Electronic Control of π-Facial Diastereoselection. Electrophilic Additions to 7-Methylenenorbornanes

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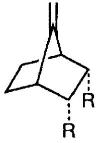
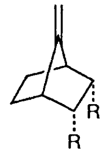
The approach of electrophiles to the sterically unbiased 7-methylenenorbornanes **2a–c** can be remote controlled through electronic modification of 2,3-*endo,endo*-substituents.

The role of stereoelectronic effects in π-facial diastereoselection during nucleophilic and electrophilic additions has been vigorously probed in recent years.[1] However, little attention has been paid to the control of electrophilic stereoselections through remote electronic influences in sterically neutral situations. A noteworthy exception[1c] in this context is the stereoinduction by the distal 5-fluoro substituent in the approach of the electrophiles to 5-fluoro-2-methylene-adamantane. In a recent study, we have demonstrated the profound effect of the electronic modification of 2,3-*endo,endo*-substituents on the diastereoselectivity at the carbonyl group in nucleophilic additions to the sterically neutral 7-norbornonones **1a–c**.[2] To further extend the scope of this new finding, we have ventured to investigate the electrophilic additions to 2,3-*endo,endo*-7-methylenenorbornanes **2a–c** which have the same advantageous feature of sterically equivalent π-faces in a conformationally rigid framework. Herein, we report that electronic modifications at remote 2,3-substituents dramatically alter facial selection at the C-7-alkenic centre during electrophilic additions.

7-Methylenenorbornanes **2a–c** were readily synthesised from the corresponding ketones **1a–c**[2] *via* Wittig alkenation ($Ph_3P^+CH_3Br^-$, $t\text{-}C_5H_{11}O^-Na^+$, 70–80%) and the appearance of C-5, C-6 resonances in the δ ~20 region[3] in the ^{13}C NMR spectra of **2a–c** ensured that the 2,3-substituents had retained their *endo,endo*-disposition.† The 7-methylenenorbornanes **2a–c** were subjected to epoxidation, hydroboration and oxymercuration reactions (Scheme 1) and the results are presented in Table 1. The stereostructures to *E,Z*-epoxides **4a–c**, **5a–c**, *E,Z*-primary alcohols **6a–c**, **7a–c** and *E,Z*-tertiary alcohols **8a-c**, **9a-c**† were unambiguously assigned on the basis of relatively greater deshielding of the 2,3-*exo*-protons in the *Z*-series compared to the *E*-series. This could be further confirmed through lanthanide induced shift (LIS) studies. In the case of hydroboration alcohols **6a–c**, **7a–c**, greater



1; a R = $\overset{O}{\overset{\|}{C}}\text{—OMe}$
b R = $CH_2\text{—}O\text{—}Me$
c R = $CH_2\text{—}Me$



2a, b, c

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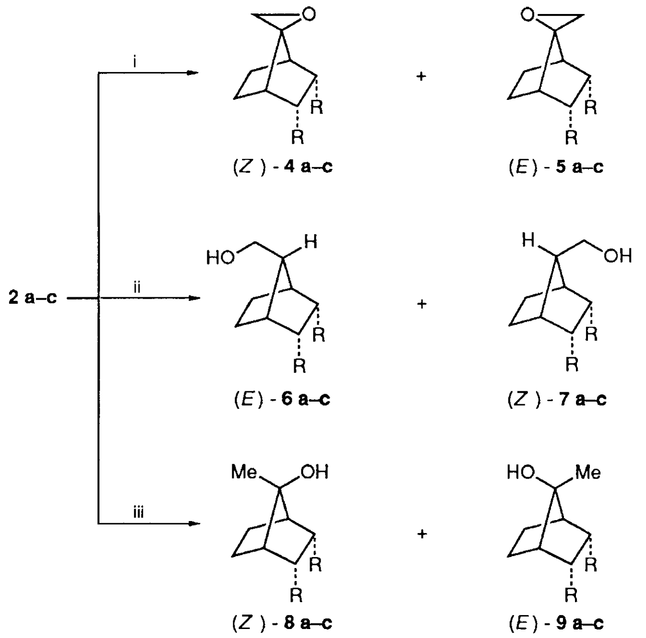
† All new compounds were characterised on the basis of their spectral and analytical data.



Scheme 1 *Reagents*: i, *m*-Chloroperbenzoic acid, CH$_2$Cl$_2$, 5–10 °C, 75–85%; ii, B$_2$H$_6$–THF, H$_2$O$_2$–aq. NaOH, 70–80%; iii, Hg(OAc)$_2$ aq. THF, NaBH$_4$–NaOH (3 mol dm^{-3}) 75–85%

shielding (δ 3–4) of C-5, C-6 resonances in the *E*-series compared to the *Z*-series provided additional support for the stereochemical assignment.

The results displayed in Table 1 show a complete crossover in *syn*/*anti* aproach of the electrophiles in going from **2a** to **2c**. The π-face stereoselection observed here is moderate in the case of additions proceeding through cyclic transition states (epoxidation and hydroboration) but is significantly enhanced in the case of the more polar addition (oxymercuration). The electrophiles attack **2a** and **2c** predominantly from the *syn*- and *anti*-face, respectively. The dimethoxy compound **2b** shows a modest preference for the *anti*-approach. These results appear to be consistent with the Cieplak hyperconjugative model[1g,4,5] in which the stabilising interaction between the electron rich antiperiplanar σ bond and the developing σ* orbital lowers the transition-state energy. Accordingly, irrespective of which reacting partner contributes the bonding electrons, the σ* orbital would attract electron density through the same directional preference, *i.e.* from the more electron rich σ bond.[1c] In agreement with this prediction, electrophiles exhibit the same face-selectivity in approach to **2a–c**, as do nucleophiles[2] in their approach to **1a–c**.

Table 1 Product ratios in electrophilic additions to **2a–c**

	syn : *anti* approach (%)[a]		
Substrate	epoxidation	hydroboration	oxymercuration[b]
2a	74 : 26 **4a 5a**	59 : 41 **6a 7a**	>95 : trace **8a 9a**
2b	45 : 55 **4b 5b**	44 : 56[c] **6b 7b**	40 : 60 **8b 9b**
2c	30 : 70[c] **4c 5c**	38 : 62[c] **6c 7c**	17 : 83 **8c 9c**

[a] Ratios based on ^{1}H NMR integration of crude reaction (±5%). [b] Oxymecurations were carried out under conditions of reversible formation of mercurinium ion; CO bond formation is the rate-limiting step. [c] The *E*–*Z* mixture could not be separated for full characterisation of each isomer. However, 300 MHz ^{1}H NMR data enabled identification of each isomer.

In conclusion, we have demonstrated, for the first time, that π-facial selectivities in electrophilic additions to 7-methylenenorbornanes can be electronically tuned through 2,3-*endo*,*endo*-substitution. Further work, both theoretical and experimental, is in progress.

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