ORBITAL INTERACTIONS THROUGH SPACE I. A NEW REACTION PROBE FOR INVESTIGATING

THE ELECTRONIC REQUIREMENTS OF $[_\pi4_s + _\pi2_s]$ PERICYCLIC REACTIONS.

Michael N. Paddon-Row and Ronald N. Warrener

Department of Chemistry, Australian National

University, Canberra, A.C.T. 2600 Australia.

Cyclopropenes(*1*), and to a lesser extent cyclobutenes(*2*), by virtue of
their strain behave as highly reactive dienophiles in $[_\pi4_s + _\pi2_s]$ pericyclic
reactions towards both normal dienes (electron rich) and dienes possessing
inverse electron demand (electron poor). Reactions with dienes of the latter
type such as *s*-tetrazines are facilitated by increasing electron availability
in the dienophile, as deduced from studies on substituent-rate correlations(*3*).
In general these substituents are chosen such that they operate on the electron
availability at the reaction zone through perturbations of the σ- and π-bonds
directly connecting the two. To our knowledge, marked substituent effects on
the reactivity of dienophiles are only observed when one σ-bond separates the
(non conjugating) substituent from the reaction zone. It has been established
by volume activation studies(*4*) that the transition state in $[_\pi4_s + _\pi2_s]$ (Diels-
Alder) reaction is smaller than the adduct and so the rate of reaction is
particularly sensitive to steric effects. Indeed it is difficult to separate
the steric from the electronic influence in the above-mentioned substituent-
rate correlations.

We propose that judicious use of orbital interactions through space
allows these effects to be completely separated, since electronic modification
of the reaction centre can be achieved without introducing concomitant steric
perturbations. This can be illustrated by the reaction of the cyclobutenes
(II a,b,c) with 3,6-di(2'-pyridyl)-*s*-tetrazine(I). In this reaction the
dienophile approaches from the least hindered side of the cyclobutene, [see
III→V, Scheme] , while the electronic modificand is on the opposite side at the

9-position of the tricyclic system. The details of this reaction have not been delineated*, however the loss of N_2 from the initially formed adduct is extremely facile and so the kinetic results should truely reflect the reactivity of II a,b,c.

a) X = Y = H   b) X = Y = O   c) X = H ; Y = OCH$_3$

Py = 2'-pyridyl
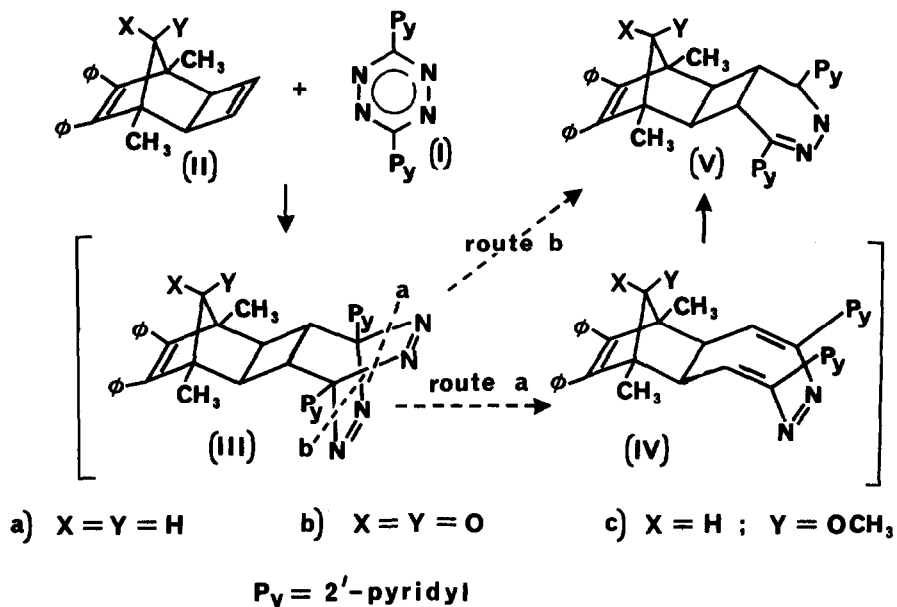
In order to evaluate the magnitude of the electronic effect of this reaction we have carried out a kinetic study of the reaction. The reaction was followed spectrophotometrically using the peak at 550 nm due to the tetrazine as the monitor.

---

*   Rapid loss of N_2 from the first formed intermediate adduct (III) preculdes its direct identification. However we feel that attack by (I) onto the least hindered face of the cyclobutene (II) is strongly favoured. We prefer loss of that nitrogen which enables participation by the cyclobutane σ-bond (i.e. route a), since there is excellent precedent in similar systems(5). The p.m.r. spectrum of each final product (Va,b,c) confirms that it exists in the tetracyclic form (V), obviously derived from the tricyclic form (IV) via the thermally allowed disrotatory 6Π-electrocyclic valence isomerisation. Satisfactory analytical data was obtained for compounds (Va,b,c) and spectral data were in accord.

Table: Kinetic Data

for the reaction of (I) with (II) at 23.8° in chloroform solution.

Compound	Rate ($10^2 K$, $1 \text{ m}^{-1} \text{s}^{-1}$)	Relative Rates
IIa[+]	26.7	$k_a/k_b = 22.3$; $k_c/k_a = 27.3$
IIb[+]	1.2	
IIc[‡]	729	

+for preparation see ref 2b.   ‡ new compound. Prepared from
the hydroxy compound, by methylation of the Na Salt in DMSO
with MeI, m.p. 104°

With respect to the unsubstituted compound (IIa) we observe (see table) that the rate of the 9-methoxy compound (IIc) is enhanced by a factor of 22, whereas the 9-carbonyl compound (IIb) is diminished by a comparable amount. Considering that four σ-bonds intervene between the substituents and the cyclobutene double bond, these substituent effects are substantial. In agreement with the known reverse-electron demand of s-tetrazines(3) the decrease in the rate of the 9-carbonyl compound (IIb) indicates that the cyclobutene is more electronegative than that in (IIa); similarly that in (IIb) is more electron rich. These effects are those intuitively assigned to these compounds in view of the known electronic effects of such groups.* The nature of the orbital interactions which allow this through space effect is elaborated upon in the accompanying letter.

E =
COOC₂H₅

(VI)   (VII)   (VIII)
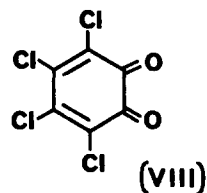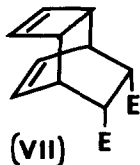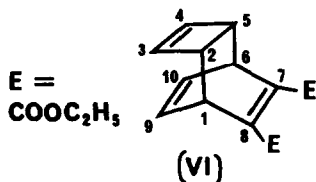
While kinetic studies have only been carried out in the above-mentioned series, other systems have been studied qualitatively. Indeed the decreased reactivity of the cyclobutene (VI) relative to the cyclobutene (VII) in its reaction with s-tetrazine (I) or with o-chloranil (VIII) is quite marked (6).

---

*   Intuitive reasoning is not always correct, even qualitatively. See accompanying communication.

The reason is not obvious, except when viewed in terms of the present orbital effect. Thus the 7,8-dicarbomethoxy groups in (VI) make the $\Delta_{7,8}$-olefin electron deficient. This effect is transferred to the $\Delta_{3,4}$-position (either through bond or via orbital overlap involving the $\Delta_{9,10}$ olefinic group).[†] No such effect is possible in (VII). This results in the relative electron density of the $\Delta_{3,4}$-dienophilic centre in (VI) being less than that in (VII), and accounts for the decreased reactivity of (VI) compared with (VII), as both the $_{\pi}4_{s}$ components display reverse electron demand. As predicted this order is reversed when 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-2,4-diene is used as the $_{\pi}4_{s}$ component.

REFERENCES

1. *inter alia* a) K.B. Wiberg and W.J. Bartley, *J. Amer. Chem. Soc.*, **82**, 6375 (1960). b) W. Dittmar, G. Heinrichs, A. Steigel, T. Troll and J. Sauer, *Tetrahedron Letters*, 1623 (1970).

2. *inter alia* a) R.J. Shozda and R.E. Putman, *J. Org. Chem.*, **27**, 1557 (1962). b) C.M. Anderson, I.W. McCay and R.N. Warrener, *Tetrahedron Letters*, 2735 (1970).

3. J. Sauer, *Angew. Chem. internat. edit.*, **6**, 16 (1967).

4. R.A. Grieger and C.A. Eckert, *J. Amer. Chem. Soc.*, **92**, 7149 (1970).

5. E.L. Allred and J.C. Hinshaw, *Chem. Comm.*, 1021 (1969).

6. It has been established that these cycloadditions occur exclusively at the $\Delta_{3,4}$-position. R.N. Warrener, E.E. Nunn and W.S. Wilson, *unpublished results*.

† A more detailed treatment has been carried out (M.P-R), but further discussion of this will be reserved for the full paper.