HETEROCYCLES, Vol 22, No 5, 1984

STEREOCHEMICAL ASPECTS OF 1,3-DIPOLAR CYCLOADDITION OF BENZ[*de*]ISOQUINOLINIUM-1-IDE AND NAPHTHO[1,8-*cd*]THIOPYRAN

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Abstract —— In contrast to naphtho[1,8-*cd*]thiopyran which undergoes 1,3-dipolar cycloaddition with maleimides to give exclusively or predominantly *exo*-adducts, 2-methylbenz[*de*]isoquinolinium-1-ide has been shown to react with maleimides to give exclusively *endo*-adducts. These results are rationalized in terms of frontier orbital theory.

2-Methylbenz[*de*]isoquinolinium-1-ide (**1**)(R=Me) was found to undergo 1,3-dipolar cycloaddition with maleimides to give exclusively *endo*-adducts (Table 1).[1,2] In contrast, naphtho[1,8-*cd*]thiopyran (**5**) has been known to give exclusively or predominantly *exo*-adducts when allowed to react with maleimides (Table 2).[1,3] We have now attempted to rationalize these conflicting results using frontier orbital theory.

Before discussing the results of calculations, the reaction of (**1**)(R=Me) with dimethyl maleate and dimethyl fumarate should be mentioned. Thus, treatment of 2,3-dihydro-2-methyl-1*H*-benz[*de*]isoquinoline *N*-oxide[1] with acetic anhydride and triethylamine in the presence of dimethyl maleate at -10°C gave the *endo*- (**2d**)[4] and *exo*-adducts (**3d**)[4] in 6 and 52% yields, respectively. A similar reaction of (**1**)(R=Me) with dimethyl fumarate afforded the single adduct (**4**)[4] in 83% yield. The structures of these adducts can be readily assigned on the basis of the ^{1}H-nmr spectra. The fact that the stereospecific *cis*-1,2-cycloaddition was observed

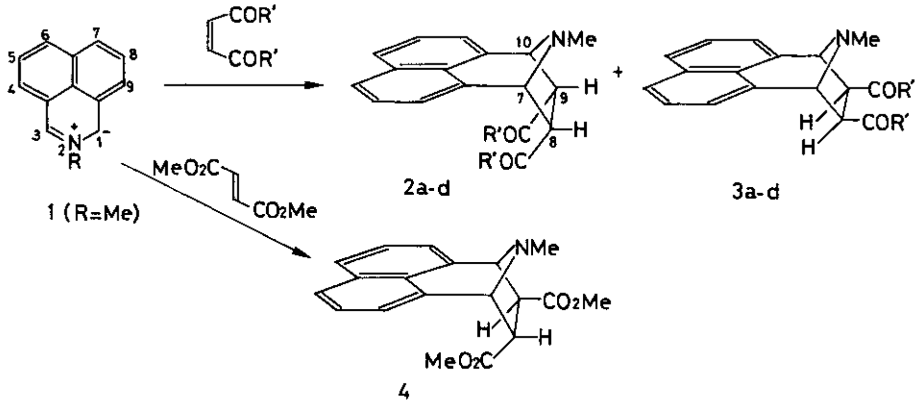


Table 1. Yield for cycloaddition of (1) (R=Me) to various dipolarophiles

	dipolarophile	R' R'	isolated yield (%) (2)	 (3)	reference
a	N-methylmaleimide	-NMe-	80	0	1
b	N-phenylmaleimide	-NPh-	59	0	1
c	maleic anhydride	-O-	65	0	unpublished[5]
d	dimethyl maleate	OMe OMe	6	52*	this work

* GLC analysis showed that the product ratio of (2d) to (3d) is 1:6.

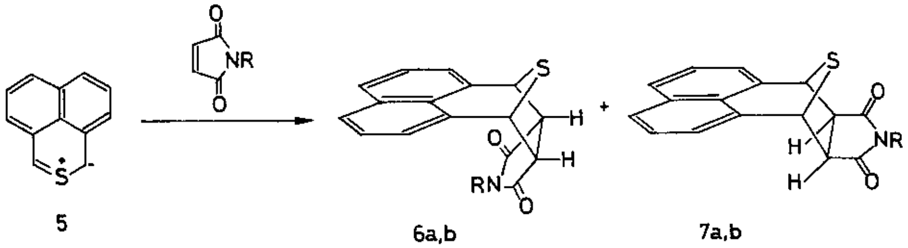


Table 2. Yield for cycloaddition of (5) to maleimides

	dipolarophile	R	isolated yield (%) (6)	 (7)	reference
a	N-methylmaleimide	Me	13	52	1
b	N-phenylmaleimide	Ph	0	55	3

in these reactions, indicates that the reaction takes place in a concerted manner. Frontier orbitals of (1) (R=H), (5), and maleimide (R=H) were calculated by using *ab initio* procedures at the STO-3G level.[6] The computer program employed is IMSPACK which contains Gaussian 70.[7] The results, summarized in Fig. 1, clearly indicate that both the reactions are dipole-HOMO-controlled ones.[8]

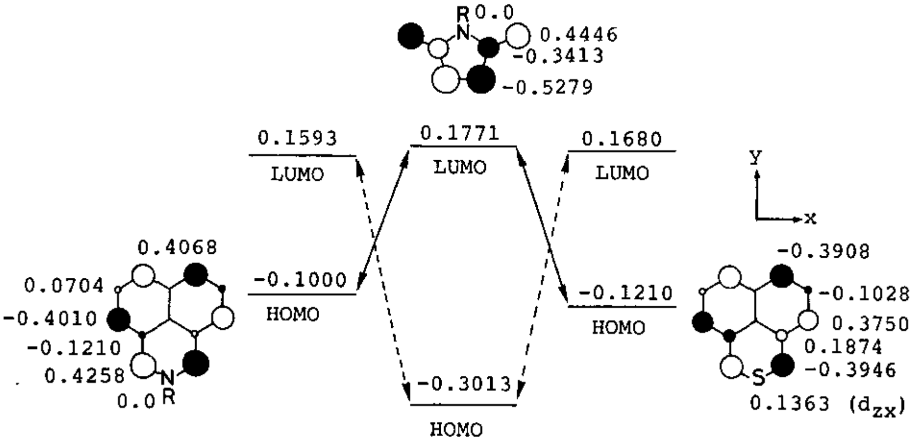
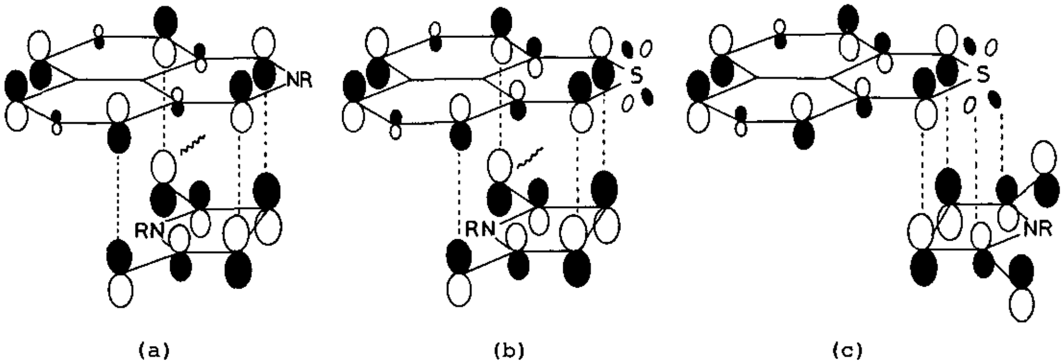


Fig. 1. Frontier energy levels (a.u.) and orbital coefficients for (1) (R=H), (5), and maleimide (R=H)

The secondary orbital interactions in the transition states are shown in Fig. 2. The interactions between the lobes on C-3a and C-9a of the dipoles and the carbonyl carbons of maleimide are antibonding (wavy lines). However, the coefficients of the HOMO of (1) at C-3a and C-9a are relatively small and the bonding interactions between the lobes of C-4 and C-9 of the dipoles and the carbonyl oxygens of

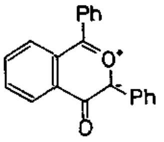


(a) (b) (c)

Fig. 2. The secondary orbital interactions in the transition states

maleimide are dominant (Fig. 2a) and lead to a preference for endo addition. In sharp contrast, relatively large HOMO coefficients on C-3a and C-9a in (5) make the endo transition state (Fig. 2b) disfavorable. In addition, the exo transition state (Fig. 2c) is stabilized by the favorable interaction between the d_{zx} component of the sulfur and the carbonyl carbons of maleimide.

The remaining problem to be accounted for is why the reaction of (1)(R=Me) with dimethyl maleate gave the exo-adduct (3d) as the major product.[9] One possible interpretation is that the molecule of dimethyl maleate is rather flexible compared to maleimides and maleic anhydride, so that the secondary interactions in the endo transition state are expected to be less important and the steric repulsion between the naphthalene ring and the ester groups may become significant. A similar exo-selectivity of dimethyl maleate has been reported with some six-membered heteroaromatic betaines [e.g., (8)[10] and (9)[11]].



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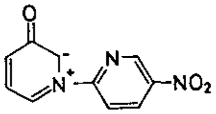

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4. The adduct (2d), mp 140-142°C; nmr ($CDCl_3$) δ 2.16 (s,3H, NCH_3), 3.20 (s, 6H, $2xOCH_3$), 3.90 (m, 2H, 8- amd 9-H), 4.42 (m, 2H, 7- and 10-H), 7.1-7.7 (m, 6H, arom. H); the adduct (3d), mp 135-136°C; nmr ($CDCl_3$) δ 2.18 (s, 3H, NCH_3), 3.26 (s, 2H, 8- and 9-H), 3.72 (s, 6H, $2xOCH_3$), 4.57 (s, 2H, 7- and 10-H), 7.1-7.75 (m, 6H, arom. H); the adduct (4), mp 110-111°C; nmr ($CDCl_3$) δ 2.14 (s, 3H, NCH_3), 3.40 (s, 3H, endo-CO_2CH_3), 3.46 (d, 1H, J=6 Hz, 9-H), 3.75 (s, 3H, exo-CO_2CH_3), 4.12 (bt, 1H, 8-H), 4.50 (d, 1H, J=7 Hz, 7-H), 4.55 (s, 1H, 10H), 7.0-7.75 (m, 6H, arom. H).
5. The adduct (2c), mp 154-155°C; nmr ($CDCl_3$) δ 2.20 (s, 3H, NCH_3), 4.19 (m, 2H,

8- and 9-H), 4.57 (m, 2H, 7- and 10-H), 7.15-7.8 (m, 6H, arom. H).

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   The molecular geometries of (**1**)(R=H), (**5**), and maleimide (R=H) were taken from appropriate references [R. E. Marsh, E. Ubell, and H. E. Wilcox, *Acta Cryst*., 1962, **15**, 35; J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory," McGraw-Hill, New York, N. Y., 1970]. A value of 1.55 Å for the C-S bond length in (**5**) was used ["Tables of International Distances," ed. by L. E. Sutton, The Chemical Society London, London, 1958, Supplement 1965]. The calculations were performed on a FACOM M-200 computer at the Computation Center of Fukuoka University.
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9. It has been reported that the reaction of (**1**)(R=Ph) with dimethyl maleate gave the *endo*- and *exo*-adducts in a ratio of *ca*. 70:30.[2] The *endo*-selectivity was considerably lowered.
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Received, 8th July, 1983