Rationalisation of the Variation of Reactivity towards Cycloaddition with Structure in 3-Oxido-pyridinium and -azinium Betaines and a Study of 1-(4,6-Dimethyl-2-pyrimidinyl)-3-oxidopyridinium

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Summary Frontier M.O. theory rationalises the effects of aza-substitution on the dimerisation tendency in 3-oxidopyridiniums, the 1-(2-pyrimidinyl) betaine displaying the predicted high reactivity; fulvenes add as 6 π-electron systems across the 2,6-positions of 3-oxidopyridiniums.

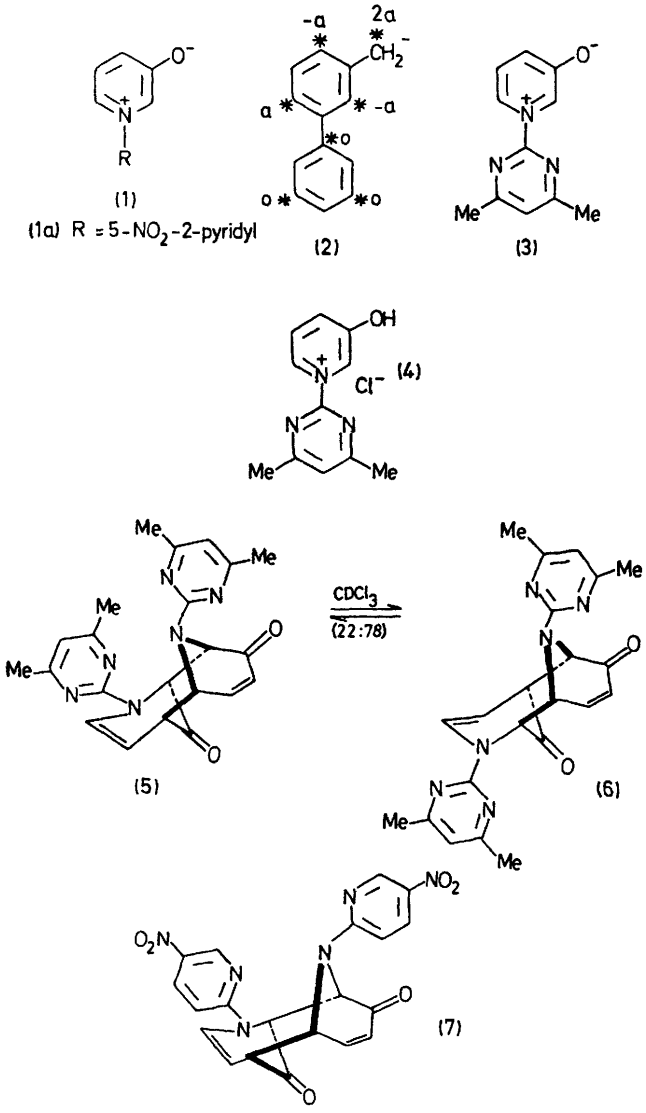
THE betaines 1-methyl-, 1-phenyl-, 1-(2,4-dinitrophenyl)- and 1-(5-nitro-2-pyridyl)-3-oxidopyridinium [*cf.* (**1**)] form a series which displays increasing reactivity in pericyclic reactions with olefinic dipolarophiles.[1] The frontier molecular orbital approximation utilising equation (1) has previously[2a] successfully accounted for the reactivity of various dipolarophiles towards a common dipole. In equation (1), ΔE is a measure of the stabilisation of the transition state between addends R and S reacting at the positions *r*, *r'* of R and *s*, *s'* of S (*cf.* ref. 2a).

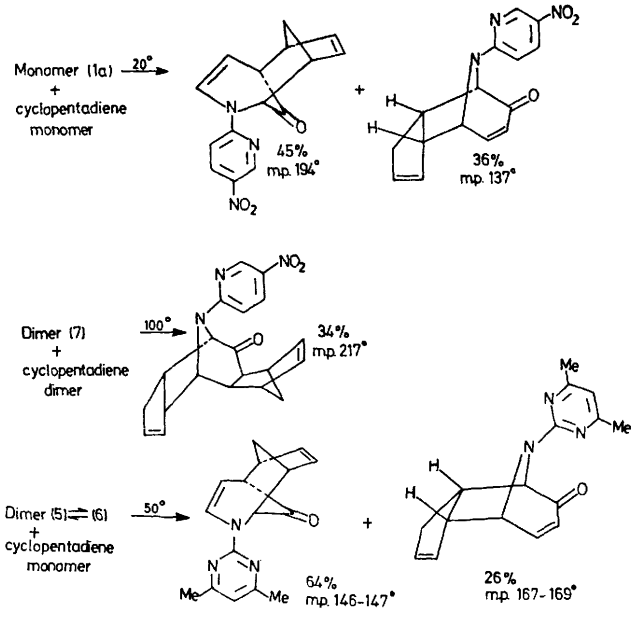
$$\Delta E = 2\{[C_r^{HO}C_s^{LU} + C_{r'}^{HO}C_{s'}^{LU})\gamma]^2/(E_R^{HO} - E_s^{LU}) + [(C_r^{LU}C_s^{HO} + C_{r'}^{LU}C_{s'}^{HO})\gamma]^2/(E_s^{HO} - E_R^{LU}) \quad (1)$$

The tendency to dimerise by a pericyclic reaction accordingly depends on the difference between HOMO and LUMO in the molecule; extended conjugation narrows the gap, hence the 1-aryl betaines are more reactive than 1-alkyl. The effects of substituents can be correlated using equation (2) in which the 1-aryl-3-oxido-betaines are considered to be derivatives of the 3-phenylbenzyl anion (**2**).

$$\Delta E = \sum_r C_r^2 \Delta\alpha_r \quad (2)$$

In the 3-phenylbenzyl anion (**2**) the NBMO [corresponding to HOMO in the 1-aryl betaine (**1**)] has zero coefficients at all the phenyl carbon atoms. According to equation (2), aza-substitution of the unstarred C-atom of the pyridine ring of (**1**), and of any of the C-atoms of the phenyl ring, thus has no effect on HOMO.[2b] However, such aza-substitution will generally lower LUMO. Hence the inter-frontier energy separation will be reduced and consequently the absolute value of ΔE of equation (1) will increase leading





SCHEME 1. Reaction of nitropyridyl betaine [monomer (**1a**) and dimer (**7**)] and pyrimidinyl betaine dimer (**5**) ⇌ (**6**) with cyclopentadiene (monomer and dimer).

to a greater tendency towards dimerisation. Aza-substitution in the 2′,6′-positions of the phenyl ring, in addition to the substitution effect mentioned above, allows the two rings to attain coplanarity which is necessary for efficient conjugation. In the case of the 2′,4′-dinitrophenyl betaine, marked deviation from coplanarity of the two rings decreases conjugation.

The betaines react with (*a*) electron deficient (*e.g.* CH_2=CHCN), (*b*) electron rich (*e.g.* CH_2=CHOEt), and (*c*) conjugated olefins (*e.g.* CH_2=CHPh). CNDO/2 calculations show that in (*a*) the reactions are controlled by the betaine HOMO interacting with olefin LUMO, in (*b*) by betaine LUMO interacting with olefin HOMO whereas in (*c*) both interactions are important.

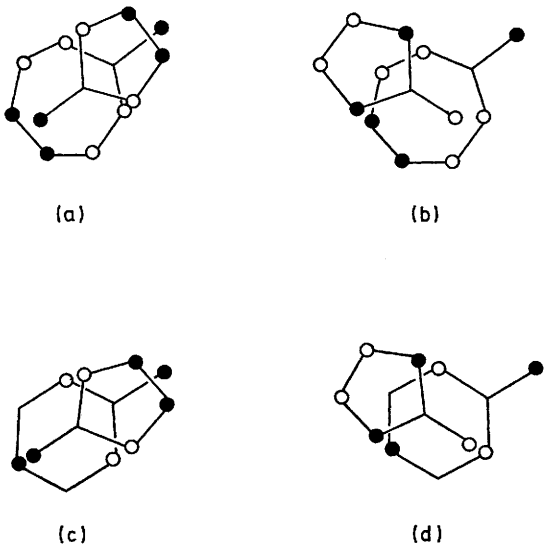
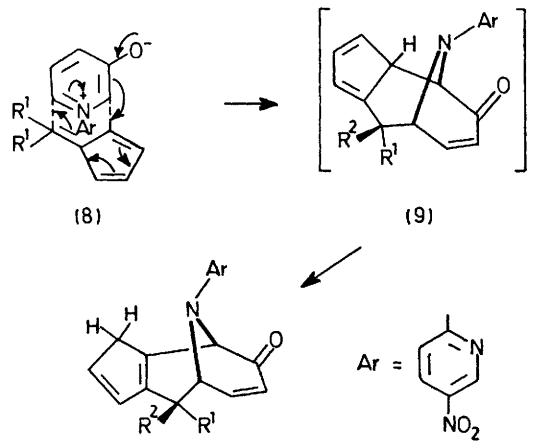


FIGURE. (a) and (b): Alternative stereochemistry for adduct formation between fulvene and tropone (the filled and unfilled circles indicate the signs of the coefficients for the fulvene[7] LUMO and tropone[9] HOMO). (c) and (d): Alternative stereochemistry for adduct formation between 1-methyl-3-oxidopyridinium and fulvene (signs of the coefficients for the fulvene[7] LUMO and betaine[10] HOMO are indicated).

Reactions of type (*a*) occur with all the pyridinium betaines; the unreactivity of 1-methyl-3-oxidopyridazinium[3] and 2-methyl-4-oxidobenzotriazinium[4] towards cycloaddition and the reduced reactivity of 3-methyl-1-oxidophthalazinium[3] and 2-methyl-3-oxidocinnolinium[3] is rationalised by the fact that heteroatom substitution at the starred positions in (**2**) lowers the HOMO. Reactions of type (*c*) occur only with arylpyridinium betaines and reactions of type (*b*) only with the nitropyridyl betaine (**1a**), in agreement with the increased importance of the betaine LUMO in such reactions.

The above considerations suggest that the pyrimidinylpyridinium betaine (**3**) should be of particular interest. Its attempted preparation from (**4**) led to formation of dimers (**5**) and (**6**) originally in the ratio >10:1 which changed on standing to 22:78. The structure and stereochemistry of the dimers (**5**) and (**6**) were elucidated by n.m.r. spectroscopy, including extensive decoupling experiments. The preferential formation of dimer (**5**) under kinetically controlled conditions is well explained by a frontier M.O. treatment of the type used by Houk *et al.*[5] PMO calculations using equation (1) show that the transition state for formation of the *exo*-2,2′-4,6′ adduct (**5**) should be lower than that for (**6**).[2a,5]

We have now isolated the monomeric nitropyridyl betaine (**1a**); it readily forms the known[6] dimer (**7**). Comparison of the reactivity of (**1a**), (**7**), and (**5**) ⇌ (**6**) with cyclopentadiene (Scheme 1) demonstrates the great reactivity of the pyrimidinylpyridinium betaine dimers (**5**) ⇌ (**6**).



(10) $R^1 = R^2 = Me$
(11) $R^1 = Ph$, $R^2 = H$
(12) $R^2 = p\text{-}MeOC_6H_4$, $R^1 = H$

SCHEME 2.

Finally, we have demonstrated that fulvenes add as 6π-electron components across the 2,6-positions, as predicted.[7] From 6,6-dimethyl-, 6-phenyl-, and 6-*p*-methoxyphenylfulvene and the *N*-pyridyl betaine (**1a**), (**10**)—(**12**) were isolated by rearrangement of initial products (**9**). The pyrimidinyl betaine dimer [(**5**) ⇌ (**6**)] gives several products with fulvenes deriving from further addition to initial 1:1-adducts. Addition reactions of fulvenes with tropone were previously reported[8] to give regioisomers of the same type as (**9**) in which the initially formed tropone 1:1 adducts also underwent facile [1,5] hydrogen shifts; the stereochemistry of addition was established as that of

Figure (a) by deuterium labelling at C-2 and C-5 of the fulvene. Our results now show the corresponding approach (Figure c) for addition to 3-oxidopyridinium. The strong favourable secondary orbital overlap in both (a) and (c) compared to the unfavourable ones in (b) and (d) rationalises both the stereospecificity and the regiospecificity.

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