1,3-Cycloaddition of Heterocyclic Zwitterions to Dienes†

By King-Leung Mok and Martin J. Nye*

(Department of Chemistry, University of Guelph, Guelph, Ontario, Canada)

Summary The frontier molecular orbital method was used to predict that certain heterocyclic zwitterions should cycloadd to dienes, and the first case of this type was experimentally observed in the formation of adducts between 1-methylquinolinium-3-olate (**1**) and several dienes.

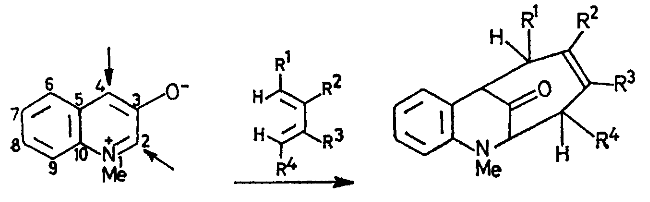
It is remarkable that while hundreds of examples of 1,3-cycloadditions of heterocyclic zwitterions have been reported,[1] not one involves a diene rather than an ene as dipolarophile. The known systems can all therefore be designated as $(4n + 2)$-electroselective‡ rather than $(4n)$-electroselective. However there is *a priori* no reason why

---

† Presented in part at the 4th International Congress of Heterocyclic Chemistry, Salt Lake City, Utah, U.S.A., 1973.

‡ *i.e.* Reactive in cycloaddition reactions towards systems containing $4n+2$ π-electrons between the reaction termini. Normally $n=0$, and the addend is an alkene.

($4n$)-electroselective zwitterionic systems should not exist, and it was of interest to develop a method of predicting such systems and then to test the predictions.



(1) (2) (3)

TABLE

	a	b	c	d	e	f	g	h
R^1	H	Me	H	H	H	Me	H	H
R^2	H	H	H	Me	H	H	H	Me
R^3	H	H	H	H	Me	H	H	Me
R^4	H	H	Me	H	H	H	Me	H
Yield of (**3**)/%	40	25	45	20 or 62	62 or 20	15	15	57

Several groups of workers[2] have applied molecular orbital calculations (such as CNDO/2) within the framework of Fukui's frontier molecular orbital (FMO) method[3] to rationalise the various aspects of cycloaddition behaviour. We have found[4] that even the simplest Hückel treatment of π-systems within the FMO method satisfactorily explains periselectivity,[2b] electroselectivity, regioselectivity, and stereoselectivity of over one hundred diverse cycloadditions (including reactions of heteroatomic species and 1,3-dipoles). This technique was applied to the postulated cycloaddition between 1-methylquinolinium-3-olate (**1**) and buta-1,3-diene (**2a**). Application of the Hückel method gave the eigenvalues and eigenvector coefficients of the various energy levels (Figure). The highest occupied molecular orbital (HOMO) of (**1**) interacts with the lowest unoccupied molecular orbital (LUMO) of (**2a**), as well as the LUMO of (**1**) interacting with the HOMO of (**2a**).§ Inspection of the eigenvector coefficients of both the HOMO and the LUMO at the proposed reaction sites C-2 and C-4 of (**1**) shows that the symmetry is correct for bonding, and that the values are large ($>$ 0·3) and therefore appreciable bond strength might be expected. Hence (**1**) is predicted to cycloadd to dienes across atoms C-2–C-4.

We report that (**1**) can be generated *in situ* by treating a solution of 3-hydroxy-1-methylquinolinium iodide with triethylamine, and gives the predicted 1 : 1 adducts (**3a**—**h**) with the dienes (**2a**,**b**,**d**,**f**,**h**) respectively. The adducts have the expected C, H, and N analyses, molecular ions, and ^{1}H n.m.r. spectra. In the i.r. each shows a carbonyl band between 1700 and 1725 cm^{-1} and the u.v. spectra are similar.¶

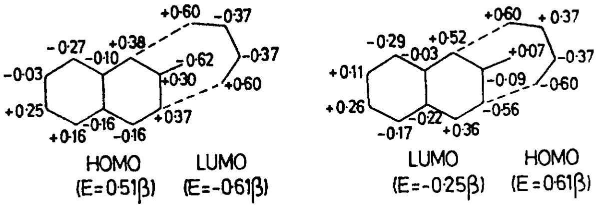
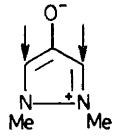
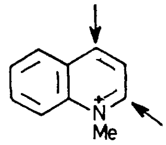


FIGURE. Eigenvector coefficients and eigenvalues (E) for the frontier molecular orbitals of (**1**) and buta-1,3-diene.

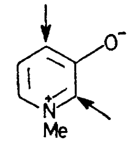
The number and yields (see Table) of isomeric cycloadducts produced is in accordance with minimal regioselectivity but exclusive *exo–endo* selectivity. The former is expected[2c] from the FMO theory since the eigenvector coefficients at C(2) and C(4) are very similar in magnitude. The latter can also be predicted[2d] by consideration of secondary interaction of the FMO's. Of the possible interactions the most repulsive would occur between the LUMO of (**1**) at N(1), C(5), and C(10) and the HOMO of (**2**) at C(2) and C(3) in an *endo* attack. Hence *exo* attack might be expected. Double resonance ^{1}H n.m.r. at 220 MHz¶ of (**3b**) followed by coupling constant–dihedral angle correlations of vicinal protons supports a boat conformation of the seven-membered ring with the methyl group *trans* to the aromatic ring, which must have arisen by *exo* attack.



(4)



(5)



(6)

Systems (**4**)—(**6**) are also predicted to be ($4n$)-electroselective across the sites indicated. However (**4**) and (**5**) were recovered under similar conditions which yielded adducts of (**1**). Substitution of diphenyl-, dimethyl-, and diethoxycarbonyl-groups at C(3) and C(5) of (**4**) again did not result in addition. The behaviour of (**6**) towards dienes

---

§ The latter reaction between the closer lying levels should be greater. So (**1**) would behave as an electron acceptor and would react more quickly with more electron-rich reagents.

¶ We are grateful to the Ontario Research Foundation for running and analysing these spectra. Full results will be published later. For example, (**3e**): ν_{CO} (nujol) 1715 *m/e* 241 (M^+, 28%), 159 ($M^+ - C_6H_{10}$, 100%), 131 ($M^+ - C_6H_{10} - CO$, 56%); δ (CD_3CN–Me_4Si) 1·27 (s, 3H, C–CH_3), 1·68 (s, 3H, C–CH_3), 2·00—2·75 (m, 4H, 2CH_2), 2·84 (s, 3H, N–CH_3), 3·49—3·88 (m, 2H, 2CH), 6·36—7·24 (m, 4H, arom); λ_{max} (hexane) 323 (ϵ 1400), 303 (2500), 293 (sh, 1700), 260 nm (11,400).

is currently being studied[5] by Katritzky *et al.*, who have previously shown[6] that the system adds to electron deficient enes across C(2) and C(6).††

Financial support of the National Research Council of Canada is acknowledged. We thank Dr. C. A. Fyfe for guidance with the HMO work.

(*Received, 2nd May* 1974; *Com.* 496.)

†† An analogous cycloaddition of an ene across C(2) and C(10) of (**1**) is not symmetry disallowed, but would be disfavoured because of the low eigenvector coefficient at C(10) and the thermal instability of the product. The referee was interested in the possibility that the observed adduct formation might be explained by visualising initial cycloaddition of the diene as an ene across C(2) and C(10) (**1**) followed by Cope rearrangement of the unstable adduct. Consideration of steric effects in (**2b**) reveals that the wrong stereoisomers with the methyl groups *cis* to the aromatic ring should be strongly preferred and hence the mechanism seems unlikely.

[1] M. Ohta and H. Kato in 'Nonbenzenoid Aromatics,' ed. J. P. Snyder, Academic Press, New York, 1969, p. 117.

[2] (a) R. Sustmann and H. Trill, *Angew. Chem. Internat. Edn.*, 1972, **11**, 838; R. Sustmann and R. Schubert, *ibid.*, 1972, **11**, 840; K. N. Houk, J. Sims, R. E. Duke Jr., R. N. Strozier, and J. K. George, *J. Amer. Chem. Soc.*, 1973, **95**, 7287; (b) K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *ibid.*, 1973, **95**, 7301; (c) O. Eisenstein, J.-M. Lefour, and N. T. Anh, *Chem. Comm.*, 1971, 969; (d) F. Hoffmann and R. B. Woodward, *J. Amer. Chem. Soc.*, 1965, **87**, 4388.

[3] K. Fukui, 'Theory of Orientation and Stereoselection,' Springer Verlag, Heidelberg, 1970.

[4] K. Mok, M.Sc. thesis, University of Guelph, 1974; K. Mok and M. J. Nye, to be published.

[5] A. R. Katritzky, personal communication.

[6] A. R. Katritzky and Y. Takeuchi, *J. Amer. Chem. Soc.*, 1950, **92**, 4134.