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The Importance of Secondary Orbital Interactions in the Stabilization of Isomeric Transition State Structures in the Cyclopropene Addition to Furan

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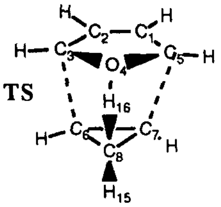
Summary: Density Functional Theory (DFT) computational studies were performed on two isomeric transition state structures for the cyclopropene cycloaddition to furan in order to determine the importance of secondary orbital interactions (SOI) on the stability of transition state structures. © 1997 Elsevier Science Ltd. All rights reserved.

Computational methods are becoming increasingly popular practical tools for the experimentalist to predict a reaction's outcome and the physical properties of the chemical system prior to performing the experiment and, consequently, to explain their experimental observations.[1] Some of the most promising computational approaches to organic chemistry are the Density Functional Theory (DFT) computational methods.[2] They are of relatively recent origin thus there are fewer computational studies conducted with them than with the widely used ab initio methods. One of the goals of our research is to implement computational methods into finding solutions to our everyday synthetic problems. Because cycloaddition reactions are very important in the stereoselective formation of hydrocarbon skeletons during the preparation of many natural products, we have decided to closely examine the *exo-endo* selectivity of these reactions. We have demonstrated that DFT methods have high accuracy when predicting the geometries[3], vibrational spectra[4], heats of formation[5], bond dissociation energies[6], ionization energies[7], electron affinities[8], and activation barriers[9] for many chemical systems. Here we will present the DFT study of the *exo-endo* selectivity of Diels-Alder reactions on the example of the cyclopropene addition to furan.

exo TS



endo TS

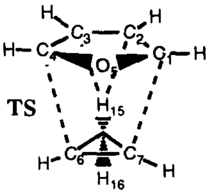


Table 1. Structural parameters for transition state structures computed with ab initio and DFT methods

			Exo Transition State Structure			
Theory Model	r63/Å	r62/Å	r164/Å	r67/Å	r43/Å	a763/°
HF/6-31+G(d)	2.214	2.741	2.391	1.338	1.343	100.3
B3LYP/6-31+G(d)	2.265	2.781	2.386	1.351	1.366	100.3
BLYP/6-31+G(d)	2.281	2.805	2.274	1.365	1.385	100.3
			Endo Transition State Structure			
Theory Model	r64/Å	r63/Å	r153/Å	r67/Å	r54/Å	a764/°
HF/6-31+G(d)	2.193	2.786	2.595	1.340	1.348	100.4
B3LYP/6-31+G(d)	2.234	2.814	2.576	1.354	1.370	100.5
BLYP/6-31+G(d)	2.236	2.836	2.612	1.368	1.389	100.6

The activation activation barrier for the addition of cyclopropene to furan has not been determined experimentally. Binger and coworkers[10] observed a slight *exo* preference in the cyclopropene addition to 1,3-diphenylisobenzofuran, however previous studies reported that the major product of this cycloaddition reaction is the *endo* cycloadduct.[11] The*exo* cycloadduct is the major of cyclopropene addition to furan, contrary to the cycloadduct product obtained in the reaction between cyclopropene and butadiene.[12] On the other hand, Breslow and coworkers[13] isolated only the *exo* cycloadduct from the reaction between cyclopropenone and 1,3-diphenylisobenzofuran. This was confirmed by determining the crystal structure of the product.[14]

The computed geometries[15] for two isomeric transition states are presented in Table 1. All computational methods predict a synchronous formation of the two new C-C bonds and a concerted mechanism for the cycloaddition reaction. If we consider the two isomeric transition state structures obtained with DFT (B3LYP and BLYP) methods, then the *exo* transition state structure is the closest structure to the reactants. According to the Hammond postulate[23], the *exo* transition state structure should then have a lower energy than the isomeric *endo* transition state structure. Of course, these observations are only of a qualitative nature. To obtain a better picture of the kinetic control of the cyclopropene addition to furan, the computation of an activation barrier is necessary.

We have demonstrated that the hybrid B3LYP DFT method produces extraordinarily accurate activation barriers while the gradient-corrected BLYP DFT method slightly underestimates (by approximately 1-3 kcal/mol) barriers for Diels-Alder reactions.[24] On the other hand, HF ab initio methods substantially overestimate and MP2 underestimate activation barriers for Diels-Alder reactions.[25] Our computed activation barrier for the cyclopropene addition to furan fit perfectly with these observations (Table 2). If the HF computed energy were the activation barrier, then the reaction between furan and cyclopropene would not be possible. On the other hand, MP2 computed that the reaction is occurs almost without any barrier. When considering the experimental procedure conducted with 1,3-diphenylisobenzofuran and cyclopropene, the activation barrier should be around 16 kcal/mol with a slight preference (~0.5 kcal/mol) of the *exo* over the *endo* transition state structure. The B3LYP/6-31+G(d) theory model computed energies which one would expect. Recently, we performed DFT computational studies on the cyclopropene addition to butadiene.[26] This reaction produced the *endo* cycloadduct exclusively. B3LYP/6-31+G(d) computed the activation energy to be 13.5 kcal/mol with a 1.9 kcal/mol *endo* preference. Considering that furan is a poorer diene than butadiene for Diels-Alder additions, our results agree very well.

Table 2. Total energies (a.u.) and activation barriers (kcal/mol) computed using 6-31+G(d) basis set

Method	E_I	E_{II}	E_{III}	E_{IV}	ΔE_{exo}	ΔE_{endo}
HF	-115.823048	-228.625214	-344.394891	-344.393367	33.5	34.4
MP2	-116.203921	-229.307501	-345.500590	-345.499585	6.8	7.4
B3LYP	-116.619038	-230.020576	-346.613746	-346.612620	16.2	16.9
BLYP	-116.556554	-229.939403	-346.471417	-346.470083	15.4	16.2

E_I=cyclopropene total energy; E_{II}=furan total energy; E_{III}=*exo* transition state structure total energy; E_{IV}= *endo* transition state structure total energy; ΔE_{exo}=activation barrier through *exo* transition state; ΔE_{endo}=activation barrier through *endo* transition state

It is well known that the majority of Diels-Alder reactions will form the *endo* cycloadduct predominantly, which is in agreement with Alder's *endo* rule.[27] Woodward and Hoffmann used secondary orbital interactions (SOI) between the diene and dienophile to explain the *endo* stereoselectivity.[28] Our DFT computational results[26] are in full agreement with Apeloig and Matzner's ab initio calculations which provide evidence for the dominant role of secondary orbital interactions in dictating the *endo:exo* ratio of cycloadducts. One of the most reliable ways to determine SOI is through bond orders.[29] The $BO_{6\text{-}2}$ and $BO_{6\text{-}3}$ represent secondary π–π bonding interactions (π–π SOI) in the transition state structure between the diene and dienophile in the *exo* and *endo* transition state structures, respectively (Table 3). As previously determined true bond distances, the π–π SOI is dominant in the *exo* transition state structure (BOs are 0.00843 and 0.00663 in the *exo* and *endo* transition state structures, respectively) contrary to the majority of Diels-Alder reactions. This suggests that there might be other SOI that are of a stronger nature than the π–π SOI. There are two SOI that stabilize both transition state structures. They are the orbital interaction between the methylene hydrogen of cyclopropene and the lone pair of furan (H-n SOI) and the methylene hydrogen of cyclopropene and the π MO of furan (H-π SOI) in the *exo* and *endo* transition state structures, respectively. The H-n SOI in the *exo* transition state structure is stronger than the H-π SOI in the *endo* transition state structure. For instance, B3LYP computed 0.02282 for the H_{16}-O bond order in the *exo* transition state structure and 0.01717 for the H_{15}-C_3 bond order in the *endo* transition state structure. This indicates a greater stabilization of the *exo* transition state structure by SOI (Table 3). As an effect of these SOI, corresponding changes in atomic charges and frontier molecular orbital[31] energies are observed. Thus there is a higher atomic charge difference for the hydrogen of the H-n SOI in the *exo* transition state structure than for the atomic charge difference for the H-π SOI in the *endo* transition state structure (Table 3). Furthermore, the B3LYP computed difference between the frontier orbitals in the *exo* transition state structure (0.22255 a.u.) is substantially lower than for the *endo* transition state structure (0.22831 a.u.). These results clearly indicate a stronger secondary orbital overlap in the *exo* transition state structure.

Table 3. Computed Mullikan bond orders (BO)[30], atomic charges (AC), and frontier orbital energies for two isomeric transition state structures using the 6-31+G(d) basis set

Theory Model	BO_{6-3}	BO_{6-2}	BO_{16-4}	BO_{15-4}	AC_{15}	AC_{16}	HOMO	LUMO
				Exo Transition State Structures				
HF	0.36231	-0.00508	0.01234	0.00045	0.196712	0.209217	-0.30447	0.15431
B3LYP	0.33395	0.00843	0.02282	0.00089	0.209578	0.218010	-0.21432	0.00823
BLYP	0.34263	0.01281	0.02619	0.00104	0.217797	0.209390	-0.17656	-0.01646
				Endo Transition State Structures				
	BO_{6-4}	BO_{6-3}	BO_{15-3}	BO_{16-3}	AC_{15}	AC_{16}	HOMO	LUMO
HF	0.37688	-0.00269	0.01139	0.00012	0.196968	0.201530	-0.30938	0.15810
B3LYP	0.35389	0.00663	0.01717	0.00033	0.208687	0.213501	-0.21884	0.00947
BLYP	0.37017	0.00860	0.01910	0.00039	0.209767	0.213201	-0.18023	-0.01606

BO=bond order; AC=atomic charge; the numbers of atoms are the same as presented in Table 1, for example BO_{6-3} is the bond order between carbon atoms 6 and 3 in the *exo* transition state structure.

In conclusion, we can state that both the HF and MP2 ab initio computational methods, which are applicable to larger molecular systems of interest for experimental chemists, are not capable of computing activation barriers for the cyclopropene addition to furan. HF produced activation barriers which were too high while MP2 produced activation barriers which were too low. The very reliable B3LYP hybrid DFT method generated the expected activation barriers with a slight preference of the *exo* product formation over the *endo* product. The higher stability of the *exo* transition state structure is more stable due to a strong secondary orbital overlap between the methylene hydrogen of the cyclopropene moiety with the *n*-orbital of furan.

REFERENCES

1. Hehre, W. J.; Radom, L.; Schleyer, P.v.R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*, Wiley, New York, 1986; Clark, T. *A Handbook of Computational Chemistry*, Wiley, New York, 1986.
2. Parr, R. G.; Yang, W. *Density Functional Theory of Atoms and Molecules* , Oxford University Press, New York, 1989; Labanowski, J.; Andzelm, J. W. Eds., *Density Functional Methods in Chemistry* , Springer-Verlag, New York, 1991.
3. Jursic, B. S. *J. Mol. Struct. (Theochem)* **1996**, *366*, 97; Jursic, B. S. *J. Mol. Struct. (Theochem)* **1996**, *365*, 47; Jursic, B. S. *Int. J. Quantum Chem.* **1996**, *57*, 213.
4. Jursic, B. S. *Int. J. Quantum Chem.* in press; Jursic, B. S. *J. Mol. Struct. (Theochem)* in press.
5. Jursic, B. S. *J. Mol. Struct. (Theochem)* in press.

6. Jursic, B. S. *J. Mol. Struct. (Theochem)* **1996**, *366*, 103; Jursic, B. S.; Timberlake, J. W.; Engel, P. S. *Tetrahedron Lett.* **1996**, *37*, 6473; Jursic, B. S. *Int. J. Quantum Chem.* **1996**, *59*, 495.

7. Jursic, B. S. *J. Chem. Soc. Perkin Trans 2* **1996**, 1921.

8. Jursic, B. S. *Int. J. Quantum Chem.* in press.

9. Jursic, B. S. *J. Chem. Phys.* **1996**, *104*, 114.

10. Binger, P.; Wedemann, P.; Goddard, R.; Brinker, U. H.*J. Org. Chem.* **1996**, *61*, 6462.

11. Geibel, K; Heindl, J. *Tetrahedron Lett.* **1970**, *11*, 2133; Battiste, M. A.; Sprouse, C. T., Jr. *Tetrahedron Lett.* **1970**, *11*, 3165; Battiste, M. A.; Sprouse, C. T., Jr. *Tetrahedron Lett.* **1970**, *11*, 4661.

12. Wiberg, K. B.; Barley, W. J., *J. Am. Chem. Soc.* **1960**, *82*, 6375.

13. Breslow, R.; Oda, M. *J. Am. Chem. Soc.* **1972**, *94*, 4787; Oda, M. Breslow, R.; Pecoraro, J. *Tetrahedron Lett.* **1972**, *13*, 4419

14. Cordes, M. H. J.; deGala, S.; Berson, J. A. *J. Am. Chem. Soc.* **1994**, *116*, 11161.

15. All computational studies were performed with the Gaussian 94 computational package.[16] The Hartree-Fock (HF)[17] and the second order Møller-Plesset (MP2)[18] perturbation ab initio computational studies were the only ab initio computational methods employed. Two of the most popular DFT methods were used, B3LYP and BLYP. The hybrid B3LYP is based on Becke's three parameter functional[19] and the correlation is provided by the LYP[20] expression. The BLYP gradient-corrected DFT method combines Becke's 88 exchange functional[21] and Lee-Yang-Parr's correlation functional. Explanations for these DFT methods, basis sets, and ab initio methods can be obtained elsewhere.[22]

16. Gaussian 94, Revision B.3, M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 1995.

17. Roothaan, C. C. *Rev. Mod. Phys.*, **19951**, *23*, 69; Hall, G. G. *Proc. Roy. Soc. (London)*, **1951**, *A205*, 541.

18. Raghavachari, K.; Pople, J. A.; Replogle, E. S.; Head-Gordon, M. *J. Phys. Chem.* **1990**, *94*, 5579.

19. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

20. Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

21. Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.

22. Frisch, M. J.; Frisch, Æ.; Foresman, J. B. Gaussian 94 User's Reference, Gaussian, Inc. Pittsburgh, PA, 1995.

23. Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 344; For analytical functions that describe the reaction coordinates and reproduce the Hammond behavior see LeNoble, W. J.; Miller, A. R.; Hamann, S. D. *J. Org. Chem.* **1977**, *42*, 338; Miller, A. R. *J. Am. Chem. Soc.* **1978**, *100*, 1984.

24. Jursic, B. S. *Computing Transition State Structures with Density Functional Theory Methods*, IN: *Recent Developments and Applications of Modern Density Functional Theory*, Seminario, J. M. Ed.; Elsevier, Amsterdam, 1996.; Jursic, B. S.; Zdravkovski, Z. *J. Chem. Soc. Perkin Trans. 2* **1995**, 1223.

25. Houk, K. N. Lin, Y.-T.; Evanseck, J. D. *Angew. Chem. Int. Ed. Eng.* **1992**, *31*, 682.

26. Jursic, B. S. *J. Org. Chem.* submitted.

27. Alder, K.; Stein, G. *Angew. Chem.* **1937**, *50*, 510.

28. Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlage Chemie: Weinheim, 1971.

29. For an excellent article concerning bond orders as a method for characterization of the reactivity, see Lendvay, G. *J. Phys. Chem.* **1994**, *98*, 6098 and references therein

30. Bond orders are computed with SPARTAN computational package. SPARTAN version 4.0. Wavefunction, Inc., 18401 Von Karman Ave., #370, Irvine, CA92715 U.S.A.

31. Fukui, K.; Fujimoto, H. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2018; Fukui, K.; Fujimoto, H. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2018; Fukui, K. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 801.

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