

1,3-Dipolar Character of Six-membered Aromatic Rings. Part XXI.¹ Thermal Cycloadditions of 1-(5-Nitro-2-pyridyl)- and 1-(4,6-Dimethylpyrimidin-2-yl)-3-oxidopyridinium with 2, 4, and 6 π -Electron Components

By Nicholas Dennis, Badreldin Ibrahim, and Alan R. Katritzky,* School of Chemical Sciences, University of East Anglia, Norwich NR4 7TJ

The regio- and stereo-selectivities of reactions of the title compounds at the 2- and 6-positions with mono- and di-substituted ethylenes are elucidated and rationalised by FMO theory including secondary orbital overlap and taking into account steric and dipolar effects. For monosubstituted ethylenes, FMO theory correctly predicts that electron donor, electron acceptor, and conjugated olefins all add in the same regioselective sense. Stereoselectivity is shown to depend rationally on the structures of the betaine and the addend.

Buta-1,3-diene, its 2,3-dimethyl and 1-monomethyl derivatives, and cyclopentadiene add as 4 π -electron addends at the 2- and 4-positions of the betaines. Such reactions are favoured kinetically, but under thermodynamic control reaction also occurs with the diene acting as a 2 π -addend at the 2- and 6-positions of the betaine. The periselectivities and stereoselectivities are discussed in terms of FMO theory: the reversal of electron demand leading to easier reaction with electron-rich dienes is explained by PNIFLS.

Fulvenes add at the betaine 2- and 6-positions. Peri-, regio-, and stereo-selectivity are successfully rationalised in terms of FMO theory.

THE preceding paper¹ describes the preparation of dimers [(1) and (2)] of the nitropyridyl betaine (3) and the pyrimidinyl betaine (4) and, in impure form, of the monomer of the betaine (3). MO predictions that the betaines (3) and (4) should undergo thermal suprafacial cycloaddition reactions with both 2 and 6 π -electron components across the 2- and 6-positions and with 4 π -electron components across the 2- and 4-positions were supported by the structure of the dimers.¹ We now report a variety of such reactions.

Relative Reactivity of the Dimers (1) and (2) and the Monomer (3).—The dimers are stable crystalline compounds, which can be stored unchanged indefinitely, and which form convenient sources of nascent monomer. That the dimer (2a) changes spontaneously to a mixture rich in the dimer (2b), whereas the dimer (1) does not readily undergo analogous change, suggests that the dissociation into monomer is more rapid for (2): we do find that (2) is considerably more reactive in cycloadditions than (1). Moreover the dimer (1) is considerably less soluble in dipolarophile-solvent mixtures than

the pyrimidinyl dimer (2a and b) and hence less convenient to use. Additionally, there is evidence¹ that the pyrimidinyl dimer (2) is in equilibrium with significant amounts of the monomer even at 20° C.

For reactions with volatile dipolarophiles, the monomer (3) has been used: it is extremely reactive, but its use is inconvenient for three reasons, (a) it cannot be obtained pure; (b) yields are low as large quantities of the dimer (1) are formed during the reaction; and (c) the monomer (3) deteriorates on storage.

In all the cycloadditions studied, quinol was added to minimize polymerisation of the dipolarophiles.

Cycloadditions to 2 π -Electron Addends

Monosubstituted Ethylenes (Table 1).—The nitropyridyl betaine dimer (1) gives good yields of the mixed *exo*- (8) and *endo*-adducts (7) with acrylic addends. Methyl vinyl ketone gave with the nitropyridyl betaine monomer the same *exo*- and *endo*-adducts in the same ratio but

¹ Part XX, N. Dennis, B Ibrahim, and A. R. Katritzky, preceding paper.

poorer yield than with the dimer. With styrene, substituted styrenes, and 4-vinylpyridine, good yields were again obtained from dimer (1) but the *endo*-adduct (7) greatly predominated: traces of the corresponding

istic splitting patterns simplify structure elucidation. For example, in the spectrum of the *endo*-adduct (7c), the double doublets at δ 5.91 (J 9.7 and 1.4 Hz) and 7.29 (J 9.7 and 5.0 Hz) were assigned to H-3 and H-4,

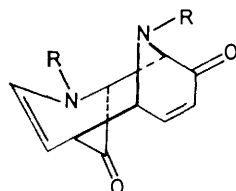
TABLE 1

Yields of *endo*- and *exo*-adducts [cf. (7) and (8)] formed from 1-substituted 3-oxidopyridiniums with monosubstituted ethylenes

Ethylene substituent	N-Substituent of 3-oxidopyridinium											
	Methyl ^a		Hydrogen ⁴		Phenyl ²		2,4-Dinitrophenyl ⁵		5-Nitro-2-pyridyl ^a		4,6-Dimethylpyrimidin-2-yl ^a	
	<i>exo</i>	<i>endo</i>	<i>exo</i>	<i>endo</i>	<i>exo</i>	<i>endo</i>	<i>exo</i>	<i>endo</i>	<i>exo</i>	<i>endo</i>	<i>exo</i>	<i>endo</i>
CO ₂ Me		75	50	50	24	41	25	25	75	25		
CN	21	21	50	50	31	39	37	28	32	48		<i>b</i>
COMe		<i>b</i>		<i>b</i>		<i>b</i>	<i>b</i>	<i>b</i>	59	21		<i>b</i>
C ₆ H ₅		0		<i>b</i>	0	50	>5	50	7	83	0	68
<i>p</i> -MeO·C ₆ H ₄		<i>b</i>		<i>b</i>		<i>b</i>		<i>b</i>	0	69		<i>b</i>
<i>p</i> -ClC ₆ H ₄		<i>b</i>		<i>b</i>	0	63		<i>b</i>	0	77		<i>b</i>
<i>p</i> -BrC ₆ H ₄		<i>b</i>		<i>b</i>	0	60		<i>b</i>	0	69		<i>b</i>
4-Pyridyl		<i>b</i>		<i>b</i>	0	55		<i>b</i>	0	52		<i>b</i>
OEt		<i>b</i>		<i>b</i>	0	0	0	0	0	25		<i>b</i>

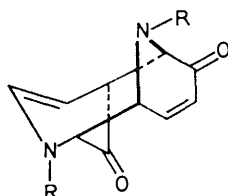
^a Reactions with dimers except in the case of CH₂=CH-OEt. ^b Reaction not attempted.

exo-adducts (8) were detected by t.l.c. and, in the case of styrene itself, isolated. In a single reaction with the pyrimidinyl dimer (2), styrene gave the *endo*-isomer [cf. (7j)] in 68% yield. Ethyl vinyl ether afforded only the *endo*-isomer (7i) (25%) with the nitropyridyl monomer (3).

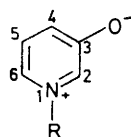


(1) R = 5-nitro-2-pyridyl

(2a) R = 4,6-dimethylpyrimidin-2-yl



(2b) R = 4,6-dimethylpyrimidin-2-yl

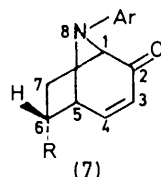


(3) R = 5-nitro-2-pyridyl

(4) R = 4,6-dimethylpyrimidin-2-yl

(5) R = 2,4-dinitrophenyl

(6) R = Ph



(7)

a: R = CO₂Me, Ar = 5-nitro-2-pyridyl

b: R = CN, Ar = 5-nitro-2-pyridyl

c: R = COMe, Ar = 5-nitro-2-pyridyl

d: R = Ph, Ar = 5-nitro-2-pyridyl

e: R = *p*-MeO·C₆H₄, Ar = 5-nitro-2-pyridyl

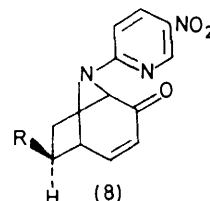
f: R = *p*-ClC₆H₄, Ar = 5-nitro-2-pyridyl

g: R = *p*-BrC₆H₄, Ar = 5-nitro-2-pyridyl

h: R = 4-pyridyl, Ar = 5-nitro-2-pyridyl

i: R = OEt, Ar = 5-nitro-2-pyridyl

j: R = Ph, Ar = 4,6-dimethylpyrimidin-2-yl



(8)

a: R = CO₂Me

b: R = CN

c: R = COMe

d: R = Ph

The regio- and stereo-structures of the foregoing adducts were based on the n.m.r. spectra (Table 2). We have already discussed such spectra,² whose character-

and the broad double doublet at δ 5.51 for the bridgehead proton H-5 (J 5.0, 6.0 Hz) to collapse to a broad doublet

² N. Dennis, A. R. Katritzky, T. Matsuo, S. K. Parton, and Y. Takeuchi, *J.C.S. Perkin I*, 1974, 746.

(J 6.0 Hz). Similarly the H-5 signal collapsed to a doublet (J 5.0 Hz) on irradiation at the frequency of the multiplet due to H-6-*exo* at δ 3.68. Irradiation at the frequency of H-1 (δ 4.76) removed the long-range W-coupling between H-1 and H-3 and caused the octet at δ 2.82 of H-7-*exo* (J 8.5, 10.5, and 13.7 Hz) to collapse to a double doublet (J 10.5 and 13.7 Hz). The large *cis*-coupling constant ($J_{6-exo,7-exo}$ 10.5 Hz) also confirms this assignment. The quartet at δ 2.17 was assigned to

(δ 2.11) was identified by its geminal coupling constant of 14.0 Hz to H-7-*exo*. The double doublet at δ 3.13 was assigned to H-6-*endo* on the basis of its coupling to H-7-*exo* by 4.0 and to H-7-*endo* by 9.5 Hz. Irradiation at frequency of the vinylic proton H-4 (δ 7.35) caused collapse of the H-5 signal (δ 5.51) to a singlet, indicating the absence of any appreciable coupling of H-5 to H-6, which confirms the *endo*-configuration of H-6 and hence the *exo*-configuration of the acetyl group.

TABLE 2

Proton n.m.r. spectra of cycloadducts * derived from monosubstituted ethylenes ^a													
	(7a) ^b	(7b) ^c	(7c) ^b	(7d) ^b	(7e) ^b	(7f) ^b	(7g) ^b	(7h) ^b	(7i) ^b	(7j) ^b	(8a) ^b	(8b) ^b	(8c) ^b
Chemical shifts (δ)													
1	4.80 ^d	5.10 ^d	4.76 ^d	4.91 ^d	4.90 ^d	4.90 ^d	4.91 ^d	4.86 ^d	4.67 ^d	5.17 ^d	4.91 ^d	4.84 ^d	4.85 ^d
3	5.99 ^d	6.18 ^d	5.91 ^d	6.03 ^d	6.05 ^d	5.97 ^d	6.07 ^d	6.02 ^d	6.06 ^d	5.98 ^d	5.98 ^d	5.90 ^d	5.95 ^d
4	7.28 ^d	7.60 ^d	7.29 ^d	6.89 ^d	6.94 ^d	6.81 ^d	6.91 ^d	6.85 ^d	7.20 ^d	6.85 ^d	7.38 ^d	7.22 ^d	7.35 ^d
5	5.53 ^d	5.68 ^d	5.51 ^d	5.52 ^d	5.48 ^d	5.44 ^d	5.53 ^d	5.56 ^d	5.30 ^d	5.52 ^d	5.58 ^e	5.47 ^e	5.51 ^e
6- <i>endo</i>											3.15 ^d	3.22 ^d	3.13 ^d
6- <i>exo</i>	3.66 ^f	3.93 ^f	3.68 ^f	4.07 ^f	4.00 ^f	3.95 ^f	4.03 ^f	4.00 ^f	4.49 ^e	4.01 ^f			
7- <i>endo</i>	2.27 ^d	2.01 ^d	2.17 ^d	2.20 ^d	2.16 ^d	2.07 ^d	2.17 ^d	2.16 ^d	1.78 ^d	2.05 ^d	2.17 ^d	2.40 ^d	2.11 ^d
7- <i>exo</i>	2.87 ^f	3.06 ^f	2.82 ^f	3.05 ^f	3.01 ^f	2.97 ^f	3.08 ^f	3.03 ^f	2.97 ^f	2.93 ^f	3.00 ^f	2.95 ^f	2.81 ^f
3'	6.57 ^e	7.03 ^e	6.57 ^e	6.61 ^e	6.63 ^e	6.55 ^e	6.64 ^e	6.60 ^e	6.53 ^e		6.34 ^e	6.61 ^e	6.59 ^e
4'	8.23 ^d	8.37 ^d	8.21 ^d	8.22 ^d	8.26 ^d	8.18 ^d	8.29 ^d	8.24 ^d	8.19 ^d		8.23 ^d	8.20 ^d	8.18 ^d
5'										6.38 ^g			
6'	8.98 ^e	8.90 ^e	9.00 ^e	9.00 ^e	9.07 ^e	8.96 ^e	9.08 ^e	9.02 ^e	8.98 ^e		8.97 ^e	8.97 ^e	8.97 ^e
CO ₂ Me	3.73 ^g										3.73 ^g		
C(O)Me			2.24 ^g										
CMe													2.26 ^g
Ph				7.26 ^h						7.27 ^h			
ArMe										2.30			
O-Me					3.82 ^g								
2''					7.20 ^e	7.22 ^e	7.50 ^e	8.57 ^e					
3''					6.90 ^e	7.12 ^e	7.15 ^e	7.13 ^e					
OCH ₂ -CH ₃										3.57			
OCH ₂ -CH ₃										1.21 ^f			
Coupling constants (Hz)													
1, 3	1.4												
1, 7- <i>exo</i>	8.3	8.3	8.5	8.5	8.2	8.5	8.5	8.2	8.0	8.5	8.2	8.2	8.2
3, 4	9.7	10.0	9.7	9.7	10.0	9.7	9.7	10.0	9.7	10.0	9.7	10.0	9.7
4, 5	4.9	5.0	5.0	5.0	4.7	5.0	5.0	5.0	5.0	5.0	5.1	5.0	5.2
5, 6- <i>exo</i>	6.4	6.1	6.0	6.0	6.3	6.0	6.0	6.0	6.0	6.5			
6- <i>endo</i> , 7- <i>endo</i>			1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.4		1.4
6- <i>endo</i> , 7- <i>exo</i>											9.8	9.2	9.5
6- <i>exo</i> , 7- <i>endo</i>	6.5	6.1	7.0	7.3	7.5	7.4	7.0	7.0	4.8	7.0	3.5	3.4	4.0
6- <i>exo</i> , 7- <i>exo</i>	10.5	10.5	10.5	9.7	9.5	10.0	10.0	9.5	8.0	10.0			
7- <i>endo</i> , 7- <i>exo</i>	14.0	13.9	13.7	14.0	14.0	14.0	14.0	14.0	14.0	14.0	14.5	14.0	14.0
3', 4'	9.2	9.2	9.3	9.2	9.2	9.2	9.3	9.2	9.3	9.3	9.3	9.2	9.3
4', 6'	2.8	2.8	2.7	2.7	2.8	2.7	2.8	2.8	2.7		2.7	2.7	2.6
1,7- <i>endo</i>	1.3						1			1.5			
2'', 3''					9.0	8.5	8.5	6.0					
CH ₂ CH ₃											7.0		

^a In p.p.m. relative to Me₄Si as internal standard. ^b In CDCl₃. ^c In (CD₃)₂SO. ^d Double doublet. ^e Doublet. ^f Octet. ^g Singlet. ^h Multiplet. ⁱ Quartet. ^j Triplet.

* For numbering see formula (7); single primes for 8-substituent; double primes for 6-substituent.

H-7-*endo* since it was coupled to H-7-*exo* (J 13.7 Hz), characteristic of a geminal coupling constant. Thus the acetyl group must be at C-6, having the *endo*-configuration.

Again in the spectrum of the *exo*-adduct (8c), irradiation at the frequency of a doublet at δ 4.85 removed the fine splitting (1.4 Hz) in the signals of H-3, and simplified an octet at δ 2.81. Accordingly the doublet was assigned to H-1 and the octet to H-7-*exo*. The H-7-*endo* signal

In all the above cycloadducts, the *exo*-protons at C-6 and C-7 are deshielded by 0.6–1.0 p.p.m. with respect to their *endo*-counterparts, by the enhanced anisotropy of the bridge nitrogen.

Regioselectivity in Addition of Monosubstituted Ethylenes.—In none of the foregoing reactions were any of the 7-substituted regioisomers (9) detected: similar behaviour has been observed with 1-methyl-,³ 1-phenyl-,² and 1-unsubstituted-3-oxidopyridinium,⁴ and only in

³ A. R. Katritzky and Y. Takeuchi, *J. Chem. Soc. (C)*, 1971, 874.

⁴ J. Banerji, N. Dennis, J. Frank, A. R. Katritzky, and T. Matsuo, *J.C.S. Perkin I*, 1976, 2334.

the reaction of 1-(2,4-dinitrophenyl)-3-oxidopyridinium with acrylonitrile was a small quantity of the 7-regioisomer isolated.⁵ For the electron-deficient dipolarophiles, this regioselectivity could be explained by the high electron density of the 2-position of a pyridinium ring 3-substituted with an electron-donor; *cf.* the electrophilic substitution pattern of 3-substituted pyridines⁶ and the electron densities calculated (see *e.g.* ref. 1) by the CNDO/2 MO method (10).

plexing phenomenon which has led some investigators to propose⁷ a stepwise diradical mechanism for such reactions. A rationalisation within the framework of a concerted mechanism is provided by PMO treatments at various levels of sophistication.⁸ Equation (1) was derived within the Hückel approximation and although it accounts only for the interactions of the frontier orbitals of addends R through the positions r and r' and S through the positions s and s' , it successfully predicts

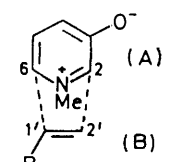
TABLE 3

Calculated frontier orbital energies and coefficients of 1-methyl-3-oxidopyridinium, methyl vinyl ether, acrylonitrile, and methyl acrylate

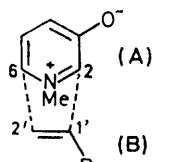
E/eV	1-Methyl-3-oxidopyridinium		H ₂ C=CH·OMe		H ₂ C=CH·CN		H ₂ C=CH·CO ₂ Me	
	HOMO	LUMO	HOMO	LUMO	HOMO	LUMO	HOMO	LUMO
C ₁	-8.912 9	1.293 2	-13.62 6	5.605 8	-14.647 5	3.540 0	-14.069 4	2.728 9
C ₂	0.528 6	0.487 2	0.397 4	0.722 3	0.481 9	0.534 9	0.296 2	0.429 3
C ₄	0.344 2	-0.488 3	0.623 2	-0.664 1	0.592 5	-0.653 1	0.379 7	0.619 1
C ₆	-0.384 1	0.415 2						

TABLE 4

Perturbation energy (ΔE /eV) for formation of regioisomers in the cycloadditions of 1-methyl-3-oxidopyridinium (A) to methyl acrylate, acrylonitrile, and methyl vinyl ether (B)



(A)
(B)



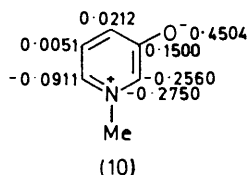
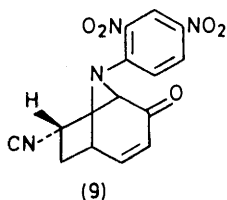
(A)
(B)

R	2,2'-6,1'			2,1'-6,2'		
	HOMO (A)- LUMO (B) contribution	HOMO (B)- LUMO (A) contribution	Total energy	HOMO (A)- LUMO (B) contribution	HOMO (B)- LUMO (A) contribution	Total energy
CO ₂ Me	-0.041 6	-0.012 3	-0.053 9	-0.037 1	-0.011 9	-0.049 0
CN	-0.048 7	-0.030 0	-0.078 7	-0.045 7	-0.029 0	-0.074 7
OMe	-0.054 4	-0.029 4	-0.083 8	-0.055 9	-0.027 4	-0.083 3

However, this explanation does not account for the similar regioselectivity found for the styrenes, and especially for the electron-rich dipolarophile ethyl vinyl ether. The matter can be treated by the FMO method already previously briefly discussed in the preceding

the correct orientation in many Diels-Alder⁹ and 1,3-dipolar cycloaddition reactions.¹⁰

The total interaction energy ΔE measures the transition state stabilisation during the process of bond formation, and larger values of ΔE therefore signify more ready reactions. Frontier energy levels and coefficients at possible positions of reaction of 1-methyl-3-oxidopyridinium, methyl vinyl ether, acrylonitrile, and methyl acrylate calculated by the CNDO/2 method¹¹ are given in Table 3. These energies and coefficients have been used to calculate the perturbational energies for adduct formation at the two possible orientations which are given in Table 4. It is apparent in the case of addition to methyl acrylate and acrylonitrile that both FMO interactions lead to larger values of ΔE for the observed regioisomer 2,2'-6,1' than for 2,1'-6,2'. In the case of



paper¹ with regard to the orientation of dimer formation.

Regioselectivity in cycloaddition has long been a per-

⁵ N. Dennis, B. Ibrahim, A. R. Katritzky, I. G. Taulov, and Y. Takeuchi, *J.C.S. Perkin I*, 1974, 1883.

⁶ A. R. Katritzky and J. M. Lagowski, 'Principles of Heterocyclic Chemistry,' Methuen, London, 1967, p. 33.

⁷ R. A. Firestone, *J. Org. Chem.*, 1968, **33**, 2285; *J. Chem. Soc. (A)*, 1970, 1570; *J. Org. Chem.*, 1972, **37**, 2181.

⁸ W. C. Herndon, *Chem. Rev.*, 1972, **72**, 157; A. R. Katritzky, N. Dennis, and Y. Takeuchi, *Angew. Chem. Internat. Edn.*, 1976, **15**, 1.

⁹ J. Feuer, W. C. Herndon, and L. H. Hall, *Tetrahedron*, 1968, **24**, 2575.

¹⁰ K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Amer. Chem. Soc.*, 1973, **95**, 7301.

¹¹ G. P. Ford, unpublished results.

addition to methyl vinyl ether, although the HOMO (betaine)-LUMO (dipolarophile) interaction which favours formation of isomer 2,1'-6,2' is unexpectedly large, the total FMO interaction is still in favour of the observed isomer 2,2'-6,1'. The disadvantage of using calculated rather than experimentally determined FMO energy levels in the calculations resulted in the unexpectedly large value of ΔE for the HOMO(betaine)-LUMO(dipolarophile) interaction in the case of addition to methyl vinyl ether which then led to the wrong prediction that the latter dipolarophile should add faster than methyl acrylate and acrylonitrile to 3-oxidopyridinium.

$$\Delta E = \frac{2[(C_r^{\text{HO}} C_s^{\text{LU}} + C_r^{\text{HO}} C_s^{\text{LU}})\gamma]^2}{E_R^{\text{HO}} - E_S^{\text{LU}}} + \frac{2[(C_r^{\text{LU}} C_s^{\text{HO}} + C_r^{\text{LU}} C_s^{\text{HO}})\gamma]^2}{E_S^{\text{HO}} - E_R^{\text{LU}}} \quad (1)$$

Stereoselectivity in Reactions of Monosubstituted Ethylenes.—The stereoisomeric composition of the cycloadducts isolated from the reactions of 1-substituted-3-oxidopyridiniums with monosubstituted ethylenes are collected in Table I. Stereoselection in 1,3-dipolar additions and Diels-Alder reactions has been reviewed.¹² Alder and Stein¹³ proposed that the transition state with the maximum accumulation of double bonds leads to the product, and this rule was developed quantitatively.¹⁴ Hoffmann and Woodward¹⁵ rationalised stereoselection by secondary orbital overlap of the frontier orbitals in the transition state, between centres in the two addends not directly involved in bond-formation. Such overlap is essentially positive in $[2_s + 4_s]$ processes and negative in $[4_s + 6_s]$ processes. Consequently the former proceed preferentially *via* the *endo*-transition states while the latter favour the *exo*-transition state. Restricting Alder's rule to $[2_s + 4_s]$ cycloaddition thus gives it a theoretical basis. Secondary orbital control of stereoselection has, since then, been confirmed in a variety of concerted cycloadditions.

In the addition of a conjugated addend to an aromatic betaine, distinction between *exo*- and *endo*-addition is not immediately straightforward. Addition to the 2- and 6-positions of 3-oxidopyridinium may be considered to involve either the five-atom fragment [as in (b)] or the three-atom fragment [as in (a); Figure 1]: in both cases the betaine behaves as a 4π -component. Although the distinction between *exo*- and *endo*-addition is thus apparently lost, if stereoselection is controlled by secondary orbital overlap, the five-atom fragment (b) should be more important in this respect, and additions in which the bulk of the π -system of the addend points towards this fragment should be regarded as *endo*. Hence for the present cycloadditions, both *exo*- and *endo*-modes of addition will be subject to secondary

overlap interactions, but with some preference for the *endo*-mode.

Dipole-dipole interactions are particularly important for polar dipolarophiles, since the betaine itself is highly polar. Berson and his co-workers¹⁶ used an electrostatic model for the Diels-Alder addition of methyl acrylate, methyl *trans*-crotonate, and methyl metha-

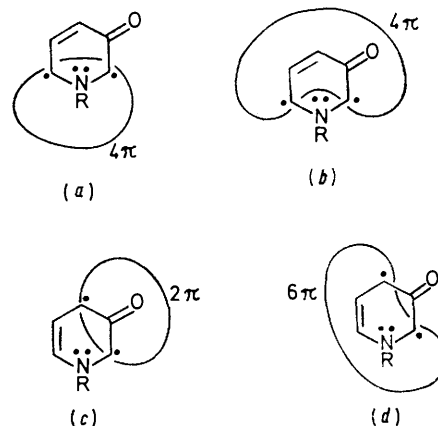


FIGURE 1 π -Components involved in cycloaddition to the 2- and 6- and the 2- and 4-positions of 3-oxidopyridinium

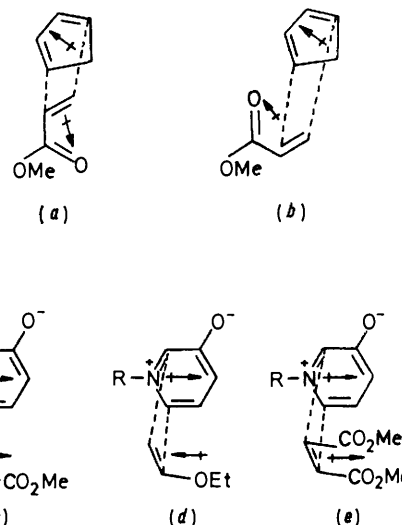


FIGURE 2 Dipole-dipole interactions during cycloadditions to cyclopentadiene and 3-oxidopyridinium

crylate to cyclopentadiene to calculate *exo* : *endo* ratio as a function of the solvent polarity. Permanent dipoles in the *exo*-transition state [Figure 2(a)] are opposite in direction and attract, whereas in the *endo*-orientation (b) they are parallel and repel each other. Increase in the solvent polarity progressively stabilised the *endo*-orientation (b). The model predicted correctly the effect of solvent polarity on the *exo* : *endo* ratio. Neglect of secondary orbital overlap in this model led to the incorrect finding that the *exo*-isomer will predominate

¹⁶ J. A. Berson, Z. Hamlet, and W. A. Mueller, *J. Amer. Chem. Soc.*, 1962, **84**, 297; J. A. Berson and W. A. Mueller, *Tetrahedron Letters*, 1961, 131.

¹² R. Huisgen, *Angew. Chem. Internat. Edn.*, 1963, **2**, 633; S. Seltzer, *Adv. Alicyclic Chem.*, 1968, **2**, 1.

¹³ K. Alder and G. Stein, *Angew. Chem.*, 1937, **50**, 510.

¹⁴ E. W. J. Butz and L. W. Butz, *J. Org. Chem.*, 1942, **7**, 199.

¹⁵ R. Hoffmann and R. B. Woodward, *J. Amer. Chem. Soc.*, 1965, **87**, 4388.

in non-polar solvents. The third main factor which affects stereoselectivity in cycloadditions is steric repulsion by bulky groups in the addends: thus although most addends gave the *endo*-adducts with 1,3-diphenylisobenzofuran¹⁷ and 1,3-diphenyl-4-oxidobenzopyrylium betaine, dimethyl maleate gave the *exo*-adducts.

all these adducts are 6-regio-substituted isomers: in particular for (11) the H-1 and H-5 signals appear as a doublet and a doublet ($J_{1,7-exo}$ 8.2, $J_{4,5}$ 5.2 Hz) respectively while the H-7-*exo* signal (δ 3.21) appears as a doublet with geminal coupling of 14.0 Hz to H-7-*endo*.

TABLE 5
Proton n.m.r. spectra of cycloadducts^b derived from disubstituted ethylenes^a

Chemical shifts (δ)	(11) ^b	(12) ^b	(13) ^b	(16) ^b	(17) ^c	(18a, b) ^{b, d}		(19) ^b	(20) ^b
1	4.76 ^e	4.91 ^e	4.80 ^e	5.35 ^f	5.49 ^e	4.92 ^e	4.62 ^e	5.12 ^f	5.20 ^e
3	6.10 ^e	5.73 ^e	6.10 ^e	6.00 ^e	6.16 ^e	6.12 ^e	5.86 ^e	5.99 ^e	6.00 ^e
4	7.31 ^e	7.09 ^e	7.40 ^e	7.42 ^e	7.56 ^e	7.34 ^e	7.39 ^e	7.28 ^e	7.43 ^e
5	5.38 ^f	5.49 ^f	5.50 ^f	5.68 ^f	5.77 ^e	5.28	5.05	5.61 ^e	5.56 ^f
6- <i>endo</i>				3.54 ^f					3.65 ^f
6- <i>exo</i>					4.49 ^e			4.03 ^e	
7- <i>endo</i>	1.68 ^f	2.60 ^f	2.64 ^f	3.42 ^f				3.51 ^f	
7- <i>exo</i>	3.21 ^e	2.64 ^e	3.18 ^e		4.72 ^e				4.20 ^e
3'	6.59 ^f	6.63 ^f	6.46 ^f	6.77 ^f	7.08 ^f	6.52 ^f	6.52 ^f	6.63 ^f	6.63 ^f
4'	8.23 ^e	8.23 ^e	8.13 ^e	8.24 ^e	8.41 ^e	8.16 ^e	8.18 ^e	8.13 ^e	8.25 ^e
6'	8.97 ^f	9.00 ^f	8.98 ^f	8.99 ^f	8.94 ^f	8.93 ^f	8.93 ^f	8.97 ^f	9.13 ^f
CO ₂ Me				3.72 ^g				3.80 ^g	3.78 ^g
				3.69 ^g				3.78 ^g	3.73 ^g
Ph		7.28 ^h	7.30 ^h						
Norbornane						0.7—2.6 ^h	0.7—2.6 ^h		
CMe	1.28 ^g	1.60 ^g	1.54 ^g						
CH(O)	9.61 ^g								
Coupling constants (Hz)									
1, 3	1.5	1.4	1.5	1.4	1.4	1.5	1.5	1.4	1.4
1, 7- <i>exo</i>	8.2	7.3	9.0		8.7				8.0
3, 4	9.7	9.8	9.6	9.7	9.7	9.7	9.7	9.7	9.7
4, 5	5.2	5.0		5.3	5.1	5.0	6.0	4.8	5.3
5, 6- <i>exo</i>					7.1			6.3	
6- <i>endo</i> , 7- <i>endo</i>				9.5					
6- <i>endo</i> , 7- <i>exo</i>									4.5
6- <i>exo</i> , 7- <i>exo</i>					9.2				
7- <i>endo</i> , 7- <i>exo</i>	14.0	13.6	14.2						
3', 4'	9.3	9.2	9.3	9.2	9.1	9.3	9.3	9.2	9.3
4', 6'	2.7	2.8	2.8	2.7	2.8	2.8	2.8	2.7	2.8
6- <i>exo</i> , 7- <i>endo</i>								6.3	

^a In p.p.m. relative to Me₄Si as internal standard. ^b In CDCl₃. ^c In (CD₃)₂SO. ^d Numbered as in formula (7); the numbering used in structure (18) is non-systematic, for comparison only. ^e Doublet. ^f Doublet. ^g Singlet. ^h Multiplet.

In the present investigation the formation of the *endo*-adduct prevails in the addition of 3-oxidopyridinium to styrene, *para*-substituted styrenes, 4-vinylpyridine, and ethyl vinyl ether. Stereoselectivity is lost in the addition of the *N*-aryl betaines to acrylonitrile, methyl acrylate, and methyl vinyl ketone: here, the secondary overlap is weaker, and the steric and dipole-dipole interactions [Figure 2(c)] stronger which leads to considerable formation of the *exo*-adduct.

Conjugated dipolarophiles give mainly the *endo*-adduct (83% *endo*, 7% *exo* in the case of styrene), evidently owing to the predominance of secondary overlap over the weak dipole-dipole interaction.

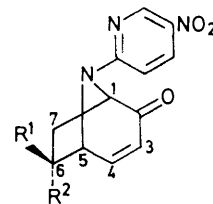
Reversal in polarity of ethyl vinyl ether leads to a favourable dipole-dipole interaction [Figure 2(d)] which is responsible for the sole formation of the *endo*-adduct.

1,1-Disubstituted Ethylenes.—Methacrylaldehyde gave a single adduct (11) (58%) and α -methylstyrene the two adducts (12) (51%) and (13) (30%) with the nitropyridyl dimer (1). N.m.r. spectra (Table 5) show clearly that

¹⁷ J. W. Lown and K. Matsumoto, *Canad. J. Chem.*, 1971, **49**, 3443.

¹⁸ N. Dennis, A. R. Katritzky, and R. Rittner, following paper.

The stereostructure of the methacrylaldehyde adduct was elucidated by lanthanide shift (LIS) effects (see Figure 3). The high LIS on H-1 and H-3 indicate



(11) R¹ = Me, R² = CHO

(12) R¹ = Me, R² = Ph

(13) R¹ = Ph, R² = Me

preferential complexation of the lanthanide to the ring carbonyl group: this very fact indicates the *endo*-orientation of the formyl group because in the analogous series [(14) and (15)], whereas the *exo*-methoxycarbonyl derivative (14) complexes by chelation with the nitrogen and CO₂Me, the *endo*-derivative (15) complexes again at the ring carbonyl group.¹⁸

Structures were assigned to the stereoisomeric α -methylstyrene adducts from the fact that only (12) underwent ring closure (see discussion in ref. 19). The

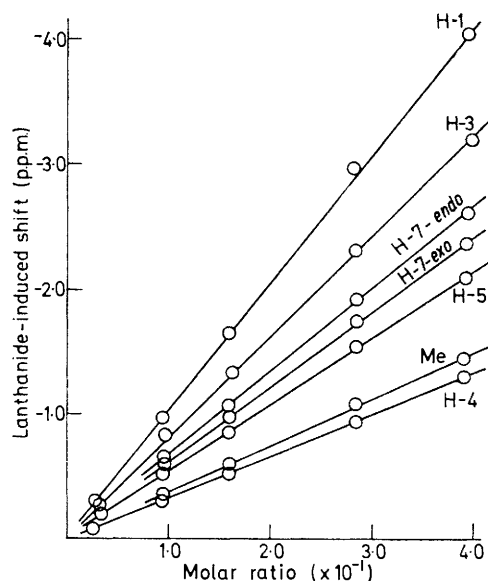
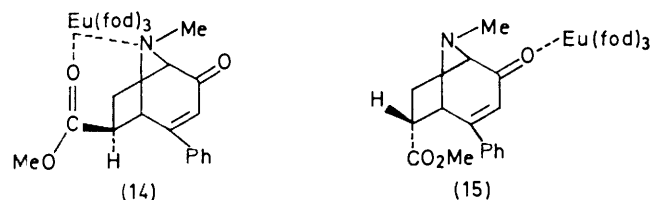
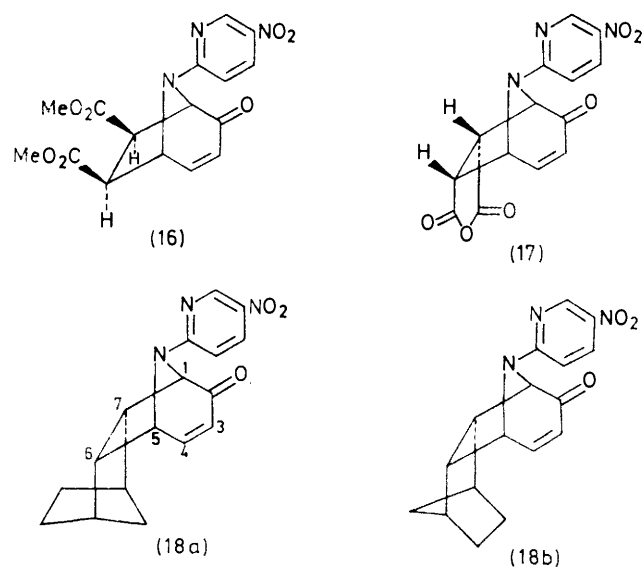


FIGURE 3 $\delta\Delta$ vs. molar ratio of lanthanide $[\text{Eu}(\text{fod})_3]$ to substrate for compound (11)

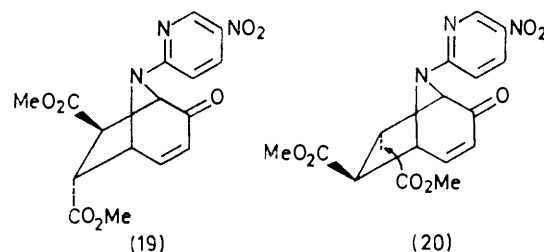
fact that methacrylaldehyde gives mainly the *endo*-formyl adduct whereas methyl vinyl ketone gives both



stereoisomers underlines the importance of steric repulsion by the methyl groups.

1,2-Disubstituted Ethylenes.—Several *cis*-1,2-disubstituted ethylenes react with the nitropyridyl betaine dimer (1) to give single adducts in good yields: dimethyl maleate gave the *exo*-adduct (16) (90%), whereas maleic anhydride formed the *endo*-adduct (17) (92%). Norborn-2-ene gave a mixture of adducts (18a and b) (59%).

The nitropyridyl dimer was less reactive towards *trans*-1,2-disubstituted olefins: no reaction occurred with stilbene, and β -methyl-, β -bromo-, and β -nitro-styrene gave poor yields of mixed stereoisomeric adducts which were not isolated pure. However dimethyl fumarate afforded the two adducts (19) (36%) and (20) (54%).



Structures (16)—(20) were assigned from the n.m.r. spectra (Table 5). In the ^1H n.m.r. spectrum of (19) (Table 5) the double doublet at δ 5.61 was assigned to H-5 on the basis of its coupling to the vinylic H-4 ($J_{4,5}$ 4.8 Hz). The *exo*-configuration of H-6, and consequently the *endo*-configuration of the methoxycarbonyl group at C-6, is proved by the large coupling (6.3 Hz) with H-5. The appearance of the H-1 signal as a fine doublet at δ 5.12 with no appreciable coupling to H-7 indicated the *endo*-configuration of the latter proton and accordingly the *exo*-configuration of the methoxycarbonyl group at C-7. However in the ^1H n.m.r. spectrum of the adduct (20) the absence of appreciable coupling between H-5 (a doublet at δ 5.56) and H-6 (a doublet at δ 3.65), indicates the *exo*-configuration of the methoxycarbonyl group at C-6. The large coupling (J 8.0 Hz) between H-1 (a double doublet at δ 5.20) and H-7 (double doublet at δ 4.20) indicates the *endo*-configuration of the methoxycarbonyl group at C-7. In the case of the adduct (16) the lack of coupling between H-5 and H-6, and between H-1 and H-7, fixes both methoxycarbonyl groups at C-6 and C-7 in the *exo*-configuration. The large *cis*-coupling constant ($J_{6\text{-endo},7\text{-endo}}$ 9.5 Hz) supports this configuration. Furthermore, H-6-*endo* (δ 3.54) and H-7-*endo* (δ 3.42) are not deshielded by the bridge nitrogen atom which effectively deshields H-6-*exo* (δ 4.03) in (19) and H-7-*exo* (δ 4.20) in (20). The *endo*-structure was indicated clearly in the ^1H n.m.r. spectrum of the maleic anhydride adduct (17) by the large coupling constants ($J_{5,6}$ 7.1, $J_{1,7}$ 8.7 Hz). ^1H n.m.r. spectra (Table 5) of the norborn-2-ene adducts exhibited the expected pattern for H-4 and H-3. The bridgehead protons, H-1 and H-5, gave

¹⁹ N. Dennis, B. Ibrahim, and A. R. Katritzky, *Synthesis*, 1976, 105.

broad absorptions, but the H-1 signal is evidently not a singlet in both isomers, indicating that we are dealing with the two possible *endo*-isomers (18a and b).

Cycloadditions with dimethyl fumarate to give (19) and (20) and with dimethyl maleate to give (16) occur with complete retention of the stereochemistry about the ethylenic double bond: t.l.c. of the crude reaction mixture from dimethyl fumarate showed no detectable trace of (16) and that from dimethyl maleate no trace of (19) or (20). This provides good evidence for the concerted character of these cycloaddition reactions.

As already discussed, *endo*-addition of conjugated olefins is favoured by secondary orbital overlap,¹⁵ and disfavoured by steric factors and dipole-dipole interactions (Figure 2e).^{16,20} With maleic anhydride and *N*-phenylmaleimide, steric factors are minimal, allowing the favourable formation of the *endo*-adducts (*cf.* Figure 4). There is a weak positive secondary interaction between the HOMO of 1-methyl-3-oxidopyridinium and

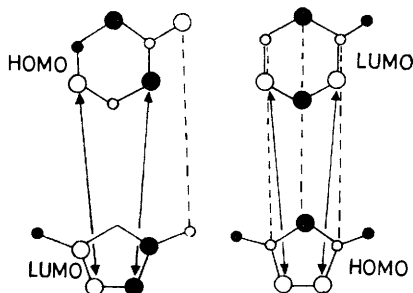


FIGURE 4 Secondary orbital interactions in the *endo*-addition of maleic anhydride (ref. 21) to 3-oxidopyridinium

the LUMO²¹ of maleic anhydride which, according to the interfrontier energy separation, is the predominant interaction. However, 1-methyl-3-oxidopyridinium³ (10) gives the *exo*-adduct (72%) with *N*-phenylmaleimide; here dipole-dipole interactions are evidently more important than secondary overlap.

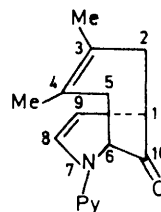
However, interaction between the LUMO of the betaine and the HOMO of maleic anhydride incurs a strong positive secondary overlap. In agreement, changing the structure of the betaine to lower the LUMO increases the proportion of the *endo*-isomer. Thus 1-phenyl-3-oxidopyridinium (6) gives 45% of the *endo*-adduct and 36% of the *exo*-adduct with *N*-phenylmaleimide,² whereas the dinitrophenyl (5)⁵ and the nitropyridyl betaines (3) give exclusively the *endo*-adducts.

With dimethyl maleate, steric factors prevent the formation of the *endo*-adducts. 1,3-Diphenylisobenzofuran¹⁷ and 1,3-diphenyl-4-oxidobenzopyrylium betaine¹⁷ generally gave *endo*-adducts with various dipolarophiles but gave *exo*-adducts with dimethyl maleate and *cis*-stilbene.

Cycloadditions to 4 π -Electron Addends

1,3-Dienes can react either as 2 π -electron components across the betaine 2- and 6-positions or as 4 π -electron components across the 2- and 4-positions. The different

types of adduct are clearly distinguished spectroscopically. The type of reaction entered into depends on the

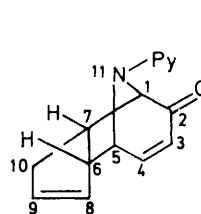


(21) Py = 5-nitro-2-pyridyl

(22) Py = 4,6-dimethylpyrimidin-2-yl

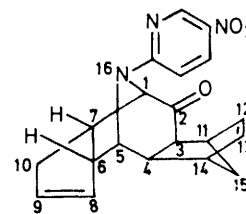
diene substitution pattern, thus 2,3-dimethylbuta-1,3-diene yields predominantly single adducts (21) (90%) and (22) (71%) with the relevant betaine dimers, while penta-1,3-diene forms with both complex mixtures.

Temperature also appears to influence the orientation; thus cyclopentadiene with the nitropyridyl betaine dimer (1) gives only (24) (34%), evidently formed by initial attack as a mono-ene at the 2- and 6-positions to give (23), which then undergoes Diels-Alder reaction with more cyclopentadiene to give (24). The nitropyridyl betaine monomer forms a mixture of the primary 2,6-adduct (23) (45%) together with the 2,4-adduct (25) (37%). By contrast the pyrimidinyl betaine dimer gives appreciable quantities of the 2,4-adduct (26) (42%) and the 2,6-adduct (27) (21%). We believe that this dependence on temperature is a result of the 2,6-adducts being

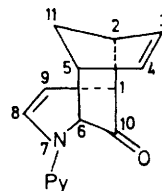


(23) Py = 5-nitro-2-pyridyl

(27) Py = 4,6-dimethylpyrimidin-2-yl



(24)



(25) Py = 5-nitro-2-pyridyl

(26) Py = 4,6-dimethylpyrimidin-2-yl

thermodynamically the more stable, with the 2,4-adducts formed preferentially under conditions of kinetic control.

Additions to 2,3-Dimethylbuta-1,3-diene.—The nitropyridyl betaine dimer (1) reacted at 50–60 °C in chlorobenzene with this diene to afford the stable 2,4-adduct

²⁰ J. A. Berson, A. Remanick, and W. A. Mueller, *J. Amer. Chem. Soc.*, 1960, **82**, 5501.

²¹ W. C. Herndon and L. H. Hall, *Theor. Chim. Acta*, 1967, **7**, 4.

(21) (90%). The pyrimidinyl betaine dimer (2a or b) similarly gave the stable adduct (22) (71%) in 1,2-dichloroethane at 60 °C.

The i.r. spectra of (21) and (22) show strong $\nu(\text{C}=\text{O})$ bands at 1720 cm^{-1} for the saturated cyclic ketone, and medium $\nu(\text{C}=\text{C})$ bands at ca. 1640 cm^{-1} for the enamine double bond. The ^1H n.m.r. spectrum of (21) (Table 6

at δ 2.40 (J 14.7 and 6.7 Hz) to a doublet (J 14.7 Hz). No appreciable coupling between H-1 and H-2-*endo* was observed. Protons at position 1 as well as 6 are greatly affected by the shift reagent owing to their proximity to the complexation site. Irradiation at the frequency of H-6 reduced the double doublet of H-5-*exo* originally at δ 3.05 (J 14.9 and 7.2 Hz) to a doublet

TABLE 6
Proton n.m.r. spectra of cycloadducts * derived from dienes ^a

Chemical shifts (δ)	(21) ^{b,c}	(22) ^{b,d}	(23) ^{b,e,f}	(24) ^{b,f,g}	(25) ^{b,f,h}	(26) ^{b,f,i}	(29), (31) ^{b,j}	(33) ^{b,k}	(34) ^b	(35), (36) ^{b,m}
1	3.15 ⁿ	3.07 ⁿ	4.36 ^o	4.51 ^o	3.05 ^q	2.95 ^q	2.00—3.80 ^p	4.70 ⁿ	5.00 ⁿ	3.25 ^p
2- <i>endo</i>	2.40 ⁿ	2.40 ⁿ					2.00—3.80 ^p			2.40—3.40 ^p
2- <i>exo</i>	2.40 ⁿ	2.40 ⁿ			3.05	2.95	2.00—3.80 ^p			2.40—3.40 ^p
3			5.95 ⁿ	2.57 ⁿ	6.26 ⁿ	6.20 ⁿ	5.30—5.90 ^p	5.97 ⁿ	5.95 ⁿ	5.00—5.5 ^p
4			7.00 ⁿ	2.38 ⁿ	6.00 ⁿ	6.00 ⁿ	5.30—5.90 ^p	7.16 ⁿ	7.18 ⁿ	5.00—5.5 ^p
5- <i>endo</i>	2.40 ^o	2.40 ^o	5.38 ⁿ	5.19 ^o	3.56 ^p	3.57 ^p	2.00—3.80 ^p	5.15 ⁿ	5.26 ⁿ	2.40—3.40 ^p
5- <i>exo</i>	3.05 ⁿ	3.18 ⁿ	5.38 ⁿ				2.00—3.80 ^p			
6	4.90 ^o	5.04 ^o	3.93 ^q	3.61 ^q	4.64 ^o	4.85 ^o	5.00	3.25 ^p	3.22 ^p	4.50 ^p
7- <i>endo</i>								1.60 ⁿ	1.49 ⁿ	
7- <i>exo</i>			3.50 ⁿ	3.05 ^p				2.78 ^q	2.68 ^q	
8	7.19 ^o	7.68 ^o	6.50 ⁿ	5.72 ^p	7.46 ^o	7.90 ^o	7.15 ^o		5.20 ⁿ	7.20 ^o
9	4.95 ⁿ	4.66 ⁿ	6.71 ^q	5.72 ^p	5.17 ⁿ	4.89 ⁿ	5.00 ⁿ		5.61 ^r	4.94 ⁿ
10- <i>endo</i>			2.06 ^q	2.06 ^q				5.15 ⁿ		4.32 ^p
10- <i>exo</i>			2.40 ^q	2.45 ^q				5.64 ^r		4.32 ^p
11- <i>endo</i>					2.49 ^o	2.55 ^o				
11- <i>exo</i>				3.18 ^p	1.72 ^q	1.72 ^q				
3'	6.73 ^o		6.53 ^o	6.28 ^o	6.76 ^o		6.75 ^o	6.47 ^o		7.00 ^o
4'	8.30 ⁿ		8.18 ⁿ	8.14 ⁿ	8.29 ⁿ		8.30 ⁿ	8.15 ⁿ		8.25 ⁿ
5'		6.42 ^s				6.46 ^s			6.34 ^s	
6'	9.10 ^o		9.00 ^o	8.99 ^o	9.07 ^o		9.08 ^o	8.95 ^o		9.00 ^o
CMe	1.50 ^s	1.50 ^s					1.21 ^o	1.59 ^o	1.64 ^o	1.10 ^o
	1.70 ^s	1.70 ^s					1.23 ^o			
ArMe		2.32 ^s				2.32 ^s			2.26	
Coupling constants (Hz)										
1, 3			1.5						1.5	
1, 7- <i>exo</i>			8.5	8.3				8.5	8.5	
1, 9	5.7	5.8			6.5	6.0	6.0			6.0
3, 4			9.6	8.8	6.0	6.0		9.7	10.0	
4, 5			5.0	ca. 0	2.7	3.0		5.0	5.0	
5, 6- <i>exo</i>			7.5	7.3				5.0	6.0	
5- <i>exo</i> , 6	7.2	7.3			4.0					
6- <i>exo</i> , 7- <i>exo</i>			10.0	9.5				10.0	10.0	
6- <i>exo</i> , 8			2.5	1.0				8.0	8.5	
8, 9	8.0	8.6	6.0		8.0	8.0	8.0	14.5	15.0	8.5
3', 4'	9.4		9.3		9.3		9.5	9.2		9.5
4', 6'	2.8		2.8		2.8		2.8	2.8		2.8

* For numbering see formulae.

^a In p.p.m. relative to Me_4Si as internal standard. ^b In CDCl_3 . ^c $J_{1,2\text{-exo}}$ 6.7; $J_{2\text{-endo},2\text{-exo}}$ 14.7; $J_{5\text{-exo},5\text{-endo}}$ 14.9 Hz. ^d $J_{1,2\text{-exo}}$ 6.8; $J_{2\text{-endo},2\text{-exo}}$ 15.0; $J_{5\text{-exo},5\text{-endo}}$ 14.2 Hz. ^e $J_{7\text{-exo},10\text{-endo}}$ 4.5; $J_{7\text{-exo},10\text{-exo}}$ 10; $J_{9,10\text{-endo}}$ 2.0; $J_{9,10\text{-exo}}$ 2.0; $J_{10\text{-exo},10\text{-endo}}$ 18.0 Hz. ^f The numbering used in this structure is non-systematic, for comparison only. ^g H-12 5.75ⁿ; H-13 5.50ⁿ; H-14 2.93^p; H-15-*endo* 1.29^q; H-15-*exo* 1.32^q; $J_{3\text{-endo},11}$ 4.5; $J_{4\text{-exo},14}$ 3.1; $J_{7\text{-exo},10\text{-endo}}$ 4.3; $J_{7\text{-exo},10\text{-exo}}$ 9.7; $J_{9,10\text{-endo}}$ 1.8; $J_{9,10\text{-exo}}$ 3.6; $J_{11,15\text{-endo}}$ 1.5; $J_{11,15\text{-exo}}$ 1.5; $J_{13,14}$ 3.0; $J_{14,15\text{-endo}}$ 1.5; $J_{14,15\text{-exo}}$ 1.5; $J_{15\text{-exo},15\text{-endo}}$ 8.6 Hz. ^h $J_{2\text{-exo},11\text{-exo}}$ 4.0; $J_{2\text{-exo},3}$ 2.5; $J_{5\text{-exo},11\text{-exo}}$ 4.0; $J_{11\text{-exo},11\text{-endo}}$ 12.0 Hz. ⁱ $J_{2\text{-exo},3}$ 3.0; $J_{11\text{-exo},11\text{-endo}}$ 12.0 Hz. ^j $J_{\text{Me},\text{H}}$ 7.0 Hz. ^k $J_{8\text{-exo},7\text{-endo}}$ 6.0; $J_{7\text{-exo},7\text{-endo}}$ 14.0; $J_{9,\text{Me}}$ 6.0 Hz. ^l $J_{8\text{-exo},7\text{-endo}}$ 6.5; $J_{7\text{-exo},7\text{-endo}}$ 14.0; $J_{9,\text{Me}}$ 6.0 Hz. ^m $J_{\text{Me},\text{H}}$ 7.0 Hz. ⁿ Double doublet. ^o Doublet. ^p Multiplet. ^q Octet. ^r Double quartet. ^s Singlet.

and Figure 5) is consistent only with a 2,4-adduct; the patterns due to the vinylic and bridgehead protons are very similar to those of H-2, H-4, H-5, and H-6 of the dimer (1). The downfield doublet at δ 7.19 was assigned to the vinylic H-8 and the double doublet at δ 4.95 to H-9. The vinylic methyl groups absorb at δ 1.5 and 1.7. The spectrum was further analysed by using $\text{Eu}(\text{fod})_3$ in conjunction with double-resonance experiments. Irradiation at the frequency of H-9 simplified the H-8 signal to a singlet and the double doublet originally at δ 3.15 to a doublet. Thus the signals at δ 3.15 were assigned to H-1. Irradiation at the frequency of H-1 caused collapse of the double doublet (H-2-*exo*) originally

(J 14.9 Hz). Again there is no observable coupling between H-6 and H-5-*endo*. The *endo*-structure of the adduct was demonstrated by the LIS technique (Figure 6) and the application of the Karplus relationship.²² The LIS is greater at H-2_n and H-5_n than at H-2_x and H-5_x. The former protons point toward the carbonyl group (the complexation site) and the latter away from it. In the *exo*-structure (28) all four protons are equidistant from the carbonyl group. Furthermore the small LIS of the methyl groups confirms the *endo*-structure.

The dihedral angles between H-1 and -2 and H-6 and -5 are particularly sensitive to the stereochemistry of the

²² M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11.

adduct. Thus, in the *endo*-structure (Figure 7) Φ (H-1,-H-2 x) = Φ (H-6,H-5 x) \approx 25°, consistent with the large observed coupling constants (*ca.* 7 Hz). Again, Φ (H-1,-H-2 n) = Φ (H-6,H-5 n) \approx 95°, consistent with the

In spectra of both (21) and (22) H-5 x absorbs about 0.7 p.p.m. downfield of H-5 n owing to the anisotropy of the nitrogen atom in the *endo*-structure. The anisotropy of the aryl substituent can be neglected since the

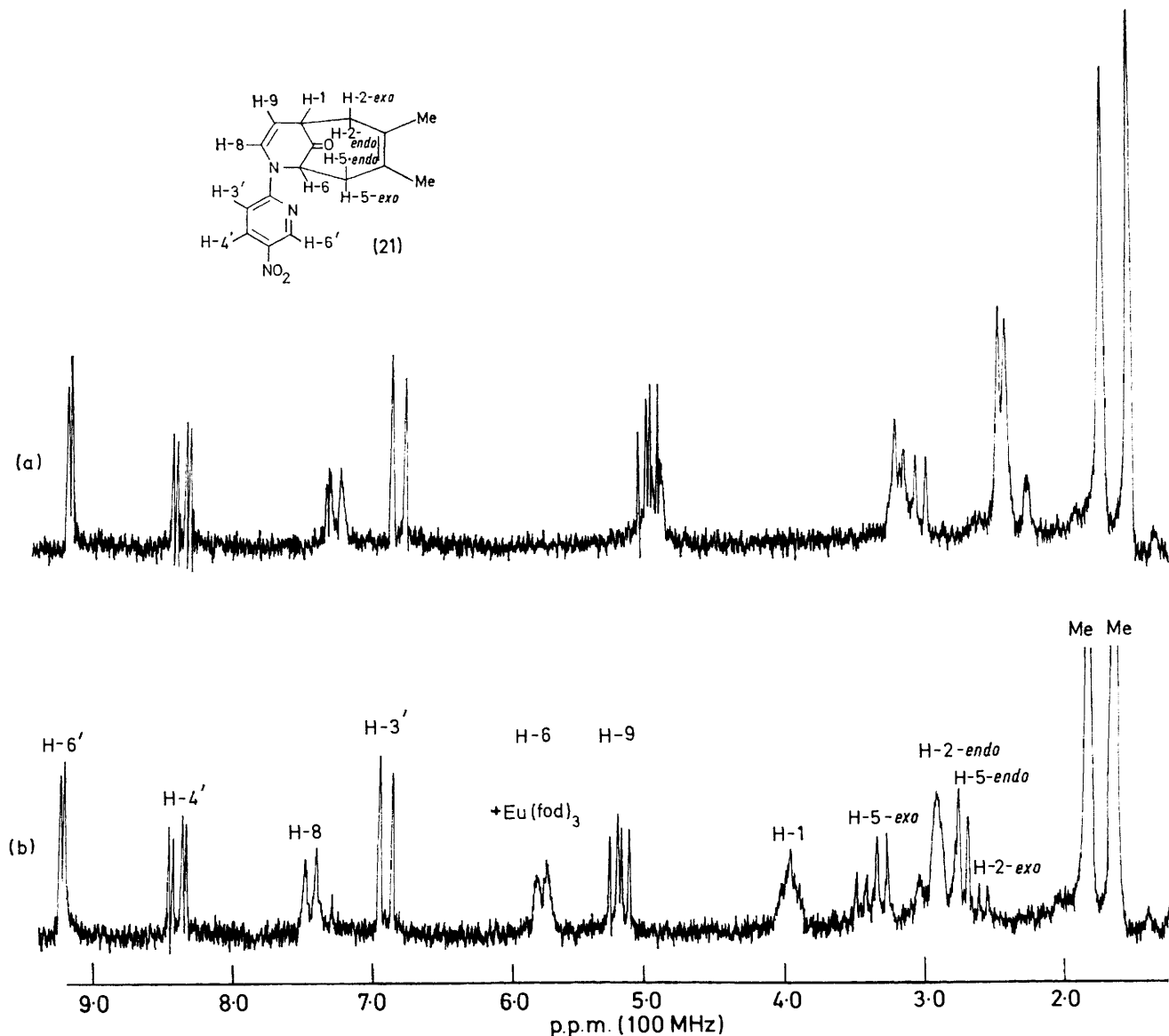
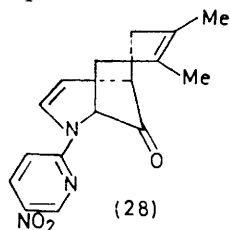


FIGURE 5 ^1H N.m.r. spectrum of compound (21): (a) simple; (b) $+\text{Eu}(\text{fod})_3$

absence of coupling between H-1 and H-2 n . However in the *exo*-structure (Figure 7) the corresponding angles are 25 and 145°, resulting in large coupling constants for both *exo*- and *endo*-protons.



chemical shift of H-5 x is similar in both compounds. Again the difference in chemical shifts of the methyl groups (0.2 p.p.m.) is similarly explained by the anisotropy of the nitro-function.

The cycloadducts (21) and (22) undergo ready electron-impact-induced retro-reaction in the mass spectrometer to give as base peaks the molecular ions of the respective betaines, (3) and (4).

Addition to trans-Penta-1,3-diene.—The reaction of the betaine (3) at 20 °C or the betaine dimer (1) at 40 °C with *trans*-penta-1,3-diene gave a mixture of 2,4- and 2,6-cycloadducts. The 2,4-cycloadducts (29) and (31) were

obtained as a deep yellow crystalline mixture in 20% yield. Structures were assigned from the following spectral properties. The i.r. spectrum shows a $\nu(\text{C}=\text{O})$ band at 1710 and enamine $\nu(\text{C}=\text{C})$ at 1650 cm^{-1} . In the ^1H n.m.r. spectrum (Table 6) two doublets at δ 1.21 and

vinyl protons H-3 and H-4 in the pentadiene gave a multiplet centred at δ 5.60 (4 H). The overlapping doublets of H-1 and H-9 were separated by addition of a small amount of $\text{Eu}(\text{fod})_3$. Thus structures (29) and (31) have the *endo*-orientation with the methyl group at

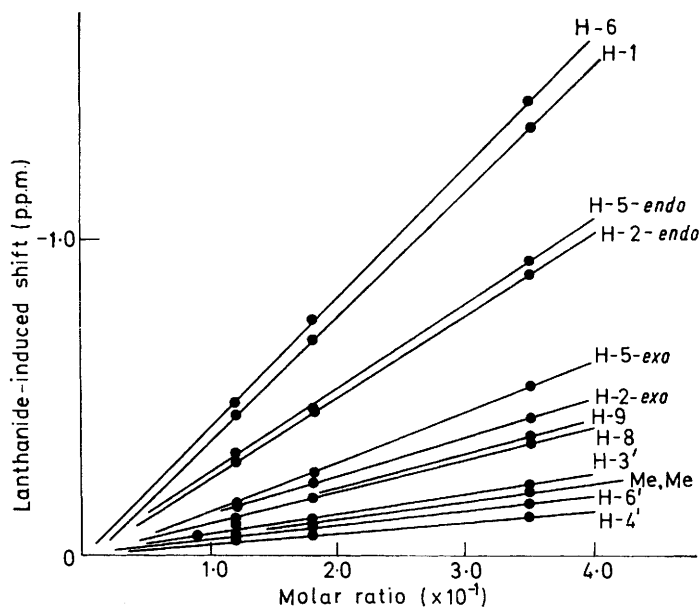


FIGURE 6 $\delta\Delta$ vs. molar ratio of lanthanide $[\text{Eu}(\text{fod})_3]$ to substrate for compound (21)

1.23 of equal intensity, assigned to allylic methyl groups, indicated that the mixture contained equal

C-2-*endo* in one isomer and at C-5-*endo* in the other, as confirmed by the high LIS on the methyl groups. In both cases H-6 is coupled to H-5-*exo* alone, thus establishing that the adducts have the *endo*-structures.

The mass spectrum of the isomeric mixture of (29) and (31) gave the correct molecular weight (285), and

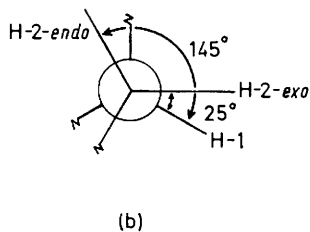
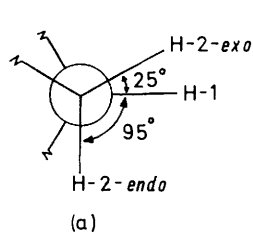
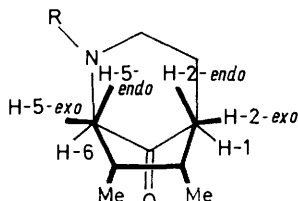
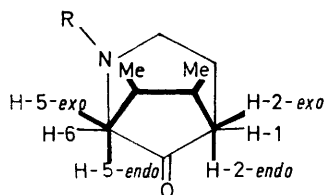
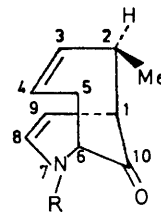


FIGURE 7 Geometries of (a) the *endo*- and (b) the *exo*-adducts of 2,3-dimethylbuta-1,3-diene

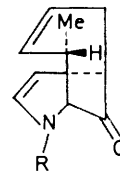
amounts of (29) and (31). Most of the remaining signals of the isomers are coincident. The pattern due to the enamine is clearly shown. The H-8 signal is a doublet (δ 7.15) coupled to H-9 (δ 5.00) ($J_{8,9}$ 8.0 Hz). The

indicated a ready electron-impact-induced retro-cyclo-addition.



(29) R = 5-nitro-2-pyridyl

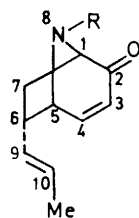
(30) R = 4,6-dimethylpyrimidin-2-yl



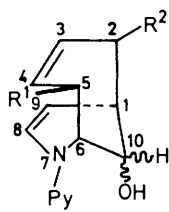
(31) R = 5-nitro-2-pyridyl

(32) R = 4,6-dimethylpyrimidin-2-yl

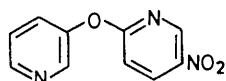
The 2,4-cycloadduct (33) was isolated as pale yellow crystals in 10% yield. The i.r. spectrum shows a $\nu(\text{C}=\text{O})$ band at 1680 cm^{-1} . The complex ^1H n.m.r. spectrum (Table 6) was elucidated by LIS coupled with double resonance. The vinylic methyl protons (doublet δ 1.59) are coupled to the vinylic H-9 by 6.0 Hz. The pattern due to the protons of the azabicyclic ring is very similar to those described for the other 2,6-adducts earlier in this paper and indicates the *endo*-structure. The large coupling constant ($J_{8,9}$ 14.5 Hz) demonstrates *trans*-orientation of H-8 and H-9 in the propenyl group.



(33) R = 5-nitro-2-pyridyl

(35) R¹ = Me, R² = H

(34) R = 4,6-dimethylpyrimidin-2-yl

(36) R² = Me, R¹ = H

(37)

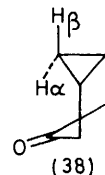
A deep orange crystalline solid, m.p. $171\text{ }^\circ\text{C}$, which showed $\nu(\text{O}-\text{H})$ 3500 cm^{-1} and no $\nu(\text{C}=\text{O})$ was also isolated. The ^1H n.m.r. spectrum (Table 6) is similar to that of (29) and (31). The mass spectrum indicated a molecular weight of 287. A reduced structure such as (35) and (36) is compatible with the above physical data, and is probably formed by the reduction of the initially formed cycloadduct (29) or (31) by hydroquinone added to minimise polymerisation. We also isolated 6% of 3-(5-nitro-2-pyridyloxy)pyridine (37).

Analogous products were obtained from *trans*-penta-1,3-diene with the pyrimidinyl betaine dimers (2a and b). The 2,6-adduct (34) was isolated in 20% yield and is characterised by a $\nu(\text{C}=\text{O})$ band at 1685 cm^{-1} . The ^1H n.m.r. spectrum (Table 6) confirms structure (34) [cf. discussion for (33)]. The 2,4-adducts (30) and (32) were isolated as a 1:1 mixture which could not be separated. The i.r. spectrum showed a $\nu(\text{C}=\text{O})$ band at 1720 cm^{-1} and the ^1H n.m.r. spectrum is very similar to that of (29) and (31).

Addition to Cyclopentadiene.—Cyclopentadiene readily reacted with the nitropyridyl betaine (3) at $20\text{ }^\circ\text{C}$ to give two products. The 2,4-adduct (25) was isolated in 37% yield. The i.r. spectrum shows a $\nu(\text{C}=\text{O})$ band at 1740 and enamine $\nu(\text{C}=\text{C})$ at 1640 cm^{-1} . The ^1H n.m.r. spectrum (Table 6) shows the characteristic signals of the enamine protons, H-8 a doublet at δ 7.46, and H-9 a double doublet at δ 5.17 ($J_{8,9}$ 8.0 Hz). The vinylic protons H-3 and H-4 appear as double doublets at δ 6.26 and 6.00, respectively. The signals of the methylene bridge protons, H-11-*exo* and -*endo*, were assigned

on the basis of the Karplus equation.²² In both the *exo*- and the *endo*-models, θ (H-11-*exo*, H-2) and θ (H-11-*exo*, H-5) $\cong 30^\circ$ and thus H-11-*exo* was assigned to the upfield multiplet at δ 1.72, while θ (H-11-*endo*, H-2) and θ (H-11-*endo*, H-5) $\cong 90^\circ$ and was assigned to the downfield doublet at δ 2.49 ($J_{11-*exo*, 11-*endo*}$ 12.0 Hz).

Further evidence of the *exo*-structure of the adduct is provided by the following spectral features. The $\nu(\text{C}=\text{O})$ value (1750 cm^{-1}) is high compared to those of the *endo*-adducts (21), (22), and (29)—(32) (1710 — 1720 cm^{-1}), but close to those of the dimers (1) and (2a and b) (1735 cm^{-1}), indicating a strained system in the *exo*-structure. The adduct (25) failed to complex with either $\text{Eu}(\text{fod})_3$ or $\text{Pr}(\text{fod})_3$ as did the *exo*-dimers (2a and b), indicating considerable crowding about the carbonyl group. The value of $J_{5-*exo*, 6}$ (4.0 Hz) is small compared to those of (21) and (22) (7.2 and 7.3 Hz, respectively) indicating a different geometry. From the *exo*-model, Φ (H-5-*exo*, H-6) = 40° is consistent with a small J value while in the *endo*-model the dihedral angle of 5° demands a larger coupling constant than was observed. The *exo*-structure is also indicated by the chemical shifts of the bridge methylene protons. In β -thujone (38) the considerable shielding of the α -proton of the cyclopropane methylene group (δ -0.05) relative to the β -proton (δ 1.39) is attributed to the anisotropy of the carbonyl group.²³ Since the geometry of (38) is similar to that of the *endo*-structure of the adduct, H-11-*endo* should be shielded as is the α -proton of (38). However, this proton is considerably deshielded (δ 2.49), an observation consistent with the *exo*-structure where H-11-*endo* is situated in the deshielding zone of the carbonyl group. Final evidence is provided by a small **W**-type coupling between H-1 and H-6 demanding a planar four-bond system connecting the two protons, consistent with the *exo*-model.



(38)

The reaction of cyclopentadiene with (3) gave also the 2,6-adduct (23) (45%), $\nu(\text{C}=\text{O})$ 1680 cm^{-1} . The ^1H n.m.r. pattern (Table 6) is similar to those of other 2,6-adducts. The *endo*-structure is confirmed by the substantial couplings between H-1 and -7-*exo* and H-5 and -6-*exo*. The position of the double bond in the cyclopentene ring is indicated by the coupling of H-6-*exo* to the vinylic H-8 by 2.5 Hz, and the coupling between H-7-*exo* and the methylene protons. These assignments were further confirmed by double resonance.

Dicyclopentadiene reacted with the nitropyridyl betaine dimer (1) at $120\text{ }^\circ\text{C}$ to give a single isolable product (24) in 34% yield. This 2:1 adduct (24) shows $\nu(\text{C}=\text{O})$ 1710 cm^{-1} . The complex ^1H n.m.r. spectrum (Table 6) was elucidated by LIS coupled with double

²³ K. Tori, *Chem. and Pharm. Bull. (Japan)*, 1964, **12**, 1439.

resonance. The *endo*-configuration of the initial attack of cyclopentadiene to the 2,6-positions of the betaine is indicated by the large couplings between H-1 and -7-*exo* and H-5 and -6-*exo*. Again the position of the double bond in the cyclopentene ring is indicated by the coupling of H-6 to the vinylic H-8 and by the coupling of H-7 to the methylene protons at C-10. The stereochemistry of addition of the second cyclopentadiene to the conjugated double bond of the initially formed cycloadduct is indicated by the absence of H-4, H-5 coupling, where the dihedral angle is almost 90°. The coupling of the bridgehead H-11 to H-3-*endo*, H-15-*endo*, and H-15-*exo*, and the coupling of the bridgehead H-14 to H-4, H-13, H-15-*endo*, and H-15-*exo* were ascertained by double resonance. The small geminal coupling constant ($J_{15\text{-}exo,15\text{-}endo}$ 8.6 Hz) is characteristic²⁴ of the angle-strained methylene bridge of bicyclo[2.2.1]heptenes.

LIS has confirmed the above general structure: H-10-*endo* is remarkably affected by the shift reagent and the LIS values of the other protons fit the geometry of the adduct where the lanthanide cation is complexing with the carbonyl oxygen atom. The enhanced LIS of the vinylic H-12 and H-13 relative to that of the methylene bridge protons, H-15-*endo* and H-15-*exo*, confirms the stereostructure of (24).

Cyclopentadiene reacts also with the pyrimidinyl betaine dimer (2a and b) at 50 °C to form a mixture of two adducts. The 2,4-adduct (26) (45% yield) displays spectral properties similar to those of (25). The structure of the 2,6-adduct (27) (21% yield) was determined in similar manner to that of the adduct (23).

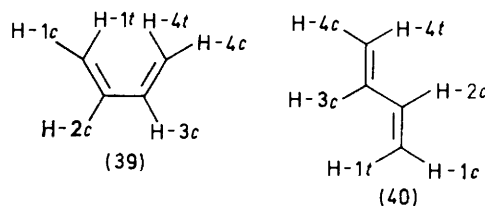
Other Attempted Cycloadditions.—The following 4 π -electron cycloaddends did not react with the nitropyridyl betaine system: (a) dienes: furan, 2-methylfuran, 1,3-diphenylisobenzofuran, hexachlorocyclopentadiene, tetraphenylcyclopentadienone, and anthracene; (b) 1,3-dipoles: 1,2,3-triphenylazomethine ylide (generated from the corresponding aziridine),²⁵ the tetracyano-carbonyl ylide generated from tetracyanoethylene oxide,²⁶ 3-phenylsydnone,²⁷ and 3-methyl-5-oxido-2-phenyl-4-trifluoroacetyl-1,3-oxazolinium.²⁸

Peri-selectivity.—These reactions of 1,3-dienes with 3-oxidopyridinium provide interesting examples of orbital symmetry control of dipolar cycloadditions. No stepwise mechanism can account for the peri-specificity observed in these reactions. Unlike many cycloadditions, the geometry of approach of the addend is similar for reactions across the 2- and 6- or the 2- and 4-positions of the betaine. Consequently the complete peri-specificity observed in compliance with the Woodward-Hoffmann rules must be derived from electronic factors. A conjugated diene can add across one of its

double bonds to the 2- and 6-positions of the betaine in a [2 + 4] process, or across both the double bonds to the 2- and 4-positions of the betaine in a [4 + 6] process. Such selectivity within the allowed pericyclic modes of cycloadditions has been termed 'peri-selectivity',¹⁵ and it is controlled by both electronic and steric factors. The coefficient magnitudes¹⁰ at the addition sites slightly favour the [4 + 6] process over the [2 + 4] process; however secondary orbital overlap favours the [2 + 4] *endo*-process. Hence, overall, electronic factors do not decisively favour one type of addition and primary and secondary steric effects determine the peri-selectivity.

Methyl groups at potential addition sites evidently exert considerable primary steric repulsions; thus no [2 + 4] adducts were obtained across the methyl-substituted double bonds of 2,3-dimethylbuta-1,3-diene or *trans*-penta-1,3-diene.

Acyclic dienes must assume a *cisoid* conformation prior to reaction as a 4 π -component. The *cisoid* form of buta-1,3-diene is less stable by 2.3 kcal mol⁻¹ than the *transoid* form²⁹ and only ca. 1% exists in the equilibrium mixture. Substitution of H-1c and/or H-4c by methyl exerts only small steric effects which are similar for both conformers (39) and (40). However methyl substitution for H-1t and/or H-4t disfavors (39) strongly (*cf.* ref. 30). Methyl substitution of H-2c and/or H-3c disfavors (40): in agreement 2,3-dimethylbuta-1,3-diene is a good 4 π -electron addend giving exclusively the [4 + 6] adduct with 3-oxidopyridinium.



Stereoselectivity.—Addition to the 2- and 4-positions of 3-oxidopyridinium can be considered as involving either fragment (c), a 2 π -component or (d) a 6 π -component (Figure 1). The addition of a diene can thus be simultaneously an *endo*- [2 + 4] {involving (c)} and an *exo*- [4 + 6] process {involving (d)}. Such an orientation is favoured by secondary orbital overlap (Figure 8).¹⁵ Inspection of secondary interactions in the alternative {*exo*- [2 + 4] or *endo*- [4 + 6]} transition state indicates predominant negative overlap especially between the diene HOMO and the betaine LUMO.

The foregoing simply explains the formation of the *exo*-adduct with cyclopentadiene. The apparent formation of the *endo*-adducts with 2,3-dimethylbuta-1,3-diene and *trans*-penta-1,3-diene is more complex. The

²⁷ C. J. Thoman and D. J. Voaden, *Org. Synth.*, Coll. Vol. V, 1973, p. 962.

²⁸ C. V. Greco, R. P. Gray, and V. G. Grosso, *J. Org. Chem.*, 1967, **32**, 4101.

²⁹ E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962, p. 331; J. G. Aston, G. Szasz, H. W. Woolley, and F. G. Brickwedde, *J. Chem. Phys.*, 1946, **14**, 67.

³⁰ D. Craig, *J. Amer. Chem. Soc.*, 1943, **65**, 1006.

²⁴ R. C. Cookson, T. A. Crabb, J. J. Frankel, and J. Hudec, *Tetrahedron*, 1966, Suppl. 7, 355.

²⁵ H. W. Heine, R. Peavy, and A. J. Durbetaki, *J. Org. Chem.*, 1966, **31**, 3924.

²⁶ W. J. Linn, O. W. Webster, and R. E. Benson, *J. Amer. Chem. Soc.*, 1965, **87**, 3651; W. J. Linn and R. E. Benson, *ibid.*, p. 3657; W. J. Linn, *ibid.*, p. 3665.

2,4-adduct from pentadiene and the pyridyl dimer possesses a *cis*-methyl group. Adducts of 1,3-dienes to *N*-methyl-3-oxidoquinolinium³¹ were originally assigned *exo*-structures from ¹H n.m.r. data. Later the *trans*-pentadiene adduct was found by X-ray crystallography³²

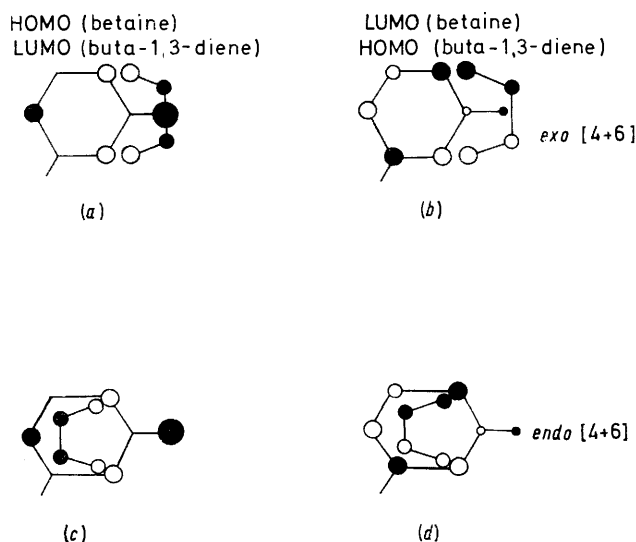
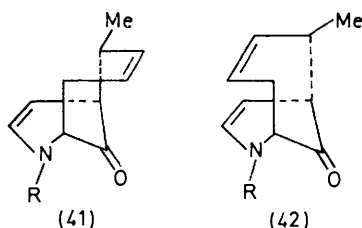


FIGURE 8 Secondary orbital overlap in the *exo*- and *endo*-additions of buta-1,3-diene to 3-oxidopyridinium

to have a distorted chair conformation (*endo*) with a *cis*-pentadiene unit, in agreement with our results. Since isomerisation of *trans*-pentadiene to *cis*-pentadiene prior to addition is highly improbable under the conditions employed, the formation of these apparently *endo*-adducts must arise from an initial *exo*-addition to give (41) followed by a conformational flip to the *endo*-orientation (42) by which the initially *trans*-methyl group suffered rotation to the *cis*-configuration. By analogy, it is highly probable that 2,3-dimethylbuta-1,3-diene also gives initially the *exo*-adducts which then flip to the thermodynamically more stable *endo*-forms. The high carbonyl frequency of the *exo*-adducts indicates strain and thus a driving force for conformational interconversion.



Reactivity.—Cycloaddition to 3-oxidopyridinium at the 2- and 4-positions is controlled by the betaine LUMO. Dimerisation as well as ability to add to dienes is enhanced by the lowering of the LUMO by strongly electron-withdrawing groups on the nitrogen atom. Although 3-oxidopyridiniums generally react better

with electron-deficient dipolarophiles across the 2- and 6-positions, the electron demand is reversed for additions across the 2- and 4-positions. Thus 3-oxidopyridiniums react readily with the electron-rich 2,3-dimethylbuta-1,3-diene, *trans*-penta-1,3-diene, and cyclopentadiene but do not add to the electron-deficient tetraphenylcyclopentadienone and 3-phenylsydnone.

In the betaine HOMO the coefficient at C-6 (0.38) is larger than that at C-4 (0.34). Accordingly interaction with a LUMO is slightly greater at C-6. In the LUMO the coefficient at C-4 (0.49) is larger than that at C-6 (0.41), leading to a preferential interaction with a HOMO at C-4. However the differences in the coefficient sizes are small and reversal in electron demand needs further explanation.

The PMO method utilises ground state frontier eigenvalues and eigenvectors in equation (1) and provides knowledge of the energetics of the transition state between the two addends. A better approximation is to use a transition state model somewhere between reactants and products. Calculations³³ of the hypothetical Diels–Alder reaction of butadiene and ethylene show that the HOMO levels of both addends are raised and the LUMO levels are lowered by the deformation of bond lengths of the addends during the reaction. This leads to stronger interaction between the frontier orbitals in the transition state, and was termed by Fukui and Fujimoto³³ the principle of a narrowing of the inter-frontier level separation (PNIFLS).

Qualitatively, orbital energy changes due to bond length deformation can be deduced by inspection: they are a function of bond length deformation and the sizes and signs of the coefficients at the two atoms of the bond. Thus stretching at a bonding overlap site will raise and contraction will lower the orbital energy. The opposite effect is produced at antibonding sites.

Application of the PNIFLS to additions of 3-oxidopyridinium shows that the HOMO level has pseudo-NBMO properties, *i.e.* the coefficients at the alternate positions, 1, 3, and 5 are almost zero. Consequently its energy level is insensitive to bond length deformations. However, the LUMO level has large coefficients at C-1, -2, -4, -5, and -6 and is consequently sensitive to bond-length deformations.

During addition to the 2- and 6-positions double bonds are developing between the oxygen atom and C-3 and between C-4 and -5 while single bonds develop between the other adjacent atoms. Bond length deformation in the transition state (Figure 9a) will accordingly produce two lowering and two raising effects in the LUMO level of the betaine, resulting in an almost zero net effect. Therefore 2,6-addition will gain no benefit from the PNIFLS. On the other hand during addition to the 2- and 4-positions a double bond is progressively forming between C-5 and -6. Thus all bond length deformations in the transition state will contribute substantially to lower the LUMO level (Figure 9b).

³¹ K.-L. Mok and M. J. Nye, *J.C.S. Chem. Comm.*, 1974, 608.

³² M. J. Nye, personal communication.

³³ K. Fukui and H. Fujimoto, *Bull. Chem. Soc. Japan*, 1969, **42**, 3399.

When the (betaine) LUMO–(diene) HOMO separation is initially small, as in the case of addition to electron-rich dienes, further narrowing of this separation by the PNIFLS produces an amplified effect in the interaction

selectivity. Addition of fulvene to 3-oxidopyridinium could form the peri-isomers (43)–(45), each in the form of various regio- and stereo-isomers, all allowed by the Woodward–Hoffmann rules.⁴¹

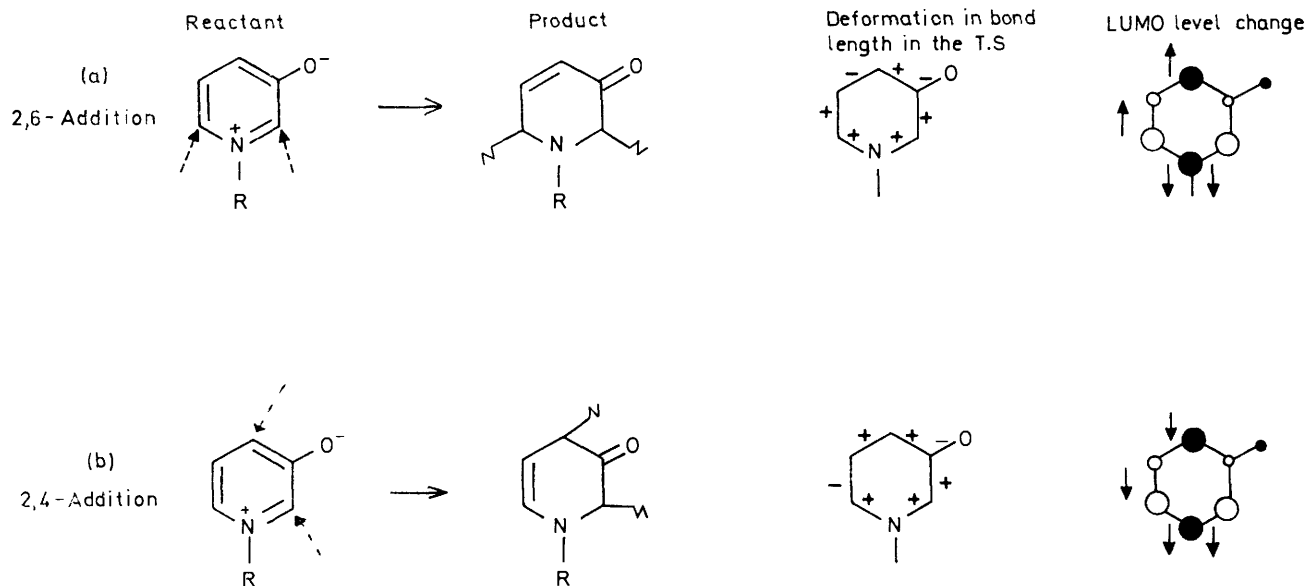


FIGURE 9 PNIFLS effects in 2,4- and 2,6-addition to 3-oxidopyridiniums

energy leading to an acceleration of the reaction. This enhanced effect is a consequence of the presence of the energy separation term in the denominator of the PMO term in equation (1).

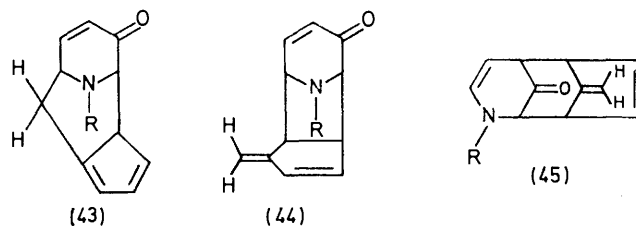
When the (betaine) LUMO–(diene) HOMO energy separation is initially large, as in the addition of the betaine to electron-deficient dienes, the effect of the PNIFLS is small.

Cycloadditions to 6 π -Electron Addends

Introduction.—Addition of 6 π -electron addends to the 2- and 6-positions constitutes the third possible symmetry-allowed thermal mode of cycloaddition to 3-oxidopyridinium. Tropones³⁴ and azepines³⁵ have previously been used as 6 π -addends. Fulvenes undergo [4 + 6] cycloadditions with tropone across the 2- and 6-positions³⁶ with acyclic 1,3-dipoles as 2 π -electron addends^{10,11,37,38} and as 6 π -electron addends,^{37,39} and also dimerise in a [4 + 2] process.⁴⁰

Fulvenes were selected for the present work. The mode of addition provides tests of electronic theory and organic reactivity, and of stereo-, regio-, and peri-

6,6-Dimethylfulvene reacted with the nitropyridyl betaine (3) to give an adduct (47) (31%) *via* the unisoluble (46). The strong conjugated ketone $\nu(\text{C}=\text{O})$



band at 1690 cm^{-1} suggested addition across the 2- and 6-positions of the betaine. The ^1H n.m.r. pattern (Table 7) of H-1, -3, -4, and -5 is similar to those for other 2,6-adducts, except that the long-range **W**-type coupling is reduced between H-1 and -3. The ^1H n.m.r. spectrum of (47) also shows singlets at δ 3.01 (2 H) and 6.40 (2 H). $\text{Eu}(\text{fod})_3$ removed the accidental equivalence of the two protons in each of these signals and changed their appearance to the slightly broadened AB quartets for H-10-*exo* and H-10-*endo* ($J_{10\text{-exo},10\text{-endo}}$

³⁷ P. Caramella, P. Frattini, and P. Grünanger, *Tetrahedron Letters*, 1971, 3817.

³⁸ R. A. W. Johnstone, 'Mass Spectrometry for Organic Chemists,' Cambridge University Press, 1972, p. 68.

³⁹ K. N. Houk and L. J. Luskus, *Tetrahedron Letters*, 1970, 4029.

⁴⁰ (a) M. N. Paddon-Row, P. L. Watson, and R. N. Warrener, *Tetrahedron Letters*, 1973, 1033; (b) K. N. Houk and L. J. Luskus, *J. Org. Chem.*, 1973, **38**, 3836.

⁴¹ R. B. Woodward and R. Hoffmann, 'The Conservation of Orbital Symmetry,' Verlag Chemie–Academic Press, Weinheim, 1970.

³⁴ R. C. Cookson, B. V. Drake, J. Hudec, and A. Morrison, *Chem. Comm.*, 1966, 15; K. N. Houk and C. R. Watts, *Tetrahedron Letters*, 1970, 4025.

³⁵ I. C. Paul, S. M. Johnson, J. H. Barrett, and L. A. Paquette, *Chem. Comm.*, 1969, 6; L. A. Paquette, J. H. Barrett, and D. E. Kuhla, *J. Amer. Chem. Soc.*, 1969, **91**, 3616.

³⁶ (a) K. N. Houk, L. J. Luskus, and N. S. Bhacca, *J. Amer. Chem. Soc.*, 1970, **92**, 6392; (b) N. S. Bhacca, L. J. Luskus, and K. N. Houk, *Chem. Comm.*, 1971, 109; (c) K. N. Houk, L. J. Luskus, and N. S. Bhacca, *Tetrahedron Letters*, 1972, 2297; (d) H. Tanida, T. Irie, and K. Tori, *Bull. Chem. Soc. Japan*, 1972, **45**, 1999; (e) H. R. Pfaendler and H. Tanida, *Helv. Chim. Acta*, 1973, **56**, 545.

24.1 Hz) near δ 3.0 and to H-8 and H-9 ($J_{8,9}$ 5.5 Hz) near δ 6.4. The coupling constants are characteristic of a cyclopentadiene moiety.^{24,42} The allylic methyl groups (δ 1.28 and 1.32) confirm the general structure. The regiostructure shown (47) is supported by the H-1 signal being downfield of that of H-5, indicating that it is

regio-structure is unambiguously assigned by the direct coupling of H-5 to H-6-*exo* (J 6.0 Hz). The H-1 signal is close to that of H-1 in (47); the downfield shift of the

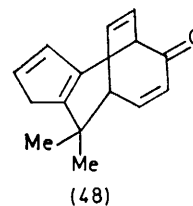
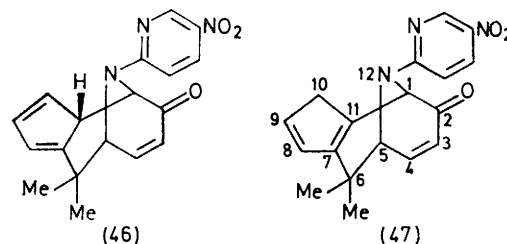
TABLE 7
Proton n.m.r. spectra of cycloadducts derived from fulvenes^a

Chemical shifts (δ)	(47) ^{b,c}	(49) ^{b,c}	(51) ^{b,c}	(52) ^{b,c}
1	5.42 ^d	5.47 ^d	5.58 ^d	
3	5.87 ^e	6.05 ^e	5.95 ^e	
4	6.99 ^f	7.15 ^f	7.06 ^f	
5	5.53 ^g	5.86 ^f	5.32 ^e	
6- <i>exo</i>		4.42 ^e		
6- <i>endo</i>			3.88 ^d	4.7 ^d
8	6.40 ^d	6.40 ^g	6.45 ^g	
9	6.40 ^d	6.55 ^g	6.15 ^g	
10- <i>exo</i>	3.01 ^d	3.06 ^e	3.18 ^e	3.8 ^h
10- <i>endo</i>	3.01 ^d	2.74 ^e	3.18 ^e	3.8 ^h
3'	6.64 ^e	6.72 ^g	6.15 ^e	
4'	8.19 ^f	8.30 ^f	7.99 ^f	
6'	9.00 ^g	9.13 ^g	8.87 ^e	
Me	{1.32 ^d 1.28 ^d }			{2.4 ^d 2.4 ^d }
Ph		7.30 ^g		
2''			7.02 ^e	
3''			6.72 ^e	
O-Me			3.70 ^d	3.8 ^d
Coupling constants (Hz)				
3, 4	10.5	10.0	10.0	
4, 5	5.1	5.5	5.5	
5, 6- <i>exo</i>		6.0		
8, 9	5.5	5.5	5.5	
10- <i>endo</i> , 10- <i>exo</i>	24.1	24.5	24.5	
3', 4'	9.5	9.5	9.5	
4', 6'	2.8	3.0	3.0	
2'', 3''			8.5	

^a In p.p.m. relative to Me₄Si as internal standard. ^b In CDCl₃. ^c For numbering see formula (47); this is non-systematic, for comparison only. ^d Singlet. ^e Doublet. ^f Doublet. ^g Multiplet. ^h Overlap with OMe.

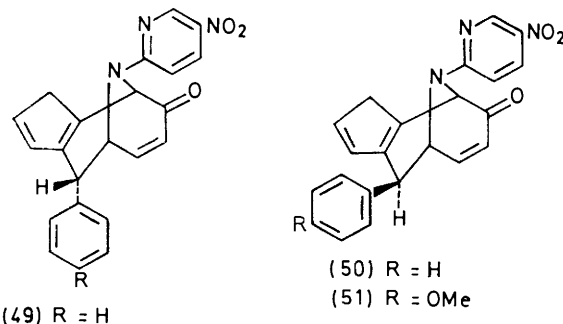
H-1 which is allylic. Furthermore the LIS values of the methyl groups are lower than those of H-5 and the methylene protons. The high shift of H-10-*endo* can only be explained by the methylene group *anti* to the methyl groups. The isomerised dimethylfulvene tropone adduct^{36a} (48) with the *syn*-configuration has methyl signals at δ 0.81 and 0.96. The product (47) evidently results from a rapid [1,5] sigmatropic hydrogen shift in the originally formed adduct (46) which has many analogies⁴³ (*cf.* the addition of tropone^{36a} to fulvenes, where again the initial adduct could not be isolated owing to rapid isomerisation).

6-Phenylfulvene reacts readily with the betaine (3) at 20 °C to give two products. The first (49) (38%) has a ν (C=O) (conjugated) band at 1 685 cm⁻¹. The ¹H n.m.r. pattern (Table 7) is similar to that observed for (47), but here signals for H-10-*endo* and -*exo* and H-8 and -9 were not overlapped ($J_{10-*exo*, 10-*endo*}$ 24.5, $J_{8,9}$ 5.5 Hz). The



H-5 signal must be due to the anisotropy of the *endo*-phenyl group.

The second isomeric 1:1 adduct (17%) shows a ν (C=O) (conjugated) band at 1 690 cm⁻¹, and its u.v. and mass spectra are very similar to those of (49). It is thought to be the stereoisomer (50) with an *exo*-phenyl group, however confirmation by ¹H n.m.r. was prevented by lack of solubility.

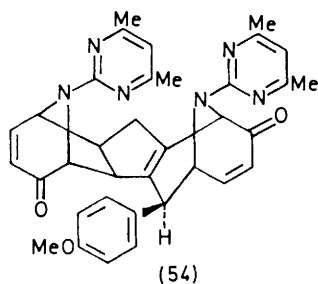
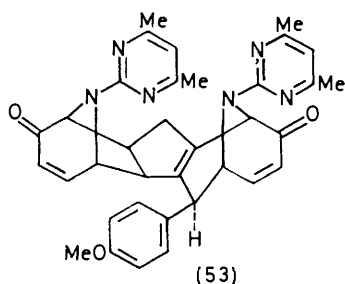
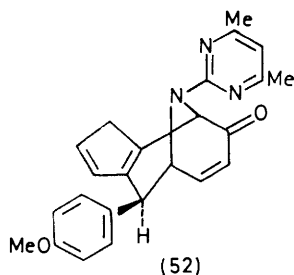


6-(*p*-Methoxyphenyl)fulvene with the dimer (1) gives a mixture of products with ν (C=O) (conjugated) bands at 1 680—1 690 cm⁻¹. The single major product (51), isolated pure (49%), had a ¹H n.m.r. pattern (Table 7) similar to that of (49). The *exo*-orientation of the *p*-methoxyphenyl group is indicated by the absence of coupling between H-5 and H-6-*endo*. The H-1 signal occurs downfield of that of H-1 in (49) while H-5 absorbs at the normal position (δ 5.32) owing to the disappearance of the anisotropic effect. An exothermic reaction of the pyrimidinyl betaine dimer (2a or b) with *p*-methoxyphenylfulvene gave a mixture of five products with ν (C=O) bands at 1 680—1 690 cm⁻¹. Three of these products were isolated by t.l.c. Analytical and ¹H n.m.r. data indicate that one of the products is a 1:1 adduct, possibly (52), while the other two are 2:1

⁴² G. Bergson, *Acta Chem. Scand.*, 1964, **18**, 2003.

⁴³ V. A. Mironov, E. V. Sobolev, and A. N. Elizarova, *Tetrahedron*, 1963, **19**, 1939; E. Hedaya, D. W. McNeil, P. Schissel, and D. J. McAdoo, *J. Amer. Chem. Soc.*, 1968, **90**, 5284; W. R. Roth, *Tetrahedron Letters*, 1964, 1009; S. McLean and P. Haynes, *Tetrahedron*, 1965, **21**, 2313.

adducts (betaine : fulvene) with the possible structures (53) and (54). Complete assignments of the structures of these products was hindered by low solubility and



overlap. In the spectrum of (52) (Table 7) the absorption at δ 2.4 (6 H) is assigned to the pyrimidine methyl groups and that at δ 3.8 (5 H) to the methoxy-group together with the two protons at C-10. The broad singlet at δ 4.7 (1 H) is assigned to H-6-*endo*, by analogy with the spectrum of (51). The spectra of (53) and (54) are more complicated. However in both cases the intensity of the pyrimidinyl methyl peaks is four times that of the methoxy-peak.

The dimethylfulvene adduct (47) decomposed in the mass spectrometer; however the adducts (49), (51), and (52) gave the corresponding molecular ion peaks. The strong peaks due to the betaine and fulvene indicate electron impact retro-reaction. This implies the occurrence of a [1,5] hydrogen shift before or after electron impact to give the radical ion corresponding to (46). The variable relative intensities of the betaine and fulvene peaks are in good agreement with the mechanism of the above reaction as the charge should appear on the fragment with the lower ionization potential.³⁸ Thus

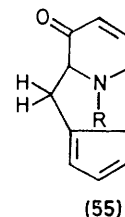
⁴⁴ K. N. Houk, J. K. George, and R. E. Duke, jun., *Tetrahedron*, 1974, **30**, 523.

the betaine : fulvene relative peak intensities are 1 : 1 in (50) and 1 : 6 in (51), reflecting a considerable resonance stabilisation of 6-(*p*-methoxyphenyl)fulvene radical cation. The adducts fragment alternatively by loss of R¹, R², CHO·, or C₃H₃O·. The betaine : fulvene relative peak intensity given by (52) is 1 : 0.75 while that given by the 2 : 1 adducts (53) and (54) is accordingly 1 : 0.25.

Peri- and Regio-selectivity.—MO calculations for fulvenes by using CNDO/2 EH⁴⁴ and other methods⁴⁵ all indicate that the HOMO possesses a node or a near-node through C-6, whereas the LUMO has its largest coefficient at this position. Addition at C-6 is thus sensitive to the electron demand of the other addend: electron-deficient dienes^{40b} and electron-deficient 1,3-dipoles³⁷ interact mainly with the fulvene HOMO and hence avoid C-6 and give normal [2 + 4] adducts across the 2- and 3-positions of the fulvene. Electron-rich dienes⁴⁴ and electron-rich 1,3-dipoles^{37,39} interact mainly with the fulvene LUMO and give [4 + 6] adducts across the 2- and 6-positions. The formation of the *peri*-isomer (43) is thus explained on the basis that the betaine behaves as an electron-rich addend.

The observed regio-structure of adducts (47), (49), (51), and (52) is not controlled by primary orbital overlap. The coefficients at C-2 (betaine HOMO) and C-6 (fulvene LUMO) are somewhat larger than those at C-6 (betaine HOMO) and C-2 (fulvene LUMO). Hence equation (1) predicts¹⁰ that the alternative regioisomer (55) should be formed.

The observed regioselectivity derives from secondary orbital overlap. For addition of the 2- and 6-positions of fulvene to the 2- and 6-positions of the betaine four geometries of approach are possible. The *endo*-approaches (a) and (b) (Figure 10) are compared with the similar approaches (c) and (d) of addition of fulvene to tropone. In both (a) and (c) all interactions have positive overlap leading to the observed adducts while the strong negative secondary orbital overlap in (b) and



(d) prevents these approaches. The adducts in both reactions underwent ready [1,5] hydrogen shift whereby the indications of the stereochemistry of approach were lost.

In the reaction with tropone however the stereochemistry of addition was established as that of (c) by deuterium labelling at C-2 and C-5 of the fulvene.^{36c}

The result underlines the need to incorporate secondary overlap into the simple perturbation expression equation

⁴⁵ L. Praud, P. Millie, and G. Berthier, *Theor. Chim. Acta*, 1968, **11**, 169; W. C. Herndon and E. Silber, *J. Chem. Educ.*, 1971, **48**, 502.

(1) for successful prediction of regioselectivity¹⁰ especially for cycloadditions of large π -addends.

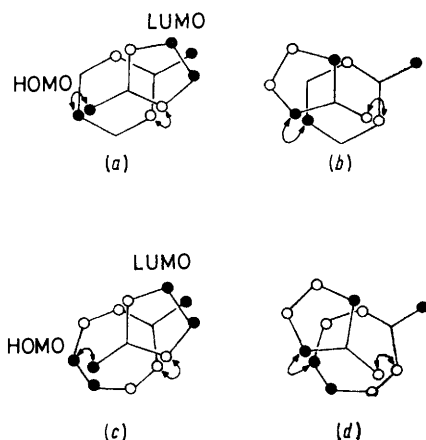


FIGURE 10 Secondary overlap in the additions of 3-oxidopyridinium and tropono to fulvenes

With a little modification, approach (a) (Figure 10) can lead to the *peri*-isomer (45) when new σ bonds are formed to the 2- and 4- and 2- and 5-positions of the

scopic reversibility can be established between the two *peri*-isomers through a transition state of geometry (a) (Figure 10) (43) is thermodynamically more stable than (45) as the two double bonds in the cyclopentadiene unit are conjugated in (43) and isolated in (45). The ready [1,5] hydrogen shift which is possible only in (43) could be another factor which freezes the structures of the adducts in the form isolated.

EXPERIMENTAL

M.p.s. were determined with a Reichert apparatus. Spectra were recorded with a Perkin-Elmer 257 grating i.r. spectrophotometer, a Perkin-Elmer SP 800 u.v. spectrophotometer, a Hitachi-Perkin-Elmer RMU-6E mass spectrometer, and a Varian HA-100 MHz n.m.r. spectrometer. Compounds were purified until they were obtained as single spots on t.l.c. (Kieselgel PF 254). For the preparations of 1-(5-nitro-2-pyridyl)-3-oxidopyridinium (3), 1-(4,6-dimethylpyrimidin-2-yl)-3-oxidopyridinium (4), the nitropyridyl dimer (1), and the pyrimidinyl dimer (2) see preceding paper.

Dimethyl 8-(5-Nitro-2-pyridyl)-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-endo,7-exo- and 6-exo,7-endo-dicarboxylate [(19) and (20)].—The dimer (1) (1.9 g, 0.0044 mol), dimethyl fumarate (2 g, 0.0138 mol), and chlorobenzene (20 ml)

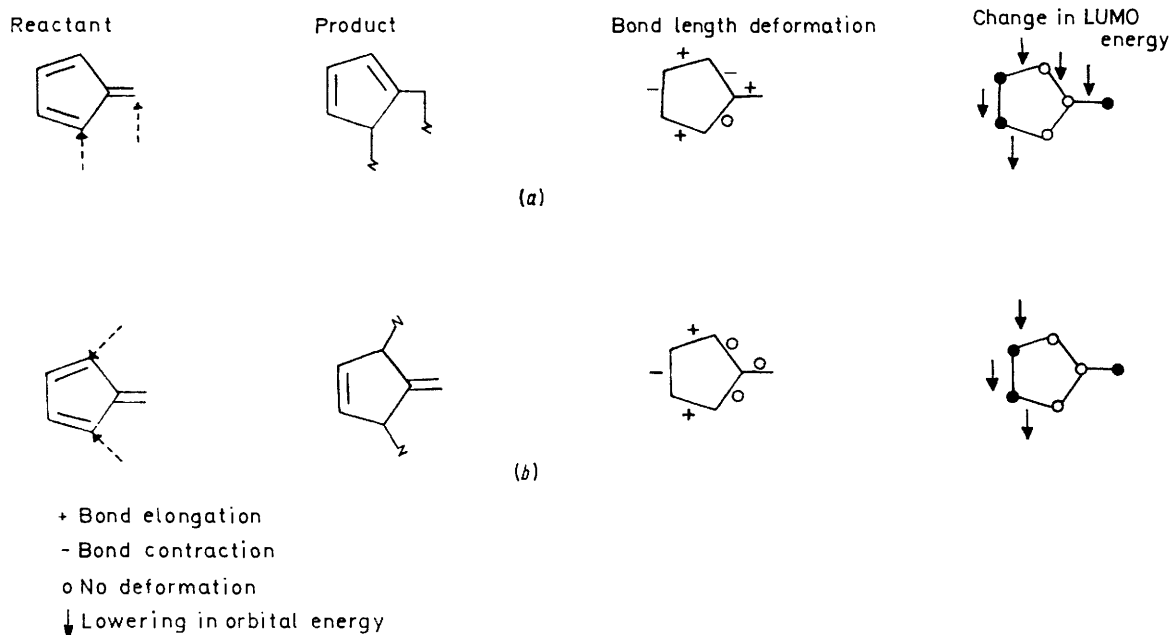


FIGURE 11 Energy changes in the fulvene LUMO caused by bond length deformations during (a) 2,6- and (b) 2,4-addition

betaine and fulvene, respectively. However an adduct of structure (45) has not been detected in the crude mixtures of the reactions reported here [(45) is expected to show carbonyl absorption in the range 1710–1750 cm^{-1}]. The sole formation of the isomer (43) can be explained on the basis of a kinetic and/or a thermodynamic control. Kinetically, coefficient size at new bond formation sites favours the formation of (43). Also in favour of (43), the PNIFLS³³ lowers the fulvene LUMO considerably during bond formation at the 2- and 6-positions (Figure 11). Furthermore if micro-

were heated under reflux for 17 h. The solvent was evaporated off (50 °C at 10 mmHg) and the product chromatographed on alumina (B.D.H. aluminium oxide, neutral) eluted first with toluene, then with toluene-EtOAc (2:1). The second eluate was evaporated to leave a solid residue (2.82 g, 90%), a mixture of two components, separated by preparative t.l.c. on silica gel (Kieselgel PF 254, CHCl_3). The 6-endo,7-exo-dicarboxylate (19) (1.15 g, 36%) formed prisms from (CHCl_3 -Et₂O), m.p. 174 °C (Found: C, 53.3; H, 4.4; N, 11.4. $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_7$ requires C, 53.2; H, 4.2; N, 11.6%); ν_{max} (Nujol) 1735, 1680, 1590, 1570, 1510, and 1335 cm^{-1} ; λ_{max} (EtOH) 210 (log ϵ 4.23), 226

(4.34), and 348 nm (4.36); m/e 361. The 6-exo,7-endo-dicarboxylate (20) (1.71 g, 54%) formed needles ($\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 141—142 °C (Found: C, 53.1; H, 4.2; N, 11.7%); ν_{max} (Nujol) 1740, 1680, 1590, 1500, and 1345 cm^{-1} ; λ_{max} (EtOH) 210 (log ϵ 4.22), 225 (4.34), and 348 nm (4.35); m/e 361.

Dimethyl 8-(5-Nitro-2-pyridyl)-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-exo,7-exo-dicarboxylate (16).—The dimer (1) (1.25 g, 0.0029 mol), dimethyl maleate (4 g, 0.028 mol), and chlorobenzene (25 ml) were heated under reflux for 5 h, the solvent was evaporated off (70 °C at 10 mmHg), and the solid residue chromatographed on alumina (B.D.H. aluminium oxide, neutral), eluted first with toluene then with toluene-EtOAc (1:1). The second eluate gave the *cycloadduct* (16) (1.9 g, 90%), as pale yellow needles (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 129—130 °C (Found: C, 53.3; H, 4.4; N, 11.7. $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_7$ requires C, 53.2; H, 4.2; N, 11.6%); ν_{max} (Nujol) 1740, 1690, 1590, 1575, 1500, and 1330 cm^{-1} ; λ_{max} (EtOH) 210 (log ϵ 4.25), 226 (4.36), and 348 nm (4.36); m/e 361.

8-(5-Nitro-2-pyridyl)-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-endo,7-endo-dicarboxylic Anhydride (17).—The dimer (1) (1 g, 0.0023 mol), maleic anhydride (0.45 g, 0.0046 mol), and $\text{CH}_2\text{Cl}\cdot\text{CH}_2\text{Cl}$ (10 ml) were heated under reflux for 20 min. The mixture was cooled to 30 °C and without delay chromatographed on alumina (B.D.H. aluminium oxide, neutral; $\text{CH}_2\text{Cl}\cdot\text{CH}_2\text{Cl}$) to give the *endo-adduct* (17) (1.36 g, 91.5%), pale yellow prisms (from CHCl_3), m.p. 220 °C (decomp.) (Found: C, 53.2; H, 3.1; N, 12.9. $\text{C}_{14}\text{H}_9\text{N}_3\text{O}_6$ requires C, 53.3; H, 2.9; N, 13.3%); ν_{max} (Nujol) 1860, 1785, 1695, 1595, 1575, 1510, and 1345 cm^{-1} .

Methyl 8-(5-Nitro-2-pyridyl)-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-endo- and -6-exo-carboxylate, (7a) and (8a).—The dimer (1) (0.5 g, 0.0012 mol), methyl acrylate (5 ml), and tetrahydrofuran (THF) (5 ml) were heated under reflux for 18 h. The solvent was evaporated off (50 °C at 10 mmHg) to leave a solid (0.7 g, 100%) mixture of two components. The mixture was separated by preparative t.l.c. on silica gel [Kieselgel PF 254; light petroleum (60—80 °C)-EtOAc (4:1)]. The *endo-6-carboxylate* (7a) crystallised (25%) as prisms (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 170 °C (Found: C, 55.9; H, 4.5; N, 13.9. $\text{C}_{14}\text{H}_{13}\text{N}_3\text{O}_6$ requires C, 55.5; H, 4.3; N, 13.9%); ν_{max} (Nujol) 1740, 1680, 1595, 1570, 1510, and 1350 cm^{-1} ; λ_{max} (EtOH) 210 (log ϵ 4.11), 227 (4.26), and 356 nm (4.27); m/e 303. The *exo-6-carboxylate* (8a) crystallised (75%) as prisms (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 158 °C (Found: C, 55.9; H, 4.4; N, 13.9%); ν_{max} (Nujol) 1725, 1690, 1590, 1575, 1500, and 1345 cm^{-1} ; λ_{max} (EtOH) 210 (log ϵ 4.11), 228 (4.26), and 359 nm (4.28); m/e 303.

8-(5-Nitro-2-pyridyl)-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-endo- and -6-exo-carbonitrile, (7b) and (8b).—The dimer (1) (2 g, 0.0046 mol) and an excess of acrylonitrile were heated under reflux for 5 h. The mixture when set aside at room temperature for 12 h gave the *6-endo-carbonitrile* (7b) (1.2 g, 48.2%) as pale yellow prisms (from $\text{THF-H}_2\text{O}$), m.p. 208—209 °C (Found: C, 58.0; H, 3.9; N, 20.5. $\text{C}_{13}\text{H}_{10}\text{N}_4\text{O}_3$ requires C, 57.8; H, 3.7; N, 20.7%); ν_{max} (Nujol) 2240 ($\text{C}\equiv\text{N}$), 1685 ($\alpha\beta$ -unsat. ketone $\text{C}=\text{O}$), 1600 (arom. $\text{C}=\text{C}$), 1510 (antisym. NO_2), and 1350 cm^{-1} (sym. NO_2); λ_{max} (EtOH) 210 (log ϵ 4.10), 228 (4.27), and 356 nm (4.26); m/e 270. The mother liquors were chromatographed [preparative t.l.c. on Kieselgel PF 254; light petroleum (b.p. 60—80 °C)-EtOAc (4:3)] to obtain the *6-exo-carbonitrile* (8b) (0.8 g, 32.2%) as pale yellow prisms

(from toluene), m.p. 163—165 °C (Found: C, 57.7; H, 3.9; N, 20.2%); ν_{max} (Nujol) 2240 ($\text{C}\equiv\text{N}$), 1690 ($\alpha\beta$ -unsat. ketone $\text{C}=\text{O}$), 1600 (benzene $\text{C}=\text{C}$), 1510 (antisym. NO_2), and 1345 cm^{-1} (sym. NO_2); λ_{max} (EtOH) 208 (log ϵ 4.12), 225 (4.29), and 350 nm (4.26); m/e 270.

6-endo-Acetyl- and 6-exo-Acetyl-8-(5-nitro-2-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-one, (7c) and (8c).—The dimer (1) (1 g, 0.0023 mol) was heated under reflux with an excess of methyl vinyl ketone for 3 h. The solvent was evaporated off and the product chromatographed on alumina (B.D.H. aluminium oxide, neutral; CHCl_3) to give a pale yellow gum (1.6 g) (two components by t.l.c.). Preparative t.l.c. [Kieselgel PF 254; light petroleum (b.p. 60—80 °C)-EtOAc (2:1)] gave (a) the *6-endo-acetyl adduct* (7c) (0.285 g, 21%) as pale yellow prisms (from toluene), m.p. 146—147 °C (Found: C, 58.0; H, 4.8; N, 14.2. $\text{C}_{14}\text{H}_{13}\text{N}_3\text{O}_4$ requires C, 58.5; H, 4.6; N, 14.6%); ν_{max} (Nujol) 1710 (acetyl $\text{C}=\text{O}$), 1690 ($\alpha\beta$ -unsat. ketone $\text{C}=\text{O}$), 1590, 1570, 1510, and 1335 cm^{-1} ; λ_{max} (EtOH) 209 (log ϵ 4.28), 225 (4.40), and 348 nm (4.38); m/e 287, and (b) the *6-exo-acetyl adduct* (8c) (0.785 g, 59%) as pale yellow prisms (from toluene), m.p. 151—152 °C (Found: C, 58.4; H, 4.8; N, 14.2%); ν_{max} (Nujol) 1710, 1690, 1590, 1570, 1510, and 1340 cm^{-1} ; λ_{max} (EtOH) 210 (log ϵ 4.27), 228 (4.39), and 352 nm (4.38); m/e 287.

6-endo-Formyl-6-exo-methyl-8-(5-nitro-2-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (11).—The dimer (1) (1.2 g, 0.0028 mol) was heated under reflux in an excess of methacrylaldehyde for 24 h. The solvent was evaporated off and the product chromatographed on alumina (B.D.H. aluminium oxide, neutral; CHCl_3) to give *compound* (11) (0.91 g, 57.7%) as pale yellow prisms, m.p. 168—169 °C (from $\text{CHCl}_3\text{-Et}_2\text{O}$) (Found: C, 58.2; H, 4.7; N, 14.7. $\text{C}_{14}\text{H}_{13}\text{N}_3\text{O}_4$ requires C, 58.5; H, 4.6; N, 14.6%); ν_{max} (Nujol) 2710 (formyl $\text{C}-\text{H}$), 1730 (formyl $\text{C}=\text{O}$), 1685 ($\alpha\beta$ -unsat. carbonyl $\text{C}=\text{O}$), 1590, 1580 (benzene $\text{C}=\text{C}$), 1510 (antisym. NO_2), and 1345 cm^{-1} (sym. NO_2); λ_{max} (EtOH) 210 (log ϵ 4.14), 227 (4.29), and 354 nm (4.30); m/e 287.

8-(5-Nitro-2-pyridyl)-6-endo- and -6-exo-phenyl-8-azabicyclo[3.2.1]oct-3-en-2-one, (7d) and (8d).—The dimer (1) (8 g, 0.018 mol), styrene (50 ml), and MeCN (35 ml) were heated under reflux for 3 h. The solvent was evaporated off to leave a solid residue which was chromatographed on alumina (B.D.H. aluminium oxide, neutral; toluene-EtOAc). The eluate gave the *6-endo-phenyl-cycloadduct* (7d) as yellow needles (9.8 g, 83%) (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 176—177 °C (Found: C, 66.9; H, 4.8; N, 13.2. $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}_3$ requires C, 67.3; H, 4.7; N, 13.1%); ν_{max} (Nujol) 1680, 1600, 1575, 1510, and 1340 cm^{-1} ; λ_{max} (EtOH) 212 (log ϵ 4.33), 225 (4.34), and 352 (4.32) nm; m/e 321. Preparative t.l.c. of the mother liquor afforded the *6-exo-phenyl-cycloadduct* (8d) as yellow needles (0.5 g, 4%) (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 160—165 °C (Found: C, 67.1; H, 4.8; N, 13.3%); ν_{max} (Nujol) 1680, 1600, 1580, 1510, and 1345 cm^{-1} .

8-(4,6-Dimethylpyrimidin-2-yl)-6-endo-phenyl-8-azabicyclo[3.2.1]oct-3-en-2-one (7j).—The dimer (2a and b) (3.4 g, 0.0085 mol) was heated in an excess of styrene at 90 °C for 3 h. Unchanged styrene was removed (100 °C at 10 mmHg) and the residual gum chromatographed on alumina (B.D.H. aluminium oxide, neutral; CHCl_3). The eluate was decolourised with animal charcoal to afford a colourless gum which solidified on cooling (solid CO_2 -acetone). The *endo-phenyl adduct* (7j) (3.5 g, 68%) was

obtained as prisms (from Et₂O), m.p. 91—92 °C (Found: C, 74.6; H, 6.3; N, 13.8. C₁₉H₁₉N₃O requires C, 74.7; H, 6.3; N, 13.8%); ν_{\max} (Nujol) 1 690 ($\alpha\beta$ -unsat. carbonyl C=O), 1 580, and 1 565 cm⁻¹ (arom. C=C); λ_{\max} (EtOH) 213 (log ϵ 4.23), 242 (4.37), and 295 nm (3.54); m/e 305.

6-endo-(4-Methoxyphenyl)-8-(5-nitro-2-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (7e).—The dimer (1) (1 g, 0.002 3 mol), *p*-methoxystyrene (2 g, 0.015 mol), and 1,2-dichloroethane (7 ml) were heated under reflux for 24 h. The cooled mixture was chromatographed on alumina (B.D.H. aluminium oxide, neutral; CHCl₃) to give the *methoxyphenyl compound* (7e) (1.11 g, 68.5%) as pale yellow prisms (from CHCl₃-Et₂O), m.p. 216–217 °C (Found: C, 64.5; H, 4.9; N, 11.7. C₁₉H₁₇N₃O₄ requires C, 65.0; H, 4.9; N, 12.0%); ν_{\max} (Nujol) 1 680 ($\alpha\beta$ -unsat. carbonyl C=O), 1 600, 1 570, 1 510, 1 340, 1 300, and 1 250 cm⁻¹; λ_{\max} (EtOH) 215 (log ϵ 4.37), 226 (4.37), and 350 nm (4.33); m/e 351. The mother liquor contained a mixture of three isomers (0.36 g) which were not separated.

6-endo-(4-Chlorophenyl)-8-(5-nitro-2-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (7f).—The dimer (1) (3.4 g, 0.008 mol), *p*-chlorostyrene (4 g, 0.029 mol), and toluene (10 ml) were heated under reflux for 3 h. On cooling, the crude *compound* (7f) (4.25 g, 76.5%) precipitated as dark yellow needles, m.p. 196—198 °C. Chromatography on alumina (B.D.H. aluminium oxide, neutral; CHCl₃) gave the *chlorophenyl derivative* (7f) (3.1 g, 56%) as pale yellow needles (from CHCl₃-Et₂O), m.p. 199 °C (Found: C, 60.5; H, 4.1; Cl, 10.1; N, 11.6. C₁₈H₁₄ClN₃O₃ requires C, 60.8; H, 4.0; Cl, 10.0; N, 11.8%); ν_{\max} (Nujol) 1 680 ($\alpha\beta$ -unsat. carbonyl C=O), 1 590, 1 570, 1 510, 1 340, and 1 290 cm⁻¹; λ_{\max} (EtOH) 215 (log ϵ 4.33), 227 (4.33), and 349 nm (4.29); m/e 355.

6-endo-(4-Bromophenyl)-8-(5-nitro-2-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (7g).—The dimer (1) (2.7 g, 0.006 2 mol), *p*-bromostyrene (4 g, 0.022 mol), and toluene (10 ml) were heated under reflux for 4 h. The mixture was decolourised with animal charcoal. *Compound* (7g) (3.4 g, 68.5%) was isolated as pale yellow needles (from CHCl₃-Et₂O), m.p. 206 °C (Found: C, 53.9; H, 3.7; Br, 20.0; N, 10.5. C₁₈H₁₄BrN₃O₃ requires C, 54.0; H, 3.5; Br, 20.0; N, 10.5%); ν_{\max} (Nujol) 1 690 (conj. ketone C=O), 1 590, 1 570, 1 510, 1 345, and 1 290 cm⁻¹; λ_{\max} (EtOH) 212 (log ϵ 4.36), 225 (4.36), and 353 nm (4.30).

8-(5-Nitro-2-pyridyl)-6-endo-(4-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (7h).—The dimer (1) (1 g, 0.002 3 mol) and 4-vinylpyridine (10 ml) were heated at 100 °C for 5 h. The cooled mixture was chromatographed on alumina (B.D.H. aluminium oxide, neutral; EtOAc). Evaporation left a residue which was extracted into hot light petroleum (b.p. 60—80 °C) (15 ml) giving when set aside *compound* (7h) (0.764 g, 51.5%), as pale yellow prisms (from toluene), m.p. 215—216 °C (Found: C, 63.4; H, 4.5; N, 16.9. C₁₇H₁₄N₄O₃ requires C, 63.4; H, 4.4; N, 17.4%); ν_{\max} (Nujol) 1 680 ($\alpha\beta$ -unsat. ketone C=O), 1 590, 1 570 (arom. C=C), 1 510 (antisym. NO₂), and 1 345 cm⁻¹ (sym. NO₂), λ_{\max} (EtOH) 212 (log ϵ 4.41), 225 (4.36), and 340 nm (4.30); m/e 322.

6-exo-Methyl-6-endo-phenyl- and 6-endo-Methyl-6-exo-phenyl-8-(5-nitro-2-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-one, (12) and (13).—The dimer (1) (0.8 g, 0.001 9 mol) was heated at 100 °C with an excess of α -methylstyrene for 4 h. The cooled mixture was chromatographed on alumina [B.D.H. aluminium oxide, neutral; light petroleum (b.p. 60—80 °C)-EtOAc (50 : 50)]. The eluate was eva-

porated and the residue crystallised from toluene to give the 6-exo-*methyl-6-endo-phenyl adduct* (12) (0.628 g, 51%) as pale yellow prisms, m.p. 192—193 °C (Found: C, 67.9; H, 5.2; N, 12.2. C₁₉H₁₇N₃O₃ requires C, 68.1; H, 5.1; N, 12.5%); ν_{\max} (Nujol) 1 700, 1 600, 1 580, 1 505, 1 340, and 1 300 cm⁻¹; λ_{\max} (EtOH) 210 (log ϵ 4.36), 227 (4.37), and 360 nm (4.38); m/e 335. The 6-endo-*methyl-6-exo-phenyl adduct* (13) (0.358 g, 30%) was obtained as pale yellow prisms, m.p. 187—188 °C, from the mother liquor by preparative t.l.c. [Kieselgel PF 254; light petroleum (b.p. 60—80 °C)-EtOAc (9 : 2)] followed by recrystallisation from light petroleum (b.p. 40—60 °C)-CHCl₃ (Found: C, 67.8; H, 5.2; N, 12.1%); ν_{\max} (Nujol) 1 700, 1 600, 1 580, 1 505, 1 340, and 1 300 cm⁻¹; λ_{\max} (EtOH) 210 (log ϵ 4.36), 227 (4.38), and 360 nm (4.38).

6-endo-Ethoxy-8-(5-nitro-2-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (7i).—A mixture of the hydrochloride (1.06 g, 0.004 2 mol) of (3), triethylamine (0.424 g, 0.004 2 mol), and ethyl vinyl ether (15 ml) was stirred at room temperature for 3 days, then filtered, and the solid was washed well with EtOAc. The combined filtrate and washings were chromatographed on alumina (B.D.H. aluminium oxide, neutral; EtOAc) to give *compound* (7i) (0.3 g, 25%) as pale yellow rods (from CHCl₃-Et₂O), m.p. 108—109 °C (Found: C, 57.9; H, 5.2; N, 14.5. C₁₄H₁₅N₃O₄ requires C, 58.1; H, 5.2; N, 14.5%); ν_{\max} (Nujol) 1 690 ($\alpha\beta$ -unsat. ketone C=O), 1 590, 1 570 (arom. C=C), 1 505 (antisym. NO₂), and 1 345 cm⁻¹ (sym. NO₂); λ_{\max} (EtOH) 209 (log ϵ 4.11), 225 (4.24), and 350 nm (4.28); m/e 289.

12-(5-Nitro-2-pyridyl)-12-azatetracyclo[6.3.1.1.3^e.0^{2,7}]-tridec-10-en-9-one (18a or b).—The dimer (1) (0.8 g, 0.001 8 mol), norborn-2-ene (3 g), and toluene (20 ml) were heated at 90 °C for 24 h. The solvent and the excess of norbornene were evaporated off (100 °C at 10 mmHg) and the residue was chromatographed on alumina [B.D.H. aluminium oxide, neutral; toluene-EtOAc (3 : 1)]. The eluate was evaporated to dryness and the residual gum dissolved in warm light petroleum (b.p. 60—80 °C)-Et₂O (50 : 50). After 24 h at room temperature the two stereoisomers of *compound* (18) (0.67 g, 58.5%) precipitated as fine pale yellow needles, m.p. 140 °C, and yellow rods, m.p. 164—166 °C. The two isomers could not be separated by chromatography; however fractional recrystallisation from toluene afforded a low yield of *rods* (18a or b), m.p. 165—166 °C (Found: C, 65.4; H, 5.5; N, 13.2. C₁₇H₁₇N₃O₃ requires C, 65.6; H, 5.5; N, 13.5%); ν_{\max} (Nujol) 1 690 ($\alpha\beta$ -unsat. ketone C=O), 1 600, 1 580, 1 510, 1 340, and 1 300 cm⁻¹; λ_{\max} (EtOH) 209 (log ϵ 4.34), 227 (4.50), and 362 (4.54) nm; m/e 311.

3,4-Dimethyl-7-(5-nitro-2-pyridyl)-7-azabicyclo[4.3.1]deca-3,8-dien-10-one (21).—The dimer (1) (8 g, 0.037 mol), 2,3-dimethylbuta-1,3-diene (8 g, 0.098 mol), and toluene (40 ml) were heated (70 °C). After 6 h a second portion of the butadiene (7 g, 0.085 mol) was added and heating was continued for 6 h. The cooled mixture was filtered through alumina [B.D.H. aluminium oxide, neutral (50 g)]. Elution with toluene gave *compound* (21) (10 g, 90%) as orange prisms (from toluene), m.p. 123—124 °C (Found: C, 64.1; H, 5.8; N, 13.6. C₁₆H₁₇N₃O₃ requires C, 64.2; H, 5.7; N, 14.0%); ν_{\max} (Nujol) 1 720 (sat. ketone C=O), 1 640 (enamine C=C), 1 590, 1 570 (arom. C=C), 1 500 (antisym. NO₂), 1 335 (sym. NO₂), and 1 295 cm⁻¹; λ_{\max} (CHCl₃) 255 (log ϵ 4.11) and 392 nm (4.41); m/e 299.

3,4-Dimethyl-7-(4,6-dimethylpyrimidin-2-yl)-7-azabicyclo[4.3.1]deca-3,8-dien-10-one (22).—The dimeric mixture (2a

and b) (0.9 g, 0.002 24 mol), 2,3-dimethylbuta-1,3-diene (1 g, 0.012 2 mol), and 1,2-dichloroethane (10 ml) were stirred under reflux (60 °C) for 3 h. The product was cooled and chromatographed on alumina (B.D.H. aluminium oxide, neutral; $\text{ClCH}_2\cdot\text{CH}_2\text{Cl}$) to give *compound* (22) (0.91 g, 71%) as prisms, m.p. 102–103 °C (Found: C, 72.2; H, 7.4; N, 14.4. $\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}$ requires C, 72.1; H, 7.5; N, 14.8%); $\nu_{\text{max.}}$ (Nujol) 1 720 (sat. ketone C=O), 1 645 (enamine C=C), 1 585, 1 570 (arom. C=C), and 1 295 cm^{-1} ; $\lambda_{\text{max.}}$ (EtOH) 206 (log ϵ 3.98), 226 (3.86), and 274 nm (4.51); *m/e* 283.

Reaction of the Dimer (1) with trans-Penta-1,3-diene.—The dimer (1) (2.5 g, 0.005 7 mol), *trans*-penta-1,3-diene (15 ml), MeCN (15 ml), and hydroquinone (1 g) were heated under reflux for 3 days. The solvent was evaporated off and the residue extracted with hot methanol. After methanol was evaporated off the dark residue (3.7 g) was chromatographed on alumina (B.D.H. aluminium oxide, neutral; CHCl_3) to give a yellow mixture (2.16 g) of products. The major bands were separated by preparative t.l.c. on silica gel (Kieselgel PF 254; CHCl_3). The first band (highest R_F value) gave a (50 : 50) mixture of 2-methyl-7-(5-nitro-2-pyridyl)-7-azabicyclo[4.3.1]deca-3,8-dien-10-one (29) and 5-methyl-7-(5-nitro-2-pyridyl)-7-azabicyclo[4.3.1]deca-3,8-dien-10-one (31) (0.644 g, 19.6%) as fine rods (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 140–150 °C (Found: C, 63.2; H, 5.4; N, 14.9. Calc. for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_3$: C, 63.2; H, 5.3; N, 14.7%); $\nu_{\text{max.}}$ (Nujol) 1 710 (sat. ketone C=O), 1 650 (enamine C=C), 1 600, 1 570 (arom. C=C), 1 500 (antisym. NO_2), 1 335 (sym. NO_2), and 1 295 cm^{-1} ; $\lambda_{\text{max.}}$ (EtOH) 209 (log ϵ 4.08), 250 (4.08), and 385 nm (4.34); *m/e* 285. The second band gave a pale yellow gum (0.72 g) containing at least three products; $\nu_{\text{max.}}$ (Nujol) 1 680 cm^{-1} . The mixture was further separated by preparative t.l.c. on silica gel [Kieselgel PF 254; cyclohexane-EtOAc (3 : 1)] to give 8-(5-nitro-2-pyridyl)-6-endo-(*trans*-1-*prop*-1-enyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (33) (0.32 g, 9.8%) as pale yellow needles (toluene), m.p. 95–97 °C (Found: C, 63.0; H, 5.3; N, 14.9. $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_3$ requires C, 63.2; H, 5.3; N, 14.7%); $\nu_{\text{max.}}$ (CHBr_3) 2 920, 2 850, 1 680, 1 590, 1 570, 1 505, 1 330, and 1 295 cm^{-1} ; *m/e* decomp. (no M^+ given). The third band gave an orange gum (0.37 g) which was further separated by preparative t.l.c. on silica gel [Kieselgel PF 254; cyclohexane-EtOAc (3 : 2)] to give 5-methyl-7-(5-nitro-2-pyridyl)-7-azabicyclo[4.3.1]deca-3,8-dien-10-ol (35) or 2-methyl-7-(5-nitro-2-pyridyl)-7-azabicyclo[4.3.1]deca-3,8-dien-10-ol (36) (0.121 g, 3.7%) as orange prisms (from CHCl_3) m.p. 171 °C (Found: C, 61.8; H, 6.0; N, 13.7. $\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_3$ requires C, 62.7; H, 6.0; N, 14.6%); $\nu_{\text{max.}}$ (Nujol) 3 500 (OH), 3 080 (vinylic CH), 1 640 (enamine C=C), 1 590, 1 570 (arom. C=C), 1 495 (antisym. NO_2), 1 340 (sym. NO_2), and 1 290 cm^{-1} ; $\lambda_{\text{max.}}$ (EtOH) 208 (log ϵ 4.17), 253 (4.17), and 392 nm (4.42); *m/e* 287. 3-(5-Nitro-2-pyridyloxy)pyridine (37) (0.143 g, 5.7%) was also isolated as pale yellow prisms (from Et_2O), m.p. 94 °C (lit.⁴⁶ 95 °C).

15-(5-Nitro-2-pyridyl)-15-azapentacyclo[7.5.1.1^{3,6}.0^{2,7}.0^{10,14}]hexadeca-4,12-dien-8-one (24).—(1) (2 g, 0.004 6 mol) and dicyclopentadiene (15 ml) were heated at 120 °C for 4 h, unchanged dicyclopentadiene was evaporated off (90 °C at 10 mmHg), and the residue was chromatographed on alumina (B.D.H. aluminium oxide, neutral), eluted first with toluene, then with toluene-EtOAc (3 : 2). Evaporation of the second eluate gave the 2 : 1 *adduct* (24) (1.1 g, 34%) as pale yellow needles (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 216–218 °C (Found: C, 68.7; H, 5.4; N, 11.8. $\text{C}_{20}\text{H}_{19}$

N_3O_3 requires C, 68.8; H, 5.5; N, 12.0%); $\nu_{\text{max.}}$ (Nujol) 3 150, 3 060, 1 710, 1 600, 1 520, and 1 345 cm^{-1} ; $\lambda_{\text{max.}}$ (EtOH) 207 (log ϵ 4.18), 228 (4.29), and 370 nm (4.05); *m/e* 349.

Reaction of the Betaine (3) with Cyclopentadiene.—The mixture of the betaine (3) together with $\text{NEt}_3\cdot\text{HCl}$ [0.8 g, containing 0.002 2 mol of (3)] and freshly distilled cyclopentadiene (10 ml) were stirred together at room temp. for 48 h. The mixture was then filtered and the solid washed with EtOAc (40 ml). The combined filtrate and washings were evaporated to dryness and the residual mixture separated by preparative t.l.c. on Kieselgel PF 254 [light petroleum (b.p. 60–80 °C)-EtOAc (3 : 1)]. (1RS,2RS,6SR,7RS)-11-(5-nitro-2-pyridyl)-11-azatricyclo[5.3.1.0^{2,6}]undeca-3,9-dien-8-one (23) (0.28 g, 44.5%) was isolated as pale yellow prisms (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 194 °C (Found: C, 63.8; H, 4.8; N, 14.8. $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_3$ requires C, 63.6; H, 4.6; N, 14.8%); $\nu_{\text{max.}}$ (Nujol) 3 080 (vinyl C-H), 1 680 (α,β -unsat. ketone C=O), 1 640 (enamine C=C), 1 600, 1 570 (arom. C=C), 1 520 (antisym. NO_2), 1 340 (sym. NO_2), and 1 300 cm^{-1} ; $\lambda_{\text{max.}}$ (EtOH) 207 (log ϵ 4.00), 228 (4.19), and 355 nm (4.25); *m/e* 283. 7-(5-Nitro-2-pyridyl)-7-azatricyclo[4.3.1.1^{2,5}]undeca-3,8-dien-10-one (25) (0.231 g, 36.5%) was isolated as yellow prisms (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 137 °C (Found: C, 63.3; H, 4.7; N, 15.2. $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_3$ requires C, 63.6; H, 4.6; N, 14.8%); $\nu_{\text{max.}}$ (Nujol) 1 740 (sat. ketone C=O), 1 590, 1 575 (arom. C=C), 1 500 (antisym. NO_2), 1 330 (sym. NO_2), and 1 300 cm^{-1} ; $\lambda_{\text{max.}}$ (CHCl_3) 252 (log ϵ 4.04) and 385 nm (4.38); *m/e* 283.

8-(4,6-Dimethylpyrimidin-2-yl)-6-endo-(*trans*-*prop*-1-enyl)-8-azabicyclo[3.2.1]oct-3-en-2-one (34).—The mixture of dimers (2a and b) (0.5 g, 0.001 3 mol), *trans*-penta-1,3-diene (7 ml), hydroquinone (50 mg), and 1,2-dichloroethane (7 ml) was heated under reflux (50 °C) for 12 h. The solvent was evaporated off and the mixture of products separated by preparative t.l.c. on silica gel [Kieselgel PF 254; light petroleum (b.p. 60–80 °C)-EtOAc (3 : 1)]. *Compound* (34) (0.138 g, 20.4%) was isolated as rods (from $\text{CHCl}_3\text{-Et}_2\text{O}$), m.p. 128–130 °C (Found: C, 71.0; H, 6.9; N, 15.3. $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}$ requires C, 71.4; H, 7.1; N, 15.6%); $\nu_{\text{max.}}$ (CHBr_3) 1 685 (α,β -unsat. ketone C=O), 1 580, 1 560 (arom. C=C), and 1 340 cm^{-1} ; *m/e* 269. *Compounds* (30) and (32) (0.28 g) were isolated as a gum which resisted both crystallisation and separation by chromatography; $\nu_{\text{max.}}$ (CHBr_3) 1 720 cm^{-1} .

7-(4,6-Dimethylpyrimidin-2-yl)-7-azatricyclo[4.3.1.1^{2,5}]undeca-3,8-dien-10-one (26) and (1RS,2RS,6SR,7RS)-11-(4,6-dimethylpyrimidin-2-yl)-11-azatricyclo[5.3.1.0^{2,6}]undeca-3,9-dien-8-one (27).—The mixture of dimers (2a and b) (1 g, 0.002 5 mol), freshly distilled cyclopentadiene (7 ml), and 1,2-dichloroethane (7 ml) were heated under reflux (60 °C) for 3 h. The mixture was decolourised with animal charcoal and chromatographed on alumina (B.D.H. aluminium oxide, neutral; $\text{ClCH}_2\cdot\text{CH}_2\text{Cl}$). The solvent was removed to leave a crystalline mixture (1.4 g) (two components by t.l.c.) from which *compound* (26) (0.6 g, 44.9%) was isolated as prisms (by fractional recrystallisation from Et_2O), m.p. 146–147 °C (Found: C, 71.9; H, 6.5; N, 15.5. $\text{C}_{16}\text{H}_{17}\text{N}_3\text{O}$ requires C, 71.9; H, 6.4; N, 15.7%); $\nu_{\text{max.}}$ (Nujol) 3 080 (vinyl CH), 1 735 (sat. ketone C=O), 1 615 (C=C), 1 590, 1 575 (arom. C=C), and 1 260 cm^{-1} ; $\lambda_{\text{max.}}$ (CHCl_3) 278 nm (log ϵ 4.51); *m/e* 267. Preparative t.l.c. of the mother liquor gave a further *solid* (27) (0.29 g, 21%),

⁴⁶ F. Yoneda, *J. Pharm. Soc. Japan*, 1957, **77**, 944.

m.p. 167—169 °C (Found: C, 71.7; H, 6.3; N, 15.5%; ν_{\max} (Nujol) 1 680 cm^{-1}).

(1RS, 8RS)-7,7-Dimethyl-12-(5-nitro-2-pyridyl)-12-azatricyclo[6.3.1.0^{2,6}]dodeca-2(6),4,9-trien-11-one (47).—A mixture of the hydrochloride (0.709 g, 0.002 8 mol) of (3), triethylamine (0.28 g, 0.002 8 mol), 6,6-dimethylfulvene (b.p. 43 °C; lit.,⁴⁷ 40—43 °C) (5 ml), and diethyl ether (10 ml) was stirred at 20 °C for 2 h, then evaporated (40 °C at 10 mmHg). The residue was chromatographed on alumina [B.D.H. aluminium oxide, neutral; EtOAc-toluene (50 : 50)]. The brown gum (0.6 g) was further purified by preparative t.l.c. on silica gel [Kieselgel PF 254; cyclohexane-EtOAc (4 : 1)] to give compound (47) (0.27 g, 31%) as a pale yellow gum which resisted crystallisation, ν_{\max} (Nujol) 3 060, 3 020 (vinyl CH), 1 690 (α,β -unsat. ketone), 1 590, 1 570 (arom. C=C), 1 500 (antisym. NO₂), and 1 330 cm^{-1} (sym. NO₂); λ_{\max} (CHCl₃) 366 nm (log ϵ 3.99); decomp. in mass spectrometer (no M^{++} given).

(1RS, 7RS, 8RS)-12-(5-Nitro-2-pyridyl)-7-phenyl-12-azatricyclo[6.3.1.0^{2,6}]dodeca-2(6),4,9-trien-11-one (49) and (1RS, 7SR,8RS)-12-(5-Nitro-2-pyridyl)-7-phenyl-12-azatricyclo[6.3.1.0^{2,6}]dodeca-2(6),4,9-trien-11-one (50).—The mixture of the betaine (3) together with NEt₃.HCl [0.33 g, containing 0.001 3 mol of (3)], 6-phenylfulvene (b.p. 98—100 °C at 5 mmHg; lit.,⁴⁸ 85—87 °C at 2.5 mmHg) (1 g, 0.006 5 mol), and diethyl ether (10 ml) were stirred at 20 °C for 2 h, then evaporated (100 °C at 10 mmHg). The residue was chromatographed on alumina [B.D.H. aluminium oxide, neutral; toluene-EtOAc (50 : 50)] to give a mixture of two products separated by preparative t.l.c. on silica gel [Kieselgel PF 254; light petroleum (b.p. 60—80 °C)-EtOAc (3 : 1)] to give the 4-endo-phenyl isomer (49) (0.2 g, 38.2%) as pale yellow prisms (from EtOAc), m.p. 186—187 °C (decomp.) (Found: C, 70.8; H, 4.9; N, 10.9. C₂₂H₁₇N₃O₃ requires C, 71.2; H, 4.6; N, 11.3%); ν_{\max} (Nujol) 3 050, 3 010 (vinyl CH), 1 685 (α,β -unsat. ketone), 1 590, 1 570 (arom. C=C), 1 500 (antisym. NO₂), 1 340 (sym. NO₂), and 1 300 cm^{-1} ; λ_{\max} (EtOH) 209 (log ϵ 4.36), 227 (4.30), and 360 nm (4.23); m/e 371. The 4-exo-phenyl isomer (50) (0.09 g, 17.3%) was obtained as pale yellow prisms (from EtOAc-Et₂O), m.p. 223—224 °C (decomp.) (Found: C, 70.9; H, 4.8; N, 11.1. C₂₂H₁₇N₃O₃ requires C, 71.2; H, 4.6; N, 11.3%); ν_{\max} (Nujol) 3 050, 1 690, 1 590, 1 570, 1 500, 1 335, and 1 300 cm^{-1} ; λ_{\max} (EtOH) 210 (log ϵ 4.35), 228 (4.29), and 360 nm (4.21); m/e 371.

(1RS,7SR,8RS)-7-(4-Methoxyphenyl)-12-(5-nitro-2-pyridyl)-12-azatricyclo[6.3.1.0^{2,6}]dodeca-2(6),4,9-trien-11-one (51).—The dimer (1) (0.88 g, 0.002 mol), 6-(*p*-methoxy-

phenyl)fulvene (m.p. 70 °C; lit.,⁴⁹ 70 °C) (0.8 g, 0.004 3 mol), and 1,2-dichloroethane (20 ml) were heated under reflux for 2 h. The solvent was removed (50 °C at 10 mmHg) to leave a pale yellow gum (2.2 g). Preparative t.l.c. on silica gel [Kieselgel PF 254; light petroleum (b.p. 60—80 °C)-EtOAc (3 : 1)] gave compound (51) (0.79 g, 49%) as pale yellow prisms (from EtOAc), m.p. 170—171 °C (Found: C, 68.3; H, 5.0; N, 10.2. C₂₃H₁₉N₃O₄ requires C, 68.8; H, 4.8; N, 10.5%); ν_{\max} (Nujol) 3 100, 3 060 (vinyl CH), 1 685 (α,β -unsat. ketone C=O), 1 595, 1 575 (arom. C=C), 1 510 (antisym. NO₂), 1 335 (sym. NO₂), and 1 290 cm^{-1} ; λ_{\max} (CHCl₃) 368 nm (log ϵ 4.29); m/e 401.

Reaction of 6-(*p*-Methoxyphenyl)fulvene with the Pyrimidinyl Dimer (2a and b).—The dimer (2a and b) (1 g, 0.002 5 mol), 6-(*p*-methoxyphenyl)fulvene (0.65 g, 0.003 5 mol), and 1,2-dichloroethane (10 ml) were warmed (50 °C for ca. 5 s). An exothermic reaction followed with loss of the orange colour of the fulvene. The cooled mixture was chromatographed on alumina (B.D.H. aluminium oxide, neutral; ClCH₂.CH₂Cl) to give a pale yellow gum (1.35 g) a mixture of many components separated by preparative t.l.c. on silica gel [Kieselgel PF 254; light petroleum (b.p. 60—80 °C)-EtOAc (3 : 1)] to give (1RS,7SR,8RS)-12-(4,6-dimethylpyrimidin-2-yl)-7-(4-methoxyphenyl)-12-azatricyclo[6.3.1.0^{2,6}]dodeca-2(6),4,9-trien-11-one (52) (0.156 g, 8%) as prisms (from CHCl₃-Et₂O), m.p. 171—173 °C (Found: C, 75.0; H, 6.0; N, 10.3. C₂₄H₂₃N₃O₂ requires C, 74.8; H, 6.0; N, 10.9%); ν_{\max} (Nujol) 1 685, 1 610, 1 580, 1 575, and 1 510 cm^{-1} ; m/e 385. The 2 : 1 adduct (53) (0.105 g, 3.6%) was isolated as prisms (from CHCl₃-Et₂O), m.p. 229—230 °C (decomp.) (Found: C, 71.4; H, 5.9; N, 13.6. C₃₅H₃₄N₆O₃ requires C, 71.6; H, 5.8; N, 14.3%); ν_{\max} (Nujol) 1 690, 1 680 (sh) 1 610, 1 580, 1 560, and 1 510 cm^{-1} ; m/e 385 ($M - 201$). The second 2 : 1 adduct (54) (0.242 g, 8.3%) was isolated as needles (from EtOAc), m.p. 232—233 °C (decomp.), (Found: C, 71.0; H, 5.9; N, 13.6. C₃₅H₃₄N₆O₃ requires C, 71.6; H, 5.8; N, 14.3%); ν_{\max} (Nujol) 1 690br, 1 610, 1 580, 1 560, and 1 510 cm^{-1} ; m/e 385 ($M - 201$).

We thank Dr. A. D. McNaught for help with nomenclature and the Sudan Government for a Scholarship (to B. I.).

[5/2475 Received, 18th December, 1975]

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