2328 *J. Org. Chem.* **1995,** *60,* 2328–2329

Origin of Facial Selectivity in the Diels–Alder Reactions of 5-Substituted 1,3-Cyclopentadienes

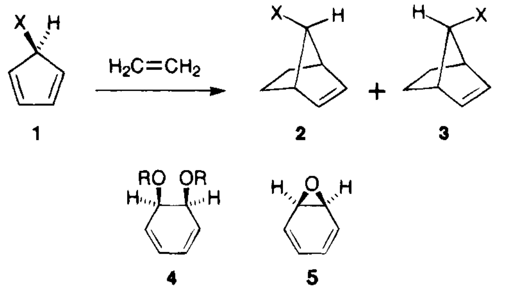
Raymond A. Poirier,* Cory C. Pye,
James D. Xidos, and D. Jean Burnell*

Department of Chemistry, Memorial University of Newfoundland, St. John's, Newfoundland, Canada A1B 3X7

Received February 17, 1995

1,3-Cyclopentadienes substituted at C-5 (**1**) show an intriguing range of facial selectivity in their Diels–Alder reactions.[1] Heteroatom substituents from the first row (X = F, NH_2, OH, OAc) lead overwhelmingly to reaction onto the diene face syn to the heteroatom to give **2**.[2–4] Diene **1** with a heteroatom substituent from the second row (X = Cl, SPh) leads to both syn and anti adducts,[3,5,6] but with a substituent from the third or fourth rows (X = Br, SePh, I) the anti-addition adduct **3** is the exclusive product (Scheme 1).[3,6] The facial selectivity in Diels–Alder reactions has been rationalized in a number of ways, but we can now disclose, based on an ab initio computational examination of the problem, that none of these rationalizations can be correct for an archetypal diene system, the simple 5-substituted 1,3-cyclopentadiene **1**.

Scheme 1



We examined **1** with substituents for which some experimental results are available, or can be inferred, and we added a few more dienes for which experimental results are not yet available. The reactants and their syn and anti Diels–Alder transition states, with ethene as the dienophile, were fully optimized[7] with the $3\text{-}21G^{(*)}$ basis set using gradient optimization methods. Energies were obtained by single-point calculations with the HF/$6\text{-}31G^*$ basis set or Huzinaga basis sets for X = Se, Br, and I. The calculated facial selectivities are in good accord with the available experimental data (Table 1). The relative positions of the carbon atoms proved to be strikingly similar in all the transition states that we examined. The atom on C-5 that is syn to the incoming dienophile lies very close to the plane of the four carbons of the diene moiety, and the bond to the anti C-5 atom is almost perpendicular to that plane. The syn bond on C-5 is somewhat shortened, and the anti bond lengthened, relative to the ground state bond lengths. It is important to note that the range of calculated activation energies is significantly larger for the syn than the anti transition states (a range of 57.9 kJ/mol for the syn transition states versus a 8.9 kJ/mol range for the anti transition states). The latter are clustered near the calculated activation energy for the reaction of cyclopentadiene itself.

A significant steric interaction[9] between the incoming dienophile and the syn substituent at C-5 of **1** seems inevitable, but calculation of "deformation energies"[10] (Table 1) reveals that deformation of the addends at the transition state is the major factor responsible for determining the facial selectivity, not a direct interaction between the diene and the dienophile. Thus, in every case we examined, when the deformation energies of the two addends are summed for the syn and the anti transition states, the difference between these sums accounts for most of the difference in the activation energies for syn and anti addition. The remaining contributor to the difference in activation energies for syn and anti addition must arise from differences in the direct diene–dienophile interactions, but *these are all relatively small.* Thus, it appears that direct interactions such as steric effects between the addends have already translated largely into changes in the geometries of the addends at the transition state.[11]

In most instances a very large degree of facial selectivity results from the difference between the deformation energies of only the diene moiety in the syn and anti transition states. This is not surprising since the amount of geometric change at the transition state is much larger in the diene moiety. For example, the H–C–H bond angles in the ethene moieties (115.6 ± 1.1°) are very similar to the angle in ethene itself (116.2°), but the C-2–C-1–C-5 bond angles of the diene moieties (107.7 ± 2.6°) are already close to tetrahedral. Indeed, the activation energies for syn addition correlate very well (*r* = 0.989, slope = 1.23) with the diene deformation energies for syn addition (Figure 1). In contrast, the activation energies for anti additions are all close to that of cyclopentadiene

---

[1] Fallis, A. G.; Lu, Y.-F. In *Advances in Cycloaddition*; Curran, D. P., Ed; JAI Press, Inc.: Greenwich, CT, 1993; Vol. 3, pp 1–66.

[2] (a) Winstein, S.; Shatavsky, M.; Norton, C.; Woodward, R. B. *J. Am. Chem. Soc.* **1955**, *77*, 4183. (b) McClinton, M. A.; Sik, V. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1891.

[3] Macaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 1136 and refs therein.

[4] In this paper we define syn addition as an addition to the face of the diene on the same side as the substituent. Anti addition is to the opposite face.

[5] Williamson, K. L.; Hsu, Y.-F. L.; Lacko, R.; Youn, C. H. *J. Am. Chem. Soc.* **1969**, *91*, 6129.

[6] Ishida, M.; Beniya, Y.; Inagaki, S.; Kato, S. *J. Am. Chem. Soc.* **1990**, *112*, 8980.

[7] Poirier, R. A.; Peterson, M. R.; Yadav, A. *MUNGAUSS*, Department of Chemistry, Memorial University of Newfoundland, St. John's, Newfoundland, Canada. C_s symmetry was imposed to speed up geometry optimization. The transition state of cyclopentadiene is C_s symmetric at the 3-21G[12a] and 6-31G* levels.[12b] Where applicable, staggered conformations of X are reported, because all of these computed transition states proved to be first-order saddle points.

[8] Huzinaga, S.; Andzelm, J.; Klobukowski, M.; Radzio-Andzelm, E.; Sakai, Y.; Tatewaki, H. In *Gaussian Basis Sets for Molecular Calculations*; Huzinaga, S., Ed.; Elsevier Science Publishers: Amsterdam, 1984.

[9] Differences in the steric interactions in the syn and anti transition states have been used to explain the influence of carbon substituents at C-5 of 1,3-cyclopentadiene: (a) Burnell, D. J.; Valenta, Z. *J. Chem. Soc., Chem. Commun.* **1985**, 1242. (b) Burnell, D. J.; Valenta, Z. *Can. J. Chem.* **1991**, *69*, 179 and refs therein.

[10] A "deformation energy" is defined here as the difference in energy between the diene (or dienophile) in its initial reactant geometry and *alone* in its transition state geometry.

[11] The most obvious differences in geometry between the syn and the anti transition states of **1** are in the extra-annular angles about C-5. Attack on a face of **1** is generally disfavored when these angles experience large changes from the ground state. Thus, for **1** with X = F the sum of the changes in the angles X–C-5–H, X–C-5–C-1, and H–C-5–C-1 on going from the ground state to the favored, syn transition state is only 2.5° (compared to 9.3° for cyclopentadiene itself), whereas going to the the anti transition state requires a 12.2° change. In contrast, for **1** with X = SiH_3 there is a very large (30.9°) angular change for the syn transition state, but for the favored, anti transition state it is 4.5°. However, this simple analysis only works for the extreme cases, for **1** with X = NH_2, C≡CH, and C≡N it does not.

0022-3263/95/1960-2328$09.00/0

Table 1. Facial Selectivities and Transition State Properties Computed for 5-Substituted 1,3-Cyclopentadienes

substituent	facial selectivity (% syn)		E_{act}[a] (kJ/mol)		diene deformation energy[a] (kJ/mol)		dienophile deformation energy[a] (kJ/mol)	
at C-5	exptl	calcd[b]	syn	anti	syn	anti	syn	anti
F	100[c]	99.99	−25.9	−2.9	−19.0	−0.4	−7.5	−3.3
NH_2	100[d]	99.9	−13.1	4.9	−7.9	3.3	−8.4	−1.3
OH	100[e]	99	−11.1	−1.3	−9.2	2.3	−3.0	−3.4
C≡CH		97	−4.8	2.8	−0.9	4.7	−4.3	0.4
C≡N		90	−5.5	−0.5	0.5	3.0	−2.7	−0.5
Cl	79[f]	73	−3.7	−1.4	−0.9	−1.0	−6.4	−0.2
CH_3	16[g]	23	8.8	6.0	6.3	2.1	−3.0	0.8
Br	17[f]	5	5.6	−1.2	9.0	−2.4	−5.1	0.6
SH	40[h]	3	12.9	4.4	10.7	2.0	−3.6	−0.1
SeH	0[h]	0.1	20.7	5.2	18.0	0.6	−2.6	1.5
PH_2		0.1	19.4	2.8	16.4	−2.4	−1.2	1.8
I	0[f]	0.03	17.3	−1.2	18.9	−3.7	−4.3	1.2
SiH_3		0.001	32.0	5.5	27.0	−1.2	1.6	4.1

[a] Relative to cyclopentadiene and/or ethene. [b] Calculated for 0 °C. [c] With unsymmetrical ethenic dienophiles.[2b] [d] Inferred from the pentamethyl system.[3] [e] Acetate derivative with ethene.[2a] [f] With *N*-phenylmaleimide: Wellman, M. A.; Burnell, D. J. Unpublished results. [g] 1,2,3,4,5-Pentamethyl-1,3-cyclopentadiene with symmetrical ethenic dienophiles (±5%).[9a] [h] Phenylthio or phenylseleno ethers with maleic anhydride.[6b] These larger groups may be quite different conformationally from the calculated substituents.

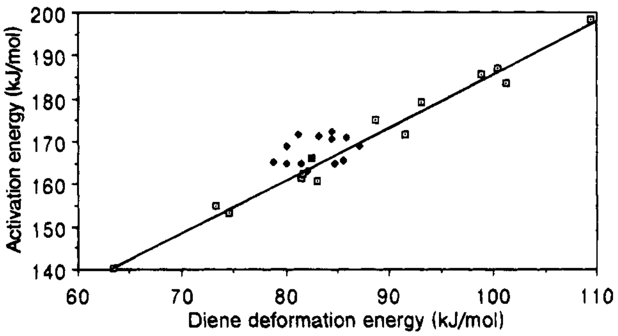


Figure 1. Plot of computed diene deformation energies versus computed activation energies. Open squares are syn transition states (with least-squares line indicated); filled diamonds are anti transition states; the filled square is for cyclopentadiene.

itself. In the three cases in which the diene deformation energies happen to be close to that of cyclopentadiene (X = C≡CH, C≡N, and Cl), the deformation of the dienophile emerges as an important factor in determining facial selectivity, and in these cases one should expect the facial selectivity to be sensitive to the nature of the dienophile, unlike with the other substituents.[12]

The fact that the diene deformation energies for syn addition of **1** with X = F, NH_2, and OH are significantly lower than that for cyclopentadiene itself indicates that these dienes, deformed into their transition state geometries, are stabilized by the X group. The mechanism of this stabilization is not clear. While it may be tempting to speculate that stabilization could arise via electron donation from the (coplanar) syn substituent, in every case that we studied there is an insignificant difference in the hybridization of the X group in the syn and anti transition states, and bond orders between X and C-1 or C-4 and between X and the dienophile carbons are negligible. Furthermore, there is no significant correlation between the Hammett constants (σ_m or σ_p)[13] for the substituents and the facial selectivity. Also, orbital diagrams of the transition states do not show consistent trends, so it appears that syn stabilization may arise by more than one mechanism. Computational work is ongoing in order to pinpoint these mechanisms.

Many groups have postulated that facial selectivity in Diels–Alder reactions is controlled by a direct interaction between the diene and the dienophile. In addition to simple steric interactions,[9] phenomena that have been implicated are favorable admixture of the C-5 substituent's lone pair with the LUMO of a syn-adding dienophile;[14] energetically different interactions of a dienophile with a π-system that is facially biased, in terms of either electron density[15] or nucleophilicity,[16] by a C-5 substituent; dienophile interactions with tilted p components of occupied π-orbitals of a plane-nonsymmetric diene;[6,17] and direct, facially different dipole–dipole,[5] electrostatic,[18] or filled-orbital[19] diene–dienophile interactions. Obviously, such phenomena should be evident at the transition state if they play a significant role in deciding facial selectivity. However, we have shown that even if direct diene–dienophile interactions are energetically significant at the syn and anti transition states, these interactions do not have much importance in determining facial selectivity with **1**. Furthermore, the proposal[2b,3,20] of facial control by the mechanism postulated by Cieplak for carbonyl reactions[21] can also be obviated because it operates by donation from a σ-donor on the anti face of the diene, i.e., the mechanism would predict a large range of activation energies for anti additions, but as can be seen in Figure 1, these activation energies are all similar to that of cyclopentadiene.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for financial support.

JO950303P

---

(12) Experiments with **1**, X = CH_3,[9a] and with other sp^3 carbon substituents[9b] led to very small changes in facial selectivity when various dienophiles were employed.

(13) Oxner, O. In *Correlation Analysis in Chemistry*; Chapman, N. B., Shorter, J. Eds.; Plenum Press: New York, 1978; Chapter 10.

(14) Anh, N. T. *Tetrahedron* **1973**, *29*, 3227.

(15) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4054.

(16) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 663.

(17) Paquette, L. A.; Gugelchuk, M. *J. Org. Chem.* **1988**, *53*, 1835 and references therein.

(18) Ginsburg, D. *Tetrahedron* **1983**, *39*, 2095.

(19) Coxon, J. M.; Fong, S. T.; McDonald, D. Q.; Steel, P. J. *Tetrahedron Lett.* **1993**, *34*, 163.

(20) (a) Chung, W.-S.; Turro, N. J.; Srivastava, S.; Li, H.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 7882. (b) Halterman, R. L.; McCarthy, B. A.; McEvoy, M. A. *J. Org. Chem.* **1992**, *57*, 5585.

(21) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 8447.