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THE ROLE OF SECONDARY ORBITAL INTERACTIONS IN CYCLOADDITION REACTIONS

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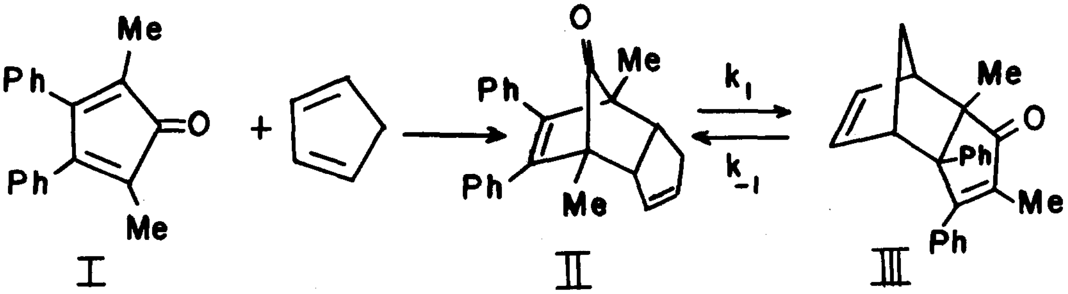
The Alder rule of maximum accumulation of unsaturation[1] has stimulated a number of rationalizations including stabilization of the *endo* transition state of Diels-Alder reactions by (A) inductive (van der Waals or dipolar) forces[2], (B) charge transfer,[3] (C) favorable geometry for overlap,[4] (D) secondary bonding forces,[5] and (E) secondary orbital interactions.[6] In their consideration of secondary orbital interactions, Woodward and Hoffmann made the prediction that these same interactions which stabilize the *endo* [4 + 2] transition state should destabilize the *endo* [6 + 4] transition state[6] - a prediction amply verified by experiment in that all known [6 + 4] cycloadditions proceed stereospecifically *exo*.[7]

While the importance of secondary orbital interactions seems established, the predominantly *endo* cycloadditions of cyclopentadiene with the mono-olefins cyclopentene,[8] norbornene,[9] cyclopropene,[10] and propene[11]-systems in which no secondary orbital stabilization is possible - have indicated that (A) or (C) may be of over-riding importance, or that the *exo* transition state is destabilized in these cases by steric repulsion of the methylene hydrogen of cyclopentadiene and the alkyl groups of the mono-olefins.[1b,2b]

We report experimental support for the importance of secondary orbital interactions in stabilization of the *endo* Diels-Alder transition state, and suggest that the steric repulsion hypothesis[1b,2b] accounts satisfactorily for the stereoselective *endo* Diels-Alder additions of mono-olefins with cyclopentadiene.

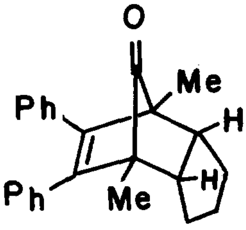
Since the reactive diene, 2,5-dimethyl-3,4-diphenylcyclopentadienone, I, undergoes stereospecific *endo* [4 + 2] cycloadditions with cycloheptatriene[78] and azepines[12] and stereospecific *exo* [6 + 4] cycloadditions with cycloheptatriene and tropone,[78], it was of interest to study the cycloadditions of I with mono-olefins to determine whether stereoselectivity might be observed in the absence of extending conjugation in the dienophile.

Reaction of I[13] and cyclopentadiene (90°, 3 hours, benzene) resulted in the formation of the Diels-Alder adduct, II, mp 137° (lit.[14] mp 139°) (90%) and a second adduct, III,[15] mp 120° (10%). The presence of an α, β-unsaturated ketone (ir, CCl_4: 5.98μ, 6.02μ), tertiary and olefinic methyl groups (nmr, C_2Cl_4: 1.0ppm (3H)s; 1.95ppm (3H)s), and two olefinic protons (nmr, C_2Cl_4: 6.2ppm (2H)) established the structure of III.

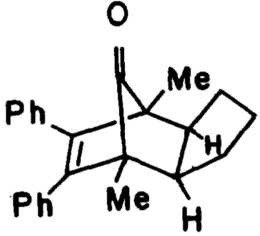


When II was heated at 105°, a rapid equilibrium with III was established consisting of 50 ± 3% of both II and III. When either II or III was heated in tetrachloroethylene at 90 ± 1°, rapid first order reactions occurred, ($k_1 \approx k_{-1} \cong 4 \times 10^{-4}$ sec^{-1}) yielding an equilibrium mixture (II/III ≅ 48/52). Although Cope rearrangements are common in such systems,[5,7g,16] the nearly equal stability of II and III was surprising in light of the strain expected in the bridged ketone. However, steric interaction of the 2-Me and 6-Ph appears severe from models. Most importantly, the Cope rearrangement established adduct II as the endo Diels-Alder adduct.

Reaction of I and excess cyclopentene (115°, 3 days, benzene) gave an oily mixture of adducts which were inseparable by tlc, but could be separated by fractional crystallization from ethanol. The structure of endo adduct IV, mp 109.5-110.0° (lit.[14] mp 106°)(i.r., CCl_4; 5.64μ) was proven by its identity to the product of catalytic hydrogenation of cyclopentadiene adduct II. The nmr of the endo isomer IV displayed a sharp methyl resonance at 1.32ppm ($CDCl_3$). The exo isomer V,[15] mp 180.0-180.5° (i.r., CCl_4; 5.64μ) had a sharp methyl resonance at 1.15ppm in the nmr.



IV



V

The nmr of the crude reaction product of I and cyclopentene displayed sharp methyl resonances at 1.15 and 1.32ppm in a ratio of 56 ± 2:44 ± 2. Since both cyclopentene adducts proved to be stable upon prolonged heating at 120°, the rates of exo and endo adduct formation are essentially identical.

To determine the stereoselectivity of the addition of cyclopentadiene to I, the crude mixture from the reaction of I and cyclopentadiene was catalytically hydrogenated (5%Pd/C). The nmr of the crude hydrogenate showed an intense resonance at 1.32 ppm due to IV, and a very minor resonance at 1.15 ppm whose area amounted to less than 3% of the area of the 1.32 ppm resonance. The cyclopentadiene addition is, therefore, at least 97% stereoselective. Similarly, the reaction of I and cycloheptene produced a mixture of exo and endo adducts, while cycloheptatriene gave only the endo [4 + 2] adduct with I.[7g,17]

The presence of the second double bond in the dienophile transforms a nonselective process into a stereoselective process and appears to stabilize the endo transition state by 2.5-5.0 kcal/mole. We have considered the possibility of stabilizing inductive forces between saturated centers[18,19] and between dipoles[2] in the transition states and conclude that neither of these forces provide a viable explanation of the results.

Since I reacts in a nonselective fashion with cyclopentene, it may be tentatively concluded that the stereoselectivity of cyclopentadiene reactions with mono-olefins is due to steric repulsions of the methylene hydrogen of cyclopentadiene with the mono-olefin substituent. In our cases, only introduction of a second double bond in the dienophile results in stereoselectivity, testifying to the importance of secondary orbital interactions in the stabilization of the endo transition state.

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REFERENCES

(1) (a) K. Alder and G. Stein, Angew. Chemie., 50, 510 (1937); K. Alder Ann., 571, 87 (1951); (b) J. G. Martin and R. K. Hill, Chem. Reviews, 61, 537 (1961).

(2) (a) A. Wassermann, J. Chem. Soc., 828, 1511 (1935), 432 (1936), Trans, Farad. Soc., 35, 841 (1939); "Diels-Alder Reactions", Elsevier, New York, 1965); (b) E. W. Garbisch, Jr., and R. F. Sprecher, J. Amer. Chem. Soc., 91, 6758 (1969); (c) L. Horner and W. Dürckheimer, Chem. Ber., 95, 1219 (1962); (d) W.C. Herndon, unpublished results.

(3) R. B. Woodward and H. Baer, J. Amer. Chem. Soc., 66, 645 (1944).

(4) W.C. Herndon and L.H. Hall, Tetrahedron Letters, 3095 (1967).

(5) R. B. Woodward and T.J. Katz, Tetrahedron, 5, 70 (1959).

(6) R. Hoffmann and R. B. Woodward, J. Amer. Chem. Soc., 87, 4388 (1965); R. B. Woodward and R. Hoffmann Angew. Chemie internat. ed., 8, 781 (1969). These results may be generalized for all suprafacial cycloadditions: For [4m + 2] cycloadditions, the endo transition state will be stabilized when extending conjugation is present in the 2π system; for [(4m) + (4n + 2)] cycloadditions, (n≠ o) the endo transition state will be destabilized.

(7) (a) R. C. Cookson, B.V. Drake, J. Hudec and A. Morrison, Chem. Comm., 15 (1966); S. Itô, Y. Fujise, T. Okuda and Y. Inoue, Bull. Chem. Soc. Japan, 39, 135 (1966); S. Itô, K. Sakan, and Y. Fujise, Tetrahedron Letters, 775 (1969); (b) T. Nozoe, T. Mukai, K. Takase, Proc. Japan Acad., 28, 477 (1952); (c) S. Itô, Y. Fujise and M.C. Woods, Tetrahedron Letters, 1059 (1967); (d) L.A. Paquette and J.H. Barrett, J. Amer. Chem. Soc., 88, 2590 (1966); (e) L.A. Paquette, J.H. Barrett and D.E. Kuhla, ibid, 91, 3616 (1969) and references therein; (f) C. Cottrell, R.C. Dougherty, G. Fraenkel and E. Pecchold, ibid., 91, 7545 (1969) report an endo [6 + 4] cycloaddition of a pentadienyl anion to a diene. Since the major interaction will be between the NBMO (occupied) of the pentadienyl anion and ψ_3 (vacant) of the diene, the endo addition should be slightly favored; (g) K.N. Houk and R. B. Woodward, ibid., 92, 0000 (1970).

(8) P. Wilder, Jr., C.F. Culberson and G. T. Youngblood, ibid., 81, 655 (1960); S. J. Cristol, W.K. Seifert and S.B. Soloway, ibid., 82, 2351 (1960).

(9) S.B. Soloway, ibid., 74, 1027 (1952).

(10) K.B. Wiberg and W.J. Bartley, ibid., 82, 6375 (1960).

(11) N.A. Belikova, V.G. Berezkin and A.F. Platé, J. Gen. Chem. USSR, 32, 2896 (1962).

(12) L.A. Paquette, D.E. Kuhla, J. H. Barrett and L.M. Leichter, J. Org. Chem., 34, 2888 (1969).

(13) As the dissociating Diels-Alder dimer, C.F.H. Allen and J.A. Van Allan, J. Amer. Chem. Soc. 64, 1260 (1942); C.F.H. Allen and J.A. Van Allan, ibid., 72, 5165 (1950).

(14) C.F.H. Allen, J.E. Jones and J.A. Van Allan, J. Org. Chem., 11, 268 (1946).

(15) All new compounds gave satisfactory elementary analyses.

(16) P. Yates and P. Eaton, Tetrahedron, 12, 13 (1961).

(17) Partial decarbonylation of the cycloheptene adducts during the reaction prevented determination of the exo/endo ratio by simple nmr analysis.

(18) W.C. Herndon, J. Feuer, J. Amer. Chem. Soc., 90, 5914 (1969).

(19) K.L. Williamson, Y.L. Hsu, R. Lacko, C.H. Youn, ibid., 91, 6129 (1969).