

Unexpected Complexity in the Thermal $[\pi 2 + \sigma 2 + \sigma 2]$ Cycloaddition Reactions of Quadricyclane: Theory and Isotope Effects

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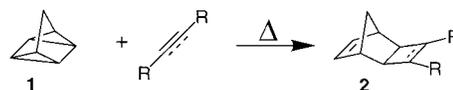
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Abstract: A combined computational and experimental study has been performed on the thermal $[\pi 2_s + \sigma 2_s + \sigma 2_s]$ cycloaddition reactions of quadricyclane with acetylene, ethylene, dicyanoacetylene, and dimethyl acetylenedicarboxylate (DMAD). The energy surfaces for the reactions were obtained using hybrid density functional theory at the B3LYP/6-31G(d) level. All attempts to locate concerted pathways for the reactions failed, since the putative transition structures for these processes correspond to second-order saddle points. Nonconcerted pathways, proceeding via biradical intermediates, were found for these reactions using unrestricted B3LYP/6-31G(d) theory. Intramolecular secondary kinetic isotope effects (SKIEs) were determined experimentally for the reaction of quadricyclane-1-*d*₁ and quadricyclane-1,5-*d*₂ with DMAD in benzene at 95 °C. The results were compared with the intermolecular SKIE for the reaction of quadricyclane-1,5,6,7-*d*₄ with DMAD under the same conditions. The $k_{\text{H}}/k_{\text{D}1}$ and $k_{\text{H}}/k_{\text{D}2}$ values are in quite good agreement with calculated values for the nonconcerted biradical mechanism. The experimental intermolecular SKIE for the addition of DMAD to quadricyclane-*d*₀ or -*d*₄ is negligible. This observation conflicts with either concerted or biradical mechanisms. Alternatives are discussed.

The concerted mechanisms of the synthetically useful thermal $[2_s + 2_s + 2_s]$ cycloaddition reactions¹ are Woodward–Hoffmann allowed processes,² and reactions such as the thermal uncatalyzed cycloadditions of alkenes and alkynes to quadricyclane **1** (Scheme 1), formally a $[\pi 2_s + \sigma 2_s + \sigma 2_s]$ reaction, have been assumed to follow a concerted pathway.^{3,4} The most convincing experimental evidence to date for a concerted mechanism for this class of reactions stems from stereochemical studies which found that the reactions of quadricyclane with several cis and trans alkenes gave products which preserved the original alkene stereochemistry.³ However, these observations would also be consistent with a nonconcerted process in which the rate of conversion of biradical intermediates into product is faster than rotation about the newly formed single bonds in the biradicals.

We have performed a B3LYP/6-31G(d) DFT study^{5,6} of the $[\pi 2_s + \sigma 2_s + \sigma 2_s]$ reactions of **1** with ethylene and acetylene, dicyanoacetylene (DCA), and dimethyl acetylenedicarboxylate (DMAD). Experimental secondary deuterium kinetic isotope

Scheme 1



effects (SKIEs) for the reaction of **1** with DMAD have also been determined and are compared with the DFT predictions.

The potential energy surfaces for the cycloaddition reactions with **1** were probed using the B3LYP/6-31G(d) theoretical model^{5,6} since it is well known that this level of theory treats well both concerted and open-shell radical and biradical systems.^{7,8} Unless stated otherwise, the following discussion

(5) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. For reviews of density-functional methods, see: (c) Ziegler, T. *Chem. Rev.* **1991**, *91*, 651. (d) *Density Functional Methods in Chemistry*; Labanowski, J., Andzelm, J., Eds.; Springer: Berlin, 1991. (e) Parr, R. G.; Yang, W. *Density-Functional Theory of Atoms and Molecules*; Oxford University Press: New York, 1989.

(6) All calculations were performed with Gaussian 94: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Latham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94* (Revision B); Gaussian Inc.: Pittsburgh, PA, 1994.

(7) Houk, K. N.; Li, Y.; Evanseck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1, 682 and references therein.

(8) B3LYP/6-31G(d) DFT has proved to give excellent results in comparisons of biradical and concerted mechanisms for pericyclic reactions. See, for example: (a) Goldstein, E.; Beno, B.; Houk, K. N. *J. Am. Chem. Soc.* **1996**, *118*, 6036. (b) Houk, K. N.; Beno, B. R.; Nendel, M.; Black, K.; Yoo, H. Y.; Wilsey, S.; Lee, J. K. *J. Mol. Struct. (Theochem)* **1997**, *398–399*, 169.

[†] University of New South Wales.

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(1) (a) Lautens, M.; Edwards, L. G.; Tam, W.; Lough, A. J. *J. Am. Chem. Soc.* **1995**, *117*, 10276 and references therein. (b) Smith, C. D. *J. Am. Chem. Soc.* **1966**, *88*, 4273. (c) Paddon-Row, M. N.; Cotsaris, E.; Patney, H. K. *Tetrahedron* **1986**, *42*, 1779. (d) Oevering, H.; Paddon-Row, M. N.; Heppener, H.; Oliver, A. M.; Cotsaris, E.; Verhoeven, J. W.; Hush, N. S. *J. Am. Chem. Soc.* **1987**, *109*, 3258. (e) Paddon-Row, M. N. *Acc. Chem. Res.* **1994**, *27*, 18.

(2) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Academic Press: New York, 1970.

(3) Tabushi, I.; Yamamura, K.; Yoshida, Z. *J. Am. Chem. Soc.* **1972**, *94*, 787.

(4) Paquette, L. A.; Kesselmayr, M. A.; Künzer, H. *J. Org. Chem.* **1988**, *53*, 5183.

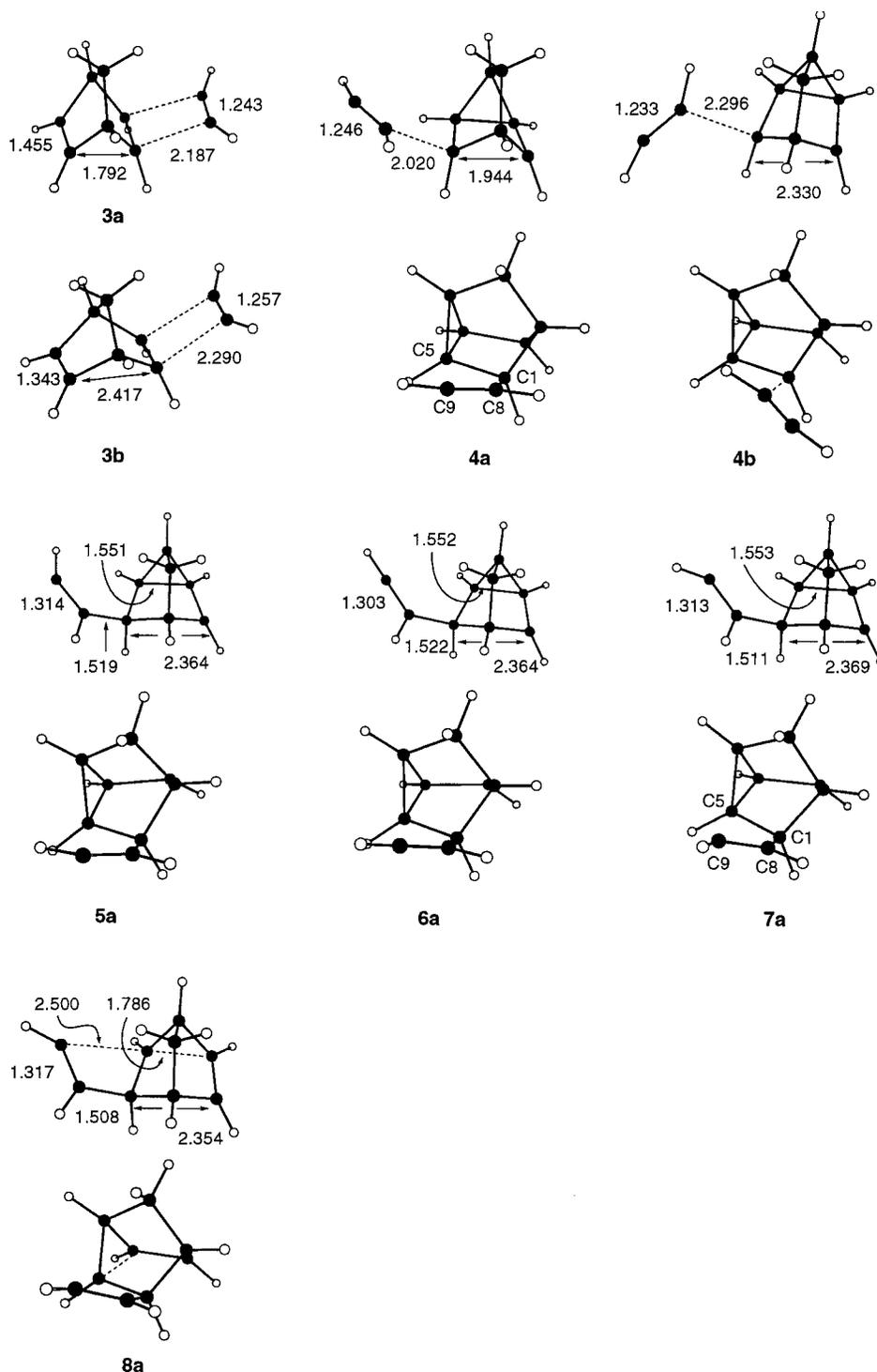


Figure 1. B3LYP/6-31G(d) structure for the second-order saddle point **3a** for the concerted pathway of the $[2 + 2 + 2]$ cycloaddition of acetylene and quadricyclane using restricted RB3LYP, and **3b** using unrestricted UB3LYP, and the biradical intermediates and transition structures (**4a**–**8a**) for the addition of acetylene to quadricyclane. All bond lengths are in angstroms.

refers to results obtained using the B3LYP/6-31G(d) level of theory. For closed-shell systems, the restricted formalism (B3LYP) was used, whereas for open-shell biradicaloid systems, the unrestricted method (UB3LYP) was employed.

Efforts to locate concerted, synchronous transition structures for the addition of either ethylene or acetylene to **1** using various spin-restricted wave functions resulted, in each case, in the location of a single stationary point possessing C_s symmetry. The lengths of the bonds undergoing first-order changes in these putative transition structures are commensurate with those

expected for concerted cycloaddition transition structures (e.g., structure **3a**, Figure 1, for the reaction between **1** and acetylene); however, harmonic frequency calculations identified these structures as second-order saddle points.

Reoptimizing the second-order saddle point for the reaction of **1** with acetylene using a spin-unrestricted formalism, UB3LYP/6-31G(d), again led to a second-order saddle point of C_s symmetry (**3b**, Figure 1) which, according to an IRC analysis, is associated with a $[\pi 2 + \pi 2]$ cycloaddition reaction between acetylene and norbornadiene, rather than with a $[\pi 2_s$

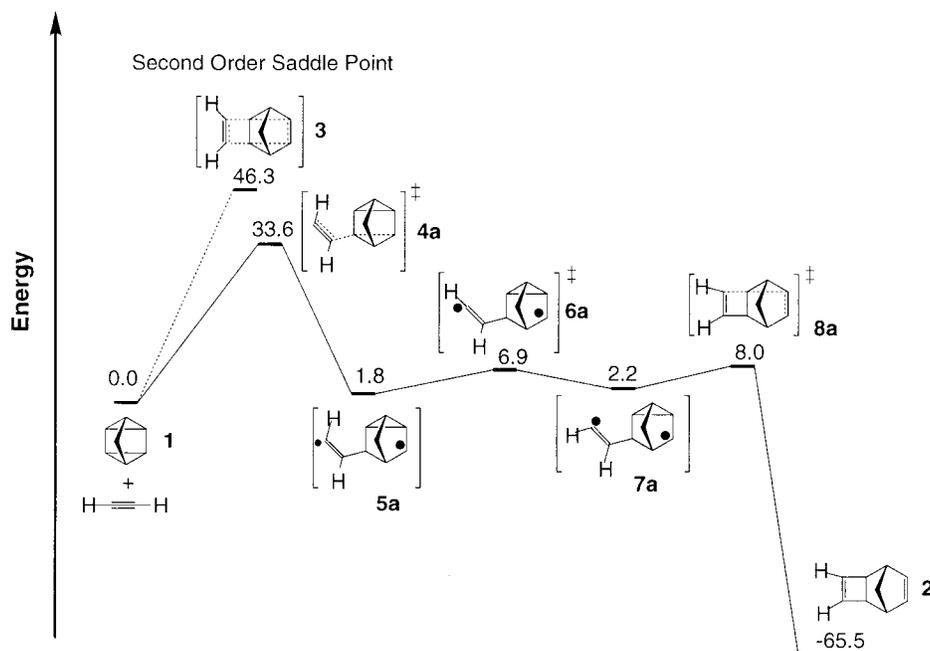


Figure 2. Energy profile for the quadricyclane–acetylene [2 + 2 + 2] cycloaddition reaction. UB3LYP/6-31G(d) energies (kcal/mol) are in plain text and are not corrected for ZPE.

+ $\sigma^2_s + \sigma^2_s$] cycloaddition between acetylene and quadricyclane. Similar results were obtained for the reaction between quadricyclane and ethylene.

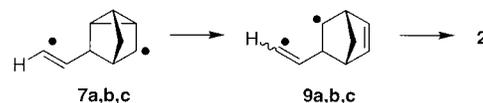
Despite an extensive search of the singlet-state energy surface using both restricted and unrestricted B3LYP/6-31(d) levels of theory, we were unable to locate a genuine transition structure for either a synchronous or a nonsynchronous concerted cycloaddition process. The same finding was also experienced using UHF/3-21G and MP2/6-31G(d) methods for the reaction of **1** with acetylene and ethylene, and using the CASSCF(6,6)/6-31G(d) method for the reaction of **1** with ethylene. In each case, only a second-order saddle point of C_s symmetry was found.

Given our failure to locate a concerted transition structure for the cycloaddition of either acetylene or ethylene to **1**, attention was then focused on nonconcerted reactions. Two singlet biradical transition structures, **4a** and **4b**, for the nonconcerted addition of acetylene to **1** were readily located (Figure 1). Both structures are, indeed, transition structures, since each possesses a single imaginary frequency whose transition vector connects the reactant with a biradical intermediate (vide infra).

The transition structures **4a** and **4b** differ only in their conformations about the forming C1–C8 bond, and **4a**, in which the C8–C9 acetylene bond nearly eclipses the C1–C5 bond of **1**, is 2.9 kcal/mol more stable than **4b**, in which the two aforementioned bonds are in nearly antiparallel alignment. Most stationary points, intermediates, and transition structures located in this work are associated with three conformations (**a**, **b**, **c**) of the type discussed above, although the third conformation, **c**, could not be found for **4**. In the interest of conciseness, we shall restrict discussion to the lowest energy conformer, **a**, for each stationary point.^{9a} Full geometric and energetic details of all conformations may be found in the Supporting Information.

(9) (a) Conformations **a**, **b**, and **c** for the acetylene–quadricyclane system are characterized by the value of the dihedral angle C9–C8–C1–C5: **a**, $\sim 0^\circ$; **b**, $\sim 130^\circ$; **c**, $\sim 230^\circ$. Conformation **4b** has a dihedral angle of 159° . Conformation **4c** does not exist. (b) Conformations for the ethylene–quadricyclane system are characterized by the dihedral angle C9–C8–C1–C5: **a**, $\sim 65^\circ$; **b**, $\sim 180^\circ$; **c**, $\sim 315^\circ$.

Scheme 2



An IRC analysis of **4a** showed that it connects the reactants with the biradical intermediate, **5a**, which possesses a Z configuration. This biradical then undergoes inversion of configuration, via transition structure **6a**, into the *E*-stereoisomer **7a**. We were unable to locate a transition structure for direct formation of cis-bent *E*-isomer **7a** from **1** and acetylene. The preference for trans- rather than cis-bending in additions to acetylenes has been rationalized on the basis of more favorable mixing of σ with π^* orbitals and π with σ^* orbitals in the trans-bent transition states.¹⁰ Direct formation of product **2** from the *E*-isomer **7a** occurs by way of transition structure **8a**.

An alternative, *indirect* route to the product from **7a** is possible and involves first the ring opening of the nortricyclic unit to give a vinylnorbornenyl biradical, **9**, which then ring closes to **2** (Scheme 2). This pathway is favored at the UHF/3-21G level, but not at the DFT level, using either 3-21G or 6-31G(d) basis sets.¹¹

The relative energies of the stationary points corresponding to **1**–**8** on the energy surface are given in Figure 2. The UB3LYP/6-31G(d) (vibrationless) energy of activation for the formation of biradical intermediate **5a** from reactants is 33.6 kcal/mol,¹² and, because the transition structure **4a** is energetically the highest point on the reaction coordinate, this represents the calculated activation barrier for the entire cycloaddition process.

(10) Strozier, R. W.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 1340 and references therein.

(11) There are two other conformations of **7**, namely **7b** and **7c**, which are able to take the indirect route depicted in Scheme 2. However, the transition structure, **8a**, for the direct conversion of **7a** into **2** lies, respectively, 3.0 and 4.2 kcal/mol lower in energy than the transition structures for the conversion of **7b** and **7c** into the respective norbornenyl biradicals **9b** and **9c**. The direct pathway, proceeding from **7a**, is therefore favored. The dihedral angle C9–C8–C1–C5 is 5.8° for **7a**, 130° for **7b**, and 236° for **7c**. See Supporting Information for further details.

(12) The $\langle S^2 \rangle$ of the UB3LYP/6-31G(d) wave function for biradical transition structure **4a** is 0.1.

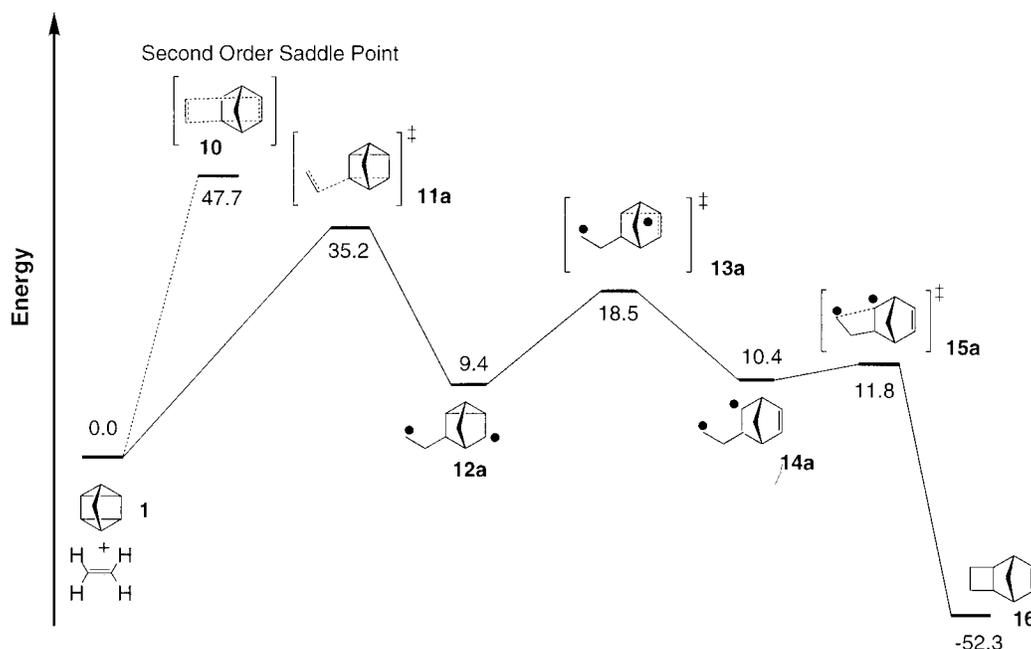
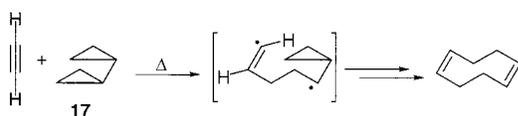


Figure 3. Energy profile for the quadricyclane–ethylene $[2 + 2 + 2]$ cycloaddition reaction. UB3LYP/6-31G(d) energies (kcal/mol) are in plain text and are not corrected for ZPE.

Scheme 3



The overall mechanism of the cycloaddition reaction between **1** and ethylene is similar to that between **1** and acetylene in that it is nonconcerted and proceeds via biradical intermediates. The UB3LYP/6-31G(d) energy surface for this reaction, involving the lowest energy conformation **a**, is shown in Figure 3.^{9b} Interestingly, unlike the quadricyclane–acetylene reaction, the formation of product **16** from **12a** does not occur directly but instead takes the indirect route by way of the ethylnorbornenyl biradical intermediate **14a**.

As with the quadricyclane–acetylene cycloaddition reaction, the rate-determining step in the reaction between **1** and ethylene is the formation of the first biradical intermediate **12a**, and so the (vibrationless) activation energy for the entire reaction is predicted to be 35.2 kcal/mol.

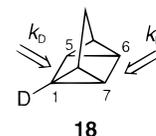
(U)B3LYP/6-31G(d) calculations were also carried out on the first steps of the cycloaddition reactions of **1** with DCA and DMAD. As with acetylene, both reactions are predicted to be nonconcerted, each proceeding by a distinct biradical intermediate resembling **4a**. The activation barriers for formation of the biradicals from the reaction of **1** with DCA and DMAD are 21.8 and 21.5 kcal/mol, respectively, i.e., 12 kcal/mol lower than that for the reaction of **1** with acetylene.

In a similar fashion, the cycloaddition reaction between acetylene and bis(cyclopropyl) (**17**) is calculated to proceed through a biradical intermediate (Scheme 3).¹³ The nonconcerted preference is thus a general feature of this $[\pi + \sigma + \sigma]$ reaction and may well arise from the difficulty in achieving overlap leading to strong bonding interactions simultaneously at both termini of the bicyclic system.

Our UB3LYP/6-31G(d) results strongly suggest a nonconcerted biradical mechanism for the reactions of **1** with alkenes

and acetylenes, notwithstanding an experimental study³ which found that the reactions of quadricyclane with several cis and trans alkenes gave products which preserved the original alkene stereochemistry. Such stereoselectivity is often taken as evidence for concerted, although zwitterionic intermediates¹⁴ or reactions involving unstabilized biradicals¹⁵ can show high stereoselectivity.

Inverse intramolecular secondary kinetic isotope effects for reactions of monodeuterated quadricyclane, **18**, with two alkenes



and an azo compound ($k_H/k_{D1} = 0.940\text{--}0.950$) and DMAD ($k_H/k_{D1} = 0.884$) had previously been interpreted in terms of an asynchronous concerted cycloaddition mechanism.^{4,16} However, a large discrepancy between the reported experimental, and our calculated¹⁷ (Table 1), k_H/k_{D1} values for the reaction of **1** with DMAD led us to redetermine the intramolecular SKIEs for this reaction and for the reaction of quadricyclane-1,5-*d*₂ in benzene at 95 °C.¹⁸ In addition, we determined the intermolecular SKIE for addition of DMAD to quadricyclane-1,5,6,7-*d*₄ under the same conditions. These data are presented in Table 1, together with the calculated^{17,19} SKIEs.

(14) Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 199.

(15) See, for example: Houk, K. N.; Nendel, M.; Wiest, O.; Storer, J. W. *J. Am. Chem. Soc.* **1997**, *119*, 10545.

(16) In this context, k_{H1}/k_{D1} is defined (ref 4) as the ratio of product arising from attack of the reagent at C6 and C7 of **18** to that formed from attack at C1 and C5.

(17) SKIEs were calculated from B3LYP/6-31G(d) vibrational frequencies scaled by 0.963 (Rauhut, G.; Pulay, P. *J. Phys. Chem.* **1995**, *99*, 3093) using either Gaussian 94⁶ or the program QUIVER (Saunders, M.; Laidig, K. E.; Wolfsberg, M. *J. Am. Chem. Soc.* **1989**, *111*, 8989.)

(18) Labeled quadricyclanes were synthesized by photochemical closure of the corresponding labeled norbornadienes, which were in turn prepared by H/D exchange and Shapiro reaction on the corresponding ketones. Details are given in the Supporting Information.

(19) See Table 1 for an explanation of SKIE nomenclature.

(13) Details can be found in the Supporting Information.

Table 1. Experimental (in Benzene, 95 °C) and UB3LYP/6-31G(d) Deuterium SKIEs for the Reactions of **1** and **22** with Acetylene, DCA, and DMAD

reactant		acetylene	DCA	DMAD	$1 \rightarrow 1^{+d}$	expt (DMAD) ^e
1	k_H/k_{D1}^a	0.963	0.968	0.965		0.970 ± 0.006
1	k_H/k_{D2}^b	0.927	0.937	0.932		0.961 ± 0.011
1	k_H/k_{D4}^c	1.002	0.921	0.921	0.983	1.006 ± 0.012
22	k_H/k_{D1}		0.975			
22	k_H/k_{D2}		0.975			

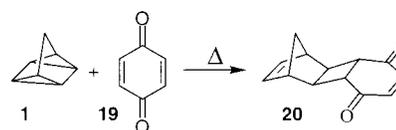
^a $k_H/k_{D1} = (\text{SKIE for attack at C6} \times \text{SKIE for attack at C7}) / (\text{SKIE for attack at C1} \times \text{SKIE for attack at C5})$. ^b $k_H/k_{D2} = (\text{SKIE for attack at C6} \times \text{SKIE for attack at C7}) / (\text{SKIE for attack at C1} \times \text{SKIE for attack at C5})$. ^c $k_H/k_{D4} = (\text{SKIE for attack at C6} \times \text{SKIE for attack at C7} \times \text{SKIE for attack at C1} \times \text{SKIE for attack at C5}) / (\text{SKIE for attack at C1} \times \text{SKIE for attack at C5})$. ^d Equilibrium isotope effect for ionization of **1-d**. ^e Experimental uncertainties correspond to standard errors in the mean for the 95% confidence interval.

The experimental intramolecular k_H/k_{D1} and k_H/k_{D2} SKIEs are in reasonable agreement with the theoretical values calculated for the biradical pathway. There is, however, a significant discrepancy between the experimental and calculated intermolecular SKIE for the system. Experimentally, no significant difference in rate constant for addition of DMAD to quadricyclane-*d*₀ or -*d*₄ is detected (1.01 ± 0.01). Had the reaction occurred by rate-limiting addition of DMAD, via transition structure **4a**, the calculations suggest that k_H/k_{D4} should be about 0.921.

The lack of an isotope effect suggests that the rate-determining step occurs before any significant bond-making or bond-breaking in quadricyclane. One possibility is that the reaction occurs by rate-limiting electron transfer (ET) from **1** to DMAD, to form a radical ion pair, followed by rapid collapse to a biradical or a zwitterion intermediate. A similar mechanism has been previously suggested for addition of azo and carbonyl compounds to **1**.²⁰ The calculated equilibrium isotope effect for ionization of quadricyclane-*d*₄ is 0.983, and if the rate of electron transfer were involved, an isotope effect between this value and 1.0 would be expected.

Energetic considerations make the ET mechanism unlikely. From the experimental oxidation potential of quadricyclane²² and the reduction potentials for DMAD,²³ the free energy change for ET from **1** to DMAD is estimated to be 50 kcal/mol endergonic. This is a very large activation barrier and is inconsistent with the observation that **1** and DMAD react at 100 °C within a few hours. However, this value refers to ET taking place between **1** and DMAD at infinite separation (in acetonitrile). The proposed species would be an intimate (inner-sphere) complex, with Coulombic attraction between the components which would lower its energy to a small extent. At 3.4 Å, point charges of opposite sign experience an attractive interaction of 95 kcal/mol, but this drops to 3 kcal/mol in the acetonitrile bulk dielectric. The true interaction is likely to be between these values.

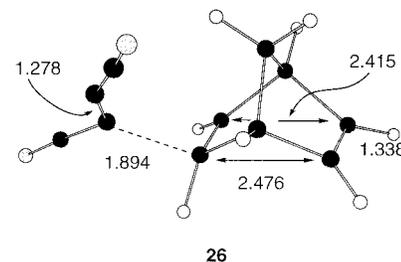
Electron transfer would be consistent with experimental observations that quadricyclane appears to react readily only with electron-accepting alkenes and acetylenes, and these reactions require mild thermal activation, e.g., 80–130 °C (Scheme 4).^{1,21} Kochi et al. have found a close relationship between excitation energies of charge-transfer reactions and

Scheme 4

activation energies of the thermal cycloaddition reactions of the same species,²⁴ but products resulting from these two processes are frequently different.^{24,25} Direct formation of a zwitterion is also a possible reaction of related species, and this route is generally preferred over ET in cycloaddition of alkenes with complementary polarities.¹⁴ However, this mechanism would also be expected to give rise to an intermolecular isotope effect.

The ET mechanism (Scheme 5) could lead also to valence tautomerism of **1**⁺ to form the norbornadiene cation radical **22**⁺; this new ion pair could undergo charge recombination to give norbornadiene or an addition reaction to give cycloadduct **25** via **24**. The conversion of quadricyclane cation radical into norbornadiene cation radical is known to be extremely facile, taking place on a microsecond time scale with an activation barrier of only 5–10 kcal/mol.²⁶

The intramolecular k_H/k_{D1} and k_H/k_{D2} SKIEs for the reaction of the ion pair **22**⁺/**21**⁻, to give biradical **24**, were estimated from the UB3LYP/6-31G(d) biradicaloid transition structure **26** for the addition of DCA to **22**.²³ Not only are both calculated



k_H/k_{D1} and k_H/k_{D2} SKIEs (0.975) in good agreement with the experimental values (0.970 and 0.961) for the reaction of **1** with DMAD, but, taken together, they are in slightly better agreement with the experimental values than are the calculated k_H/k_{D1} and k_H/k_{D2} values (0.968 and 0.937, respectively) for the direct addition of DCA to **1**.

It is also noteworthy that the photochemical reaction between **1** and benzophenone or acetophenone to give (among other products) cycloadduct **28** (Scheme 6) appears to proceed via an exciplex and the subsequent intermediacy of **22**⁺.²⁷

None of the three likely mechanisms—concerted, stepwise-biradical, or electron-transfer—fits all of the available data for this reaction. The concerted mechanism is consistent with the observed stereoselectivity of the reaction but inconsistent with the computational results, which find no such pathway. The concerted mechanism is inconsistent with the experimental isotope effects, which should have shown a larger intermolecular SKIE.

Direct formation of a biradical is consistent with the calculations, which give an activation enthalpy that appears to be in

(24) See, for example: Kim, E.; Christl, M.; Kochi, J. K. *Chem. Ber.* **1990**, *123*, 1209 and references therein.

(25) Kim, T.; Sarker, H.; Bauld, N. L. *J. Chem. Soc., Perkin Trans. 2* **1995**, 577.

(26) (a) Gebicki, J. L.; Gebicki, J.; Mayer, J. *Radiat. Phys. Chem.* **1987**, *30*, 165. (b) Bach, R. D.; Schilke, I. L.; Schlegel, H. B. *J. Org. Chem.* **1996**, *61*, 4845. (c) Ishiguro, K.; Khudyakov, I. V.; McGarry, P. F.; Turro, N. J.; Roth, H. D. *J. Am. Chem. Soc.* **1994**, *116*, 6933.

(27) Barwise, A. J. G.; Gorman, A. A.; Leyland, R. L.; Parekh, C. T.; Smith, P. G. *Tetrahedron* **1980**, *36*, 397.

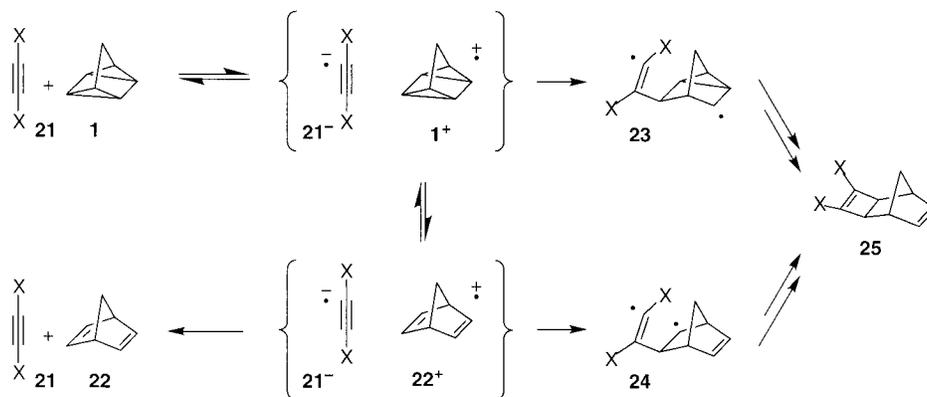
(20) (a) Landis, M. E.; Mitchell, J. C. *J. Org. Chem.* **1979**, *44*, 2288. (b) Papadopoulos, M.; Jenner, G. *Nouv. J. Chim.* **1984**, *8*, 729. See, however: (c) Papadopoulos, M.; Jenner, G. *Nouv. J. Chim.* **1983**, *7*, 463.

(21) Kaupp, G.; Prinzbach, H. *Chem. Ber.* **1971**, *104*, 182.

(22) Gassman, P. G.; Yamaguchi, R. *J. Am. Chem. Soc.* **1979**, *101*, 1308.

(23) For EA of the diethyl ester, see: Marken, F.; Compton, R. G.; Bull, S. D.; Davies, S. G. *J. Chem. Soc. Chem. Commun.* **1997**, 995.

Scheme 5



Scheme 6



qualitative accord with observed reaction rates. However, it is inconsistent with the stereoselectivity, since the barrier to formation of the second C–C bond exceeds the barrier to internal rotation. This pathway is also inconsistent with the experimentally determined lack of an intermolecular isotope effect.

Finally, the rate-determining electron transfer leading to a radical ion pair which then collapses to a biradical would be consistent with the experimental isotope effect studies but seems to be less easily harmonized with the estimated activation enthalpy.

Conclusion

Our experimental SKIE data and computational results suggest that the $[\pi 2 + \sigma 2 + \sigma 2]$ cycloaddition of quadricyclane occurs via a nonconcerted biradical mechanism, rather than by the concerted route expected on the basis of orbital symmetry arguments.² Although the calculations predict a rate-

determining formation of a biradical intermediate, this is inconsistent with the observed lack of a significant intermolecular k_H/k_{D4} SKIE. The final chapter is still to be written on this unexpectedly complex reaction.

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Supporting Information Available: Experimental details for the determination of SKIEs, including syntheses of labeled compounds as well as Cartesian coordinates and energies for all stationary points described in the manuscript (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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