J. Am. Chem. Soc. 1992, 114, 1499-1500

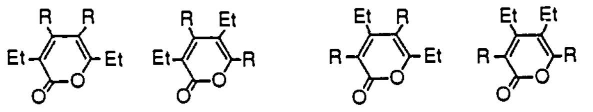

Figure 2. Four regioisomers of the co-oligomer A (R = $(CH_2)_6C{\equiv}C$—Et).

that A and B consist of one CO_2 molecule plus two diyne molecules and two CO_2 molecules plus three diyne molecules, respectively. The co-oligomer A exhibits 16 ^{13}C NMR absorptions with almost equal intensities (Figure 1b) assignable to the C=C bonds of the 2-pyrone ring, which indicates that A is composed of nearly equal amounts of four regioisomers shown in Figure 2. Homopolymerization of **1** without CO_2 gave methanol-insoluble polymers (35%, M_n = 1800)[5] whose ^{13}C NMR spectrum (Figure 1e) is quite different from those of copolymers.

Agreement of a pattern of the ^{13}C NMR C=C absorptions of copolymers **2** almost free from the C=C absorptions of homopolymers with those of co-oligomers A and B (Figure 1) indicates that alternating copolymerization of CO_2 with **1** occurs to produce poly(2-pyrone) **2**,[6] and its repeating unit[7] corresponds to the structure of the 2-pyrone ring of A.

The alternating copolymerization of diynes with CO_2 depends upon the relative reactivity of inter- to intramolecular cyclization of diynes. Thus, the reaction of 3,9-dodecadiyne and CO_2 under the standard reaction conditions of Table I produced a corresponding bicyclic 2-pyrone[2] fused with a six-membered ring as a main product (~40%) together with a small amount of polymers (~10%).

1,7-Cyclotridecadiyne (**3**), a cyclic diyne, also underwent facile alternating copolymerization with CO_2 to produce poly(2-pyrone) **4**[8] with a unique ladder structure (eq 2, Table I). Copolymers **4** are white powders.[9] They show a solubility similar to that of the copolymer **2**. Formation of alternating copolymers **4**[7] from CO_2 and **3** is demonstrated by agreement of a pattern of the ^{13}C NMR C=C absorptions of **4** (Figure 1g) free from the C=C absorptions (Figure 1h) of methanol-insoluble homopolymers[5] of **3** (22%, M_n = 840) with that (Figure 1f) of a co-oligomer C composed of one CO_2 molecule and two molecules of the diyne **3**.[10]

The TGA curve for the copolymer **2** or **4** run under nitrogen shows a rapid weight loss around 420 °C.

The present study suggests that numerous unprecedented poly(2-pyrones) can be prepared by changing the structure of diynes, for example, $RC{\equiv}C(CH_2)_mC{\equiv}CR$ ($m \geq 7$, $m \leq 2$). Their preparations, characterizations, and reactions utilizing a variety of chemical reactivities of the 2-pyrone ring[4] are interesting further subjects.

Acknowledgment. This work was sponsored by New Energy and Industrial Technology Development Organization (NEDO)/Research Institute of Innovative Technology for the Earth (RITE) under Contract of Research Commissioned.

Supplementary Material Available: Experimental section including characterization data of copolymers and co-oligomers (3 pages). Ordering information is given on any current masthead page.

---

(5) A structure of the homopolymer has not been determined at the present time. As to the structure of acetylene oligomers, see, for example, ref 3a.

(6) The copolymers **2** produced at 90 °C in THF–MeCN show no ^{13}C NMR C=C absorptions of homopolymers of **1**. The copolymers **2** produced in THF without MeCN show weak but distinct ^{13}C NMR C=C absorptions of homopolymers of **1** along with those of the 2-pyrone ring.

(7) Orientation of 2-pyrone rings along the polymer chain is reasonably assumed to be random.

(8) The copolymers **4** obtained in THF alone exhibit negligible ^{13}C NMR C=C absorptions of homopolymers of **3**.

(9) The copolymers **2** and **4** did not show satisfactory elemental analysis results. It was found that ashes were formed after combustion analyses of the copolymers. This finding suggests that nickel salts contaminate the copolymers, which was further confirmed by X-ray fluorescence analysis. Their removal by washing chloroform solutions of the copolymers with water or dilute hydrochloric acid was unsuccessful.

(10) One regioisomer among four possible regioisomers.

Exo-Lone-Pair Effect on Hetero-Diels–Alder Cycloaddition Stereochemistry

Margaret A. McCarrick, Yun-Dong Wu, and K. N. Houk*

Department of Chemistry and Biochemistry
University of California
Los Angeles, California 90024

Received October 11, 1991

In hetero-Diels–Alder reactions, we have discovered that the interactions of lone pairs on N or O with π systems can exert powerful stereochemical control. The n–π repulsion which causes this phenomenon should be very important in controlling stereochemistry in many complexation and reactivity events as well.

Hetero-Diels–Alder reactions are often key steps in stereoselective syntheses of natural products.[1,2] To learn about the transition structures of such processes, we investigated reactions of 1,3-butadiene with formaldehyde, formaldimine, diazene, and nitrosyl hydride with ab initio quantum mechanical methods. Geometry optimizations were performed at the RHF level using GAUSSIAN 86 and 88.[3] Structures were fully optimized with the 3-21G basis set, followed by vibrational frequency calculations. MP2/6-31G* calculations on 3-21G geometries were performed to evaluate the activation energies. A concerted, but nonsynchronous, reaction mechanism was presumed. The RHF/3-21G transition structure for the reaction of butadiene with ethylene is very similar to those at higher levels of theory, including MCSCF.[4] The MP2/6-31G* activation energy for this reaction is about 10 kcal/mol lower than the experimental value,[5] but substituent effects are reproduced well.[6] Predicted activation energies for hetero-Diels–Alder reactions are given in Table I, and transition structures are shown in Figure 1.

The transition structure for the reaction of butadiene with formaldehyde, **1**, resembles that for the reaction of butadiene with ethylene,[4a] with a 0.08 Å shorter C–C forming bond. The C_6–O_1 bond is 0.14 Å shorter than the C_2–C_3 bond, differing from MINDO/3 predictions.[7] Our results reflect the shorter C–O than

---

(1) Boger, D. L.; Weinreb, S. N. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic Press: San Diego, 1987. Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087. Hamer, J., Ed. *1,4-Cycloaddition Reactions*; Academic Press: New York, 1967.

(2) (a) Jung, M. E.; Shishido, K.; Light, L.; Davis, L. *Tetrahedron Lett.* **1981**, 4607. (b) Jensen, F.; Foote, C. S. *J. Am. Chem. Soc.* **1987**, *109*, 6376. (c) Nader, B.; Bailey, T. R.; Franck, R. W.; Weinreb, S. M. *J. Am. Chem. Soc.* **1981**, *103*, 7573. (d) Le Coz, L.; Veyrat-Martin, C.; Wartski, L.; Seyden-Penne, J.; Bois, C.; Philoche-Levisalles, M. *J. Org. Chem.* **1990**, *55*, 4870. (e) Danishefsky, S. J.; Larson, E.; Askin, D.; Kato, N. *J. Am. Chem. Soc.* **1985**, *107*, 1246.

(3) (a) Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; Defrees, D. J.; Seeger, R.; Whiteside, R. A.; Fox, D. J.; Fluder, E. M.; Pople, J. A. GAUSSIAN 86, Gaussian, Inc., Pittsburgh, PA 15213. (b) Frisch, M. J.; Head-Gordon, M.; Schlegel, H. B.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Kahn, L. R.; Stewart, J. J. P.; Fluder, E. M.; Topiol, S.; Pople, J. A. GAUSSIAN 88, Gaussian Inc., Pittsburgh, PA 15213.

(4) (a) Houk, K. N.; Lin, Y.-T.; Brown, F. K. *J. Am. Chem. Soc.* **1986**, *108*, 554. (b) Bach, R. D.; McDouall, J. J. W.; Schlegel, H. B.; Wolber, G. J. *J. Org. Chem.* **1989**, *54*, 2931 (c) Loncharich, R. J.; Houk, K. N. Unpublished results on the MP2/6-31G* transition structure for butadiene + ethylene. (d) Bernardi, F.; Bottini, A.; Field, M. J.; Guest, M. F.; Hillier, I. H.; Robb, M. A.; Venturini, A. *J. Am. Chem. Soc.* **1988**, *110*, 3050. Bernardi, F.; Bottini, A.; Robb, M. A.; Field, M. J. *J. Chem. Soc., Chem. Commun.* **1985**, *15*, 1051.

(5) (a) Krause, M.; Vavruska, M.; Bazant, V. *Collect. Czech. Chem. Commun.* **1957**, *22*, 484. (b) Kuchler, L. *Trans. Faraday Soc.* **1939**, *35*, 874. (c) Lewis, D. K.; Bergman, J.; Manjoney, R.; Paddock, R.; Kalra, B. L. *J. Phys. Chem.* **1984**, *88*, 4112. (d) Rowley, D.; Steiner, H. *Discuss. Faraday Soc.* **1951**, *10*, 198. (e) Smith, S. R.; Gordon, A. S. *J. Phys. Chem.* **1961**, *65*, 1124. (f) Tardy, D. C.; Ireton, R.; Gordon, A. S. *J. Am. Chem. Soc.* **1979**, *101*, 1508. Tsang, W. J. *Chem. Phys.* **1965**, *42*, 1805; Tsang, W. J. *Int. J. Chem. Kinet.* **1970**, *2*, 311. (h) Uchiyama, M.; Tomioka, T.; Amano, A. *J. Phys. Chem.* **1964**, *68*, 1878.

(6) (a) Houk, K. N.; Loncharich, R. J.; Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1989**, *111*, 9172. (b) Loncharich, R. J.; Brown, F. K.; Houk, K. N. *J. Org. Chem.* **1989**, *54*, 1129. (c) Birney, D. M.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 4127. (d) Houk, K. N.; Li, Y.; Evanseck, J. D. *Angew. Chem.*, in press.

Table I. Calculated Energies (kcal/mol) of the Hetero-Diels–Alder Transition Structures with Respect to Reactants[a]

dienophile	TS	3-21G	3-21G+ZPE[b]	6-31G*	MP2/6-31G*	ΔE_{rxn}[c]
ethylene		35.9[d]	38.3[d]	43.0[e]	17.6[e]	−43.1[d]
formaldehyde	**1**	32.5 (−3.4)	35.9 (−2.4)	46.0 (+3.0)	20.9 (+3.3)	−34.2
formaldimine, exo H	**2**	36.4 (+0.5)	39.4 (+1.1)	48.1 (+5.1)	20.1 (+2.5)	−38.0
formaldimine, endo H	**3**	31.1 (−4.8)	34.4 (−3.9)	43.8 (+0.8)	15.2 (−2.4)	
trans-diazene	**4**	29.5 (−6.4)	33.0 (−5.3)	45.3 (+2.3)	9.0 (−8.6)	−38.8
cis-diazene, exo H	**5**	39.9 (+4.0)	42.7 (+4.4)	56.0 (+13.0)	17.6 (0.0)	
cis-diazene, endo H	**6**	27.4 (−8.5)	30.6 (−7.7)	44.6 (+1.6)	6.0 (−11.6)	
nitrosyl hydride, exo H	**7**	27.3 (−8.6)	31.0 (−7.3)	45.4 (+2.4)	9.9 (−7.7)	−50.2
nitrosyl hydride, endo H	**8**	19.8 (−16.1)	23.6 (−14.7)	37.4 (−5.6)	1.8 (−15.8)	

[a] Energies relative to the reaction of butadiene with ethylene are in parentheses. [b] Corrected for zero-point energies. [c] 3-21G energies. [d] Reference 5a. [e] Reference 5b.

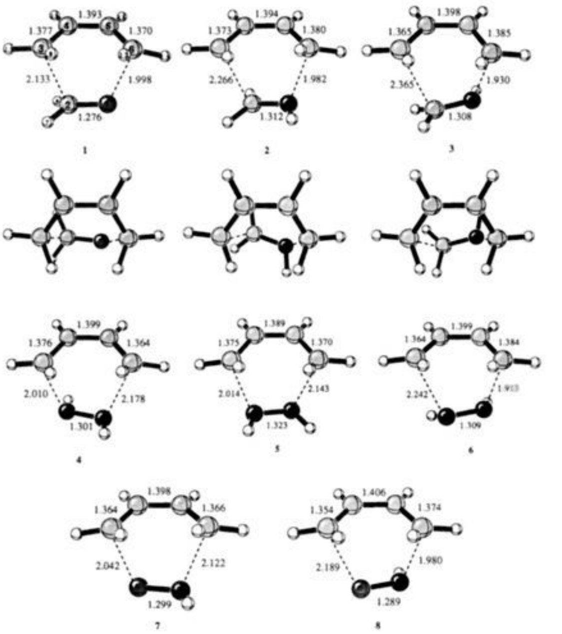

Figure 1. Computed transition structures for reactions of butadiene with heterodienophiles. All are numbered in the same fashion as **1**. For **1**, **2**, and **3**, both side and top views are shown.

C–C single bond lengths, since the geometry of the butadiene moiety indicates that the C_2–C_3 bond is more fully formed than the C_6–O_1 bond in **1**. The MP2/6-31G* activation energy is 3.3 kcal/mol higher than that for the reaction of butadiene with ethylene. Experimentally, formaldehyde does not react with 1,3-butadiene.[8]

Why is formaldehyde less reactive than ethylene, even though it has a lower LUMO energy? One factor is the lower exothermicity of the reaction (Table I); another is the repulsive interaction of an oxygen lone pair with the butadiene filled π orbitals, particularly at C_4 and C_5. The top view of **1** shows that the formaldehyde is somewhat twisted with respect to the butadiene moiety, increasing the distance from the endo lone pair to C_4 and C_5, but significant n–π repulsion is still present in the transition state.[9]

Two diastereomeric transition structures, **2** and **3**, were found for the reaction of formaldimine with butadiene. Structure **3** is predicted to have a 4.9 kcal/mol lower activation energy than **2**, highly favoring the exo lone pair. This is considerably larger than the endo preference for Diels–Alder reactions of substituted ethylenes.[6,10] With *N*-methylformaldimine, the preference for the exo lone pair is still 4 kcal/mol.[11] Experimentally, acyclic imines with similar C- and N-substituents give products with the C-substituent exo. Presumably, the N-substituent is endo in the transition state.[2c,12]

The forming N_1–C_6 bond is shorter than the forming C_2–C_3 bond in both **2** and **3**. In **3**, the attraction of the imino hydrogen to the π electrons and relief of lone pair, π repulsion causes shortening of the N_1–C_6 bond. There is significant twisting between butadiene and formaldimine in both structures. The C_6–N_1–C_2–C_3 dihedral angle is −27° in **2** and 20° in **3**. In **2**, the nitrogen lone pair is endo, where it interacts with π orbitals at C_4 and C_5 of butadiene; twisting relieves this repulsion to some extent. Constraining the C_6–N_1–C_2–C_3 dihedral angle to 0° destabilizes **2** by 2.6 kcal/mol and **3** by 1.7 kcal/mol.

Azo compounds containing electron-withdrawing groups are extremely reactive dienophiles used extensively in organic synthesis.[2b,13] Diazene exists in cis and trans forms, the trans being 6–7 kcal/mol more stable.[14] Transition structure **4** is very asynchronous. The exo-lone-pair effect is reflected in the forming bond lengths and by a 21° twisting of the dienophile with respect to butadiene. Structures **5** and **6** are the exo and endo transition structures for cis-diazene. The asymmetry of these structures results from optimization of the repulsive (**5**) or attractive (**6**) interactions, and symmetry constraint raises the energies by 0.2 and 1.4 kcal/mol, respectively. The exo-lone-pair effect causes **6** to be 12 kcal/mol more stable than **5**! Structure **4** is between **5** and **6** in energy, having one exo and one endo lone pair.

The exo (**7**) and endo (**8**) transition structures of butadiene with nitrosyl hydride are nearly synchronous and are predicted to have very low activation energies. The 8 kcal/mol endo preference is again caused by n–π repulsion in **7**, indicated by a 0.14-Å lengthening of the N_2–C_3 forming bond in **7** vs **8** and a twisting of the C_6–N_1–O_2–C_3 dihedral angle, which is −21.9° in **8** and 11.7° in **7**. This large calculated endo preference could be useful in designing reagents for enantioselective Diels–Alder reactions. For example, it has been reported that some chiral α-chloro nitroso compounds undergo Diels–Alder reactions with very high enantioselectivities.[15]

Further theoretical studies are in progress to investigate the effects of lone-pair, π interactions on other reactions.

Acknowledgment. We are grateful to the National Science Foundation and the National Institutes of Health for financial support of this research.

Registry No. Formaldehyde, 50-00-0; formaldinine, 2053-29-4; *trans*-diazene, 15626-43-4; *cis*-diazene, 15626-42-3; nitrosyl hydride, 14332-28-6; 1,3-butadiene, 106-99-0.

---

(7) (a) Le, I.; Han, E. S.; Choi, J. Y. *J. Comput. Chem.* **1984**, *5*, 606.

(8) Gresham, T. L.; Steadman, T. R. *J. Am. Chem. Soc.* **1949**, *71*, 737. Kubler, D. G. *J. Org. Chem.* **1962**, *27*, 1435.

(9) A related acetylene π, butadiene π repulsion in a Diels–Alder transition state has been suggested: Coxon, J. M.; Grice, S. T.; Maclagan, R. G. A. R.; McDonald, D. Q. *J. Org. Chem.* **1990**, *55*, 3804.

(10) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779.

(11) McCarrick, M. A.; Wu, Y.-D.; Houk, K. N. Manuscript in preparation.

(12) (a) Bailey, T. R.; Garigipati, R. S.; Morton, J. A.; Weinreb, S. M. *J. Am. Chem. Soc.* **1984**, *106*, 3240. (b) Nader, B.; Franck, R. W.; Weinreb, S. M. *J. Am. Chem. Soc.* **1980**, *102*, 1153.

(13) Moody, C. J. *Adv. Heterocycl. Chem.* **1982**, *30*, 1. Burrage, M. E.; Cookson, R. C.; Gupte, S. S.; Stevens, D. R. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1325.

(14) Whitelegg, D.; Woolley, R. G. *J. Mol. Struct* (*Theochem*) **1990**, *209*, 23.

(15) (a) Werbitzky, O.; Klier, K.; Felber, H. *Liebigs Ann. Chem.* **1990**, 267. (b) Felber, H.; Kresze, G.; Braun, H.; Vasella, A. *Tetrahedron Lett.* **1984**, 5381. (c) Felber, H.; Kresze, G.; Prewo, R.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 1137. (d) Sabuni, M.; Kresze, G.; Braun, H. *Tetrahedron Lett.* **1984**, 5377.