

Gain or loss of aromaticity in Diels–Alder transition states and adducts: a theoretical investigation[†]

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ABSTRACT: Semiempirical, *ab initio* and DFT investigations on the mechanism of the Diels–Alder reactions of a set of masked dienes (ring-fused dienes), viz. *o*-quinodimethane, anthracene and α -vinylnaphthalene, with ethylene, and reactions of α -vinylnaphthalene with maleic anhydride and *p*-benzoquinone were performed with a view to understanding the role of masking factors on the activation and reaction energies. The reactions were found to occur in a concerted fashion through synchronous transition states (TSs) in the first two reactions and through asynchronous TS in the other case. Of the compounds studied, *o*-quinodimethane is the most reactive diene both in a kinetic and a thermodynamic sense. α -Vinylnaphthalene reacts faster with maleic anhydride than *p*-benzoquinone, as expected, and two possible stereoselective TSs, one *endo* and the other *exo*, have been located for the reactions of α -vinylnaphthalene with the above dienophiles. Calculations show that the relative gain or loss of aromatic stabilization of the benzenoid ring in the transition state and in the product seems to play a major role in the kinetic and thermodynamic control of these reactions. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: aromaticity; Diels–Alder transition states; Diels–Alder adducts; reaction mechanism

INTRODUCTION

Diels–Alder reactions play an important role in organic synthesis. Its mechanism¹ remained obscure for a long time but now the regio- and stereochemistry of these reactions is well understood.² The synthetic utility of Diels–Alder reactions has expanded continuously ever since they were devised, by introducing new kinds of dienes and dienophiles. The wide range of dienes and dienophiles used have brought various factors that influence the reaction mechanism into focus and sophisticated theoretical models had to be developed to account for the mechanism and stereochemical outcome of the reactions. The dienes and dienophiles known thus far can be broadly classified as simple, substituted and masked dienes and dienophiles.^{3,4} While simple and substituted addends have expressed functionality, the masked dienes or dienophiles have hidden functionality. The mechanisms of the reactions involving the latter type of addends are complicated in the sense that, as the reacting group is a part of the whole system, the remaining part of the system reacts to changes in the functionality during the

reaction and can thus influence the reaction course to a larger extent. Therefore, in such reactions, the changes in both the functionality and the rest of the molecule are important and the final outcome depends on whether these changes reinforce or offset each other. Further, if the changes are significant before the transition state (TS) the changes affect the barrier considerably, and if they are significant after the TS the reaction energies are mostly affected.

Masked dienes and dienophiles of various kinds have been the subject of several experimental reports^{3,4} and have been studied particularly with regard to various stereochemical aspects. Masked dienes and dienophiles can be of cumulated, ring-fused, cage-fused types, etc. We selected a set of three simple masked dienes, viz. *o*-quinodimethane (QDM),^{5,6} anthracene (ANT)^{5,7} and α -vinylnaphthalene (VN),^{5,8} which are ring-fused dienes, and reacted them with ethylene to investigate factors that control the reactions. In addition to the above, the reactions of VN with maleic anhydride (MA) and *p*-benzoquinone (BQ) were also studied to observe the most preferred stereoselective TS in the reaction. A common factor in these dienes is the gain or loss aromaticity by the remaining part of the molecule when the diene reacts. The reactions selected for the investigation here have been thoroughly studied experimentally^{5–8} and the relative reactivities of the above dienes are known.

Our objective in this work was to locate the TSs of the above reactions and through them to look at the factors

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that are responsible for the reactivity trends observed with selected dienes. Especially the gain or loss of aromatic stabilization by the system in the TS and in the product was investigated. The systems were chosen such that QDM, ANT and VN are outer–outer ring, inner–inner ring and inner–outer ring conjugated dienes, respectively, and therefore are suitable for studying the influence of the above factors on the reaction.

Diels–Alder reactions of simple dienes and dienophiles have been studied^{9–12} extensively at various levels of theory, but investigations on the mechanism of the reactions involving such masked dienes are rare. It should be mentioned that a kinetic isotopic effects study of the retro–Diels–Alder reaction of ethanoanthracene has been carried out at the HF/3–21G level.^{9g} We employed AM1 and PM3 methods to investigate thoroughly the mechanism of the title reactions and, for comparison, we performed *ab initio* and DFT calculations. Higher level calculations are restricted to lower basis sets and for a selected set of reactions in view of the reasonably large size of the chemical systems investigated here.

COMPUTATIONAL METHODOLOGY

AM1 and PM3 calculations¹³ were performed using the MOPAC 6.0 program¹⁴ implemented on a Micro Vax II system and using the INSIGHT II package implemented on a Silicon Graphics workstation. For the selected set of reactions, *ab initio* and DFT computations were performed using the Gaussian 94W program.¹⁵ Equilibrium and TS structures of a set of typical reactions, involving ethylene as dienophile, were additionally optimized at the HF/3–21G¹⁶ level and single-point energy computations were performed on them with the 6–31G* basis set¹⁷ at the DFT level with the Becke3LYP functional.¹⁸ Single-point DFT calculations with the 6–31G* basis set on HF/3–21G geometry are considered to be the most reliable for such situations.¹⁹ Baker's eigenvector following (EF) routine¹⁹ has been extensively used for the location of stationary points at the semiempirical level but both EF and Berny algorithm has been used in HF/3–21G optimizations. In recent years, the EF routine has been extensively used^{11c,d,12,20} for geometry optimizations and has been found to be significantly better than the BFGS procedure. Stationary points were characterized through FORCE calculations; equilibrium and TS geometries were found to have zero and one imaginary frequency, respectively, in the diagonalized Hessian matrix. The deformation energies of dienes and dienophiles were calculated as reported earlier.^{12b,20}

Generally, in the Diels–Alder, reaction, three π bonds undergo cleavage and one π and two σ bonds are newly formed, and the bonding changes are therefore remarkable only in these bonds compared with the changes in the other parts of the reactants. For this reason, the changes in these bonds alone were quantitatively fol-

lowed through bond order analysis to monitor the progress of the reaction. The percentages of bond formation (BF_i) and cleavage (BC_j) at the TS are defined²⁰ as follows:

$$BF_i \text{ or } BC_j = \frac{BO_{i/j}^{\text{TS}} - BO_{i/j}^{\text{R}}}{BO_{i/j}^{\text{P}} - BO_{i/j}^{\text{R}}} \times 100$$

$$BFC_{\text{Ave}} = \frac{1/n_i \sum_i^{\text{forming bonds}} BF_i + 1/n_j \sum_i^{\text{cleaving bonds}} BC_j}{2}$$

where BFC_{Ave} is another index that is indicative of the early/late nature of the TSs for these reactions.

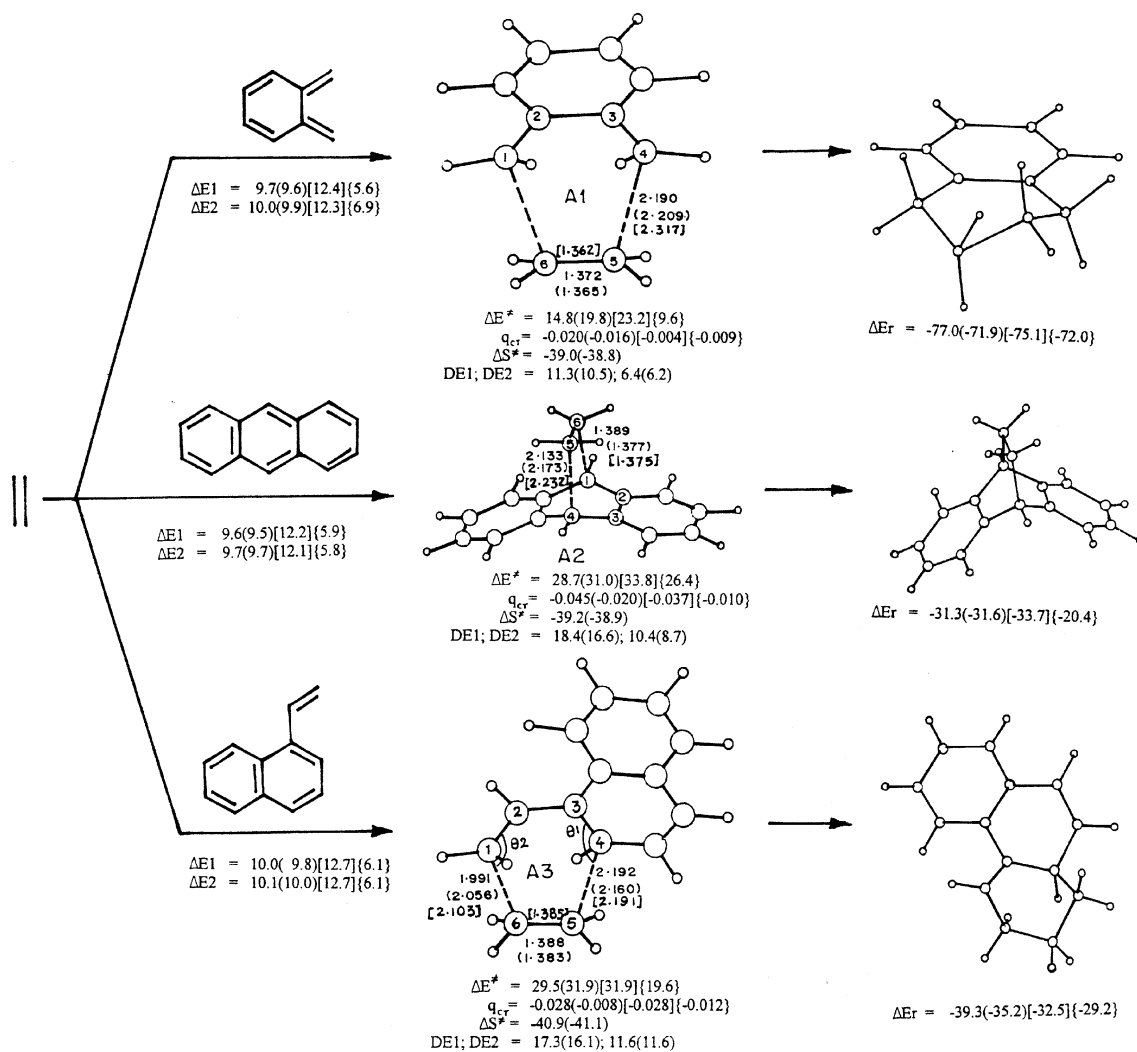
RESULTS AND DISCUSSION

A reaction scheme with TS geometries for the typical reactions, viz. ANT–ethylene, VN–ethylene and QDM–ethylene, is shown in Figure 1. The degrees of asynchronicity, frontier orbital energy (FOE) gaps, q_{CT} values, activation entropies and activation, deformation and reaction energies for the above reactions are also given in Figure 1. Computed AM1 and PM3 TSs for the reactions of VN with MA and BQ are shown in Figure 2 with the degrees of asynchronicity, selected geometric parameters, q_{CT} values and deformation energies of the reactants.

Table 1 gives the FOE gaps, activation entropies, activation and reaction energies for the reactions of VN with MA and BQ. Corresponding data for the butadiene–ethylene reactions are given for comparison and to show that the AM1 and PM3 methods give reliable activation energies. The percentages of bond making/breaking at the TS for the reactions studied here are summarized in Table 2. *Ab initio* and DFT computations were restricted to FOE gaps, q_{CT} values, activation and reaction energies.

Reactions of QDM, ANT and VN with ethylene

ANT and QDM react with ethylene to form stable Diels–Alder adducts, 9,10-dihydroethanoanthracene and aromatic tetralin, respectively, whereas VN forms an adduct that quickly isomerizes to 1,2,3,4-tetrahydrophenanthrene (Figure 1). QDM is a highly reactive diene and is usually generated⁶ *in situ* from thermal ring opening of benzocyclobutane. In QDM, there are two diene units, one endocyclic and the other exocyclic, and theoretically both units can take part in the Diels–Alder reaction. However, the exocyclic diene unit is known to react preferably over the other⁶ and it can also be verified from the frontier orbitals of QDM that the exocyclic diene unit forms the HOMO. Similarly in ANT,⁷ although different diene units are available for the reaction, it is the diene in



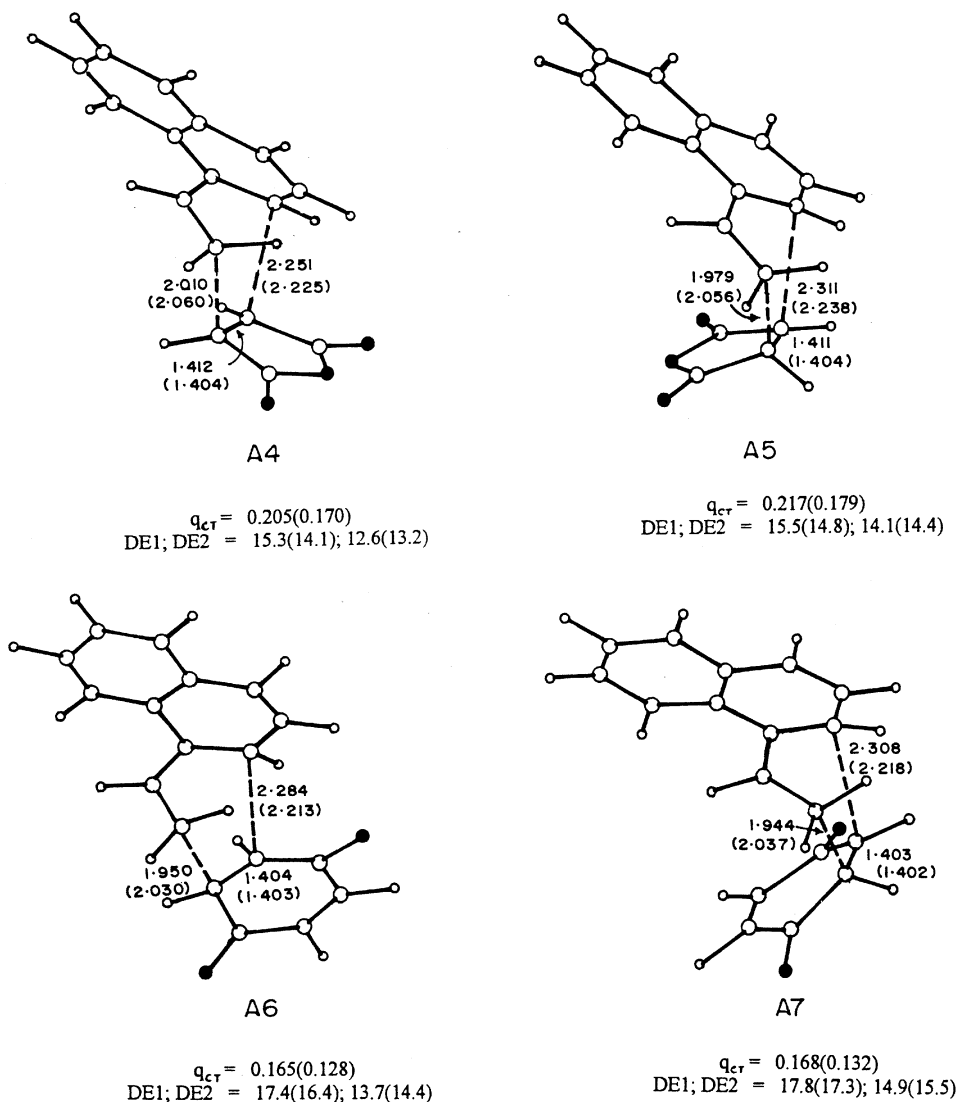
TS	α	C1—C2	C2—C3	C3—C4	θ_1	θ_2	ϕ
A1	0.000 (0.000) [0.000]	1.384 (1.377) [1.371]	1.434 (1.436) [1.439]	1.384 (1.377) [1.371]	99.2 (99.3) [100.3]	99.2 (99.3) [100.3]	0.0 (0.0) [0.0]
A2	0.000 (0.000) [0.000]	1.431 (1.426) [1.423]	1.418 (1.411) [1.400]	1.431 (1.426) [1.423]	94.5 (94.5) [94.6]	94.5 (94.5) [94.6]	0.0 (0.0) [0.0]
A3	0.048 (0.026) [0.020]	1.390 (1.381) [1.378]	1.403 (1.407) [1.396]	1.413 (1.407) [1.406]	98.4 (99.0) [100.4]	102.2 (101.3) [102.7]	-1.0 (0.0) [0.0]

Figure 1. Reaction scheme with TS geometries, frontier orbital energy gaps (eV), activation and reaction energies (kcal mol⁻¹) and activation entropy (cal K⁻¹) for the Diels–Alder reactions of QDM, ANT and VN with ethylene along with degrees of asynchronicity (α) at the TS, bond lengths (Å) and bond and torsion angles (\bullet). $\Delta E_1 = E_{\text{HOMO}}(\text{diene}) - E_{\text{LUMO}}(\text{dienophile})$ and $\Delta E_2 = E_{\text{LUMO}}(\text{diene}) - E_{\text{HOMO}}(\text{dienophile})$. The results are presented in the format AM1 (PM3) [HF/3-21G] {Becke3LYP/6-31G*//3-21G}

the central ring that is the most active;⁵ HOMO vectors also predict the same. In VN, both experimental observations⁸ and HOMO vectors show that the ring inner-outer diene is the most active in Diels–Alder reactions. Experimental reports^{5–8} suggest that, of these three reactions, the QDM reaction is considerably faster and the other two are relatively slow. Of ANT and VN, the

latter is found to react less readily than the former in Diels–Alder reactions.

Transition state geometry. Owing to the symmetrical nature of the dienes QDM and ANT and dienophile ethylene, the TSs A1 and A2 are synchronous; VN, being asymmetric, forms an asynchronous TS. The degrees of



TS	α^a	C1—C2	C2—C3	C3—C4	θ_1	θ_2	ϕ
A4	0.057 (0.039)	1.390 (1.381)	1.405 (1.410)	1.412 (1.405)	96.5 (97.3)	100.3 (99.9)	-1.9 (-3.0)
A5	0.077 (0.039)	1.391 (1.382)	1.406 (1.410)	1.410 (1.404)	98.1 (99.2)	103.9 (103.0)	2.1 (1.7)
A6	0.079 (0.043)	1.395 (1.386)	1.401 (1.405)	1.413 (1.408)	97.4 (98.4)	101.7 (100.6)	-7.8 (-5.4)
A7	0.086 (0.043)	1.396 (1.386)	1.402 (1.405)	1.412 (1.407)	98.8 (99.8)	104.8 (103.6)	-1.6 (2.0)

$$^a \alpha = |r_{4-5} - r_{6-1}| / (r_{4-5} + r_{6-1}).$$

Figure 2. AM1 (PM3) optimized TSs for the reactions of MA and BQ with VN along with degrees of asynchronicity, bond lengths (Å) and bond and torsion angles ($^\circ$)

asynchronicity (α) listed in Figure 1 show this very well. The terminal carbon atom of the vinyl unit in VN reacts first, as can be seen from the bond lengths of the newly forming bonds in the TS **A3** (Figure 1). This is due to the fact that the terminal carbon atom is more nucleophilic than the ring carbon atom of the diene, as reported by Bachmann and co-workers.^{8b,c} Also, the AM1 (PM3) [HF/3-21G] {Becke3LYP/6-31G*/3-21G} charges on the terminal and ring carbon atoms of *ca* -0.209 (-0.154)

[-0.407] {-0.345} and -0.119 (-0.101) [0.235] {-0.199}, respectively, indicate clearly the increased nucleophilicity of the former than the latter. The glide angles θ_1 and θ_2 (Figure 1) in the present set of reactions are close to those reported for the typical reaction;^{9a} the slightly greater value for θ_2 in the TS **A3** is due to the free vinyl group involved in the reaction. In all cases there is no twist from the C_s plane, as can be seen from the ϕ values in Figure 1.

Table 1. Calculated AM1 (PM3) frontier orbital energy gaps (eV), energy (kcal mol⁻¹) and entropy (cal K⁻¹) of activation and reaction energy (kcal mol⁻¹) for the reactions of VN with MA and BQ

Reaction	ΔE_1	ΔE_2	TS	ΔE^\ddagger	ΔS^\ddagger	ΔE_r
BD + ET ^a	10.8 (10.7)	11.0 (10.9)		23.2 (27.0)	-40.9 (-41.1)	-58.0 (-54.0)
VN + MA, <i>exo</i>	6.9 (7.1)	11.6 (11.2)	A4	25.5 (29.8)	-39.9 (-39.8)	-40.0 (-34.3)
VN + MA, <i>endo</i>			A5	28.3 (31.6)	-39.6 (-40.1)	
VN + BQ, <i>exo</i>	6.8 (6.9)	10.5 (10.3)	A6	31.2 (32.8)	-38.9 (-38.7)	-25.4 (-24.5)
VN + BQ, <i>endo</i>			A7	34.0 (34.3)	-38.7 (-39.1)	

^a The prototype Diels–Alder reaction between butadiene and ethylene; experimental barrier: 27.5 kcal mol⁻¹.²³

Table 2. Percentages of bond cleavage and formation in the TS of the Diels–Alder reactions involving QDM, AN and VN with ethylene and that of VN with MA and BQ

TS	Bond cleavage (BC_i) at the TS (%)			Bond formation (BF_i) at the TS (%)			BFC_{Ave}
	1–2	3–4	5–6	2–3	4–5	6–1	
A1	42.2 (35.8)	42.2 (35.8)	40.4 (33.9)	46.9 (39.5)	31.8 (26.0)	31.8 (26.0)	39.2 (32.8)
A2	49.0 (40.3)	49.0 (40.3)	50.9 (41.3)	85.6 (71.6)	41.5 (32.6)	41.5 (32.6)	52.9 (43.1)
A3	54.1 (46.5)	38.6 (33.6)	51.5 (46.7)	38.8 (33.7)	34.7 (32.1)	44.6 (38.2)	43.7 (38.5)
A4	54.3 (46.6)	37.5 (32.4)	52.5 (46.9)	37.5 (31.8)	30.2 (28.3)	44.0 (38.1)	42.7 (37.4)
A5	55.2 (47.2)	35.7 (32.6)	52.0 (47.0)	36.3 (31.8)	26.9 (27.8)	43.8 (38.6)	41.7 (37.5)
A6	58.7 (50.8)	38.7 (35.3)	55.3 (50.5)	39.7 (35.2)	29.9 (30.6)	48.3 (41.6)	45.1 (40.7)
A7	58.8 (50.8)	38.0 (35.4)	54.5 (50.2)	39.0 (35.1)	28.8 (30.6)	48.4 (41.4)	44.6 (40.6)

Energetics. The FOE gaps and quanta of charge transfer at the TS presented in Figure 1 suggest that these reactions are neutral electron demand reactions. The high negative entropy of activation for these reactions is characteristic of concerted processes. The AM1 and PM3 activation energies presented in Figure 1 show that QDM is the most reactive of the dienes chosen and in the other two ANT is slightly more reactive than VN, which is in full conformity with the experimental observations.^{6–8} It should be noted that the *ab initio* and DFT barriers in Figure 1 predict a trend in the reactivity of ANT and VN that is opposite to both the experimental observations and semiempirical predictions, but they predict the reactivity of QDM correctly. This has to be viewed in the light of earlier reports that AM1 and PM3 barriers^{10a,10f,11,12,20} are close to the experimental barrier but 3–21G^{9a} barriers are unreasonably high and Becke3LYP barriers¹⁹ are comparatively low. At the same time, AM1, PM3 and DFT calculations predict the same trend in reaction energy here whereas the 3–21G trend differs. In such a situation, we consider semiempirical activation and reaction energies to be more reliable and therefore we base our discussion on AM1 and PM3 values.

The highest reaction energy obtained for the QDM–ethylene reaction shows that it is the most favorable thermodynamically. This is in accordance with Hammond's postulate.²¹ The computed reaction energies for the ANT–ethylene and VN–ethylene reactions suggest that the former reaction is thermodynamically less favoured than the latter; this should be contrasted with

our observation from the activation energy that the former reaction is kinetically more favoured than the latter, and this is an exception to the above postulate.²¹ The considerable difference in activation energies of the reaction of QDM and the other two reactions is due to the gain in aromaticity in the former and decrease in aromaticity in the latter. In the QDM–ethylene reaction, the ring becomes partially aromatic in the TS and this results in considerable stabilization of the TS. Owing to this extra stabilization, the activation energy is significantly reduced. The ring becomes fully aromatic in the product and this gain in aromaticity from the TS to the product makes the reaction highly exothermic.

In the ANT–ethylene reaction, the central ring loses aromaticity and at the same time the side ring becomes fully benzenoid. These two opposing factors influence both the TS and the product stability. It appears that the decrease in aromaticity increases the activation energy and the gain in aromaticity increases²² the reaction energy.

In the VN–ethylene reaction, as one of the naphthalene ring double bonds is part of a diene, there is a loss of aromaticity during the reaction. Although the product in the VN reaction is metastable and quickly isomerizes by a 1,3-shift to tetrahydrophenanthrene, this reaction is found to have a slightly higher reaction energy than that of ANT. It should be noted that in 9,10-dihydroethanoanthracene the conjugation is lost and the two benzene rings are isolated by the central bicyclic ring, whereas in the other the double bonds are conjugated and this

delocalization may have led to a comparatively lower reaction energy.

Stabilization/destabilization of the TSs and products on account of a gain/loss of aromaticity can be clearly observed if the activation and reaction energies (Figure 1) of the title reactions are compared with those of the prototype butadiene–ethylene reaction (Table 1).

Deformation energy analysis shows that both the diene and the dienophile deforms to a lesser extent in the QDM–ethylene reaction and the deformation of both reactants significantly increases in the ANT and VN reactions. While differential extents of deformation in dienes (DE1) are characteristic of the molecular size, rigidity and aromaticity of the dienes, that in ethylene (DE2) in all these reactions is interestingly different. The lower deformation energy of the diene DE1 in the QDM reaction and the higher DE1 in the other two reactions is indicative of a lower activation energy for the former and a higher activation energy for the latter reactions.

Bond order analysis. Bond order analysis based on the BC_j , BF_i and BFC_{AVE} values listed in Table 2 shows the following. In the QDM reaction, the double bonds (C1—C2 and C3—C4) of the diene cleave slightly more than the ethylene double bond (C5—C6) and a newly forming π bond (C2—C3) forms to a considerably greater extent than the other forming σ bonds (C4...C5 and C6...C1). Such changes indicate the tendency of the six-membered ring to become aromatic. In the ANT reaction, the difference in cleavage is still lower and this shows that the loss of aromatic stability due to the loss of double bonds of the central ring is less. However, the new π bond is 85.6% formed and this highest value shows the tendency of the side ring to become fully benzenoid. The new σ bonds are formed to the extent of ca 40%. In the VN reaction, the terminal double bond cleaves considerably greater than the inner-ring double bond in the TS and consequently the newly forming σ bond from the terminal carbon atom is preferentially formed. This can be seen from the BC_j and BF_i values (Table 2) and the corresponding bond lengths shown in Figure 1. The BFC_{AVE} values indicate that the TS **A1** occurs 'earlier' compared with the other two and an 'early' TS would have a relatively lower activation energy.²⁰

Reactions of VN with MA and BQ

VN undergoes Diels–Alder reactions with electron-deficient dienophiles, viz. MA and BQ, more readily to form cycloadducts that are further used to synthesize steroid compounds.⁵ Two TSs (Figure 2), one an *endo* selective TS and the other *exo* TS, were obtained in these reactions and both TSs led to a single product (tetrahydrophenanthrene derivative). The high negative activation entropies (Table 1) indicate that these reactions are concerted reactions. The TSs obtained here are all

asynchronous, as would naturally be the case with an asymmetric diene. The BF_i value listed in Table 2 for the newly forming C6...C1 bond is higher than that for the C4...C5 bond as discussed in the previous section. Similarly, the outer π bond C1—C2 is found to have cleaved to a greater extent than the inner double bond C3—C4. This is explained as follows. The inner π bond is part of the aromatic system and would therefore normally resist cleavage whereas the outer π bond is free and connects the terminal atom that is highly reactive. This makes the outer π bond cleave faster than the inner π bond.

The BF_i , BC_j , BFC_{AVE} values in Table 2 for the VN–MA and VN–BQ reactions indicate that the TS for the former reaction occurs slightly 'early' compared with the latter. An 'early' TS indicates, in this case, less aromatic destabilization and will thus lead to a lower activation energy. This also supports the observation that MA is relatively more reactive than BQ. A notable difference in the geometry of the *endo* and *exo* selective TSs is in the glide angle θ_2 and twist angle ϕ , and this change seems partially to offset the crowding strain in the *endo* mode. The distortion due to crowding strain is greater in θ_2 and ϕ as they are associated with the more flexible end of the reacting site.

The FOE gaps (Table 1) and q_{CT} values (Figure 2) show that the above reactions are normal electron demand reactions. The reaction of VN with MA is predicted to be faster than that with BQ, as expected, and in agreement with the experimental observations.¹ Also, the former reaction is found to be more exothermic than the latter, as can be seen from the reaction energies in Table 1. Of the *endo* and *exo* TSs, the *endo* selective TS should be favoured over the *exo* selective TS owing to secondary orbital stabilization. Deformation energy (Figure 2) analysis shows that the dienophile has to undergo deformation to a slightly greater extent during the formation of the *endo* TS, and this happens as the atoms are crowded on one side in the *endo* approach. This difference in deformation energy could marginally increase the activation energy in the *endo* mode. Secondary orbital stabilization should be greater than this deformation energy difference and the net effect should be the stabilization of the *endo* TS over the *exo* TS. However, the AM1 and PM3 activation energies in Table 2 predict the opposite to be true, as it did on earlier occasions.^{10c,e,f,12} The BFC_{AVE} (Table 2) and q_{CT} values (Figure 2) indicate that the *endo* selective TS in both reactions occurs slightly 'earlier' than their corresponding *exo* TSs. An 'early' TS would normally correspond to a lower activation energy, but here the activation energies show the opposite trend.

CONCLUSIONS

QDM, ANT and VN act as dienes and undergo Diels–

Alder cycloadditions with ethylene through concerted processes. AM1 and PM3 calculations predict that QDM reacts more readily than the other two, in agreement with experimental observations, and the deformation energy analysis shows that the lower extent of deformation of QDM and ethylene results in a lower activation energy in this case. Of ANT and VN, ANT reacts slightly faster. HF/3–21G and Becke3LYP calculations predict a higher reactivity of QDM reliably, but their predictions for the relative reactivity of ANT and VN is the opposite of the experimental observations. Also, the QDM reaction is predicted to be more exothermic than the other two reactions. The reaction pattern and exothermicity of the reactions observed have been explained as being due to the following changes in the TSs and products: (1) there is a gain in aromatic stabilization of the benzenoid ring in the QDM reaction; (2) there is a simultaneous decrease in the aromaticity of the central ring in ANT and a marginal gain of aromatic stabilization by making the adjacent benzene ring of the ANT fully benzenoid; and (3) there is a loss of aromatic stabilization of one of the benzene rings of naphthalene in the VN reaction. The gain or loss of aromatic stabilization contributes partly to the barrier and partly to the reaction energy. In VN reactions, the terminal carbon is found to react before the ring carbon atom of the diene unit, as expected and in accordance with experimental observations. Calculations predict that in the VN reaction with MA and BQ the *exo* selective TS is slightly favoured over the *endo* form and this is in contrast with the normal expectations.

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