic ring of its hemicarcerand host.[1] We have studied the DA reaction of *o*-benzyne with benzene,[2] and the hemicarcerand using computational methods.[2]

The narrow frontier orbital gap, and especially the low LUMO energy, of *o*-benzyne make it a good dienophile.[3] Owing to the poor overlap of the sp² orbitals which combine to form the in-plane π-bond, *o*-benzyne also has a significant amount of diradical character.[4] The *o*-, *m*-, and *p*-isomers of benzyne have been the subject of extensive high-level theoretical studies,[5] and the reactivity of *o*-benzyne as a DA dienophile is well known experimentally,[6] but no computational studies of DA reactions involving *o*-benzyne have been reported.

The benzene–*o*-benzyne DA reaction has been observed experimentally. Miller and Stiles isolated benzobicyclo-[2.2.2]octatriene **4**, biphenyl and benzocyclooctatetraene in a ratio of 1 : 3 : 4, respectively, from the thermal decomposition of benzenediazonium-2-carboxylate in benzene at 45 °C.[7a] The product ratio for the reaction is strongly influenced by Ag⁺, a possible contaminant in the Miller and Stiles experiment.[7b,c] In its absence, **4** is the major product.

These results are remarkable, since the DA reactions of benzene are expected to strongly favor closed-shell concerted over stepwise diradical mechanisms.[8] The barrier for the concerted pathway of the benzene–ethene DA reaction is estimated to be 23 kcal mol⁻¹ (1 cal = 4.184 J) below that of the stepwise diradical pathway.[8a] However, the diradical character of *o*-benzyne may allow a stepwise mechanism to compete more effectively with a concerted mechanism.

The concerted and stepwise DA reactions were studied using the Becke3LYP hybrid HF-DFT method[9] and 6-31G* basis set.[10] All DFT calculations were carried out using Gaussian 94.[11] RBecke3LYP and UBecke3LYP methods were used for closed- and open-shell species, respectively. Stationary points were characterized with vibrational frequency calculations and thermodynamic quantities were calculated from unscaled frequencies. The hemicarceplex and possible *o*-benzyne–hemicarcerand DA regioadducts were calculated with Macro-Model using the MM2*, MM3* and AMBER* force-fields.[12]

The Becke3LYP/6-31G* optimized geometries of benzene **1**, *o*-benzyne **2**, the concerted transition structure **3**, and cycloadduct **4** are shown in Fig. 1. The length of the partial triple bond in **2** is predicted to be 1.251 Å, in excellent agreement with the experimental value of 1.24 ± 0.02 Å.[13] The DFT structure of **1** is also in good agreement with experiment.[14]

Concerted transition structure **3** occurs early along the reaction coordinate. The forming C(1)–C(7) and C(4)–C(8) bonds are 2.383 Å in length. The benzene moiety is relatively undistorted in the transition structure: the C(2)–C(3) and C(5)–C(6) bonds have decreased in length by 0.024 Å, about 38% of the total difference of their lengths in benzene and
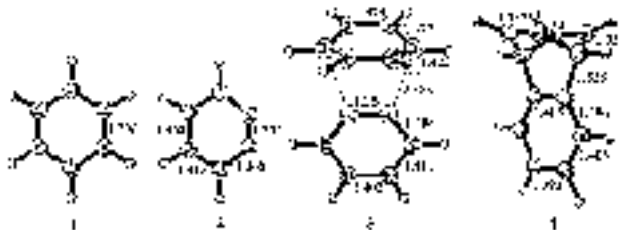

Fig. 1 RBecke3LYP/6-31G* optimized structures of the reactants (**1** and **2**), transition structure **3** and product **4** of the concerted Diels–Alder reaction of benzene with *o*-benzyne. All bond lengths are in Å.

cycloadduct **4**. The other four C–C bonds in the benzene moiety have increased in length by 0.025 Å in the transition structure, or 18% of the total change from reactants to products. The deviation of the benzene moiety from planarity is also small. These factors allow a substantial amount of the aromaticity of benzene to be conserved in the transition structure. The largest change in benzene is a 0.037 Å elongation of the partial triple bond.

The Becke3LYP/6-31G* $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ (298 K) are 10.7 kcal mol⁻¹ and −36.2 cal mol⁻¹ K⁻¹ and the ΔH_{rxn} is −48.7 kcal mol⁻¹. The $\Delta H^{\ddagger}$ for the concerted pathway of the butadiene–ethene DA reaction is 23.4 kcal mol⁻¹ at the same level.[2a] Since benzene is not an especially good DA diene, the low barrier can be attributed to the high reactivity of *o*-benzyne as a dienophile.

The $\Delta H^{\ddagger}$ predicted for the benzene–*o*-benzyne DA reaction is coincidentally close to the 12 kcal mol⁻¹ experimental value determined by Warmuth for the DA reaction of *o*-benzyne with the aromatic ring of the hemicarcerand (**5**).[1] The aromatic ring in **5** is highly substituted with electron donors, and should be electronically more reactive than benzene. However, steric effects and the difficulty of bending the aromatic ring toward the transition state should decrease its reactivity as a DA diene.

The predicted $\Delta S^{\ddagger}$ for the concerted benzene–*o*-benzyne DA reaction is 25.5 cal mol⁻¹ K⁻¹ more negative than the $\Delta S^{\ddagger}$ for the *o*-benzyne–hemicarcerand DA reaction.[1] This reflects the greater loss of mobility of the benzene in the intermolecular DA reaction, relative to the reaction within the hemicarcerand where the aryl moiety is already constrained within the framework of the host.

A diradical transition structure **6** and intermediate **7** for the stepwise addition of *o*-benzyne to benzene are shown in Fig. 2. In transition structure **6**, σ bond formation is more advanced than in concerted transition structure **3**, as shown by the relatively short C–C forming bond length of 1.976 Å. As with **3**, the benzyne moiety is relatively undistorted, except for a 0.06 Å lengthening of the partial triple bond.

The $\Delta H^{\ddagger}$ for formation of intermediate **7** is 13.1 kcal mol⁻¹; only 2.4 kcal mol⁻¹ above the $\Delta H^{\ddagger}$ for the concerted addition of benzene to *o*-benzyne. The energy of concert is nearly zero. The energy of concert for the DA reaction of ethene with cyclobutadiene, which has significant diradical character, is also smaller.[15]

The ΔH_{rxn} for formation of diradical intermediate **7** from **1** and **2** is predicted to be 2.3 kcal mol⁻¹, in good agreement with

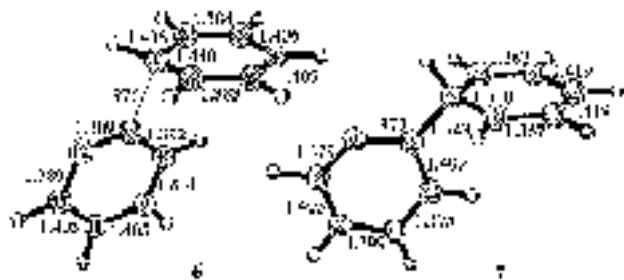**Fig. 2** UBecke3LYP/6-31G* diradical transition structure **6** and intermediate **7** in the stepwise diradical addition of *o*-benzyne to benzene. All bond lengths are in Å.

an estimate based on Benson equivalents[16] and the CASPT2 ΔH_f of benzene.[5]

Intermediate **7** may lead to biphenyl by hydrogen atom abstraction from C(1) by the C(12) phenyl radical moiety, or [2 + 2] or [4 + 2] cycloadducts *via* rotation about the C(1)–C(7) bond followed by ring closure. These mechanistic pathways are currently being explored.

NMR evidence indicates that of the two possible regioisomeric *o*-benzyne–hemicarcerand DA adducts (Fig. 4), only **8** is formed experimentally.[1] The origin of this regiospecificity was probed using force-field methods. The minimum energy conformer of hemicarceplex **10** was located using molecular dynamics and simulated annealing techniques with the MM3* force-field (Fig. 3). This force-field was also used to obtain optimized geometries and steric energies of DA adducts **8** and **9** (Fig. 4). AMBER* and MM2* gave similar results.

In **10**, the orientation of benzyne is favorable for formation of **8**, *via* a concerted DA reaction (Fig. 3). However, both carbons of the benzyne partial triple bond are >4 Å from the
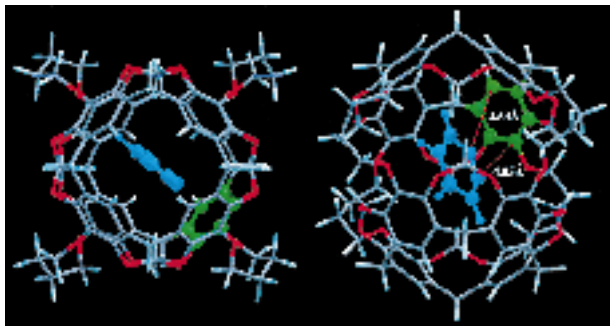

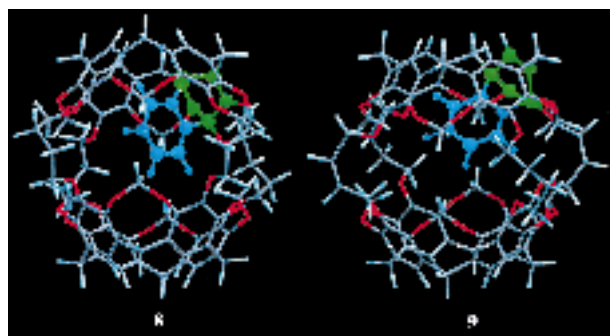**Fig. 3** MM3* minimum energy conformer of the *o*-benzyne hemicarceplex

Fig. 4 MM3* optimized stuctures of *o*-benzyne–hemicarcerand Diels–Alder adducts **8** and **9**

hemicarcerand atoms to which they are bound in **8**, and substantial motion is required to bring benzyne within bonding distance. Formation of **9** from **10** through a concerted pathway requires benzyne to rotate around its C_2 axis by *ca.* 120°. This should be sterically unfavorable. Either stepwise or concerted mechanisms should be possible.

Regioisomer **8** is predicted to be 20.0 kcal mol^{-1} more stable than **9**. It is likely that a significant fraction of this energy difference will be felt in the transition state, as well.

Unfavorable steric interactions and greater strain in **9** contribute to the thermodynamic preference for formation of **8**. The Ph group of the benzobicyclo[2.2.2]octatriene moiety is crowded into the top hemisphere of the hemicarcerand in **9**, and several unfavorable steric interactions result. In **8**, the Ph group of the benzobicyclo[2.2.2]octatriene moiety is in a less sterically hindered environment.

Calculations with MM3* on various DA adducts show that the greater transannular strain in **9** contributes significantly to the overall thermodynamic preference for formation of **8**.

Notes and References

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