

P. V. Alston and R. M. Ottenbrite

Department of Chemistry, Virginia Commonwealth University, Richmond, Virginia 23284
Received May 19, 1977

Generalizations which permit the prediction of the *syn/anti* selectivity in the $[\pi 4_s + \pi 2_s]$ cycloadditions of 7-substituted norbornadienes has been developed from perturbation molecular orbital theory. These theoretical predictions are in excellent agreement with all the experimental results reported in the literature. Furthermore, the effect of the 7-substituent of norbornenes on the double bond has been explained by the "through-space" interactions between the substituent and the *syn*-double bond.

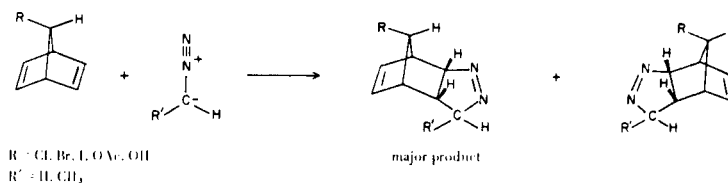
J. Heterocyclic Chem., **14**, 1443 (1977)

There is considerable interest in the *syn/anti* selectivity of the $[\pi 4_s + \pi 2_s]$ cycloaddition reactions of 7-substituted norbornadienes (1). A theory which accounts for the selectivity that has been observed in all the experimental studies has not been proposed. In this communication, perturbation molecular orbital theory is used to explain the *syn/anti* selectivity that has been observed.

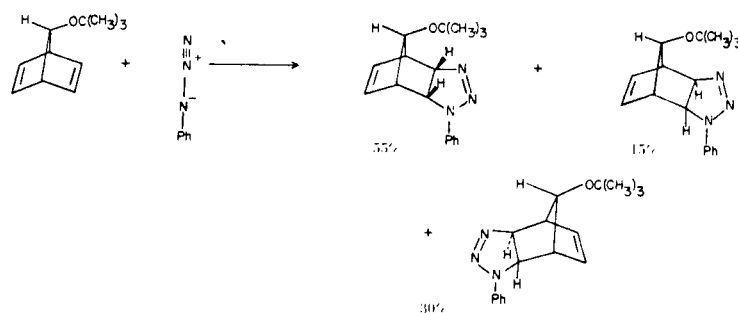
The reactivity and regioselectivity in cycloadditions have been successfully explained by considering only the

interactions between the frontier molecular orbitals (FMO) of the reacting molecules (2). This approach is based on the second-order perturbation equation for the energy change which accompanies the orbital interactions of two molecules involved in a cycloaddition (3). From the PMO equation, the following generalizations can be made: (a) the smaller the energy separation between the interacting molecular orbitals, the greater the reactivity; (b) the larger the coefficient magnitudes of the interacting orbitals,

Reaction 1 - Type I



Reaction 2 - Type II



Reaction 3 - Type II

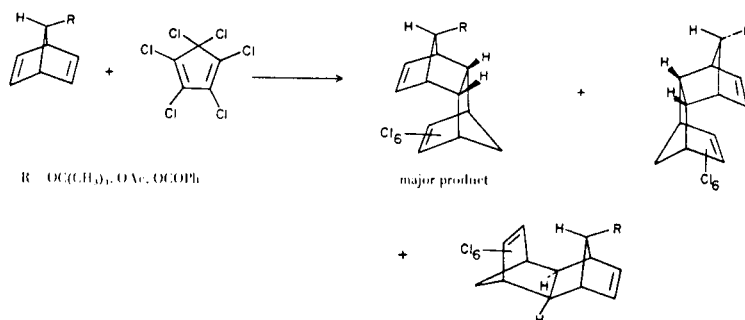


Table I

CNDO/2 Frontier Molecular Orbital Coefficients of 7-Substituted Norbornadiene

Substituent	Angle HCR	HOMO Coefficients (a)				LUMO Coefficients (a)			
		C-1	C-2	C-3	C-4	C-1	C-2	C-3	C-4
H	103.8 (opt.)	0.394	0.394	0.394	0.394	0.382	0.382	0.302	0.382
F	104.1 (opt.)	0.422	0.422	0.367	0.367	0.351	0.351	0.409	0.409
Cl	110.0	0.401	0.401	0.373	0.373	0.360	0.360	0.401	0.401
OH	106.1 (opt.)	0.415	0.415	0.375	0.375	0.355	0.355	0.404	0.404
HCOO	109	0.414	0.414	0.371	0.371	0.355	0.355	0.507	0.507
CN	104.1	0.389	0.389	0.399	0.399	0.376	0.376	0.387	0.387

(a) These are the absolute values of the P_2 coefficients. The other orbital coefficients were not zero; however, the trends in the coefficient magnitudes are the same as those of the P_2 coefficients.

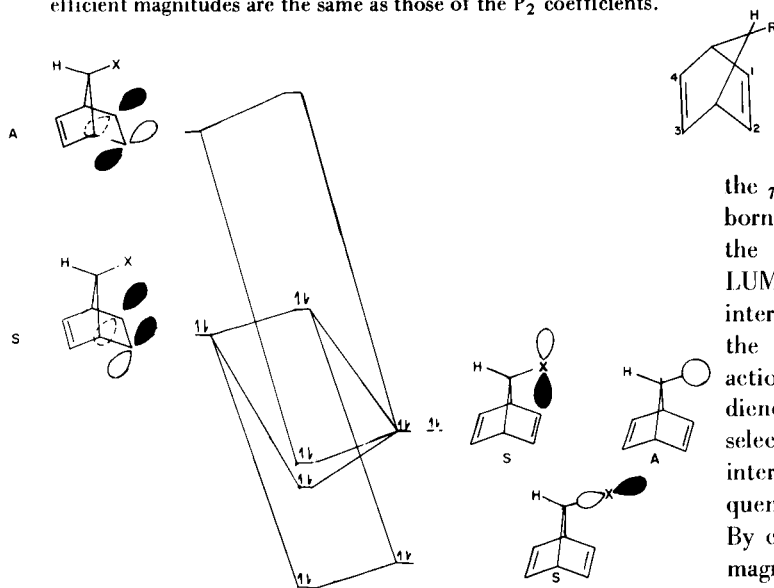


Figure 1. "Through-space" interactions between the nonbonded orbitals of the halo substituent and the *syn* double bond moiety.

the greater the reactivity. Since the π MO's of the double bond (DB) moieties of norbornadiene interact "through-space" to give more delocalized diene MO's, the effect of the 7-substituent on the magnitudes of the HOMO and LUMO coefficients of the DB moieties will determine the relative reactivity of the DB moieties and not its effect on the HOMO and LUMO energies.

CNDO/2 calculations (4,5) were carried out on various 7-oxy- and 7-halonorbornadienes to determine the effect of these substituents on the magnitudes of the FMO coefficients. In every case, the LUMO coefficients of the *anti*-DB were larger than the LUMO coefficients of the *syn*-DB while the HOMO coefficients of the *syn*-DB were larger than those of the *anti*-DB Table I. Furthermore, the [$\pi_4^s + \pi_2^s$] cycloaddition reactions of 7-substituted norbornadienes can be classified into three general types depending on the FMO arrangement of the reactants (6). In type I, the energy separation between the HOMO of

the π_4 reactants and the LUMO of the 7-substituted norbornadiene is much smaller than the separation between the HOMO of the 7-substituted norbornadiene and the LUMO of the π_4 reactant; consequently, the former FMO interaction determines the *syn/anti* selectivity. In type II, the FMO arrangement is reversed; therefore, the interaction between the HOMO of the 7-substituted norbornadiene and the LUMO of the π_4 reactant determines the selectivity. In type III, the energy separation between the interacting frontier molecular orbitals is similar; consequently, both FMO interactions can affect the selectivity. By considering the type of cycloaddition and the relative magnitudes of the FMO coefficients of the 7-substituted norbornadienes, the *endo syn/anti* selectivity can be predicted. The predictions are as follows: (a) For type I cycloadditions, *anti*-addition is preferred; (b) For type II cycloadditions, *syn*-addition is preferred; (c) For type III cycloadditions, no preference is expected. In the *exo* approach, the *anti*-addition will always be preferred because the *exo, syn*-transition state is deactivated by the closed-shell repulsion between the 7-substituent and π_4 reactant.

The experimental data that are available in the literature are in agreement with the predictions of the theory (Reactions 1, 2 and 3) except for the cycloaddition of diphenyldiazomethane with 7-*t*-butoxynorbornadiene (1,7). In this latter case, the bulkiness of the phenyl groups appears to cause steric effects to prevail over the FMO interactions (1a).

The effect of the halo- and oxy-substituents on the FMO coefficients can be predicted from the "through-space" interactions between the nonbonded orbitals of the substituent and the *syn*-DB. For example, a halo substituent has three nonbonded orbitals (8) which by symmetry interact with the HOMO and the LUMO of the *syn*-DB, thereby raising these MO's in energy (Figure 1).

Consequently, the *syn*-DB will have a LUMO and a HOMO of higher energy than the *anti*-DB. Since the π MO's of the DB moieties interact "through-space" to give more delocalized diene MO's, the LUMO of 7-halonorbornadiene will have more *anti*-DB character than *syn*-DB character. That is, the LUMO coefficients of the *syn*-DB will be smaller than those of the *anti*-DB moiety. By a similar rationale, the HOMO coefficients of the *syn*-DB are expected to be larger than those of the *anti*-DB.

Finally, if "through space" interactions are determining the coefficients magnitudes, the *endo syn/anti* selectivity should decrease as the interactions between the unoccupied MO's of the 7-substituent and the π MO's of the *syn*-DB become more important. The substituent effect on the selectivity (*Ot*-Butyl > OAc > OCOPh) in reaction 3 is in accord with this hypothesis. Further evidence for the theory was obtained from a CNDO/2 calculation on 7-cyanonorbornadiene. In this case the cyano substituent has low-lying unoccupied MO's which interact with the π MO's of the *syn*-DB and the respective CNDO/2 FMO coefficients of the DB moieties had similar magnitudes as expected from the theory (Table I).

Acknowledgment.

The authors wish to thank the Virginia Commonwealth University Computer Center for the computer time given to this study.

REFERENCES AND NOTES

- (1a) J. W. Witt and D. R. Sullivan, *J. Org. Chem.*, **40**, 1036 (1976); (b) W. Klumpp, A. Weefkind, W. de Graff, and F. Bickelhaupt, *Ann. Chem.*, **706**, 47 (1967); (c) M. Frank-Neumann and M. Sedrati, *Angew. Chem., Int. Ed. Engl.*, **3**, 606 (1974); (d) N. A. Battiste, J. F. Timberlake, and H. Malkus, *Tetrahedron Letters*, 2529 (1976); (e) K. B. Astin and K. Mackenzie, *J. Chem. Soc., Perkin Trans. II*, 1004 (1975); (f) L. T. Byrne, A. R. Rye, and D. Wege, *Aust. J. Chem.*, **27**, 1961 (1974).
- (2) P. V. Alston and R. M. Ottenbrite, *J. Org. Chem.*, **40**, 1111 (1975) and reference cited therein.
- (3) A detailed discussion of the theory is presented in a review by W. C. Herndon, *Chem. Rev.*, **72**, 157 (1972).
- (4) J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory", McGraw-Hill, New York, N. Y., 1970.
- (5) The geometries of the 7-substituted norbornadiene that were used in the calculations were a composite of Moecke and Davis' geometry of norbornadiene [*Trans. Am. Crystallogr. Assoc.*, **2**, 173 (1966)] and standard bond angles and bond lengths (4) for the 7-substituent. Reasonable variations in the bond angles and bond lengths of the 7-substituent did not effect the relative magnitudes of the FMO coefficients.
- (6a) R. Sustmann, *Tetrahedron Letters*, 2717 (1971); (b) R. Sustmann and H. Trill, *ibid.*, 839 (1972).
- (7) Houk's frontier molecular orbital energies for dipoles and dipolarphiles were used to classify the reactions with 1,3 dipoles [*J. Am. Chem. Soc.*, **95**, 7301 (1973)]. A kinetic study by Sauer [*Angew. Chem. Int. Ed. Engl.*, **6**, 16 (1967)] has shown that the Diels-Alder reactions of hexachlorocyclopentadiene are Type II.
- (8) O. Eisenstein, N. T. Anh, Y. Jean, A. Devaquet, J. C. Tocuzene, and L. Salem, *Tetrahedron*, **30**, 1717 (1974).