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FRONTIER ORBITAL CONTROL OF REGIOSPECIFICITY IN SINGLET CYCLOADDITIONS OF 2-METHYLENECYCLOPENTA-1,3-DIYLS

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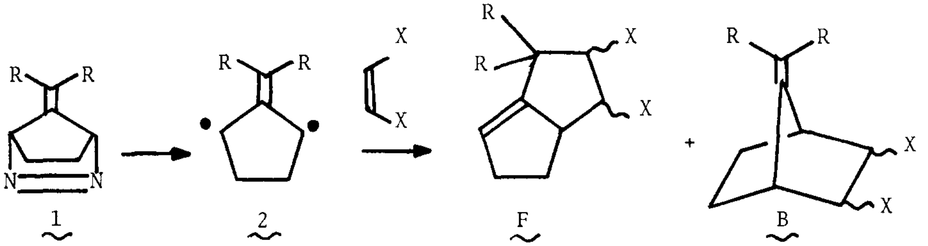
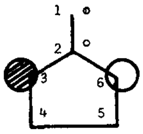
Although the reactions of the ground triplet state of the trimethylenemethane (TMM) 2-isopropylidenecyclopenta-1,3-diyl 2a, generated from diazene 1a, are nearly regiorandom, giving both fused (F) and bridged (B) cycloadducts, the singlet reactions are strongly regiospecific for fused product[1]. A rationalization of this effect[1b] suggests that the reactive singlet form of 2a may have a bisected configuration and hence that orbital overlap is unfavorable to the developing exocyclic double bond in the transition state leading to bridged cycloadduct. The present work puts forward a more satisfactory alternative explanation based upon the phase properties of the two nominally nonbonding (NB) molecular orbitals, the highest occupied (HOMO) and lowest unoccupied (LUMO), of a planar TMM. The new rationale encompasses the earlier results[1] as well as the striking reversals in regiospecificity we now observe.

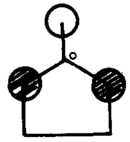


a: R = Me
b: R = H
c: R = OMe

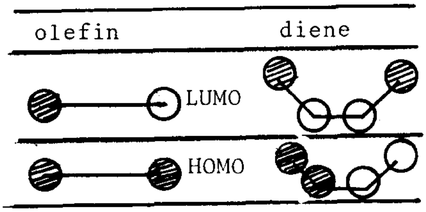
The phases of the TMM NBMOs of the dihydrogen diyl 2b may be represented as in A and S, which are, respectively, antisymmetric and symmetric under reflection in a mirror plane.



NBMO-A



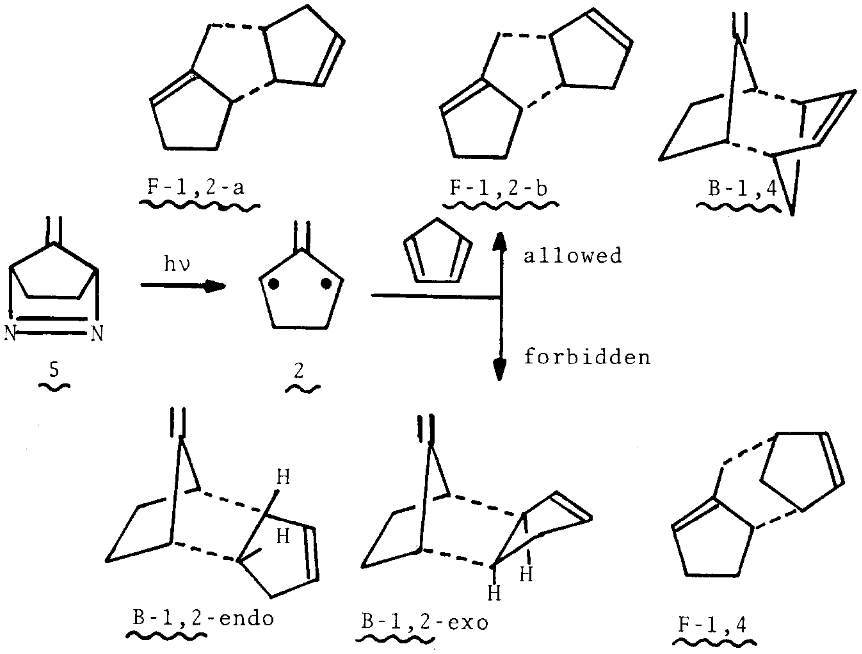
NBMO-S



If the reactive singlet has a closed shell electronic configuration and reacts concertedly with olefins[1] using the sterically preferred suprafacial-suprafacial transition state, we may deduce the symmetry allowed cycloaddition pathways from frontier orbital theory[2] by noting that positions 3 and 6 of NBMO-A or 1 and 6 of NBMO-S are in phase with an olefin LUMO. Thus, the formation of bridged or fused olefin cycloadducts will depend upon whether NBMO-A or -S, respectively, is the TMM HOMO. The observed high regiospecificity for fused product suggests the working hypothesis that in **2b** NBMO-S is the HOMO^3. A number of corollaries now are shown to agree with experiment.

The π-orbital phasings at positions 1 and 4 of a diene HOMO predict a *reversal* of regiospecificity in the cycloadditions of *dienes* to **2b**, the orbital symmetry allowed products being fused-1,2 and *bridged-1,4*. *No* such reversal is predicted by the earlier bisected diyl interpretation, since the poor orbital overlap in the bridged transition state would be equally bad for 1,2- and 1,4-cycloadditions.

Although thermolysis of diazene **1b** in the presence of the acyclic diene piperylene gives almost exclusively fused-1,2 product, some 1,4-addition can be encouraged with cyclopentadiene as the trapping agent, since the diene system now is "frozen" in the *s*-cis conformation. A convenient rate of thermal deazetation of **1b** requires temperatures above 50°, where cyclopentadiene monomer has only a short lifetime, especially at the high concentrations needed to trap singlet **2b**. Therefore, we generate the diyl by direct photolysis (350 nm,0°) of **1b** in the presence of concentrations varying from the neat hydrocarbon to dilute solutions in CH$_3$CN. The potential cycloadducts F-1,2-a (two isomers), F-1,2-b (two isomers), F-1,4 (two isomers), B-1,2 (two isomers), and B-1,4 (one isomer) are identified by gas chromatographic (gc) isolation, spectroscopic characterization, and in all cases but F-1,2, independent synthesis of the adduct or a derivative^4. The cycloaddition sites are shown with dashed lines.

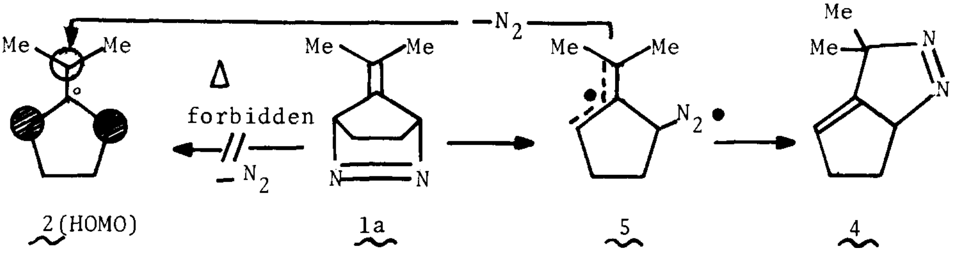


At high concentration of cyclopentadiene, the material balance of cycloadducts to reacting diazene is 98%. The dominant cycloadducts are F-1,2-a and F-1,2-b (75%) and B-1,4 (23%). Minor amounts (< 2%) of B-1,2 also are observed, but F-1,4 is not among the products (< 1%). Dilution of the reaction mixture leads to an increase in the B-1,2 isomers and one of the F-1,2 isomers, which suggests that these are largely triplet products^1. Under the highest concentration conditions achieved here, where singlet diyl reactions are optimized, the allowed products predominate over the forbidden ones by ratios of

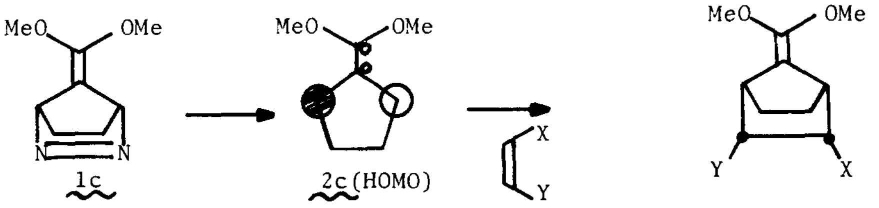
40 in the bridged series and >100 in the fused. These numbers represent minimum values for the regiospecificity, since it is not certain whether a small triplet component persists. Adduct B-14 is a single stereoisomer, the syn compound shown, in accord with the predictions of secondary orbital interactions analogous to those of *endo* Diels-Alder transition states[7].

Although the cycloadditions are most economically interpreted with the planar singlet as the *reactive* form, they are noncommittal on the relative stabilities of the planar *and bisected* diyls and on the rate of their interconversion.

Several other observations of TMM singlet chemistry find ready interpretations as orbital hierarchy phenomena. The electron-releasing effect of the methyl groups of the diyl 2a opposes[8] the energetic order A>S but apparently is insufficient to reverse it, since 2a also shows a strong preference for the formation of fused cycloadducts with olefins[1]. The thermal *cycloreversion* to diyls 2a or 2b and olefin from bridged adduct thus should be *orbital symmetry forbidden* reactions. Similar restrictions should apply to deazetation of the bridged diazenes 1a and 1b. The rearrangement to fused diazene 4 that accompanies the thermolysis of *bridged* diazene 1a[9] thus may be understood as recyclization of the diazenyl biradical 5, the *intermediate* in the nonconcerted, *stepwise* decomposition. The orbital symmetry constraints could be lifted in an *electronically* excited state of 1a, and it seems more than coincidental that the *photochemical* deazetation of 1a occurs with nearly unit quantum efficiency[10] *and without* rearrangement to 4[9].



Replacement of the Me groups of 1a by OMe increases the electron-releasing effect to the point where the LUMO-HOMO order is reversed to S>A. The switch manifests itself in two ways. First, the thermal deazetation of the bridged diazene 1c to the dimethoxy diyl 2c becomes orbital symmetry allowed and consequently much faster than that of 1a. Roughly extrapolated to a common temperature at -10°, the ratio of relative rates for 1c and 1a is about 10^4-10^5. Second, the regiospecificity of cycloaddition is reversed. With acrylonitrile (6) and dimethyl maleate (7) in Et$_2$O at 0°, the product ratios for capture of singlet 2c are 93:7 and >50:1, respectively, in favor of *bridged* adducts 8 or 9[11]. Further predictions of this model are under test[15].



6: X=H,Y=CN
7: X,Y=CO$_2$CH$_3$

8: X=H,Y=CN
9: X,Y=CO$_2$CH$_3$

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References and Notes

1. (a) J. A. Berson, C. D. Duncan, and L. R. Corwin, *J. Am. Chem. Soc.*, **96**, 6175 (1974); (b) J. A. Berson, L. R. Corwin, and J. H. Davis, *ibid.*, **96**, 6177 (1974); (c) J. A. Berson, C. D. Duncan, G. C. O'Connell, and M. S. Platz, *ibid.*, **98**, 2358 (1976).
2. (a) K. Fukui in "Molecular Orbitals in Chemistry, Physics, and Biology," P.-O. Lowdin and B. Pullman, Eds., Academic Press, New York, NY, 1964, pp. 513 ff; (b) K. N. Houk, *Accounts Chem. Res.*, **8**, 361 (1975), and references cited therein; (c) R. Sustmann, *Tetrahedron Lett.*, 2717 (1971); (d) I. Fleming, "Frontier Orbitals and Organic Chemical Reactions," Wiley, New York, NY, 1976, Chapter 4.
3. (a) A theoretical rationalization of the energy order NBMO-A>NBMO-S has been derived from extended Hückel calculations[3b]; (b) W. W. Schoeller, *J. Chem. Soc. Perkin II*, in press. We thank Dr. Schoeller for an advance copy of his paper.
4. Synthesis of ring-dihydro B-1,4 is achieved by successive steps of monohydrogenation and methylenation applied to a ketone (B-1,4 O instead of CH_2) from the reaction of cyclopentadiene and 1,3-dibromocyclopentanone in the presence of $Fe_2(CO)_9$. The latter reaction is modeled after literature precedent[5]. B-1,2-exo[9] is obtained from a second ketone product of the above reaction, while B-1,2-endo is obtained from the Diels-Alder dimer of cyclopentadienone. Compound F-1,4 is obtained by homologation and internal Wittig cyclization starting with bicyclo[3.2.1]oct-6-en-3-one[6]. All new substances gave correct elemental analyses or exact masses and concordant nmr and ir spectra.
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11. The ketene acetal cycloadducts **9** are hydrolyzed during work-up to norbornanetricarboxylic acid methyl esters and analyzed as such. Independent syntheses of these esters starts with the Diels-Alder adduct of 6-acetoxyfulvene and maleic anydride.
12. Dox Fellow, 1977-78.
13. NATO Postdoctoral Fellow, sponsored by the Science Research Council of Great Britain.
14. National Science Foundation Predoctoral Fellow, 1975-77.
15. One might preserve the bisected diyl interpretation as part of a less economical model involving *two* reactive forms of the singlet, the bisected species giving 1,2-cycloadduct and the planar giving 1,4. Similarly, the regiospecificity in the reactions of **1a** and **1b**, but *not* of **1c**, could be accounted for if the reactive singlet were a 5-alkylidenebicyclo[2.1.0] pentane.

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