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APPLICATION OF PMO THEORY TO THE PROBLEM OF PERISPECIFICITY IN CROSS-CONJUGATED SYSTEMS WITH SPECIAL ATTENTION TO THE ISOBENZOFULVENE NUCLEUS

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The number of favourable pathways open to concerted cycloaddition reactions may be obtained easily through the application of the elegant set of rules formulated by Woodward and Hoffmann(*1*). The many symmetry-favoured pathways may be characterized in terms of periselectivity (the preference for one favoured route)(*2a*), regioselectivity (orientational preference)(*2b*)and stereoselectivity (*exo vs endo* cycloaddition). The problem of stereoselectivity has been analyzed on the assumption that secondary orbital overlap is the significant factor(*1*). Regioselectivity has been treated using an expression based on perturbational molecular orbital (PMO) theory (*3*). However, this expression was derived on the assumption that only one bond is formed initially and it cannot be applied satisfactorily to the problem of periselectivity. There is scant application of PMO theory to the problem of periselectivity. Although it was foreshadowed by Herndon and his co-workers(*4*), Goe has critized(*5*) some of the PMO methods and has proposed that periselectivity may be analyzed in terms of the properties of hypothetical intermediate diradicals. However this method suffers from the disadvantage that somewhat *ad hoc* procedures are invoked when dealing with antarafacial additions and additions involving cross-conjugated systems. One of us has found recently(*6*) that an expression based on simple PMO theory does in fact predict quite accurately the major reacting pathway.

We report here its application to pericyclic reactions involving cross-conjugated systems with special reference to isobenzofulvenes (IBF) (I), recently synthesized by Tanida(*7a*) (6,6-dimethyl IBF) and by ourselves(*7b*) (6,6-dimethyl and 6,6-diphenyl IBF).

The method involves essentially, computing the second order perturbation energy which has been truncated to include only those terms involving the HOMOs and LVMOs of *both* components (eq. 1):

$$E = \frac{2\delta^2(a_r^{HO}b_s^{LV} + a_t^{HO}b_u^{LV})^2}{E_A^{HO} - E_B^{LV}} + \frac{2\delta^2(a_r^{LV}b_s^{HO} + a_t^{LV}b_u^{HO})^2}{E_B^{HO} - E_A^{LV}} \qquad \text{(eq.1)}$$

Where the two conjugated molecules A and B are interacting at the pairs of atoms r,s and t,u and a_r^{HO} is the coefficient of the atomic orbital of the rth atom in the highest occupied molecular orbital of A. The matrix element of the perturbation, δ, is taken to be the same at both bond forming sites*, and Hückel π-type MOs and energies were used. Five model cross-conjugated systems were studied and for each system *all* realistic favoured cycloaddition reactions were considered(*8*). Many of the systems which have been investigated experimentally were substituted and we make the approximation that their behaviour parallels that of the parent compounds(*9*). The results (see table) show that good agreement exists between these predictions and the available experimental data.

Table

System	No. of Modes Studied	Preferred Mode of Cycloaddition	Experimental Results	Ref.
Heptafulvalene + Ethylene	3	$[_\pi 4_s + {_\pi 2_s}]$[a] $[_\pi 14_a + {_\pi 2_s}]$[b]	$[_\pi 14_a + {_\pi 2_s}]$	*10a*
Heptafulvene + Acetylene	2	$[_\pi 8_s + {_\pi 2_s}]$	$[_\pi 8_s + {_\pi 2_s}]$	*10b*
Sesquifulvalene + Ethylene	6	$[_\pi 4_s + {_\pi 2_s}]$[c]	$[_\pi 4_s + {_\pi 2_s}]$	*10c*
Isobenzofulvene + Ethylene	3	$[_\pi 8_s + {_\pi 2_s}]$	$[_\pi 8_s + {_\pi 2_s}]$	*7a,b,c.*
Isobenzofulvene dimerization	8[d]	$[_\pi 10_s + {_\pi 8_s}]$	$[_\pi 10_s + {_\pi 8_s}]$	This work and *7a*

[a] *Calculations were based on the assumption that the molecule had planar geometry.* [b]. *The molecule was considered as having S shaped geometry - see text.* [c]. *Addition occurs across the 7,10 bond of sesquifulvalene (10c).* [d]. *Including those modes differing only in the regiochemical sense.*

If the assumption is made that heptafulvalene is planar and that interaction between the atoms 2 and 14 (and 7 and 9) are absent, then calculations suggest that the $[_\pi 4_s + {_\pi 2_s}]$ mode is favoured. However the molecule possesses an S shaped geometry(*11*) which allows for reasonable overlap between the atoms 2 and 14 (and 7 and 9). Calculations(*6*) based on this thought correctly predicted the favoured $[_\pi 14_a + {_\pi 2_s}]$ mode.

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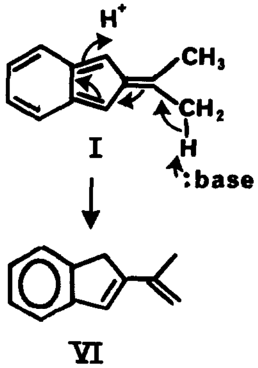
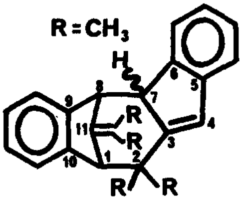
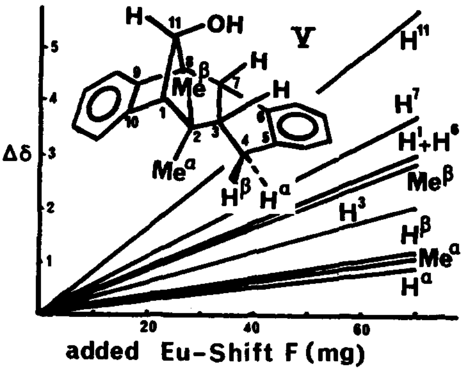
* *The assumption that the matrix elements* δ_{rs} *and* δ_{tu} *are equal implies that the new bonds are being formed synchronously.*

ISOBENZOFULVENES: Since our own results were different from those reported in the recent work of Tanida and his co-workers(*7a*) we report our findings and structure proof at this point. We find that 6,6-dimethylisobenzofulvene generated via our s-tetrazine route(*12*) undergoes spontaneous dimerization to form a *mixture of two isomers*.† The major product, m.p. 152°, was shown to be dimeric by mass spectrometry (*m/e* 312, parent, *m/e* 156 base peak) and readily formed a dihydroderivative (single isomer, m.p. 95°, *m/e* 314) upon hydrogenation (Pt/H_2), which yielded the ketone IV (m.p. 152°, *m/e* 288, $i.r._{CO}$ 1760 cm^{-1}) upon ozonolysis. Reduction with $NaBH_4$ formed a single alcohol, m.p. 124° (*m/e* 290, $i.r._{OH}$ 3300-3800 cm^{-1}) which was subjected to L.I.S. nmr spectroscopy [$Eu(Fod)_3$] and this, coupled with spin decoupling experiments, clearly supported the stereochemical assignment shown in V.





II★ H^7exo
III H^7endo
IV 3,4di-H,11-oxo
★ endo-dimer



Tanida based his structural proof on NOE experiments and his product, also assigned structure II, appears identical with this, the major isomer. Our work now clarifies the problem and the chemical reactivity is now in accord with the assigned structure.

The similarity in the p.m.r. spectrum (*inter alia,* 4 singlet methyl resonances, and three methine protons) and ultraviolet spectrum of the minor dimer (m.p. 150°, *m/e* 312) compared with the major dimer, together with its ready conversion to a dihydro compound (m.p. 94°, *m/e* 314) suggests that these isomers have related structures, simply differing by the stereochemistry about H7. This is supported by their p.m.r. spectra which show that the coupling between H7 and H8 in the major dimer is 4Hz, but less than 1Hz in the minor dimer, values consistent with the angular relationship of these protons as judged by inspection

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† *This mixture was constant over a wide range of solvents, including dioxan, and confirms the isopolar nature of the transition state. These isomers were not thermally interconvertible. The free 6,6-dimethyl IBF could not be detected, but could be trapped as its* [$_{\pi}8_s + _{\pi}2_s$] *adduct with a variety of tetraenophiles (e.g., N-methylmaleimide, exo-isomer m.p. 211°; endo-isomer m.p. 213°) or diverted to the indene VI in the presence of acid or base. The 6,6-diphenyl IBF also formed adducts but no dimeric material(7b).*

of Dreiding models (48° and 88° respectively).

Thus our finding fully confirms the high perispecificity of the reaction, but raises the question of stereospecificity in this cyclodimerization reaction. Since two isomers are formed (ratio *ca.* 4:1), it appears that the *exo*- and *endo*-transition states are not as significantly different in energy as it would appear from Tanida's report(*7a*). Consideration of HOMO/LVMO interactions based on the phase compatibilities(*1*) of the Hückel MOs of IBF does not allow a clear distinction between the two transition states in terms of secondary orbital stabilization since each transition state contains some stabilization terms. On the other hand, application of the $[_{\pi}4_{m} + (_{\pi}4_{n} + _{\pi}2)]$ rule summarized by Houk(*13*), and also our PMO calculation, favour the *exo*-transition state.

An explanation for this anomaly may involve a strong steric contribution from the 6-substituents of the IBF nucleus. Indeed we find that the 6-substituents in the IBF nucleus markedly influence the *exo/endo* isomer ratio in simple $[_{\pi}8_{s} + _{\pi}2_{s}]$ cycloadditions, e.g. the *exo/endo* ratio drops from 1:3 to 1:19 with maleic anhydride when reacting with 6,6-dimethyl and 6,6-diphenyl IBF respectively. Thus the apparent preference for the *endo*-transition state in this dimerization may simply reflect such steric contributions (expected to favour the *endo*-isomer) since pericyclic reactions are known to be subject to steric effects(*13*), and this point is currently being further investigated.

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