A Molecular Orbital and Crystallographic Study of the Structure and π-Facial Regioselectivity of 9-Chloro-1,4,5,8-tetrahydro-4a,8a-methanonaphthalene

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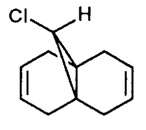
The title compound **1** undergoes reaction with electrophilic reagents such as dichlorocarbene regioselectively on the π-face *endo* to the chlorine. The crystal structure of **1** indicates significant geometrical distortions of the two rings, which we attribute to a stabilising interaction between the C–Cl σ* orbital and the *exo* π-orbital. PM3 calculations of these orbitals, the electrostatic potential and transition state models for dichlorocarbene addition all agree with the observed regioselectivity.

Stereoselection of π-faces by both nucleophilic and electrophilic reagents is currently the focus of much experimental[1] and theoretical[2,3] attention. Current theories tend to favour hyperconjugative[2] rather than electrostatic[3] models for both nucleophilic and electrophilic addition to *e.g.* carbonyl or *exo*-methylene double bonds. According to the Cieplak model,[2] stereo- or regio-selection is a consequence of specific interaction between an 'electron rich' σ orbital and an antiperiplanar σ* orbital on the electrophile or nucleophile.



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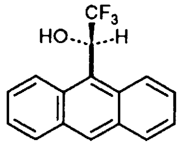

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We have recently reported[4] that the diene **1** reacts with electrophilic reagents such as dichlorocarbene or peracids regiospecifically on the double bond *endo* to the chlorine substituent, on the face of the molecule opposite the cyclopropyl ring. In a relatively rigid system apparently free from steric differentiation, regioselection could arise from either orbital or electrostatic control[5] or from specific factors present only in the transition state.[3,6] The Cieplak orbital model cannot be used to distinguish between the alkene groups in **1**, since they share common antiperiplanar σ orbitals. Electrostatic π-facial asymmetry has been proposed[7] to account for the chiral discriminatory behaviour of *e.g.* the Pirkle reagent **2**, and a similar asymmetry in the calculated PM3 electrostatic potential (MEP) for **1** was indeed noted.[7] This was attributed to stabilising antiperiplanar interactions between the Cl–C σ* orbital and the occupied *exo* π-orbital, rendering the *endo* double bond more nucleophilic in both a frontier orbital[5] and an electrostatic sense. One prediction arising out of this analysis[7] was that the Cl–C σ* *exo* π-orbital interaction would result in a geometrical distortion of the *exo* double bond towards the bridgehead carbon. Since **1** is a liquid at room temperature, verification of this prediction required specialised techniques of low temperature crystallisation and data collection.[8] We now report the crystal structure of **1**, together with a more detailed analysis of its reactivity.

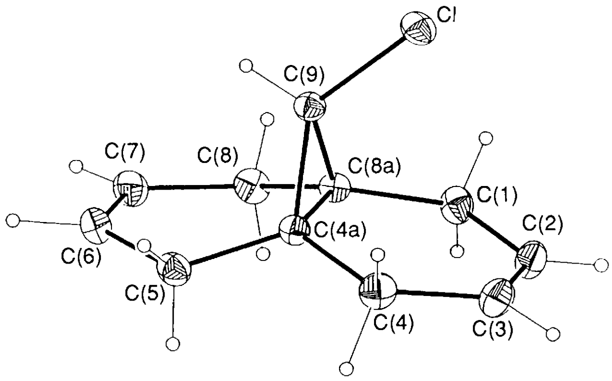

Fig. 1 Thermal ellipsoid drawing of **1**, relevant distances (Å) and angles: C(9)–Cl 1.767(1), C(1)–C(2) 1.494(2), C(8A)–C(1) 1.516(1), C(2)–C(3) 1.330(2), C(3)–C(4) 1.496(2), C(4)–C(4A) 1.517(1), C(5)–C(4A) 1.522(2), C(8A)–C(4A) 1.523(1), C(9)–C(4A) 1.508(2), C(5)–C(6) 1.499(2), C(6)–C(7) 1.335(2), C(7)–C(8) 1.497(2), C(8)–C(8A) 1.523(1), C(9)–C(8A) 1.507(1), C(9)–C(2) 3.243, C(9)–C(6) 3.000, C(4A)–C(9)–C(8A) 60.7(1)

Results and Discussion

The predicted distortion of **1** is indeed observed in the crystal structure (Fig. 1).† The distance between either of the two *exo* double bond carbons and the central bridgehead carbon was observed to be 0.24 Å shorter than the analogous *endo* distance, compared with a discrimination of 0.41 Å in the same direction predicted from the calculations.‡ Antiperiplanar overlap with the Cl–C σ* (LUMO + 2) orbital results in the *exo* π-orbital (HOMO − 1) being stabilised by 0.08 eV relative to the *endo* π-orbital (HOMO). The HOMO − 1 is also more delocalised,

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† X-ray determination of $C_{11}H_{13}Cl$: Cylindrical crystal, diameter 0.3 mm, Nicolet R3m/V diffractometer, Mo-Kα radiation, T = 120 K, a = 12.363(3), b = 6.423(2), c = 11.874(1) Å, β = 105.42(2)°, V = 909.0(4) Å^3; Z = 4, d(calc) = 1.320 g cm^{-3}, μ = 3.6 cm^{-1}, $P2_1/c$, 5027 unique ($2\theta_{max}$ 85°), 4265 observed intensities [$|F_o| > 4\sigma(F)$], 157 parameters, direct methods and full matrix least squares on F (SHELXTL-Plus). R = 0.045, R_w = 0.048, $w^{-1} = [\sigma^2(F_o) + 0.0018F_o^2]$. Hydrogen atoms were located in difference Fourier and refined without constraints. Lists of atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1992, issue 1.

‡ Calculations: Geometries were optimised at the PM3[9] level using the MOPAC program (Version 5.2) on a Tektronix CAChe workstation, which was also used to render the calculated electrostatic potentials and the molecular orbitals. Transition states were located using the eigenvector following method[10] and stationary points so located had one negative eigenvalue in the Hessian matrix as required of a transition state, with the correct displacement coordinates. Molecular entropies were calculated from the normal vibrational frequencies obtained from the mass-weighted Hessian matrix.

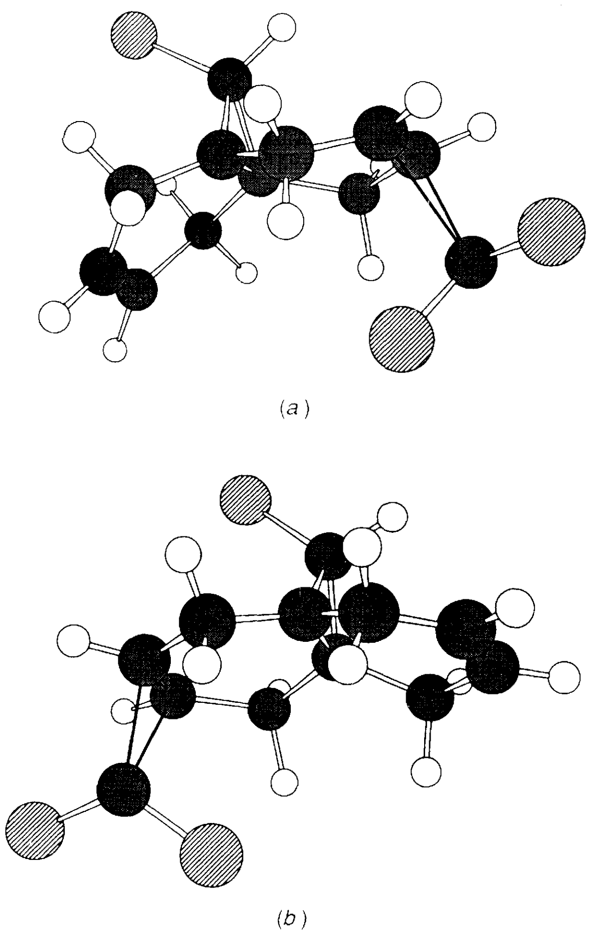

Fig. 4 Calculated PM3 transition state structures for (*a*) **3** and (*b*) **4**. The transition state C–C bond lengths were **3**: 2.020 and 2.339 Å; **4**: 2.023 and 2.314 Å.

with significant components on the π-type cyclopropyl orbital (Fig. 2). This results in smaller pπ-orbital coefficients on each of the *exo* (0.54) compared to the *endo* alkene carbons (0.58). Both effects would result in a frontier orbital prediction[5] that the *endo* alkene would be more reactive towards an electrophilic reagent. This result is also equivalent to the approach introduced by Hehre,[3] which involves superimposing the frontier orbitals onto an isovalued electron density surface. When this is done, the *endo* alkene clearly shows a larger sterically accessible π-orbital area than the *exo* alkene.

The electrostatic component of the Klopman–Salem equation[5] can be estimated from the relative sizes of the negative components of the PM3 electrostatic isopotential (Fig. 3). This clearly shows a bias towards the *endo* alkene, again in agreement with the known reactivity. The reasons for this are in some part due to the geometrical distortions of the two rings, in which overlap of the *endo* alkene π system with the central cyclopropyl pseudo π-orbital is enhanced. Finally we note that the same geometrical distortion of the *exo* ring enhances its antiperiplanar relationship with the electron rich cyclopropyl σ-bond, thus potentially promoting the *exo* alkene *via* a Cieplak-type effect. This interaction is clearly too weak to influence the observed *endo* preference.

These conclusions are all based purely on the properties of **1** as a reactant. It is of some interest to evaluate also a transition state model of the reactivity of **1**. Two isomeric transition states **3** and **4** (Fig. 4) for *exo* and *endo* addition of dichlorocarbene respectively were located. The two C–C transition bond lengths are unequal in length, the longer having a diaxial relationship to the carbene lone pair, assuming *ca.* trigonal bipyramidal coordination at the reacting carbon centre. Such asymmetry is to be expected for a thermal 4*n*-electron cheletropic process. The calculated PM3 transition state enthalpies [$\Delta H^{\ddagger}$ 98.3 (**4**), 97.5 (**3**) kcal mol^{-1}] actually show a small discrimination (0.8 kcal mol^{-1}) in favour of the *exo* transition state, although this is reduced to 0.2 kcal mol^{-1} for the corresponding free energies $\Delta G^{\ddagger}$ due to a 2.2 cal mol^{-1} K^{-1} difference in $\Delta S^{\ddagger}$ between **3** and **4**. The enthalpic result can be attributed to greater steric interactions between the methylene protons for the *endo* compared with the *exo* transition state (Fig. 4).

Inspection of the dipole moments for **3** and **4** reveals the latter to have the higher value. Using the Self-Consistent-Reaction-Field model,[11] which has been shown to provide good estimates of relative solvation energies, a relative permittivity of 10 (typical of the chlorinated solvents used in the original experiments[4]) and a reaction cavity radius of 3.68 Å, the dipole-induced solvent stabilisation was calculated as 0.1 and 0.4 kcal mol^{-1} for **3** and **4** respectively. Thus when both transition state entropy and solvation are considered, a very small 0.1 kcal mol^{-1} specificity for the *endo* isomer is predicted. In practice, this isomer is the only detectable product, which implies that the true free energy difference is significantly greater than 0.1 kcal mol^{-1} and that the PM3 transition state model is not quantitatively accurate.[9] Nevertheless this analysis does emphasise the cumulative importance of many small effects in controlling regioselectivity, and shows how stereoelectronic effects may dominate many aspects of alkene regioselection.

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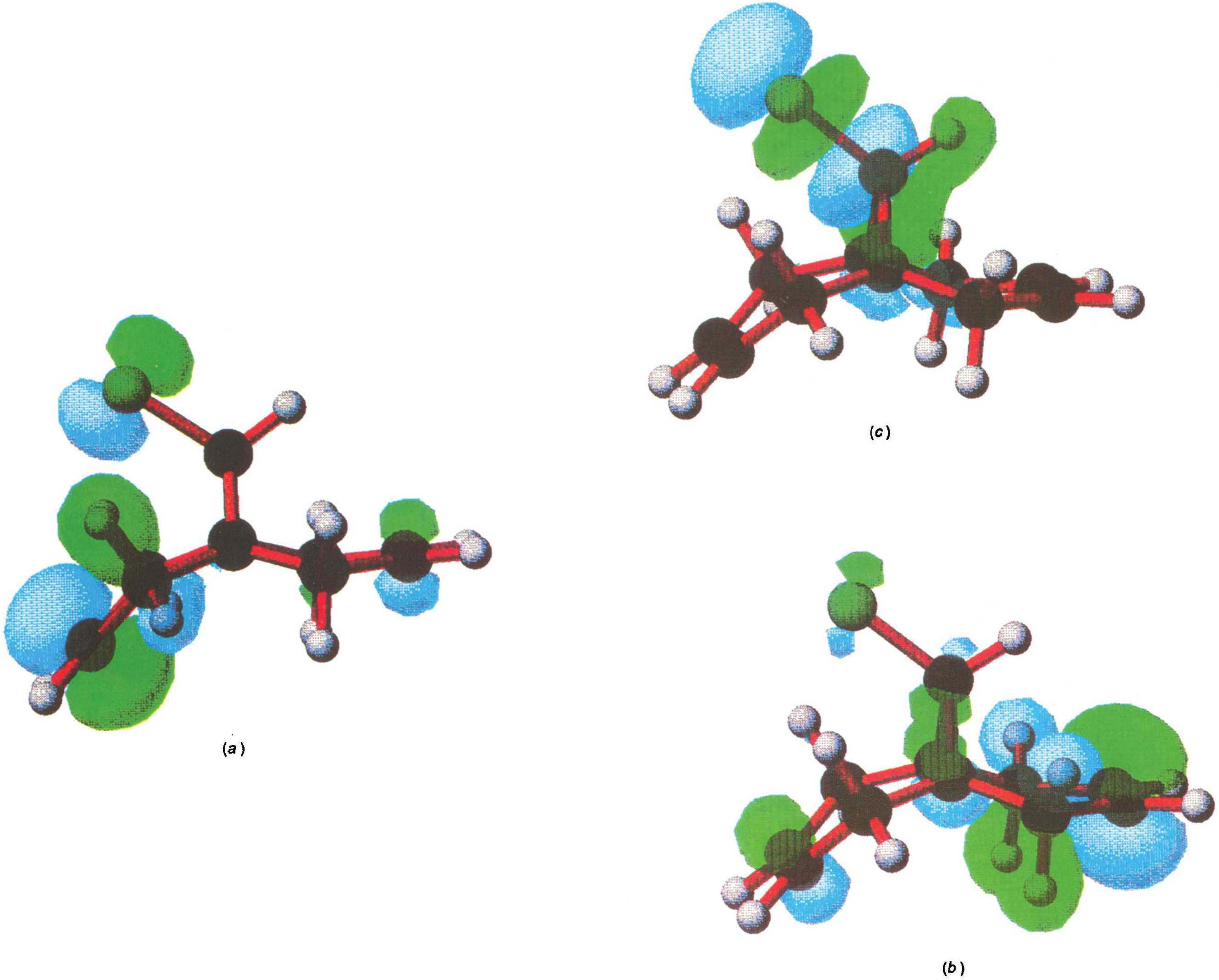
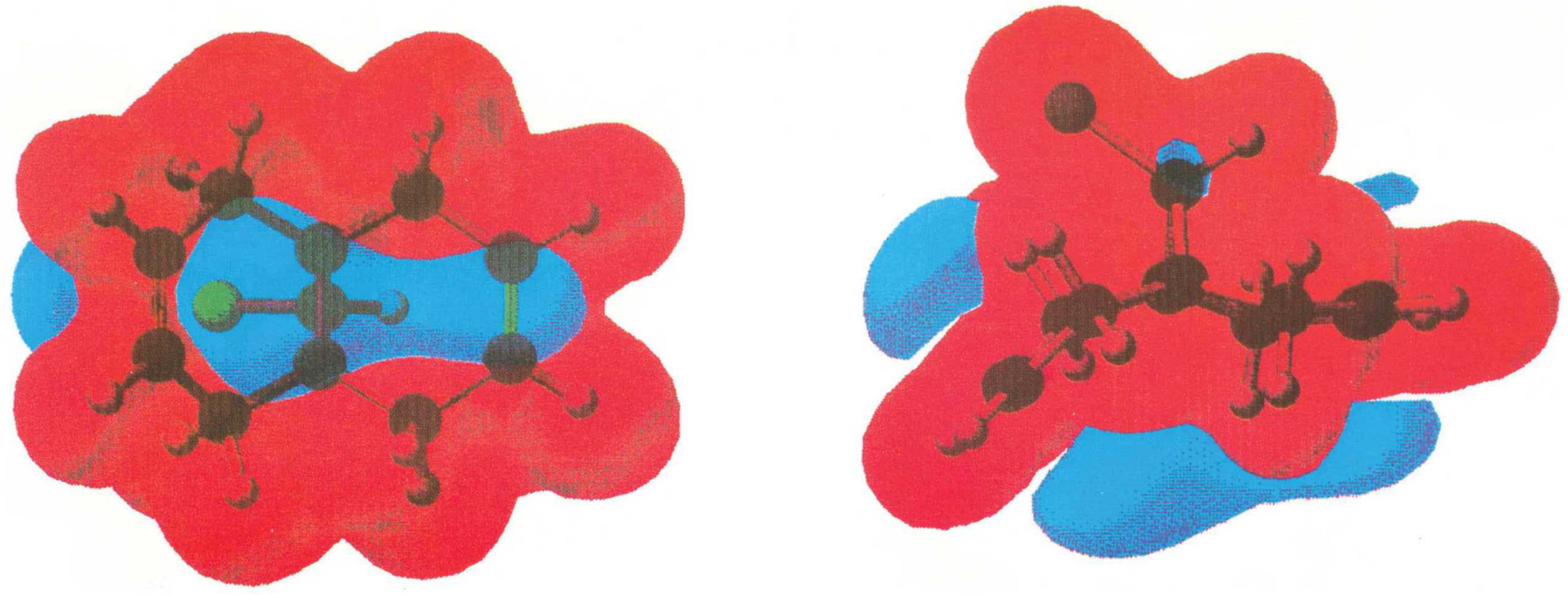


Fig. 2 Calculated PM3 orbitals for **1**, corresponding to the HOMO (*a*), the HOMO − 1 (*b*) and the LUMO + 2 (*c*), contoured at 0.04 a.u.



(*a*) (*b*)

Fig. 3 Calculated PM3 molecular electrostatic potential shown (*a*) from the face opposite the chlorine and (*b*) the side of **1**, contoured at +/− 0.025 Hartree, with the negative potential shown in blue