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Communications

Electrophilic Additions to 7-Methylenenorbornenes and 7-Isopropylidenenorbornenes: Can Remote Substituents Swamp Electrostatic Control of π -face Selectivity?[†]

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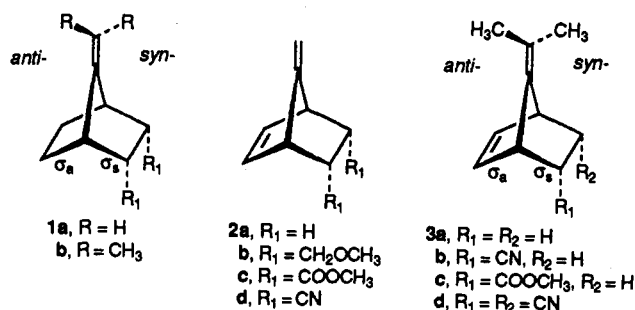
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Summary: π -Face selectivities in electrophilic additions (typically CCl_2) to 7-methylenenorbornenes and 7-isopropylidenenorbornenes are modulated by *endo*-substituents.

The role of long-range electronic effects in controlling π -facial diastereoselection during nucleophilic and electrophilic additions to trigonal carbon centers has come under incisive scrutiny in recent years and generated a lively ongoing debate.^{1,2} In particular, segregation and evaluation of the relative importance of the electrostatic

and orbital contributions are the key issues that need to be further clarified. We have recently demonstrated the profound effect of *endo*-substituents on the π -face selectivities in rigid, sterically neutral 7-methylenenorbornanes **1a** and 7-isopropylidenenorbornanes **1b**.^{2e,3} The *endo*



electron-withdrawing groups, e.g., $-\text{CN}$ and $-\text{COOMe}$, seem to consistently promote electrophile approach from the *syn*-face. These observations have been interpreted using *ab initio* electrostatic potentials and semiempirical energetics.^{3,4} The interesting results with **1a,b** have provided an impetus to probe the 7-methylenenorbornene

[†] Dedicated to Prof. C. N. R. Rao on his 60th birthday.

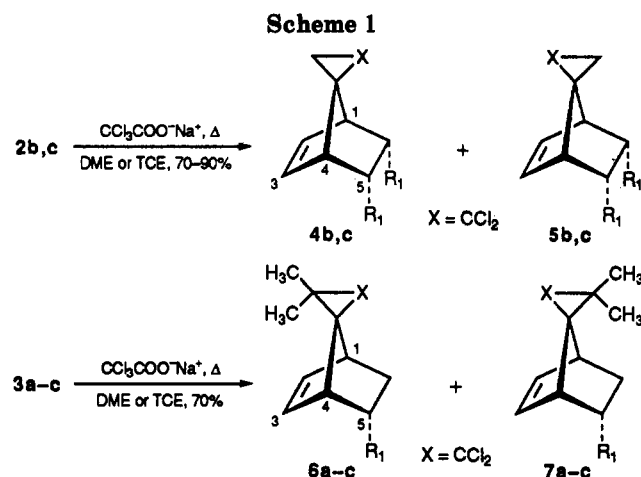
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2a and **7-isopropylidene**norbornene **3a** systems, which are of intrinsic interest due to the presence of the much acclaimed homoconjugative interaction between the two olefinic bonds.⁵ Several subtle electronic effects have also been proposed by Paquette and Gleiter to account for the dependence of the face selectivities on the nature of electrophile in additions to unsubstituted **3a**.^{2a} Therefore, studies on *endo*-substituted **3b,c** were expected to unravel the direct response of the substituent on the face selectivity without perturbing the steric environment. Herein, we report the results of addition of dichlorocarbene to **2b,c** and **3b,c** and explain the persistent directing influence of the substituent on the basis of a topographical analysis of molecular electrostatic potentials (MESP) and electron densities as well as semiempirical transition-state calculations. The results are particularly interesting in the context of a recent suggestion that reagent-specific electrostatic effects are important in determining face selectivity in electrophilic additions to *7-isopropylidene*benzenorbornenes.^{2b}

Addition of dichlorocarbene ($\text{CCl}_3\text{COO}^-\text{Na}^+$, Δ)^{2a} to **2b,c** and **3a-c** furnished the *syn*-**4b,c**, and **-6a-c** and *anti*-adducts **5b,c** and **7a-c** (separated and characterized in each case), Scheme 1 (for the sake of uniformity with the results for **1**, we retain the prefix *syn*- for additions from the side of the *endo*-substituent). The stereostructures of the 1:1 adducts were determined on the basis of ¹H and ¹³C NMR data and in particular from the greater deshielding of the C₅, C₆ *exo*-protons in the *syn*-series as compared to the *anti*-series.⁶ The *syn/anti* face selectivities, determined through ¹H NMR integrations and/or GLC, are presented in Table 1. It is quite apparent that for both **2** and **3** *syn*-approach preference increases with the placement of electron withdrawing *endo*-substitution.

In order to interpret the observed substituent effects, a topographical investigation⁷ of the electron density distribution $\rho(r)$ and molecular electrostatic potentials (MESP) for **2** and **3** was carried out at the *ab initio* level using the parallel SCF program INDMOL.^{8,9} For a bond between a pair of atoms in a molecule, there exists a (3, -1) saddle point (termed as bond critical point, CP)⁷ in $\rho(r)$. The density at these bond CPs gives an indication of donor strengths for hyperconjugative interactions and can be used to explain the stereoselection. The densities

Table 1. Observed *Syn/Anti* Product Ratios and Calculated Heats of Formation (kcal mol⁻¹) for the Transition States of CCl₂ Addition

compd	obsd <i>syn:anti</i> ratio	calcd			ΔE
		site of carbene attack	<i>syn</i>	<i>anti</i>	
2b	11:89	C-8	21.45	20.68	-0.77
		C-7	27.48	27.63	0.15
2c	23:77	C-8	-46.59	-47.07	-0.48
		C-7	-41.50	-39.62	1.88
3a	12:88 ^{2a}	C-7	99.22	99.50	0.28
		C-8	100.42	99.97	-0.45
3b	35:65	C-7	132.12	133.20	1.08
		C-8	133.97	133.55	-0.42
3c	34:66	C-7	17.87	18.71	0.84
		C-8	19.55	19.09	-0.46

Table 2. Electron Density at Bond CPs and MESP Minima (au) from *ab Initio* Calculations Using MNDO-Optimized Geometries

	σ_a	σ_b	C ₇ =C ₈		C ₂ =C ₃	
			<i>syn</i>	<i>anti</i>	<i>exo</i>	<i>endo</i>
2a	0.2134	0.2279	-0.0416	-0.0488	-0.0433	-0.0302
2aDzp	0.2363	0.2527	-0.0401	-0.0477	-0.0425	-0.0298
2b	0.2092	0.2282	-0.0416	-0.0464	-0.0393	-0.0199
2c	0.2095	0.2286	-0.0214	-0.0346	-0.0337	no min
2d	0.2083	0.2287	-0.0004	-0.0155	-0.0136	no min
3a	0.2139	0.2285	-0.0380	-0.0463	-0.0464	-0.0339
3b	0.2082	0.2288	-0.0172	-0.0305	-0.0312	-0.0243
3d	0.2085	0.2291	0.0012	-0.0015	-0.0177	no min

at bond CPs for various systems with the 6-31G basis set are reported in Table 2. A test calculation on **2a** using a Dzp basis set shows that there is no change in the relative trends of $\rho(r)$ and MESP minima. An electron-withdrawing substituent at C₅ marginally increases the density at the C₃-C₄ (σ_a) bond CP, relative to that at the C₄-C₅ (σ_b) bond CP (see structures **1** and **3**). The enhanced asymmetry should favor electrophilic attack from the *syn*-face on the basis of the Cieplak hyperconjugative model.¹⁰

The computed MESP provide valuable insight concerning the role of electrostatics in determining the face selectivities. For a typical olefin, there exist two (3, +3) minima in the scalar field of $V(r)$ on either side of the double bond ($V(r) = -0.0383$ au for ethylene with the 6-31G basis set). A negative minimum in $V(r)$ is a signature of localization of electron density. For the unsubstituted systems **2a** and **3a**, four such minima are obtained, as expected (Table 2). For the C₇=C₈ bond, the minimum toward the C₂=C₃ face is deeper. Interestingly, the isopotential surfaces for **3a** reveal that the negative contours of the two double bonds merge, providing a visual definition of homoconjugation. Thus, the two double bonds reinforce electron localization and may direct electrophilic attack from the olefin face.

The introduction of an *endo*-substituent produces a dramatic change in the MESP. The values of $V(r)$ at the minima around the exocyclic double bond are substantially

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(7) The critical point (CP) of a scalar field f is a point where $\nabla f = 0.0$. All the three eigenvalues of the Hessian at the CP are positive for a (3, +3) minimum. A (3, -1) saddle corresponds to two negative and one positive eigenvalue. For details, see: Bader, R. F. W. *Atoms in Molecules, a quantum theory*; Clarendon Press: Oxford, 1990. Kraka, K.; Cremer, D. In *Theoretical models of chemical bonding*; Maksic, Z. B., Ed.; Springer-Verlag: New York, 1990; Part 2, The concept of the chemical bond.

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reduced. The isopotential surfaces for **3b** show that the *endo*-cyano group extensively drains the negative potential contours from the reaction sites. While the minima on the *syn*- and *anti*-faces are unsymmetrical, it is unlikely that electrostatics are important in these substituted derivatives in determining face selectivities. It may be expected that the MESP minima should be deeper than a certain threshold for electrostatic effects to play any discriminating role. We suggest a value of -0.0383 au, as found in ethylene, as a practical guideline for electrostatic takeover. Invoking electrostatic effects on the basis of MESP minima or the ratio of volumes enclosed by a given closed surface⁴ may not be appropriate in systems such as **3b** with shallow MESP minima.

Transition-state energies calculated at the AM1 level¹¹ for CCl₂ addition to **2b,c** and **3a-c**, though not in quantitative agreement with all the experimental results, confirm the electronic role of *endo*-substituents in influencing face-selectivities. Transition structures for carbene addition to olefins are generally unsymmetrical, with one C-C bond being formed to a greater extent with the chlorine atoms tilted toward the other olefinic carbon.^{4,12} For the present substrates, two sets of first-order saddle points, characterized by a closer approach of the carbene to C₇ or C₈, are obtained for the *syn*- as well as *anti*-face additions. In **2b** and **2c**, the energetically favored transition states correspond to those derived by attack at C₈.

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For this mode of approach, *anti*-face addition is computed to be more stable for **2b** by 0.8 kcal mol⁻¹, in accord with the experimental trend. Significantly, the *endo*-ester substituents in **2c** reduce the *anti*-preference. Differential hyperconjugative interactions in **2c** seem to override electrostatic effects resulting from the downward-pointing chlorine atoms. In the 7-isopropylidene series, carbene attack at both C₇ and C₈ is energetically feasible. Since the facial preferences derived from the resulting transition states are in opposing directions there is some ambiguity in the predicted face selectivity. However, the effect of *endo*-substitution is clear. For C₇ attack, even a single electron-withdrawing group **3b,c** enhances the *syn*-face preference, while the transition states for C₈ attack retain their energy difference favoring the *anti*-approach. The overall consequence is that the electron-withdrawing groups reduce the preference for *anti*-face addition.

The present study demonstrates that orbital interactions involving *endo*-electron-withdrawing groups consistently reduce the preference for the electrostatically favored *anti*-face selectivity in 7-alkenylnorbornenes.

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Supplementary Material Available: ¹H and ¹³C NMR spectra of new compounds (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.