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A computational approach towards predicting π-facial selectivity in sterically unbiased olefins: an evaluation of the relative importance of electrostatic and orbital effects

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ABSTRACT

Computational studies are presented to show that electrostatic interactions significantly impact the stereochemical outcome in electrophilic addition to a number of sterically unbiased alkenes. Transition states have been located for the reaction of different electrophiles with all the sterically unbiased alkenes studied here and the calculations effectively include interactions involving the σ and σ* orbitals of the newly formed bond. Electrostatic interaction between the substrates and electrophiles was modelled by removing the electrophiles from the transition state geometry and placing the calculated charge at a distance from a selected atom as observed in TS structures. Electrostatic interactions between the electrophiles and the substrate seem to effectively determine the face selectivities in the systems studied and our model calculations indicate that it may not be important to invoke Cieplak type orbital interactions to rationalize the observed face selectivities. The face selectivities predicted for these alkenes and electrophiles with DFT B3LYP/6-31G* and ab initio MP2/6-31G* levels are generally in good agreement.

1. Introduction

Induction of face selectivity in electrophilic addition to the olefinic group through remote electronic perturbation is an elegant approach towards stereoselective bond formation. Systems have been designed where the carbonyl group is positioned in an isosteric environment but remote electronic modification through distal substituents can be used to achieve significant diastereoselectivity during electrophilic additions through face-selection (Scheme 1).[1] It is now well recognized that long range electronic effects can play decisive roles in determining π-facial selectivity. However, precise nature of these effects and how exactly they engender stereo-differentiation during electrophilic addition is still a challenge, despite devising and investigating many experimental probes and invoking a variety of theoretical models.[2] Geometric and orbital distortions, electrostatic effects, different types of specific orbital interactions (Felkin–Anh and Cieplak type) have been employed to understand the observed results.[3] The Cieplak model highlights the importance of anti-periplanar C–C σ bond donations to the σ* of the incipient bond C–H at the transition state.[3e,f] The role of electrostatic interactions, Felkin–Anh model, transition state model, desymmetrization of the π-orbital, pre-complexation model, cation complexation model[4j,k,5j–l,n] etc. constitute some of the other attempts put forward to rationalize the face selectivities.[3a–d,3h,4]

Modelling face selectivity has been a challenging task for theoretical and computational methodologies.[5] The quest for devising chemically intuitive models to predict π-face selectivity and to discern the factors responsible for such selectivities continues to engage attention. The semi-empirical MNDO model and the transition state model to predict the π-face selectivity for the nucleophilic addition to sterically unbiased ketones helped to segregate the importance of orbital and electrostatic effects.[2d,5d,6] However, segregation of the various electronic factors responsible for the π-face selectivity in electrophilic additions to sterically unbiased alkenes has received only limited attention.[1e,f,n,o,2g,7] The assessment of electrostatic effects with electrophiles is not known to fully rationalize the face selectivity in addition to trigonal carbons; presumably placing the charge on a particular position of a multi-centre electrophile is a non-trivial exercise. Recently, we have evaluated the origin of reversal of facial selectivity in peracid and diazomethane addition to 5,6-*cis*,*exo*-disubstituted bicyclic[2.2.2]oct-2-enes employing a newly developed model for the approach of electrophiles to the olefinic systems that segregates electrostatic

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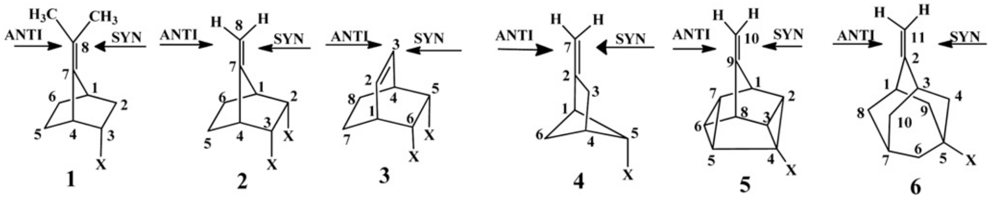


X = -CN, -COOMe, -CH_2CH_3, -F, -CH_3; X-X = -OCOO-

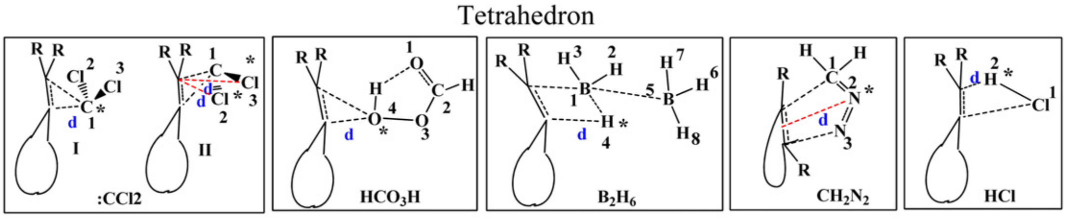
Scheme 1.

component from the orbital effects.[1o] Our intent was to invoke this electrostatic model to evaluate π-face selectivity in sterically unbiased olefins like *endo*-substituted 7-isopropylidenenorbornanes (**1**); 2,3-*endo*,*endo*-7-methylenenorbornanes (**2**); 5,6-*cis*,*exo*-disubstituted bicyclic[2.2.2]oct-2-enes (**3**); 5-*exo*-bicyclo[2.1.1]hexane (**4**); 4-substituted 9-methylenenorsnoutanes (**5**) and 2, 5-disubstituted adamantanes (**6**) during addition of different electrophiles like *m*-chloroperbenzoic acid (*m*-CPBA), diazomethane (CH_2N_2), chlorocarbene (:CCl_2), diborane (B_2H_6) and Hydrochloric acid (HCl). The origin of face selectivities observed in polycyclic systems **1**–**6** with different electrophiles were earlier considered[1c,e–h,n] in terms of the dominant role played by the Cieplak type hyperconjugative interactions. Generally, electrostatic effect were suggested to be less important to control the face selectivities in such systems, except in the case of **4**, where the diastereofacial selection was reported through the interplay of electrostatic and Cieplak type orbital effects.[1n] MESP analysis was performed in selected cases to examine the efficacy of electrostatic effects in explaining the observed diastereoselectivites in sterically unbiased olefins. However, a direct comparison of the electrostatic and orbital models was not available in these cases as was reported for the nucleophilic addition to the carbonyl groups.[5a,d] Herein, we disclose the results of a computational study to gauge the role of electrostatic and orbital interactions directly, employing the response of substrates **1**–**6** (Scheme 1) towards different electrophiles and discern their relative importance to explain the experimentally observed face selectivities. The structural diversity of substrates **1**–**6**, harbouring both *endo*- and *exo*cyclic double bonds and substitution patterns was expected to provide an intriguing testing bed for our model and the approach of the electrophiles.

2. Computational details

All the substrates and electrophiles and the transition state geometries for the *syn*- and *anti*-addition of these systems were fully optimized with B3LYP/6-31G* level of theory.[8] B3LYP/6-31G* level has been used in other π-facial studies.[4j,k,5o,t,9c] The importance of computational methods and models to qualitatively predict the π-facial selectivity of nucleophilic addition to sterically unbiased ketones has been reported.[5p] The relative energies calculated with B3LYP/6-31G* level were also corrected with zero point vibrational energies (ZPVE). Enthalpy corrected relative energies are given in the Supplementary data (Table S7). Scheme 2 shows the model transition state geometries for the addition of various electrophiles to the substrates **1**–**6**. The harmonic vibrational frequencies were computed to determine the minima and the first order saddle points in each case. Further, MP2/6-31G* calculations[10] were performed using B3LYP/6-31G* optimized geometries to calculate the energy differences for *syn*- and *anti*-addition of electrophiles to the above mentioned substrates.

To segregate the electrostatic effects from orbital effects, the charge model derived to explain the face selectivity of 5,6-*cis*,*exo*-disubstituted bicyclic[2.2.2]oct-2-enes was employed in all cases.[1o] The electrophile modelled with point charge (PC) to examine the reactivity of the acetaldehyde enolate has been reported.[11] It is important to emphasize that the charge model is not identical to the use of molecular electrostatic potential maps (MESP). The latter method is a more direct approach to examine the electrostatic effects and has indeed been successfully applied for a number of studies of regiochemical and facial selectivities in conjunction with both ab initio and semi-empirical methods.[12] However, the present procedure incorporates an additional effect. Since the wave functions are recomputed in the presence of the test charge, electronic reorganization within the substrate due to the approaching reagent is taken into account. Thus, the model includes polarization effects. The electrostatic interactions were modelled with the CHelpG charges[10,13] of the specific atom of the electrophiles obtained in the transition state calculations and placing them at the calculated distance (d) as shown in Scheme 2. The atoms modelled for the charge calculations in different electrophiles are those, which remain in the final products. In the case of dichlorocarbene (:CCl_2) addition to these substrates, there is a possibility of attack from both ends of the double bond, as shown in **I** and **II** (Scheme 2). In **I**, the charge on the carbon atom of :CCl_2 and in **II** the charge of chlorine atoms are used to perform the charge model calculations. For convenience, performic acid was considered as a model for *m*-CPBA.[14] In case of performic acid, the charge calculations are performed by removing the electrophile and adding the charge in place of the $\mathbf{O_4}$ oxygen atom. For diborane (B_2H_6) addition, the charge of the hydrogen ($\mathbf{H_4}$) is taken in each case. In the case of diazomethane (CH_2N_2), the CHelpG charge of the nitrogen atom ($\mathbf{N_2}$), which is not involved in the bond formation with the substrate is taken for the



R = H or CH_3

Scheme 2. '*' denotes the atom on which the CHelpG charge is placed in the charge model calculation using the transition state geometries.

charge model calculations.[1o] For HCl addition, charge on the Hydrogen atom (**H**$_2$) is taken to evaluate the electrostatic effect. ChelpG charges were derived from electrostatic potentials using a grid based method as suggested by Breneman and Wiberg.[15] All calculations were done by the Gaussian 03 suite of programs.[16]

3. Results and discussion

The optimized geometries of the olefins **1**–**6** do not reveal constituent features, which can be correlated with the observed face selectivity in the corresponding electrophilic additions. In particular, the alkene unit is essentially planar. The sum of the angles around the corresponding carbon atom does not deviate by more than ~1° from 360°. The presence of *endo* substituents in **1**–**6** does not lead to significant tilt of the alkene bridge towards either side of the rings. The alkene unit in these compounds is also nearly eclipsed with the bridgehead hydrogen atoms. Hence, ground state distortions and torsional interactions during the formation of the transition structures cannot be implicated for the face selectivity in these substrates.

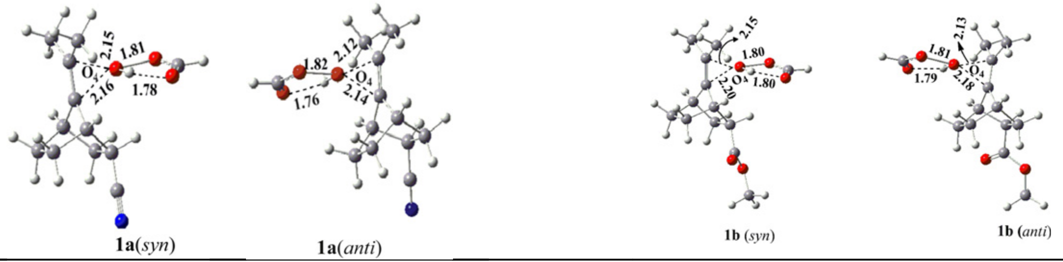
3.1. *endo*-substituted 7-Isopropylidenenorbornanes (1)

Electrophilic addition to **1** was reported by Mehta et al.[1e] The observed preferences were explained by ab initio and semi-empirical MO calculations. The calculated results suggested that the diastereoselectivites were primarily due to orbital effects. The calculations performed in the present study with *m*-CPBA and dichlorocarbene, however showed that electrostatic interactions can also explain the observed selectivity for **1** (Table 1). *endo*-Cyano-7-isopropylidenenorbornanes [**1a** (X=—CN)] and *endo*-carbomethoxy-7-isopropylidenenorbornanes [**1b** (X=—COOMe)] have been considered for the calculations. The B3LYP/6-31G* optimized butterfly transition state geometries have been located for the addition of performic acid to the olefinic double bonds of **1a** (X=—CN) and **1b** (X=—COOMe).[9] In this study the transition state energy differences showed *syn* preferences and were found to be in good agreement with the experimentally observed results for **1a** (X=—CN) and **1b** (X=—COOMe) with *m*-CPBA. These transition state calculations involve the orbital and electrostatic contributions and hence to delineate these electronic factors additional calculations are required.[5d,14a] In the present study, the calculations performed with the relative ChelpG charges taken from the respective transition states for oxygen atoms (**O**$_4$) for performic acid and placed at its location yields the *syn*-face preference compared to the *anti*-face in to **1a** (X=—CN) and **1b** (X=—COOMe), respectively. The MP2/6-31G* calculations also supported the B3LYP/6-31G* results (Table 1). The direct comparison of transition states and charge models reveals that the electrostatic effect alone can also explain the face selectivity for *endo*-substituted 7-isopropylidenenorbornanes (**1**). The importance of electrostatic agreement with observed preference for the addition of *m*-CPBA interaction was also observed in stereoselective epoxidation of α-cyclogeranyl systems and *cis*-disubstituted cyclobutenes.[9c,17]

Transition state energies determined with the B3LYP/6-31G* level for :CCl$_2$ additions to **1** are also consistent with the observed selectivities. Since the least motion pathway for the addition of carbene to an olefin is a forbidden pathway,[18] the transition structure is highly unsymmetrical. In effect, the carbene forms

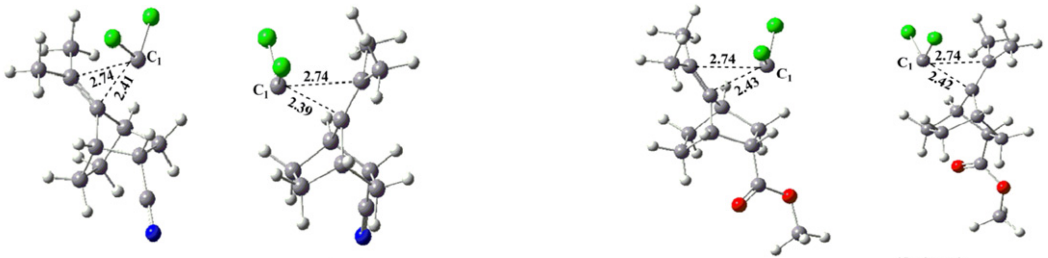
Table 1

The B3LYP/6-31G* relative energies [including zero point vibrational energy-corrected values in parenthesis ()] for *syn*- and *anti*-transition states (TS) of **1a** (X=—CN) and **1b** (X=—COOMe) with performic acid and dichlorocarbene (kJ/mol). Single point MP2/6-31G* relative energies (kJ/mol) are shown here. Bond lengths are in (Å). The relative energies (in kJ/mol) derived with charge model is also shown here [Carbon: grey; Nitrogen: blue; Oxygen: red; Hydrogen: white; Chlorine: green]



1a(*syn*) **1a**(*anti*) **1b** (*syn*) **1b** (*anti*)

B3LYP/6-31G*	TS	0.0 (0.0)	5.4 (5.0)	TS	0.0 (0.0)	3.6 (4.0)
	Charge on O$_4$	0.0	2.9	Charge on O$_4$	0.0	2.1
MP2/6-31G*	TS	0.0	6.3	TS	0.0	4.2
	Charge on O$_4$	0.0	2.9	Charge on O$_4$	0.0	1.7
Experiment		77%	23%		62%	38%



1a (*syn*) **1a** (*anti*) **1b** (*syn*) **1b** (*anti*)

B3LYP/6-31G*	TS	0.0 (0.0)	4.6 (5.2)	TS	0.0 (0.0)	3.8 (4.0)
	Charge on C$_1$	0.0	0.3	Charge on C$_1$	0.0	0.4
MP2/6-31G*	TS	0.0	4.6	TS	0.0	3.8
	Charge on C$_1$	0.0	0.1	Charge on C$_1$	0.0	0.2
Experiment		78%	22%		60%	40%

a bond to one of the olefinic carbon atoms with a C–C–C angle of about 90°. The chlorine atoms are tilted towards the other carbon, which has a planar coordination characteristic of a carbocation. In view of the unsymmetrical nature of the olefins, two sets of first order saddle points, characterized by a closer approach of the carbene to C_7 or C_8 (Scheme 1), were obtained for the *syn*- as well as *anti*-facial additions. The :CCl_2 attack at C_7 was found to be stable by ~4 kJ/mol than the corresponding attack at C_8. The transition state energies showed a clear preference for the *syn*-face attack of :CCl_2 at C_7 in **1a** (X=–CN) and **1b** (X=–COOMe), respectively. Nonetheless, the corresponding attack at C_8 also showed the similar preference for the :CCl_2 addition to **1a** (X=–CN) and **1b** (X=–COOMe) (See Supplementary data, Table S1). The calculations performed with the relative CHelpG charges taken from the respective transition states for carbon atoms (**C_1**) for :CCl_2 and placed at its location in C_7 and on chlorine atoms (**Cl 2** and **Cl 3**) for C_8 transition states yields the *syn*-face preference (Table 1 and See Supplementary data, Table S1). The charge calculated results showed larger *syn* preference with C_8 atom than C_7 atom. Direct comparison of transition states and charge calculations seem to indicate that the orbital contributions are less important for the preferential attack of *m*-CPBA and :CCl_2 to **1**. Similar charge model calculations have been performed for :CCl_2 addition to polycyclic dioxa systems, respective charges at their transition state positions.[7] Further single calculations have been performed with 6-31+G*, 6-311G** and 6-311+G** basis sets at B3LYP and MP2 levels for **1** with performic acid to examine the effect of basis set on the relative energy preferences. It appears that the relative energy preferences are independent of basis set.[19] (See Supplementary data, Table S2).

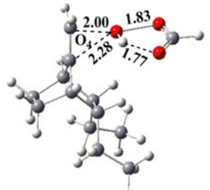
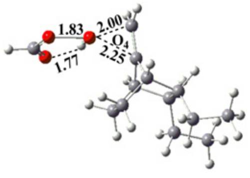
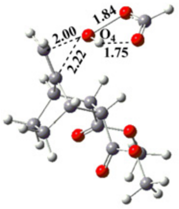
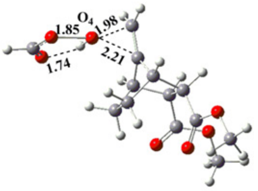
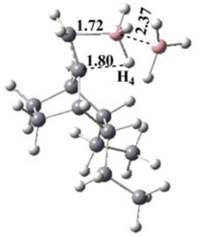
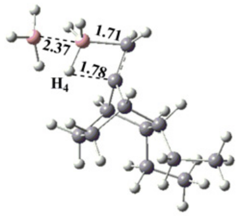
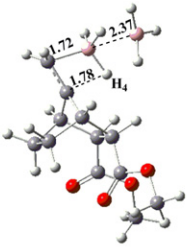
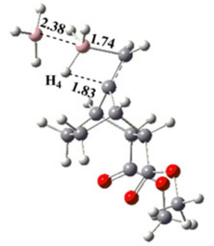
3.2. 2,3-*endo*,*endo*-7-Methylenenorbornanes (2)

Electronic control of electrophilic additions to 7-methylenenorbornanes **2** was also reported by Mehta et.al.[1c] The π-facial selectivity was tuned through remote substituents. The *endo*-substituted ethyl groups [**2a** (X=–CH_2CH_3)] directed the addition of *m*-CPBA, B_2H_6 and oxymercuration preferentially from the *anti*-face, whereas, the ester groups directed the same electrophiles from the *syn*-face of **2b** (X=–COOMe). These results can be explained by Cieplak hyperconjugative model.[3e,f] To delineate the electronic factors responsible for the face selectivity of **2**, transition state and charge model calculations have been performed. The transition state calculations for the addition of performic acid to **2a** (X=CH_2CH_3) showed *syn*-preference at both B3LYP/6-31G* and MP2/6-31G* levels of theory (Table 2), which is in contrary to the observed preferences. However, the charge calculations predicted a clear *anti* preference at both levels of theory. Going from **2a** (X=–CH_2CH_3) to **2b** (X=COOMe), the transition state results showed the *syn* preference at B3LYP/6-31G* and MP2/6-31G* levels of theory. Employing the similar charge model calculations applied for **1**, the *syn*-face preference was obtained at both B3LYP and MP2 levels of theory for **2b** (X=–COOMe) in agreement with the observed results.

Further, the electrophilic addition of B_2H_6 was modelled with *endo*-substituted 7-methylenenorbornanes **2a** (X=–CH_2CH_3) and **2b** (X=–COOMe). The transition state geometries for the B_2H_6 addition to the double bond of **2a** (X=–CH_2CH_3) and **2b** (X=–COOMe) are similar to that of hydroboration of alkenes.[20] The B_2H_6 addition to double bond is an early one and the B···H bond is significantly broken in the transition state geometries. The

Table 2

The B3LYP/6-31G* relative energies [including zero point vibrational energy-corrected values in parenthesis ( )] for *syn*- and *anti*-transition states (TS) of **2a** (X=–CH_2CH_3) and **2b** (X=–COOMe) with performic acid and diborane (kJ/mol). Single point MP2/6-31G* relative energies (kJ/mol) are shown here. Bond lengths are in (Å). The relative energies (in kJ/mol) derived with charge model is also shown here [Carbon: grey; Oxygen: red; Hydrogen: white; Boron: pink]

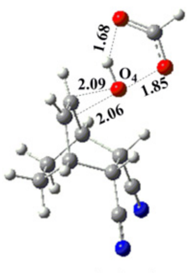
		 **2a** (*syn*)	 **2a** (*anti*)		 **2b** (*syn*)	 **2b** (*anti*)
B3LYP/6-31G*	TS	0.0 (0.0)	0.1 (0.1)	TS	0.0 (0.0)	6.3 (5.9)
	Charge on O_4	1.3	0.0	Charge on O_4	0.0	3.8
MP2/6-31G*	TS	0.0	0.8	TS	0.0	7.5
	Charge on O_4	1.3	0.0	Charge on O_4	0.0	2.9
Experiment		30%	70%		74%	26%
		 **2a** (*syn*)	 **2a** (*anti*)		 **2b** (*syn*)	 **2b** (*anti*)
B3LYP/6-31G*	TS	2.5 (1.4)	0.0 (0.0)	TS	0.0 (0.0)	4.6 (4.6)
	Charge on H_4	3.8	0.0	Charge on H_4	7.1	0.0
MP2/6-31G*	TS	2.5	0.0	TS	0.0	3.8
	Charge on H_4	5.4	0.0	Charge on H_4	8.0	0.0
Experiment		38%	62%		59%	41%

transition state geometries located for B_2H_6 addition to **2a** (X=$-$CH$_2$CH$_3$) are given in Table 2. In the case of **2a** (X=$-$CH$_2$CH$_3$), transition state and charge model calculations predicted the *anti* preference for the hydroboration with B_2H_6 in good agreement with the observed trend (Table 2). The charge of **H$_4$** was placed to calculate the electrostatic interactions between **2a**, **2b** and diborane. MESP isosurface also showed the $V_{s,max}$ on the **H$_4$** hydrogen atom (See Supplementary data, Fig. S1). The preferential addition of B_2H_6 to **2a** can possibly be dictated by the electrostatic effect. The calculated energy differences for **2b** (X=$-$COOMe) showed the *syn*-preference for the hydroboration in agreement with the observed results. However, the CHelpG charges taken from the respective transition states for hydrogen atoms (**H$_4$**) for B_2H_6 (Scheme 2) and placed at its location yields the *anti*-face preference, which are not in agreement with the observed results. These results indicate that the orbital contributions seem to be important to control the face selectivity for the hydroboration of **2b** (X=$-$COOMe). B3LYP calculations seem to underestimate the non-covalent interactions, in particular dispersive interactions, hence additional calculations have been carried out with M052X functional.[21] This DFT functional is considered to be a better model for non-covalent interactions. The single point calculations performed with M052X/6-31G* showed the similar energetic preference for both **1** and **2** as observed with the B3LYP and MP2 levels. (See Supplementary data, Table S3).

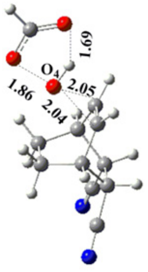
3.3. 5,6-*cis*,*exo*-Disubstituted bicyclic[2.2.2]oct-2-enes (3)

Facial selectivity for the electrophilic addition to 5,6-*cis*,*exo*-disubstituted bicyclic[2.2.2]oct-2-enes **3** was experimentally reported by Gandolfi et al.[1g] The diasterereotopic faces of **3** is both sterically and torsionally unbiased. Gandolfi et al. used different electrophiles and the *exo* substituted bicyclic[2.2.2]oct-2-enes to examine the π-facial selectivity and it was observed that Cieplak hyperconjugation effect could not predict the right selectivity in all cases. High *syn* selectivity was observed for the epoxidation of **3** bearing electron withdrawing group, such as X=$-$CN (**3a**) and X$-$X=$-$OCOO$-$ (**3b**) in agreement with Cieplak's theory, but anti selectivity was seen for diazomethane addition, which could not be explained. Density functional and ab initio calculations for these systems showed π-facial selectivity can be controlled by the atom centres of an electrophile, which is not directly involved in the bond formation while interacting with substrates.[1o] To describe properly the selectivity both transition state and charge model calculations were performed with **3a** (X=$-$CN) and **3b** (X$-$X=$-$OCOO$-$). The transition state calculations for the addition of performic acid to both **3a** (X=$-$CN) and **3b** (X=$-$OCOO$-$) showed *syn* preference at both B3LYP/6-31G* and MP2/6-31G* levels of theory (Table 3). Applying the charge model calculation, *syn*-face preference was obtained at both B3LYP and MP2 levels of theory in agreement with the (X$-$X=$-$OCOO$-$) experimental results.

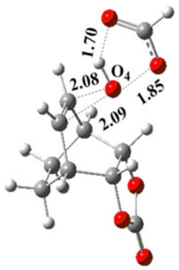
Table 3
The B3LYP/6-31G* relative energies [including zero point vibrational energy-corrected values in parenthesis ()] for *syn*- and *anti*-transition states (TS) of **3a** (X=$-$CN) and **3b** (X-X=$-$OCOO-) with performic acid and diazomethane (kJ/mol). Single point MP2/6-31G* relative energies (kJ/mol) are shown here. Bond lengths are in (Å). The relative energies (in kJ/mol) derived with charge model is also shown here [Carbon: grey; Nitrogen: blue; Oxygen: red; Hydrogen: white]



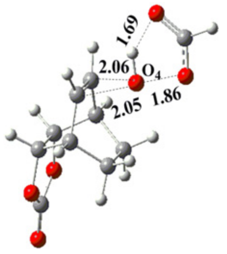
3a (*syn*)



3a (*anti*)

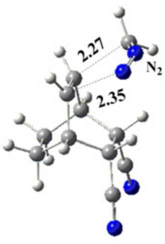


3b (*syn*)

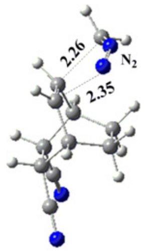


3b (*anti*)

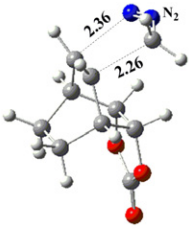
B3LYP/6-31G*	TS	0.0 (0.0)	10.9 (11.7)	TS	0.0 (0.0)	11.3 (11.8)
	Charge on O$_4$	0.0	10.0	Charge on O$_4$	0.0	12.0
MP2/6-31G*	TS	0.0	13.0	TS	0.0	14.7
	Charge on O$_4$	0.0	9.5	Charge on O$_4$	0.0	11.9
Experiment		95%	5%		96%	4%



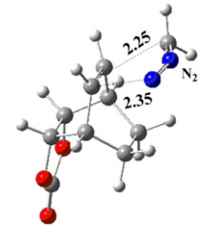
3a (*syn*)



3a (*anti*)



3b (*syn*)



3b (*anti*)

B3LYP/6-31G*	TS	3.3 (3.0)	0.0 (0.0)	TS	0.2 (0.1)	0.0 (0.0)
	Charge on N$_2$	3.9	0.0	Charge on N$_2$	0.8	0.0
MP2/6-31G*	TS	2.9	0.0	TS	0.8	0.0
	Charge on N$_2$	4.8	0.0	Charge on N$_2$	0.7	0.0
Experiment		31%	69%		38%	72%

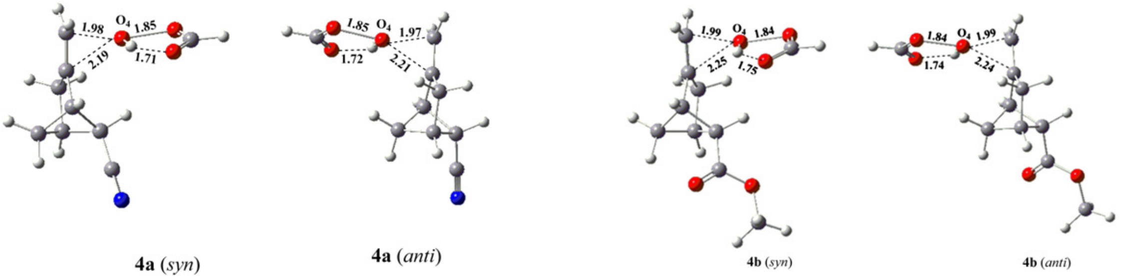
The transition states calculated for the 1,3-dipolar cycloaddition of diazomethane to **3a** (X=–CN) and **3b** (X–X=–OCOO–) concerted in nature similar to earlier reports.[22] Both B3LYP/6-31G* and MP2/6-31G* level showed *anti* preference for the addition of diazomethane to both **3a** (X=–CN) and **3b** (X–X=–OCOO–), which is in agreement to the experimental results. The dramatic reversal of π-facial selectivity of **3** with diazomethane could not be explained by the σ–σ* type hyperconjugative interaction. Electrostatic Charge model calculations and MESP analysis showed that the nonparticipating atom (**N_2**) (Scheme 2 and Supplementary data, Fig. S1) in bond formation of diazomethane predicts the facial selectivity for the electrophilic addition of diazomethane to substrate.[1o]

3.4. 5-*exo*-Substituted-2-methylenebicyclo[2.1.1]hexane

The electrophilic additions to 2-methylenebicyclo[2.1.1]hexane systems **4** have been examined.[1n] The experimental and

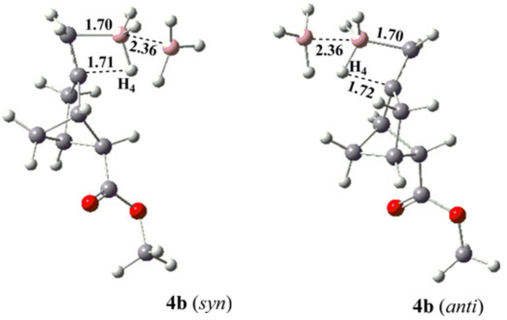
Table 4

The B3LYP/6-31G* relative energies [including zero point vibrational energy-corrected values in parenthesis ()] for *syn*- and *anti*-transition states (TS) of **4a** (X=–CN) and **4b** (X=–COOMe) with performic acid, diborane and dichlorocarbene (kJ/mol). Single point MP2/6-31G* relative energies (kJ/mol) are shown here. Bond lengths are in (Å). The relative energies (in kJ/mol) derived with charge model is also shown here [Carbon: grey; Nitrogen: blue; Oxygen: red; Hydrogen: white; Boron: pink; Chlorine: green]



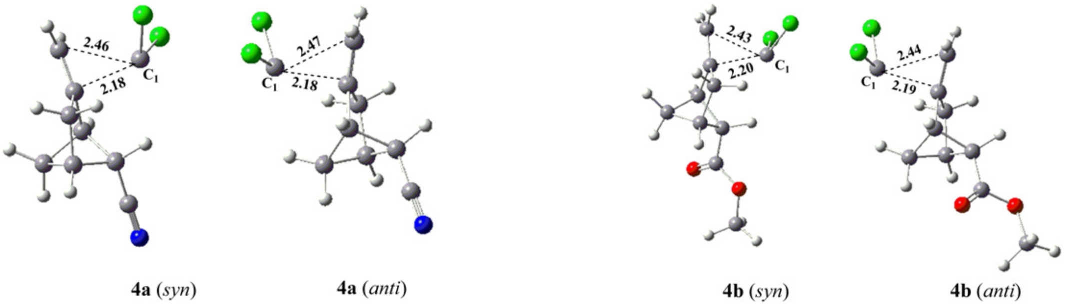
4a (*syn*) **4a** (*anti*) **4b** (*syn*) **4b** (*anti*)

B3LYP/6-31G*	TS	0.0 (0.0)	1.7 (1.8)	TS	0.0 (0.0)	2.1 (1.9)
	Charge on O_4	0.0	2.1	Charge on O_4	0.0	1.7
MP2/6-31G*	TS	0.0	2.5	TS	0.0	2.9
	Charge on O_4	0.0	2.1	Charge on O_4	0.0	1.3
Experiment		64%	36%		56%	44%



4b (*syn*) **4b** (*anti*)

B3LYP/6-31G*	TS	0.0 (0.0)	2.1 (2.2)
	Charge on H_4	1.3	0.0
MP2/6-31G*	TS	0.0	1.7
	Charge on H_4	0.8	0.0
Experiment		45%	55%



4a (*syn*) **4a** (*anti*) **4b** (*syn*) **4b** (*anti*)

B3LYP/6-31G*	TS	0.0 (0.0)	2.7 (2.8)	TS	0.0 (0.0)	2.5 (2.4)
	Charge on C_1	0.0	0.4	Charge on C_1	0.0	0.4
MP2/6-31G*	TS	0.0	3.8	TS	0.0	3.3
	Charge on C_1	0.0	0.8	Charge on C_1	0.8	0.0
Experiment		45%	55%		47%	53%

computational studies showed that the face selectivity in this system is modulated through the interplay of electrostatic and Cieplak type orbital effects whose involvement has been gleaned through MESP topographical analysis and bond density calculations. We have examined the addition of performic acid, B_2H_6 and :CCl_2 to 5-*exo*-cyano-2-methylenebicyclo[2.1.1]hexane **4a** (X=–CN) and 5-*exo*-carbomethoxy-2-methylenebicyclo[2.1.1]hexane **4b** (X=–COOMe), respectively. Both (–CN and –COOMe) substituted groups should give *syn* selectivity according to Cieplak-type hyperconjugative effect. However, the diastereoselectivity depends on the electrophiles used with these substrates. The epoxidation through *m*-CPBA addition occurs preferentially from the *syn*-face, whereas, the diborane and dichlorocarbene additions give *anti* selectivity in contrary to the Cieplak effect. Transition state and charge model calculations predict the *syn* selectivity for the *m*-CPBA addition to **4a** (X=–CN) and **4b** (X=–COOMe), respectively. These results clearly show that the selectivity can be governed by electrostatic effects. Turning to B_2H_6 addition to **4b** (X=–COOMe), the charge model calculations predicts the *anti* selectivity in agreement with the observed results (Table 4), which further corroborates the importance of electrostatic effect in controlling the face selectivity for **4**. Interestingly, the :CCl_2 additions to **4a** (X=–CN) and **4b** (X=–COOMe) gives *anti* selelctivity.[1n] In this case, the transition state and charge model calculations predicted the *syn* selectivity in contrary to the observed results, except the MP2 charge model calculation, which showed the agreement with observed trend for **4b** (X=–COOMe) (Table 4). To note that the transition states are located for **4a** (X=–CN) and **4b** (X=–COOMe) with :CCl_2, while attacking at C_2 position of the substrates (Scheme 1). Attempts failed to achieve the favoured transition states, while attacking at C_7 position of **4a** (X=–CN) and **4b** (X=–COOMe) substrates (Scheme 1). We have been able to locate a constrained transition state for **4b** (X=–COOMe) with :CCl_2 at C_7 position (See Supplementary data, Table S4). This result revealed that the transition states predicts the *syn* selectivity, whereas, the charge model gives the *anti* selectivity as observed experimentally.

3.5. 4-Substituted 9-methylenenorsnoutanes (5)

Face selectivity in electrophilic additions to 4-substituted 9-methylenenorsnoutanes **5** has been reported.[1h] The combined experimental and computational studies reveal that the face selectivity is primarily governed by through-bond interactions. The MESP topological analysis and semi-empirical calculations ruled out the importance of electrostatic interactions in governing the face selectivity for substituted 9-methylenenorsnoutanes. We have examined the factors responsible for the face selectivity of 9-methylenenorsnoutanes employing the transition state and charge model calculations. The calculations have been performed with ester-substituted 9-methylenenorsnoutanes [**5a** (X=–COOMe)] as a representative case. The :CCl_2 attack at C_9 (Scheme 1) was found to be stable by ~14 kJ/mol than the corresponding attack at C_{10} in [**5a** (X=–COOMe)] (See Supplementary data, Table S5). The transition state energies showed the preference for *syn*-face attack of :CCl_2 at C_9 and C_{10} positions with **5a** (X=–COOMe) (Scheme 1). The electrostatic interactions modelled with the previously described ChelpG charge model also explained the observed selectivity of **5a** (X=–COOMe) (Table 5). The similar analysis performed to examine the addition of performic acid to **5a** (X=–COOMe) also suggests that the electrostatic interaction can alone govern the observed face selectivity (Table 5).

Table 5
The B3LYP/6-31G* relative energies [including zero point vibrational energy-corrected values in parenthesis ()] for *syn*- and *anti*-transition states (TS) of **5a** (X=–COOMe) with performic acid and dichlorocarbene (kJ/mol). Single point MP2/6-31G* relative energies (kJ/mol) are shown here. Bond lengths are in (Å). The relative energies (in kJ/mol) derived with charge model is also shown here [Carbon: grey; Oxygen: red; Hydrogen: white; Chlorine: green]

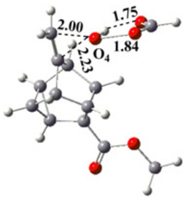
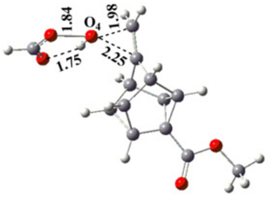
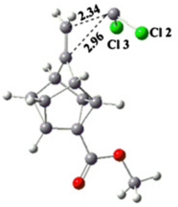
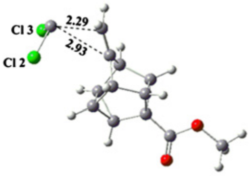
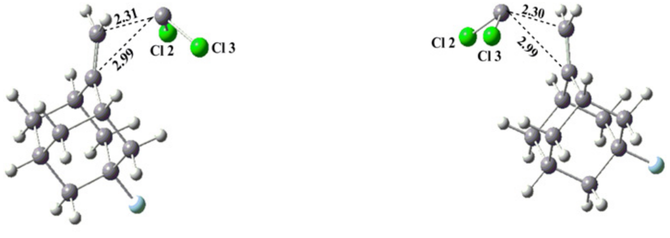
		 **5a** (*syn*)	 **5a** (*anti*)
B3LYP/6-31G*	TS	0.0 (0.0)	1.7 (1.0)
	Charge on O_4	0.0	14.2
MP2/6-31G*	TS	0.0	1.3
	Charge on O_4	0.0	14.2
Experiment		66%	34%
		 **5a** (*syn*)	 **5a** (*anti*)
B3LYP/6-31G*	TS	0.0 (0.0)	0.8 (0.6)
	Charge on Cl 2 and Cl 3	0.0	2.1
MP2/6-31G*	TS	0.0	0.2
	Charge on Cl 2 and Cl 3	0.0	1.3
Experiment		61%	39%

Table 6
The B3LYP/6-31G* relative energies [including zero point vibrational energy-corrected values in parenthesis ()] for *syn*- and *anti*-transition states (TS) of **6a** (X=–F) with dichlorocarbene (kJ/mol). Single point MP2/6-31G* relative energies (kJ/mol) are shown here. Bond lengths are in (Å). The relative energies (in kJ/mol) derived with charge model is also shown here [Carbon: grey; Fluorine: sky-blue; Hydrogen: white; Chlorine: green]



		6a (*syn*)	**6a** (*anti*)
B3LYP/6-31G*	TS	0.0 (0.0)	0.4 (0.5)
	Charge on Cl 2 and Cl 3	0.0	2.1
MP2/6-31G*	TS	0.0	0.8
	Charge on Cl 2 and Cl 3	0.0	0.5
Experiment		60%	40%

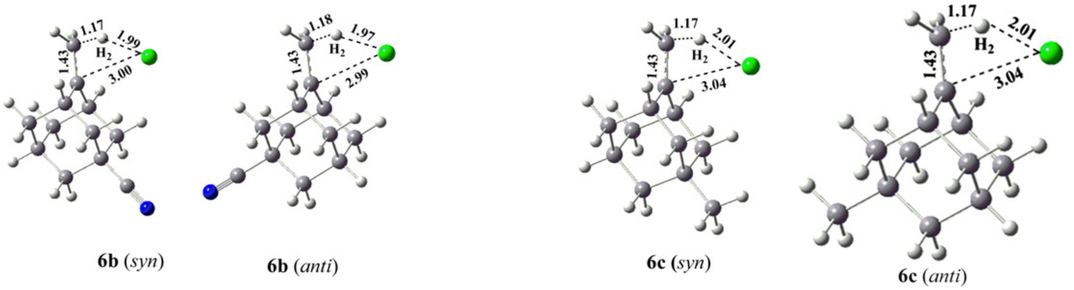
3.6. 5-Substituted-2-methyleneadamantane (6)

le Noble et al. experimentally observed that 5-fluoro-2-methyleneadamantane [**6a** (X=–F)] shows *syn* selectivity on electrophilic addition with dichlorocarbene.[1a] Further, hydrochlorination of 5-fluoro-2-methyleneadamantanes **6** with different substituents showed *syn*-face selectivity in each case.[1f] The substituents varied from electron donating group, such as methyl to electron withdrawing, such as fluoro- and cyano-groups for hydrochlorination reaction. Adcock et al. emphasized the importance of hyperconjugation as a dominant factor governing the diastereoselectivity of the hydrochlorination of 5-substitued-2-methyleneadamantane.[1f] Further, they emphasized that the $-CH_3$ substituent acts as an σ-electron withdrawing group. We have employed the transition state and charge model calculations for the electrophilic addition of dichlorocarbene and hydrochloric acid with 5-substitued-2-methyleneadamantane. Markovnikov's rule of addition of hydrochloride to alkenes is favourable than anti markovnikov addition. A detailed study has been reported on the transition state geometries of HCl addition to alkenes.[23,24] The H⋯Cl bond breaks away and C⋯H bond forms in the rate determining step for the addition of HCl to alkenes. We have modelled the transition states for HCl addition to **6** similar to that of rate determining steps for such additions.

The calculated results for the addition of $:CCl_2$ to **6a** (X=–F) are given in Table 6. The transition state calculations predict the *syn* selectivity for the addition of $:CCl_2$ to the energetically preferred C_{11} carbon position (Scheme 1) of **6a** as observed experimentally. The $:CCl_2$ attack at C_{11} (Scheme 1) was found to be stable by ∼14 kJ/mol than the corresponding attack at C_2 for **6a** (X=–F) (See Supplementary data, Table S6). Further, the charge model calculations also predicted the *syn* selectivity for $:CCl_2$ addition to **6a**.

To rationalize the observed selectivity for the addition of HCl to cyano substituted 2-methyleneadamantane [**6b** (X=–CN)] and methyl substituted 2-methyleneadamantane [**6c** (X=$-CH_3$)], transition state and charge model calculations have been employed. The calculated results show that the addition of HCl to **6b** (X=–CN) and **6c** are *syn* preferred as observed experimentally (Table 7).[1f] The charge model calculations performed with the CHelpG of hydrogen atom of HCl also predicted the *syn* selectivity in both cases (Table 7).Therefore, it appears that the π-facial addition of HCl to **6b** and **6c** is electrostatically controlled.

Table 7
The B3LYP/6-31G* relative energies [including zero point vibrational energy-corrected values in parenthesis ()] for *syn*- and *anti*-transition states (TS) of **6b** (X=–CN) and **6c** (X=$-CH_3$) with hydrochloric acid (kJ/mol). Single point MP2/6-31G* relative energies (kJ/mol) are shown here. Bond lengths are in (Å). The relative energies (in kJ/mol) derived with charge model is also shown here [Carbon: grey; Nitrogen: blue; Hydrogen: white; Chlorine: green]



		6b (*syn*)	**6b** (*anti*)		**6c** (*syn*)	**6c** (*anti*)
B3LYP/6-31G*	TS	0.0 (0.0)	1.3 (0.9)	TS	0.0 (0.0)	1.7 (1.1)
	Charge on H_2	0.0	7.5	Charge on H_2	0.0	2.1
MP2/6-31G*	TS	0.0	2.1	TS	0.0	0.7
	Charge on H_2	0.0	11.7	Charge on H_2	0.0	2.9
Experiment		87%	13%		56%	44%

4. Conclusion

In this article, we have ventured to delineate the orbital and electrostatic factors responsible for the face selectivity in sterically unbiased alkenes with varied electrophiles. The effect of electrostatic and polarization interactions is exclusively modelled using CHelpG charge of a specific atom taken from the transition state calculations. This derived charge model largely explained the face selectivity in these cases. Further, it has also been observed that the atom centre of an electrophile, which is not directly involved in the bond formation contributes towards the face selectivity. The DFT B3LYP/6-31G* and electron correlated MP2/6-31G* calculations are in good agreement to predict the facial selectivities in these sterically unbiased alkenes with different electrophiles. The application of the derived charge model should be useful to rationalize or predict the face selectivity with the electrophiles in other cases as well.

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Supplementary data

Cartesian coordinates of the electrophiles, substrates and the transition states of the different compounds are given along with the absolute energies and the imaginary frequencies. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.02.022.

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