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The nature of the electronic factor governing diastereofacial selectivity in remotely substituted (X) 2-adamantyl cations: 5-X *versus* 4-X substitution

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ABSTRACT: A limited series of 4^{eq}-substituted (X) 2-methyleneadamantanes (**6**, Y═CH_2, X═F, Cl, Br, I, and $SnMe_3$) has been synthesized and diastereoselectivities for their hydrochlorination (HCl/CH_2Cl_2) have been determined. Diastereoselectivities for the fluorination ($DAST/CH_2Cl_2$) of *secondary* alcohol mixtures, obtained from the hydride reduction of the precursor ketones (**6**,Y═O) to the alkenes, have also been measured. A comparison of this selectivity data for nucleophilic trapping of 4^{eq}-substituted (X) 2-adamantyl cations (**4**, R═H and Me) with the corresponding information for 5-substituted (X) 2-adamantyl cations (**1**, R═H and Me) has revealed important distinctions between the two series. In particular, whereas extended hyperconjugative effects appear to be the predominant electronic effect governing facial selectivity in the 5,2-series, electrostatic influences prevail in the 4,2-disposition. Copyright © 2007 John Wiley & Sons, Ltd.
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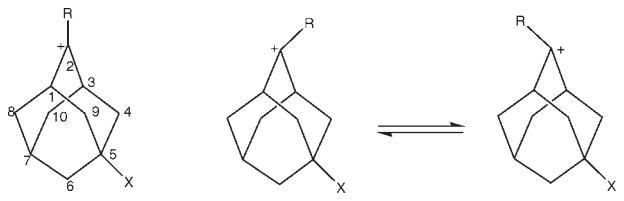
KEYWORDS: adamantane; diastereofacial selectivity; substituent effects; hyperconjugation; coulombic interactions

INTRODUCTION

The precise nature and significance of long-range electronic effects governing diastereofacial selectivity of additions to trigonal carbon centers remain a subject of continuing inquiry and debate.[1] Studies of model systems in which the electronic factor is segregated from complicating steric and conformational effects have provided crucial insight into the problem. The most widely deployed substrates of this kind are 5-substituted (X) 2-adamantyl derivatives.[2–4] Among these substrates the most conspicuous examples of diastereoselectivity are those reactions which are mediated by the formation of *secondary* (R═H) and *tertiary* (R═Me) 5-substituted (X) adamant-2-yl cations (**1**).[2,3]



1 **2** **3**

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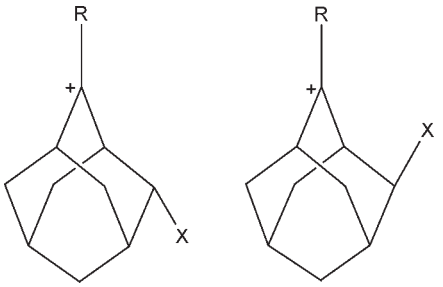
The π-facial selectivity has been ascribed to predominantly differential hyperconjugative effects induced by the substituent at C5 determining the relative stability of rapidly equilibrating pyramidalized *anti*(or *E*) and *syn*(or *Z*) epimeric ions (**2** and **3**, respectively) prior to rapid capture.[2,3] However, the situation is not completely defined as there is evidence that electrostatic effects may also be a component of the electronic influence.[5]

More recently, extensive studies in the gas phase of several of the *tertiary* ions (**1**, R═Me) have provided insight into the intrinsic factors governing face selection in these systems.[6] These results coupled with quantum chemical calculations highlight that the aforementioned model of diastereoselectivity for the *tertiary* ions (**1**, R═Me) is far from being unequivocal. In particular, the apparent occurrence of many of these ions as a single pyramidalized structure *anti*(**2**) and *syn*(**3**) for σ-electron-donating and -withdrawing substituents, respectively, in the gas phase suggests that the intrinsic diastereoselectivity of these cations is not influenced by an equilibrium population of the two *syn/anti* invertomers. The observed facial selectivity is a direct consequence of the different space available to the incoming nucleophile on the *anti* and *syn* faces of the pyramidalized cations (**2** and **3**, respectively). Furthermore, a comparison of the gas phase results with the solution data suggests that in the latter medium diastereofacial selectivity of many of the

tertiary ions (**1**, R═Me) may arise in part from the differential solvation of the two faces of a single pyramidalized ion.

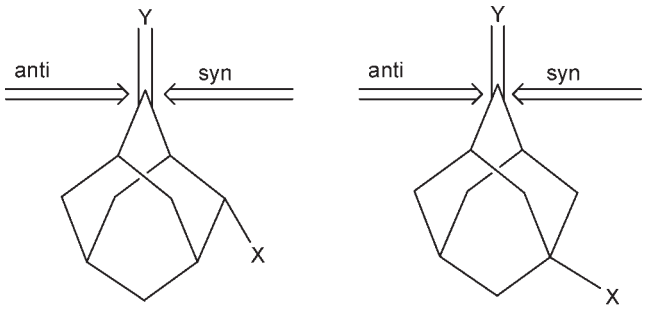
In the light of the aforementioned evolving picture of diastereoselectivity for **1** it is of interest to consider how face selection in 2-adamantyl cations will be affected by moving the substituent from the 5- to the 4-position (**4** and **5**). le Noble and co-workers[2]



4 **5**

pondered this question and perfunctorily dismissed consideration of **5** since here the *axial* disposed group will obviously affect stereochemistry in a steric way. In the case of **4**, the situation where the substituent is located in the sterically unbiased *equatorial* position, they concluded that *a priori* an answer cannot be unequivocally provided since it is not self evident that the inductive effect of a σ-electron-withdrawing group on the donor hyperconjugative ability of the C3—C4 bond with the electron deficient center (C2) will be reduced, more or less, than the extended (or double) hyperconjugative effect of a 5-substituent (antiperiplanar electron-withdrawing effect involving both the C3—C4 and C1—C9 donor bonds with C2).[3,7] Relevant to the above question are solvolysis rate studies of 5- and 4^{eq}-substituted (X) 2^{eq}-adamantyl *p*-nitrobenzenesulfonates by Grob *et al.*[8] which revealed that electron-withdrawing polar effects are transmitted more effectively in the 5,2-disposition compared to the 4,2. Consequently, a greater preference for *syn* attack in **1** (R═H) than **4** (R═H) is observed.[8]

Interestingly, Kaselj and le Noble[9] previously explored the effect on facial selectivity of moving the substituent from the 5- to the 4-position on the the hydride reduction of some appropriately substituted (X)-2-adamantanones (**6** and **7**,Y═O; X═F and Br). It was noted that despite the substituent being closer to the stereoinductive center in **6** and, therefore, with the possibility it might have a greater perturbation than in **7**, the observed expected preference for *syn* addition in **6** was unexpectedly only slightly greater than that for **7**. Moreover, it was also found that the facial selectivity for the reduction of 4^{eq},9^{eq}-dibromoadamantan-2-one (*E*/*Z* = 86/14) is not even twice that of a single bromine (**6**,Y═O; X═Br. *E*/*Z* = 76/24). It was concluded largely by default that the results probably highlight the importance of extended hyperconjugation in the transition state (TS) of **7**.[7]



6 **7**

However, a significant feature of the aforementioned results not emphasized previously is that the relative preference for *syn* addition in **1** and **4**(**1>4**) is diametrically opposite to that for the reduction of the ketones (**6** and **7**, Y═O; **6>7**)! This strongly suggests that other factors (possibly electrostatic effects)[3,5] besides delocalized electrical effects must be influencing diastereoselectivity in these systems as the trend is inexplicable in terms of purely a TS hyperconjugative model.[1a] Consequently, we were prompted to examine further how face selection in 2-adamantyl cations will be affected by having the substituent at the 4-(**4**) *versus* the 5-position (**1**). We limited our investigation of σ-electron-withdrawing groups to the halogen series since these particular substituents have similar electrostatic field constants (σ_F values)[3] but vastly different electronegativity parameters ($\sigma\chi$ values).[10] Their value lies in the fact that the pattern of induced diastereoselectivities by the halogen subset reflects importantly on the nature of the electronic effect governing diastereoselectivity. If the selectivity order parallels the σ_F values (F ~ Br ~ Cl ~ I) then through-space field effects are dominant whilst an order that follows $\sigma\chi$ values (F > Br > Cl > I) signifies dominant hyperconjugative effects (a function of the σ-inductive perturbation of C4 and C5 in 4,2- and 5,2-adamantyl derivatives, respectively).[3,5] To complete the substituent set we also included $Sn(CH_3)_3$, an electropositive substituent with virtually no electrostatic field influence ($\sigma_F \approx 0$) but with a hyperconjugative effect on diastereoselectivity in **1** opposite in direction to that of the halogens.[3b,6]

Herein, we report the results of our study which was essentially twofold. First, we wished to determine diastereoselectivities for the nucleophilic trapping of the *secondary* and *tertiary* ions of **4** (R═H and CH_3, respectively) in order to make comparisons with the corresponding data for **1**. Second, in order to provide information regarding the structure of the possible *syn*(or *Z*) and *anti*(or *E*) epimeric ions of **4** we have carried out full geometry optimizations at the B3LYP/6-31G* level of theory where X═F and Cl.

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EXPERIMENTAL

Synthesis of compounds and general procedures for hydrochlorination and fluorination

All the alkenes (**6**,Y=CH_2) and ketones (**6**,Y=O) are known compounds (X=F, Cl, Br, I, and $Sn(CH_3)_3$; see Supplementary Material). Except for the tin ketone, all were prepared essentially by literature procedures. Some essential synthetic details together with general procedures (hydrochlorination, fluorination, reduction, and methylation) are reported in the Supplementary Material.

The relative selectivity data listed in the various Tables below are the average of determinations by several methods (^{13}C, ^{1}H, and ^{19}F NMR, VPC-MS, and VPC) and are accurate to ±3%.

Computational methods. The cation calculations reported below were carried out at the B3LYP/6-31G* level of theory utilizing the GAUSSIAN 98 program package.[11] Analytical frequency calculations were performed on the minima and transition states of the density functional theory (DFT) optimized cation structures to determine zero-point vibrational energies (ZPVE) and, as well, to ensure $N_{imag} = 0$ and 1 for the minima and transition states. NBO analyses were executed using the GAUSSIAN 98 program on several of the epimeric cations of **1** and **4**. The NBO approach is described in detail by Weinhold and co-workers[12] and no detailed account is necessary here. Suffice to state that it is useful methodology for estimating quantitatively the energy of hyperconjugative effects by treating the delocalizing interactions by a standard second-order perturbation approach to provide so-called $E^{(2)}$ energies.

RESULTS AND DISCUSSION

Stereoselectivity

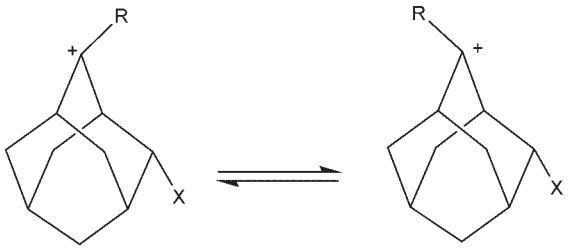
Hydrochlorination of alkenes (6, Y=CH_2). Diastereoselectivities (*Z*/*E*) for the hydrochlorination of **6** (Y=CH_2, X=Halogens) in CH_2Cl_2 and NO_2CH_3 are set out in Table 1. The corresponding values for **7** are also listed in order to facilitate comparison. Unfortunately, the protolytic instability of $Sn(CH_3)_3$ precluded a result for this group. An examination of the data reveals that the selectivity order (F ~ Br ~ Cl ~ I) for **6** essentially parallels the σ_F values of the substituents.[3] Moreover, except for F, the facial selectivity decreases on going from CH_2Cl_2 to NO_2CH_3 as solvent. This contrasts with the general picture for **7** where facial selectivity exhibits an electronegativity order (F > Cl > Br > I) and the aforementioned solvent change increases the selectivity for all the halogens. The overall pattern of results for **7** has been rationalized in terms of the relative stability of equilibrated solvated epimeric cations (**2**⇌**3**; R=CH_3) being governed predominantly by differential hyperconjugation.[5] Further, the solvent effect has been ascribed to a mechanistic difference: intimate ion-pairs in CH_2Cl_2 ($\varepsilon = 8.9$) and free ions in NO_2CH_3 ($\varepsilon = 37.5$).[5] Alternatively, if only the solvated pyramidalized *Z*-cation (**3**, R=CH_3) exists then the observed selectivity will be a function of the different physical space available to the nucleophile in its approach to the asymmetric faces of the distorted ion. In addition, differential solvation of the two faces may also play a role.[6]

Table 1. Product distributions for the hydrochlorination of 4^{eq}- and 5-substituted (X)-2-methyleneadamantanes (**6** and **7**, Y=CH_2; respectively)

	CH_2Cl_2				NO_2CH_3			
	6		**7**[a]		**6**		**7**[a]	
X	%*E*	%*Z*	%*E*	%*Z*	%*E*	%*Z*	%*E*	%*Z*
F	7	93	10	90	6	94	0	100
Cl	6	94	17	83	15	85	3	97
Br	7	93	22	78	15	85	17	83
I	13	87	34	66	21	79	26	74

[a] Taken from References 3 and 5.

If we assume that a rapid equilibrium also exists between the solvated *E*- and *Z*-cations of **4** (**8**⇌**9**, R=CH_3, respectively) then the observed selectivity order (F ~ Cl ~ Br ~ I) suggests that their relative stability is a consequence of differential electrostatic field effects. This seems reasonable if the decreased donor capacity of the C3—C4 bond by the σ-inductive effect in the *E*-cation is essentially compensated by a concominant increased donor effect from the C1—C9 bond as a result of enhanced electron demand at the reaction center (C2)[13] (see calculations below).The destabilizing electrostatic interaction between the C—X dipole and the delocalized positive charge will clearly be greater in the *E*-cation than the *Z*-cation because Coulombic repulsion



8 **9**

is maximized in the former ion due to the delocalized positive charge (including that in the CH_3 group) being towards the polar C—X bond. Within this framework the observed solvent effect noted above is probably a

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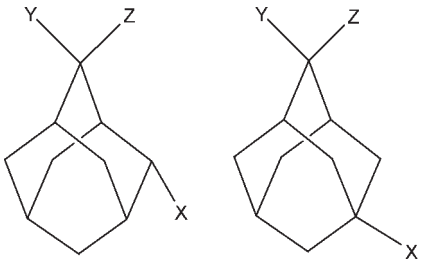
manifestation of the solvent encroaching on the space between the C—X dipole and the reaction site. Hence, the bulk dielectric of the medium impinges significantly on the effective dielectric constant.[14] An alternative explanation in terms of the existence of a single solvated *Z*-cation can also be advanced as above for **1**.[6]

Fluorination of alcohols (10, Y═OH, Z═H and Y═H, Z═OH). Product distributions for the fluorinations (DAST/CH_2Cl_2) of mixtures of *secondary* alcohols (**10**, Y═OH, *Z*═H and Y═H, *Z*═OH; *E*/*Z*∼70/30, see Supplementary Material) are set out in Table 2. It should be noted that fluorination of the 4,2 tin-alcohol



10 **11**

mixture **10** (Y═OH, *Z*═H and Y═H, *Z*═OH; X═$Sn(CH_3)_3$) did not yield any tin-fluorides. The only product detected was 2,4-dehydroadamantane (see Supplementary Material). The corresponding results for the previously reported fluoride product mixtures from similar fluorinations of 5,2-*secondary* alcohol mixtures (*E*/*Z*∼60/40) are also listed in Table 2 in order to facilitate comparison. The latter clearly display an electronegativity order of facial selectivity in accord with the dominance of extended hyperconjugation controlling the relative stability of the rapidly equilibrating ions ($E \rightleftharpoons Z$).[7b] By contrast, but similar to the results above for the *tertiary* ion (**4**, R═CH_3), the selectivity pattern for trapping of the *secondary* ion (**4**, R═H) parallels the electrostatic field-effect of the halogen substituents (F ∼ Br ∼ Cl ∼ I). Hence, it appears that differential electrostatic effects appear to predominantly govern facial selectivity in the *secondary* ions of **4** (R═H) as noted above for the corresponding *tertiary* species **4** (R═CH_3).

However, this interpretation is contingent on rapid equilibration of the ions ($E \rightleftharpoons Z$) prior to trapping by the fluoride ion. This imperative requires that the pure epimers yield identical product mixtures. Consequently, in order to test this assumption we carried out fluorinations of some of the pure epimeric alcohols (**10**; *E*- and *Z*-fluoro and -bromo alcohols, see Table 3). Most importantly, it can be seen that the product mixtures from the pure alcohols within both series are not the same. Previously,[7b] we noted this situation for the *E*- and *Z*-bromo alcohols of **11** ((*E*)-Br and (*Z*)-Br, Table 3) which agreed with the observations of le Noble and co-workers[15] for some other reactions mediated by *secondary* 2-adamantyl cations when the 5-substituent (X) is a good σ-electron acceptor. In contrast, when the 5-substituent (X) is a σ-electron donor (X═$Si(CH_3)_3$) the epimeric alcohols give identical product mixtures.[3,7] A pertinent aspect of the data in Table 3 is the reverse selectivity result ($E > Z$) for fluorination of **10** (Y═OH, *Z*═H; X═F). We believe this highlights the significant influence of extended hyperconjugation (coupling of the n-orbital of F with the electron deficiency at C2 via the C_3—C_4 σ-bond; n_F—$\sigma_{C—C}$—σ^+) on the stability of **8** (R═H, X═F). In this ion the preferred stereoelectronic requirement (antiperiplanarity of the participating orbitals)[16] for through-bond transmission is met but not in the corresponding *Z*-cation. Noteworthy, is that this resonance phenomenon does not appear to influence the relative stability of the less electron demanding *tertiary* cations (**8**⇌**9**, R═CH_3; Table 1). It is worth noting that this delocalized interaction involving fluorine as a substituent has been invoked by Nelsen *et al.*[17a] and Cieplak[17b] to explain the order of formal redox potentials for oxidation and VIP parameters for 4^{eq}-halogenated-biadamantylidene and the unusual selectivity order for the hydride reduction of **6** (Y═O, X═Halogens) utilizing $LiHAl(OC(CH_3)_3$, respectively. However, it should be

Table 2. Product distributions for the fluorination[a] of mixtures (*E* and *Z* isomers) of 4^{eq}- and 5-substituted (X) Adamantan-2-ols (**10** and **11**; Y═OH, *Z*═H and Y═H, *Z*═OH, respectively)

	10[b]		**11**[c]	
X	%*E*	%*Z*	%*E*	%*Z*
F	34	66	6	94
Cl	37	63	15	85
Br	36	64	19	81
I	35	65	35	65
$Sn(CH_3)_3$	0[d]	0[d]	>98[e]	Trace[e]

[a] DAST/CH_2Cl_2.
[b] See Table 1 ($NaBH_4$) in the Supplementary Material for composition of the *secondary* alcohol mixtures of **10** (Y═OH, *Z*═H; Y═H, *Z*═OH).
[c] Taken from Reference 5. Composition of alcohol mixtures (*E*/*Z* ≈ 60/40).
[d] No substitution product detected only propellane formation. See Supplementary Material.
[e] Fragmentation predominant.

Table 3. Product distributions for the fluorination[a] of some pure epimers of 4^{eq}- and 5-substituted (X) adamantan-2-ols (**10** and **11**; Y═OH, *Z*═H and Y═H, *Z*═OH, respectively)

	10[b]		**11**	
X	%*E*	%*Z*	%*E*	%*Z*
(*E*)-F	54	46	12[b]	88[b]
(*Z*)-F	10	90	2[b]	98[b]
(*E*)-Br	36	64	27[c]	73[c]
(*Z*)-Br	17	83	10[c]	90[c]

[a] DAST/CH_2Cl_2.
[b] This study. Alcohols available from a previous study (Reference 6a).
[c] Taken from Reference 7b.

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Table 4. Calculated energies [a,b] and zero–point vibrational energies (ZPVE)[b] of 4-substituted (X^{eq}) 2-adamantyl cations (**4**; *Z* and *E*, R═H and Me)

Systems	E_{elec}	ZPVE	E_o[c]	N_{imag}	ΔE_o[d]
R═H, X═H	−389.820158	0.23131	−389.5934766	0	0
R═H, X═H(TS)	−389.8175889	0.22082	−389.5913833	1[e]	1.31
Z(R═H, X═F)	−489.048056	0.223498	−488.824558	0	0
Z⇌*E*(TS)	−489.04467	0.222885	−488.821788	1[f]	1.74
E(R═H, X═F)	−489.045711	0.223472	−488.822239	0	1.46
Z(R═H, X═Cl)	−849.408076	0.221945	−849.186131	0	0
Z⇌*E* (TS)	−849.403993	0.221352	−849.182641	1[g]	2.19
E(R═H, X═Cl)	−849.405003	0.221887	−849.183116	0	1.89
Z(R═Me, X═F)	−528.385582	0.251509	−528.134073	0	—
Z(R═Me, X═Cl)	−888.745629	0.249896	−888.495733	0	—

[a,b] Calculations carried out at the B3LYP/6-31G* level of theory utilizing Gaussian 98. All the structures were fully optimized, and analytical frequency calculations were performed on the minima and transition state to ensure $N_{imag} = 0$ and 1, respectively.
[b] Energies given in hartrees.
[c] $E_o = E_{elec} + ZPVE$.
[d] Energy differentials given in kcal/mol.
[e] $\upsilon = -296.12\,cm^{-1}$.
[f] $\upsilon = -256.4\,cm^{-1}$.
[g] $\upsilon = -264.2\,cm^{-1}$.

noted that the latter data are puzzling in the light of the data from this study (see Table 1 and associated comments in the Supplementary Material). Interestingly, this intramolecular interaction ($n_X—\sigma_{C—C}—\sigma^*$) appears also to be significant in the neutral ground state as reflected by various nmr parameters.[18] In the extreme, when electron demand is high, extended hyperconjugation can lead ultimately to fragmentation.[19]

Theoretical calculations. The B3LYP/6-31G*-computed critical structures of the ions (**1**,R═H and **4**,R═H and CH_3; X═F and Cl) are given in Table 4. The calculation of the other ions (**1**, R═H, X═F; R═CH_3, X═F and Cl) of interest in this study were previously reported in other investigations.[6,20] To facilitate comparisons the corresponding results for **1** (R═H) are listed in Table 5. After ZPVE corrections, only a single zero-order critical structure has been identified on the potential energy surfaces (PES) of the *tertiary* ions of **1**[6] and **4** (R═CH_3). The favored invertomer of the *tertiary* ions is *syn*(or *Z*) (**3** and **9**; R═CH_3). In contrast, two zero-order critical structures have been found for the *secondary* ions (**1** and **4**, R═H). The *syn*(or *Z*) ion is favored in all cases (**3**; R═H). Relevant aspects of their geometries are displayed in Table 22 of the Supplementary Material. A pertinent feature is that the electron-deficient center (C2) is pyramidalized to varying degrees, dependent on electron demand, with the C2—H and C2—CH_3 bonds bent towards and away from the substituent in the *E* and *Z* ions, respectively. A further distortion is the concomitant tilting of the C1—C2—C3 bridge in the same direction as the C2—H and C2—CH_3 bonds (not listed in Table 22 of the Supplementary Material). These distortions allow for better overlap of the C^+ orbital with the C1—C9 (and C3—C4) and C1—C8 (and C3—C10) bonds in the *E* and *Z* conformers, respectively. The significant lengthening of these particular bonds relative to the other C—C bonds on the opposite

Table 5. Calculated energies[a,b] and zero-point vibrational energies (ZPVE)[b] of 5-substituted (X)-2-adamantyl cations (*Z* and *E*, R═H)

Systems	E_{elec}	ZPVE	E_o[c]	N_{imag}	ΔE_o[d]
Z(R═H, X═F)	−489.0501095	0.22268	−488.8318851	0	0
E⇌*Z* (TS)	−489.0429465	0.22247	−488.8249259	1[e]	4.37
E(R═H, X═F)	−489.0436883	0.22268	−488.8254648	0	4.03
Z(R═H, X═Cl)	−849.4105028	0.22160	−849.1933338	0	0
E⇌*Z* (TS)	−849.4052490	0.21921	−849.1906003	1[f]	1.72
E(R═H, X═Cl)	−849.4066456	0.22144	−849.1896364	0	2.32

[a,b] Calculations carried out at the B3LYP/6-31G* level of theory. All the structures were fully optimized, and analytical frequency calculations were performed on the minima and transition state to ensure $N_{imag} = 0$ and 1, respectively.
[b] Energies given in hartrees.
[c] $E_o = E_{elec} + ZPVE$.
[d] Energy differentials given in kcal/mol.
[e] $\upsilon = -286.47\,cm^{-1}$.
[f] $\upsilon = -230.61\,cm^{-1}$.

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face in each invertomer is clearly another manifestation of hyperconjugation. Also noticeable is the lower symmetry of the 4-X ions (**4**) compared to the 5-X species (**1**; C_s). This point is particularly exemplified by the NBO $E^{(2)}$ energies of hyperconjugative interactions (C—C → C2$^+$) in **1** and **4**. Note that the donor effects in the latter system of the four flanking C—C bonds are all different whereas in the former only those on the opposite face in each invertomer are different.

Although the calculations are for isolated molecules in the gas phase, the finding that only one structural minimum exists on the PES for the *tertiary* ions raises the possibility that the relative reactivity of the two faces of a single solvated ion may determine the stereoselectivity of these systems in solution (see above).[6] This is not the case for the *secondary* ions where two minima have been located. Interestingly, Tomoda *et al.*[21] have recently presented an excellent linear correlation ($r^2 = 0.97$) between the calculated (HF/6-31G* level of theory) energy difference between *Z*- and *E*-ions of **1** and the observed stereoselectivities (ln(*syn*/*anti*))[7b] in support of the idea that (π-facial selectivity of capture of **1** is determined by the relative stability of rapidly equilibrating pyramidalized *syn*(or *Z*) and *anti*(or *E*) epimeric ions (**2** and **3**, respectively) prior to rapid capture.[2,3] It should be noted that unlike the higher level B3LYP/6-31G* calculations in this and other studies,[6,20] the lower level HF/6-31G* calculations locate two minima on the PES of the 3^0 ions (**1**, R═CH_3). Furthermore, the authors assume incorrectly (see above) that the equilibration *Z*⇌*E* involving 2^0 ions (**1**, R═H) is complete for all substituents.

A useful way of quantitatively describing electron delocalization interactions is by the energies of the second-order perturbation analysis of the Fock matrix elements in the NBO basis ($E^{(2)}$).[12] Consequently, we carried out an NBO analysis of the *secondary* and *tertiary* ions of **1** and **4** (*Z* and *E*, R═H and Me; respectively) in order to obtain $E^{(2)}$ values for the hyperconjugative interactions between the flanking C—C bonds and the electron deficient center (C2). These parameters are set out in Table 6. One of the more significant aspects of these results is that the decreased donor capacity of the C3—C4 bond by the σ-inductive effect in the *E*-cations of system **4** (R═H) is accompanied by a concominant increased donor effect from the C1—C9 bond as a result of enhanced electron demand at the reaction center (C2). On the other hand, as expected, the donor effects of the C3—C4 and C1—C9 bonds of the corresponding ions of system **1** (R═H) are both reduced equally by extended hyperconjugation. Thus, the calculations highlight an important distinction between the substituent-induced perturbations of hyperconjugative effects in the *anti*(or *E*) epimeric ions of **1** and **4**. The result clearly supports the idea expressed above that this phenomenon is probably responsible for differential electrostatic effects being the apparent dominant factor governing facial selectivity in **4** (see subsection Hydrochlorination of Alkenes (**6**, Y═CH_2) above). A further pertinent observation is the considerable reduction in the energy of hyperconjugative interactions on reducing electron demand (cf. corresponding interactions of 2^0 and 3^0 ions (R═H and CH_3, respectively).

Finally, by use of Eqn (1) we determined the relative hydride affinities (kcal/mol) listed in Table 7. The results exemplify the pronounced destabilizing effects of the electron-withdrawing substituents on both ions (*E* and *Z*) for each structure (**1** and **4**, R═H):

$$HAd^+ + XAdH \rightarrow HAdH + XAd^+ \qquad (1)$$

For each epimeric pair, the effect is more pronounced for the *E*-cation in accord with expectations based on field inductive/hyperconjugative effects. However, the significantly larger influence for Cl *versus* F on corresponding ions for each structure is puzzling. Noteworthy though is the fact that the energy difference (kcal/mol) between the *E*- and *Z*-ions of **1** (X═F, −3.98; X═Cl, −2.38) and **4** (X═F, −1.47; X═Cl, −1.92) roughly parallels the

Table 6. Selected NBO $E^{(2)}$ energies (kcal/mol)[a,b] of hyperconjugative interactions (C–C → C2$^+$) in **1** and **4**

System	C1–C8	C1–C9	C3–C4	C3–C10
1(*Z*; R═H, X═F)	29.03	0.59	0.59	29.03
1(*E*; R═H, X═F)	1.17	25.90	25.90	1.17
1(*Z*; R═H, X═Cl)	28.07	0.74	0.74	28.07
1(*E*; R═H, X═Cl)	1.17	25.97	25.97	1.17
1(*Z*; R═Me, X═F)	20.04	1.85	1.85	20.04
1(*Z*; R═Me, X═Cl)	19.48	2.04	2.04	19.48
4(*Z*; R═H, X═F)	26.27	1.05	0.97	28.07
4(*E*; R═H, X═F)	0.92	33.73	17.98	1.87
4(*Z*; R═H, X═Cl)	27.85	0.90	0.77	27.20
4(*E*; R═H, X═Cl)	0.92	34.47	17.07	1.57
4(*Z*; R═Me, X═F)	17.95	2.46	2.21	19.60
4(*Z*; R═Me, X═Cl)	18.97	1.92	2.26	18.86

[a,b] Only energies >0.5 kcal/mol are shown.
Parent ions (X═H, R═H): 27.03, 1.02, 1.02, 27.03. (X═H, R═Me): 18.18, 2.54, 2.54, 18.18.

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Table 7. Relative hydride affinities (ΔE)[a,b] of Some *E*- and *Z*-Cations of **1** and **4**(R═H)

Structure	Epimer	ΔE (kcal/mol)
1(X═F)	*E*	7.88
1(X═F)	*Z*	3.90
1(X═Cl)	*E*	10.57
1(X═Cl)	*Z*	8.19
4(X═F)	*E*	6.62
4(X═F)	*Z*	5.15
4(X═Cl)	*E*	9.04
4(X═Cl)	*Z*	7.12

[a]Effects of substituents on the energy (kcal/mol)of the following isodesmic reaction: $HAd^+ + XAdH \rightarrow HAdH + XAd^+$.
[b]Energies calculated at the B3LYP/6-31G* level of theory

observed stereoselectivities (see Table 2) given that the equilibria (**2**⇌**3** and **8**⇌**9**, R═H) are probably incomplete (see Table 3). It should be noted that the differences between F and Cl in **1** and **4** are probably manifestations of extended hyperconjugation in the *E*-cations (**2** and **8**, R═H; $\sigma_{CX}{}^*\_\sigma_{C—C}-\sigma^+$ and $n_{F}\_\sigma_{C—C}-\sigma^+$, respectively).

CONCLUSIONS

The results of this study reveal a distinct difference in the nature of the electronic factor of polar electron-withdrawing groups governing facial selectivity in the nucleophilic trapping of 5- *versus* 4^{eq}-substituted (X)-2-adamantyl cations (**1** and **4**, respectively). Whereas the selectivity trend (*Z*/*E*) of the former ions for the halogen subset parallels their electronegativies ($F > Cl > Br > I$), by contrast, the corresponding values for the latter ions mirror their polar field constants (σ_F; $F \sim Br \sim Cl \sim I$).[3] A significant feature of this result is that if transmission of the polar inductive effect was predominantly via successive polarization of the C—C bonds (σ-inductive effect),[22] then one would have expected the selectivity for **4** to also have followed the electronegativity of the substituents. Clearly, differential electrostatic effects (through-space) prevail here in determining the relative stability of the equilibrating solvated ions (**8**⇌**9**) which govern the facial selectivity of rapid nucleophilic trapping of **4**.

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