

Electrostatic vs. Orbital Control in π -Facial Diastereoselection: A PM3 SCF-MO Study of Electrophilic Reactivity in 7-Methylenenorbornanes

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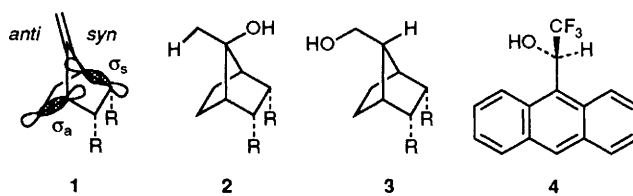
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PM3 calculations indicate that π -facial diastereoselection in the reaction between 2,3-*endo*-substituted 7-methylenenorbornanes and electrophiles such as $\text{Hg}(\text{OR})_2$ or I^+ is determined by electrostatic asymmetry whereas the reaction with BH_3 is controlled by orbital interactions.

Current theories of π -facial stereoselection by both nucleophilic and electrophilic reagents involve hyperconjugative¹ interactions between either an 'electron donor' σ -bond (the Cieplak model) or an 'electron acceptor' σ^* orbital (the Anh-Eisenstein model) antiperiplanar respectively to a developing σ or σ^* orbital on the reagent. Other factors, including electrostatic stabilisation, solvent and d-orbital metal control have also been proposed.² Amongst the many known examples of such stereoselection,³ reaction between alkene **1** ($\text{R} = \text{CO}_2\text{Me}$) and electrophilic reagents such as $\text{Hg}(\text{OAc})_2$ or B_2H_6 to give predominantly **2** or **3** respectively was suggested⁴ to be a sterically neutral example supporting

the Cieplak model, in which *syn*-attack favours the interaction between the bond marked σ_a and the antiperiplanar electrophilic σ^* orbital.



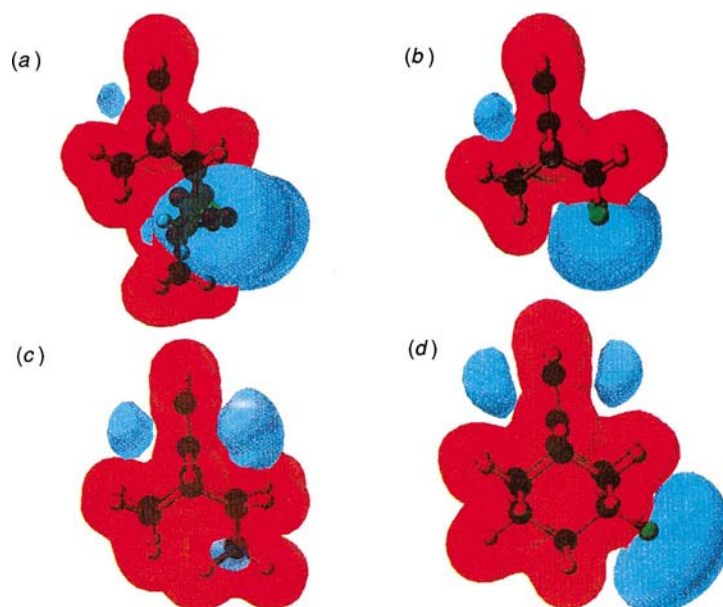
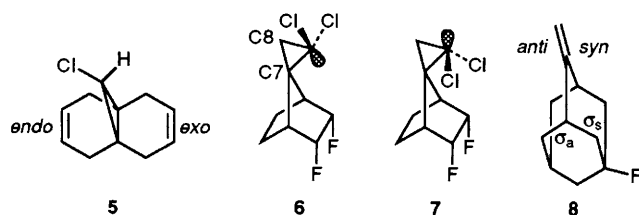


Fig. 1 Calculated PM3 electrostatic potential for (a) **1**, R = CO₂Me, (b) **1**, R = F, (c) **1**, R,R = -CH₂-, and (d) **8**, contoured at 0.025 Hartree, with the negative potential attractive to an electrophile shown in blue. A quantitative measure of the asymmetry in the negative potential surrounding the double bond is given by the ratio of either the minimum value of the potential [*antisyn* = 1.40 (PM3), 1.66 (*ab initio* 3-21G) for R = F; 1.46 (PM3) for R = CO₂Me; 0.845 (PM3) for R,R = -CH₂-, 0.91 (PM3) for R,R = -O-] or of the integrated volumes of the two negative isovalued (-0.012 Hartree) components [*antisyn* = 4.35 (PM3), 7.14 (*ab initio* 3-21G) for R = F; 4.55 (PM3) for R = CO₂Me; 0.65 (PM3) for R,R = -CH₂-, 0.78 (PM3) for R,R = -O-]. Integrations were performed using a Monte-Carlo technique over 250 000 points, within a pre-defined box which completely encapsulated a given isopotential lobe.

We have recently suggested⁵ that π -facial stereoselection in the crystal packing of the chiral resolving agent **4** is due to an asymmetry between the two π -faces in the molecular electrostatic potential (MEP), the least negative being antiperiplanar to the electron-withdrawing C-CF₃ bond. In the diene **5**, *endo*-alkene stereoselection towards electrophilic reagents such as dichlorocarbene⁵ was attributed⁶ to a combination of antiperiplanar deactivation of the *exo*- π -bond by its stabilising interaction with the Cl-C σ^* orbital, together with asymmetry in the MEP favouring *endo*-attack. Whilst in, *e.g.*, **5** the orbital and electrostatic effects cooperate, we suggest that in **1** (R = CO₂Me) they are opposed. For the electrophile Hg(OAc)₂ in particular, we believe that the electrostatic component promotes *anti*-attack, contrary to the published interpretation⁴ that the metal reacts with **1** from the *syn*-face.

Localised reactant orbital energies⁷ represent one convenient means of assessing the component due to orbital control. For **1** (R = F), the two-centre PM3 SCF-MO⁸ localised orbital σ_a is revealed to be a better electron donor (-19.09 eV) in the Cieplak sense than is σ_s (-19.58 eV), favouring antiperiplanar interaction with the σ^* orbital of an electrophile approaching specifically from the *syn*-face. The electrostatic component, as revealed by the PM3 derived MEP,⁹ shows the *anti*-face to be the most attractive to an electrophile when R is electron withdrawing such as R = F or CO₂Me (Fig. 1), but favours the *syn*-face for substituents such as R,R = CH₂- or -O- (Fig. 1). Unlike **5** therefore, electrostatic and Cieplak type orbital control appear to act in opposing directions in **1**, R = F or CO₂Me.



The overall balance between the opposing electrostatic and orbital direction for **1** (R = F) can be estimated by comparing the relative calculated enthalpies of both the *anti* and *syn*-complexes for various model electrophiles, E = Hg(OH)₂, BH₃, Zn(OH)₂, H⁺, I⁺ and :CCl₂, the last four corresponding to hitherto untested systems (Table 1). Such relative energies may be expected to be significantly more reliable than the absolute error quoted for PM3 (± 7.8 kcal mol⁻¹)⁸ due to a substantial cancellation of errors. For symmetrically bound ($r_{E-C8} \approx r_{E-C7}$) π -complexes such as Hg(OH)₂, Zn(OH)₂ or cyclic I⁺, the *anti*-isomers are calculated to be more stable, an effect we attribute in part to the large charges on the electrophile (I⁺, 0.83, Hg⁺, 0.75) favouring long-range electrostatic stabilisation by the electron-rich *anti*- π -face (Fig. 1). This predicted *anti*-preference in the preequilibrium¹⁰ would mean that subsequent rate-determining nucleophilic attack by, *e.g.*, water occurring *anti* to the complexed electrophile would result, for, *e.g.*, E = Hg(OAc)₂, in the observed alcohol **2**. This interpretation is consistent with experiment but does differ from the previously proposed *syn*-attack mechanism.⁴

In contrast, the more neutral and asymmetrical BH₃-alkene π -complexes ($r_{B-C8} < r_{B-C7}$) show a small calculated *syn*-preference, increased when the transition states for BH₃ addition to the double bond are compared (Table 1), which is consistent with the known⁴ formation of isomer **3**. In other systems where the positive charge resides not on the electrophile but more on carbon (*i.e.* the classical carbonium ions formed from E = I⁺ or H⁺) there is also a *syn*-preference, due we think to orbital rather than electrostatic stabilisation. The clearest effect is shown for the H-C₇ carbonium ion (E = H⁺); σ_a for the *syn*-complex (-23.70 eV) is stabilised relative to σ_a for the *anti*-isomer (-23.64 eV) via a Cieplak type interaction and $\sigma(H_{syn}-C7, -24.81$ eV) is more stable than $\sigma(H_{anti}-C7, -24.70$ eV) because interaction of the Anh-Eisenstein type is possible with the C-F σ^* orbital. Another potentially stereoselective⁵ electrophilic reagent is :CCl₂, for which two isomeric transition states for addition to **1** (R = F) can be located.⁵ The more stable form **7** shows a small *anti*-prefer-

Table 1 Calculated PM3 ΔH_f values in kcal mol⁻¹ for (1 cal = 4.184 J) for complexes between **1** and electrophile E

E	1 : R = F,F		1 : R,R = -CH ₂ -	
	<i>syn</i>	<i>anti</i>	<i>syn</i>	<i>anti</i>
H ⁺	139.03	139.85	256.10	255.69
I ⁺ (cyclic)	151.42	150.06	268.60	269.23
I ⁺ (classical)	149.44	149.88	265.01	264.69
Hg(OH) ₂	-130.36	-134.00	-11.56	-9.36
Zn(OH) ₂	-118.47	-122.30	1.59	0.93
BH ₃ ^a	-50.93	-50.66	85.11	84.88
BH ₃ transition state ^a	-39.49	-38.45	95.46	95.31
6	-7.36	-5.56	120.87	120.02
7	-10.41	-11.01	116.58	116.26

^a AM1 values.

ence, whereas the higher energy isomer **6**, which differs in the orientation of the carbene lone pair, clearly favours *syn* (Table 1). In each case for each pair of neutral *syn*- and *anti*-complexes, the difference in calculated dipole moment is <0.7 Debye, indicating that differential solvation effects will not appreciably influence the electrophilic stereoselectivity in moderately polar solvents.

The stereoselectivity is predicted to reverse when the electron-withdrawing R = F or CO₂Me substituents are replaced with the electron-rich R,R = -CH₂-ring (Fig. 1). Thus the electrostatically controlled reaction with, *e.g.*, Hg(OH)₂ now favours *syn*-attack whilst the reactions with *e.g.*, E = H⁺, I⁺ or BH₃ now favour *anti*-attack (Table 1). For an alkene such as **8**, electrostatic discrimination is much smaller (Fig. 1) and here we predict that, *e.g.*, electrostatically dominated oxymercuration might not be as highly selective as is observed for orbital-dominated hydroboration.¹¹ Our results also suggest that the hitherto unreported reactions between **1** and electrophiles such as E = halogen⁺ and :CCl₂ or with substituents such as R,R = -CH₂- or -O- may provide valuable further insights into the factors determining π -facial selectivity.

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