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Transmission of Polar Substituent Effects in the Adamantane Ring System as Monitored by ^{19}F NMR

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ABSTRACT: An extensive series of (*E*)/(*Z*)-5-substituted(X)adamant-2-yl fluorides (**2** and **3**, respectively) and (*E*)/(*Z*)-4-substituted(X)adamant-1-yl fluorides (**4** and **5**, respectively) were synthesized and characterized and their ^{19}F chemical shifts measured in several solvents. Correlation of the ^{19}F substituent chemical shifts (SCS) against polar field parameters (σ_F) together with comparisons against the ^{19}F SCS of 4-substituted(X)bicyclo[2.2.2]oct-1-yl fluorides (**1**) provide unequivocal evidence for the importance of electrostatic field and 'through-three-bond' electron delocalization (double hyperconjugation) effects as long-range modes of transmission of polar effects in these saturated systems. The former effect is shown to be a function not only of spatial factors (angles and distance) but also the 'stiffness' of the C—F σ bond. The latter electronic mechanism is clearly the dominant factor regulating the ^{19}F SCS of **2** and **4** but is switched 'off' in **3** and **5** as a result of specific stereoelectronic requirements.

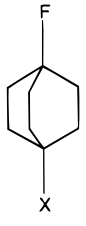
KEYWORDS: NMR; ^{19}F NMR; ^{13}C NMR; substituent chemical shifts; adamantyl fluorides; polar effects; stereoelectronic

INTRODUCTION

Several years ago we reported ^{19}F substituent chemical shifts (SCS) for an extensive series of 4-substituted(X) bicyclo[2.2.2]oct-1-yl fluorides (**1**).[1] By means of multiple regression analysis and also factorization of the SCS by a non-correlative technique, we demonstrated that the shifts seem to be dependent on both electrostatic field (σ_F effect) and electronegativity (σ_X effect) effects. The result was unprecedented since at the time all other known polar substituent perturbations in the bicyclo[2.2.2]octane ring system could be described satisfactorily in terms of an electrostatic field model.[2–4] More generally, the importance of the electronegativity factor as a long-range electronic influence is of considerable interest since analyses of many chemical and physical data failed to delineate any definitive evidence for the transmission of substituent electronegativity effects beyond the first atom of attachment of the substituent.[5]

After canvassing several possible factors with respect to the origin of the apparent electronegativity contribution to the ^{19}F SCS of **1** and bearing in mind the demonstrated sensitivity of ^{19}F chemical shifts of alkyl fluorides to the extent of delocalization of electrons into the σ^* orbital of the C—F bond,[6–8] we ascribed the phenomenon to a through-three-bond electron delocalization mechanism (double hyperconjugation) which couples the C—X and C—F bond molecular orbitals through the intervening ethano σ bonds.[1] Subsequently, we confirmed this proposal by studies of several judiciously chosen model systems.[9] In the most recent one of these we reported ^{19}F SCS for a limited series of (*E*)- and (*Z*)-5-substituted(X)adamant-2-yl fluorides (**2** and **3**, respectively).[9f] Factorization of these SCS by a non-correlative technique was achieved by calculating the respective polar-field susceptibility parameters (ρ_F values) by dividing the chemical shift differences between X = *p*-$NO_2C_6H_4$ and X = C_6H_5 by $\Delta\sigma_F$ for these substituents. Although the polar-field term ($\rho_F\sigma_F$) for **2** is significant, the solvent-independent residual contribution (^{19}F SCS $- \rho_F\sigma_F$) is clearly the dominant factor. By contrast, the latter contribution for **3** is virtually non-existent. Most importantly, the overall trend and pattern of the residual contributions to the shifts for **2** parallel to a considerable degree those observed for the corresponding derivatives of **1**. We ascribed the apparent similarity between **1** and **2** but not **1** and **3** to the stereoelectronic requirements of the through-three-bond transmission mode, namely, an antiperiplanar relationship of the participant orbitals.[10] The prevailing orbital interactions [σ^*_{CF}–σ_{CC}–σ_{CX} (or σ^*_{CX})] governing this resonance effect are optimally aligned in systems **1** and **2** but not in **3**.

The main purpose of the work described in this paper was to consolidate the conclusions drawn from the ^{19}F SCS of **2** and **3**[9f] for a very limited series of substituents [X = F, Cl, Br, I, C_6H_5, *p*-$NO_2C_6H_4$, *p*-$NH_2C_6H_4$, $Si(CH_3)_3$ and $Sn(CH_3)_3$]. Unfortunately, this database is completely inadequate for a statistical evaluation of polar substituent effects in these systems. Consequently,



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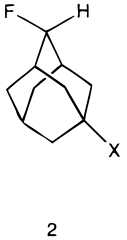

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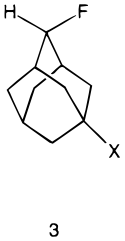

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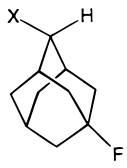

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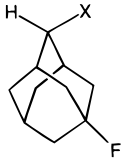

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we have synthesized and measured the ^{19}F SCS of an extensive series of **2** and **3** which cover a wide range of electronic substituent effects. In addition, we have extended the study to include a series of (*E*)- and (*Z*)-4-substituted(X)adamant-1-yl fluorides (**4** and **5**, respectively), which also embrace a diverse range of groups. Because the latter model systems differ from **2** and **3** only in that the positions of the substituents and fluorine probe have been transposed, we felt that further support for the efficacy of transmission of polar substituent effects by double hyperconjugation should emerge. Moreover, a comparison of the data for the two different sets of compounds should reveal whether or not secondary and tertiary alkyl fluorides have significantly different shift/charge density responses. Herein we report the results of our study.

RESULTS AND DISCUSSION

Before examining the results set out below, it is instructive to note that the ^{19}F chemical shifts of alkyl fluorides usually respond to the electronic influences of substituents in the *opposite* direction to expectations based on either intuition or simple shift theory.[11] For example, σ-electron-withdrawing substituents in **1** lead to *negative* ^{19}F SCS (*upfield* shifts).[1] The converse situation holds for σ-electron donor groups.[1,9b] Notwithstanding this apparent anomaly, model system studies have shown that the shift response to remote substituents appears to be systematic.[8]

^{19}F SCS of (*E*)- and (*Z*)-5-substituted(X)adamant-2-yl Fluorides (2 and 3, respectively)

The ^{19}F SCS for **2** and **3** in cyclo-C_6H_{12}, $CDCl_3$ and HFIP are shown in Table 1. Although several aspects of our previous discussion of the ^{19}F SCS of **2** and **3** for a limited range of substituents are relevant in the current context,[9f] for the sake of conciseness these will not be reiterated here. Only the most salient features of the data will be dealt with in this paper.

The most notable feature of these results (Table 1) is that the SCS of **2** (*E*-series) cover a much wider range (*ca.* 9–12 ppm) than those of **3** (*ca.* 1–3 ppm; corresponding *Z*-series). Regression analysis reveals that the SCS of **2** for all three solvents correlate poorly [$r = 0.56$ (cyclo-C_6H_{12}), 0.58 ($CDCl_3$) and 0.72 (HFIP)] against polar field constants (σ_F).[1,9a–d] A similar situation prevails for the shifts of **3** in cyclo-C_6H_{12} and $CDCl_3$, but this was expected given their very small dispersal. However, the SCS of the latter series in HFIP show a moderately strong correlation ($r = 0.95$, $n = 20$). The precision of fit of this relationship is significantly improved by omitting NH_2 and NMe_2 from the data set [Eqn (1)]:

$$^{19}F\ SCS = -4.45\sigma_F - 0.06\ (\text{system } \mathbf{3}, \text{HFIP};\ r = 0.96, n = 18) \quad (1)$$

These two groups are essentially protonated in HFIP and, therefore, act as pole not dipole substituents. Because the orientational dependences of these two types of polar substituents are different, it is unwise to group them together for correlative analyses. Proof of a significant direct field contribution to the ^{19}F SCS of **2** and **3** is demonstrated by the chemical shift difference between the *p*-$NO_2C_6H_4$ and C_6H_5 substituents. By use of the appropriate $\Delta\sigma_F$ values for these substituents [0.24 (cyclo-C_6H_{12}), 0.16 ($CDCl_3$) and 0.09 (HFIP)],[1,9e] polar field susceptibility parameters for the fluorine probe may be calculated [system **2**, $\rho_F = -0.96$(cyclo-C_6H_{12}), -1.94 ($CDCl_3$), -5.56 (HFIP); system **3**, $\rho_F = -0.50$ (cyclo-C_6H_{12}), -1.38 ($CDCl_3$), -4.44 (HFIP)]. The validity of this technique is substantiated by the fact that the ρ_F values (-4.31, -3.31 and -3.45) obtained by this methodology for the ^{13}C SCS of α-carbon centres in various unsaturated side-chain probes (Y) attached to the bridgehead of the 4-substituted(X) bicyclo[2.2.2]octyl system (Y = C_6H_5, CN and $COOC_2H_5$, respectively) agree reasonably well with those obtained (-4.60, -3.94 and -3.34) by direct correlation of the ^{13}C SCS ($CDCl_3$) against σ_F values.[12] Further strong support for this approach comes from the good correspondence between ρ_F values similarly determined for the ^{13}C SCS ($CDCl_3$) of the carbonyl group of an extensive series of 5-substituted(X)2-adamantanones[13] [-9.27 (direct correlation) *vs.* -8.63 (non-correlative method)].

Note that the ρ_F values determined by the non-correlative and correlative methods for **3** (HFIP) are in excellent agreement {-4.44 *vs.* -4.45 [Eqn (1)], respectively}. The enhancement of ρ_F values in hydrogen-bond donor (HBD) solvents has been noted previously and its origin defined.[1,8,9c,d] This phenomenon will be further discussed below in connection with the results for **4** and **5**. Factorization of the ^{19}F SCS of **2** (Table 2) reveals that the polar-field term ($\rho_F\sigma_F$) is clearly not the dominant factor regulating the shifts of system **2**. Most importantly, the SCS of **2** (cyclo-C_6H_{12} and $CDCl_3$; X = D and *p*-SC_6H_4 groups excluded except for S = H and NO_2) correlate well against the corresponding values of **1** [Eqns (2) and (3)]:

$$^{19}F\ SCS\ (\text{system } \mathbf{2}) = 0.74\ ^{19}F\ SCS\ (\text{system } \mathbf{1}) - 1.27\ (\text{cyclo-}C_6H_{12};\ r = 0.96, F\text{-test} = 205.9,\ CL = 99.99\%, n = 19) \quad (2)$$

$$^{19}F\ SCS\ (\text{system } \mathbf{2}) = 0.69\ ^{19}F\ SCS\ (\text{system } \mathbf{1}) - 1.07\ (CDCl_3, r = 0.96, F\text{-test} = 203.2, CL = 99.99\%, n = 20) \quad (3)$$

Table 1. ^{19}F substituent chemical shifts (SCS)[a–c] of (E)- and (Z)-5-Substituted(X) Adamant-2-yl fluorides (**2** and **3**, respectively)

	E-isomer (**2**)			*Z*-isomer (**3**)		
X	c-C_6H_{12}	$CDCl_3$	HFIP[d]	c-C_6H_{12}	$CDCl_3$	HFIP[d]
NO_2	−6.51	−7.05	−9.26	−0.17	−0.66	−2.73
CN	−3.46	−3.90	−5.97	−0.53	−0.99	−2.95
CF_3	−4.31	−4.34	—[e]	−0.53	−0.57	—[e]
COOH	−3.63	−3.94	−5.41	−0.22	−0.50	−1.80
$CONH_2$	−3.53	−3.99	−5.95	−0.05	−0.38	−2.02
$COOCH_3$	−3.48	−3.82	−5.23	−0.09	−0.40	−1.61
OH	−7.27	−7.62	−9.34	0.00	−0.09	−1.55
OCH_3	−6.37	−6.77	−8.74	0.25	−0.04	−1.59
$OCOCH_3$	−6.38	−6.72	−8.25	0.36	0.03	−1.34
F[f]	−7.54	−8.01	−10.03	0.24	0.17	−1.88
Cl[f]	−6.66	−7.07	−8.78	−0.15	−0.56	−2.15
Br[f]	−5.99	−6.42	−8.13	−0.21	−0.63	−2.25
I[f]	−4.63	−5.01	−6.56	−0.32	−0.72	−2.24
NH_2	−6.69	−6.92	−9.71	−0.15	−0.18	−3.03
$N(CH_3)_2$	−5.46	−5.77	−10.39	0.26	0.00	−3.53
$^{+}N(CH_3)_3$	—[e]	−8.38	—[e]	—[e]	−0.49	—[e]
$N{=}NCF_3$	−5.54	−5.94	—[e]	−0.10	−0.47	—[e]
CH_3	−4.43	−4.35	−4.33	0.00	0.00	0.00
$C(CH_3)_3$	−4.00	−4.10	—[e]	0.15	0.02	—[e]
CH_2OH	−3.38	−3.55	−4.66	0.03	−0.13	−0.95
C_6H_5 [f]	−4.18	−4.34	−5.11	0.12	−0.01	−0.69
p-$NO_2C_6H_4$ [f]	−4.41	−4.65	−5.61	0.00	−0.23	−1.09
p-CNC_6H_4	−4.37	−4.59	−5.43	0.00	−0.19	−1.00
p-$CO_2CH_3C_6H_4$	−4.26	−4.43	−5.22	0.11	−0.12	−0.80
p-FC_6H_4	−4.37	−4.45	−5.14	0.07	0.00	−0.63
p-BrC_6H_4	−4.41	−4.53	−5.23	−0.07	−0.11	−0.71
p-$CH_3OC_6H_4$	−4.24	−4.41	−5.04	0.16	0.00	−0.63
p-$NH_2C_6H_4$ [f]	−4.18	−4.33	−5.09	0.20	0.05	−0.61
p-$(CH_3)_2NC_6H_4$	—[e]	−4.39	—[e]	—[e]	−0.09	—[e]
$Si(CH_3)_3$ [f]	0.12	0.23	0.39	−0.20	−0.21	−0.19
$Sn(CH_3)_3$ [f]	1.55	1.64	1.79	−0.23	−0.25	−0.31
D	0.00	0.00	0.00	0.00	0.00	0.00

[a] Defined as the difference (in parts per million) between the ^{19}F chemical shift of the substituted compound and that of the parent compound (X = H). A negative sign denotes shielding (upfield shift).
[b] Accurate to ±0.05 ppm.
[c] X = H (relative to internal $CFCl_3$): δ −174.53 (c-C_6H_{12}) and −174.41 ($CDCl_3$).
[d] HFIP ≡ hexafluoroisopropyl alcohol.
[e] Not measured.
[f] Data taken from Ref. 9f.

The ^{19}F SCS of the latter system have been shown to be strongly regulated by an electronegativity dependent (σ_X effect) 'through-bond' electron delocalization mechanism [σ^*_{CF}–σ_{CC}–σ_{CX} (or σ^*_{CX}) orbital interactions; double hyperconjugation]. It is significant then that a slightly improved correlation is observed between the solvent-independent residual contributions (^{19}F SCS $-\rho_F\sigma_F$) of **2** and **1** ($r = 0.96$, F-test = 215.64, $n = 20$). The obvious corollary is that double hyperconjugation is the dominant mechanism conveying the polar substituent effect in **2**. Hence the fact that the stereoelectronic requirement of the participant orbitals is met in **2** (*E*-series) but not **3** (*Z*-series) readily explains the stark contrast in the relative magnitude of the ^{19}F SCS for these two systems. These conclusions are completely in line with our previous interpretation of these shift parameters based on a very limited data set.[9f]

An important point to note is that the fluorine probe is simply not just responding to the electron density fluctuations of the adjacent carbon centre. This is borne out by the fact that, in contrast to the ^{19}F SCS, the ^{13}C chemical shifts of C-2 and $^1J_{CF}$ of both systems **2** and **3** (Table 3) correlate reasonably well against σ_F (Table 4). Note, in particular, that the relative magnitudes of the ρ_F values (Table 3; **3** > **2**) are diametrically opposite to those observed for the fluorine probe (see above, **2** > **3**).

Several points concerning the residual contributions (^{19}F SCS $-\rho_F\sigma_F$) of **2** (Table 2) are noteworthy. First, the relative magnitudes of these polar contributions are governed by hyperconjugation between the relevant bond molecular orbitals, namely σ_{CC}–σ^*_{CX} and σ_{CC}–σ_{CX} for σ electron-acceptor and -donor substituents, respectively. According to simple PMO theory,[14] such conjugative interactions are proportional to $c^2\beta^2/\Delta E$, where c

Table 2. Calculated polar field ($\rho_F\sigma_F$) and residual contributions (^{19}F SCS$-\rho_F\sigma_F$) to ^{19}F SCS of (E)-5-substituted(X)adamant-2-yl fluorides (**2**)

	$\rho_F\sigma_F$			^{19}F SCS-$\rho_F\sigma_F$		
X	c-C_6H_{12}[a]	$CDCl_3$[b]	HFIP[c]	c-C_6H_{12}	$CDCl_3$	HFIP
NO_2	−0.63	−1.26	−3.84	−5.88	−5.79	−5.42
CN	−0.57	−1.09	−3.11	−2.89	−2.81	−2.86
CF_3	−0.42	−0.78		−3.89	−3.56	
COOH	−0.22	−0.62	−1.89	−3.41	−3.32	−3.52
$CONH_2$	−0.28	−0.64	−2.45	−3.25	−3.35	−3.50
$COOCH_3$	−0.21	−0.50	−1.67	−3.27	−3.32	−3.56
OH	−0.22	−0.56	−2.06	−7.05	−7.06	−7.28
OCH_3	−0.18	−0.50	−2.11	−6.19	−6.27	−6.63
$OCOCH_3$	−0.28	−0.64	−1.95	−6.10	−6.08	−6.30
F	−0.37	−0.81	−2.50	−7.17	−7.20	−7.53
Cl	−0.41	−0.83	−2.39	−6.25	−6.24	−6.39
Br	−0.42	−0.85	−2.45	−5.57	−5.57	−5.68
I	−0.40	−0.81	−2.22	−4.23	−4.20	−4.34
NH_2	−0.12	−0.37	−4.39	−6.57	−6.55	−5.32
$N(CH_3)_2$	−0.10	−0.35	−5.84	−5.36	−5.42	−4.55
$^+N(CH_3)_3$		−1.71			−6.67	
$N{=}NCF_3$	−0.49	−0.89		−5.05	−5.05	
CH_3	−0.05	−0.06		−4.38	−4.29	
$C(CH_3)_3$	−0.01	−0.04		−3.99	−4.06	
CH_2OH	−0.10	−0.27	−1.17	−3.28	−3.28	−3.49
C_6H_5	−0.14	−0.33	−1.05	−4.04	−4.01	−4.06
p-$NO_2C_6H_4$	−0.37	−0.64	−1.56	−4.04	−4.01	−4.05
p-CNC_6H_4	−0.28	−0.60	—[d]	−4.09	−3.99	—[d]
p-$CO_2CH_3C_6H_4$	−0.22	−0.49	—[d]	−4.04	−3.94	—[d]
p-FC_6H_4	−0.18	−0.41	—[d]	−4.19	−4.04	—[d]
p-BrC_6H_4	−0.21	−0.47	—[d]	−4.20	−4.06	—[d]
p-$CH_3OC_6H_4$	−0.13	−0.31	—[d]	−4.11	−4.10	—[d]
p-$NH_2C_6H_4$	−0.08	−0.23	−1.00	−4.10	−4.10	−4.09
p-$(CH_3)_2NC_6H_4$		−0.23			−4.16	
$Si(CH_3)_3$	0.00	0.00	0.00	0.12	0.23	0.39
$Sn(CH_3)_3$	0.00	0.00	0.00	1.55	1.64	1.79
D	0.00	0.00	0.00	0.00	0.00	0.00

[a] $\rho_F = -0.96$.
[b] $\rho_F = -1.94$.
[c] $\rho_F = -5.56$.
[d] Appropriate σ_F values not available.

is the coefficient of the carbon atom of attachment (or site of substitution), β is the resonance integral associated with the appropriate orbitals and ΔE is the energy gap between the orbitals. The relationship between these molecular orbital parameters and electronegativity has been discussed.[15] An approximate parallel between the polar residual contributions and group electronegativity parameters (σ_X effect) is understandable in terms of c dominating the numerator of the aforementioned expression.[14,15] The fact that the effects in **2** do not precisely parallel those in **1** ($r = 0.96$; see above) emphasizes that conjugative effects of a substituent are also a function of the reference substrate, i.e. dependent on ΔE. We have previously commented on this point in relation to the significantly smaller ^{19}F SCS of Me_3Si and Me_3Sn in **2**[9f] compared with those in **1**.[1,9b] Second, it can be seen that the alkyl groups [CH_3 and $C(CH_3)_3$], traditionally viewed as σ-electron donors when attached to an sp^3-hybridized carbon, have significant *negative* residual contributions (as large as or larger than the other carbon-based electronegative substituents such as CN, CF_3, CO_2H, $CONH_2$, CO_2CH_3 and C_6H_5 !) and are, therefore, very much σ-electron withdrawing relative to hydrogen in the *E*-series (**2**). This is in line with previous observations in **1**[1,9b] and other model polycycloalkane systems.[13] Hence, in the neutral ground state the σ^*_{C-R} bond orbital (R = alkyl) hyperconjugates significantly with the proximate antiperiplanar σ_{CC} bond orbitals. Confirmation of this point comes from replacing one of the hydrogen atoms of CH_3 with a hydroxyl group. Note that the residual contribution (^{19}F SCS $-\rho_F\sigma_F$; Table 2) for CH_2OH is significantly less negative than that for CH_3. This pronounced trend for these two groups is also observed in **1**.[9d] Based simply on σ_F[1,9c,d,16] and σ_X considerations it was expected that the shift perturbation would be in the opposite direction, i.e. the residual for CH_2OH should be more negative than that for CH_3. We believe

Table 3. ^{13}C NMR parameters ($CDCl_3$)[a,b] for C-2 of systems 2 and 3

X	*E*-isomer (**2**)				*Z*-isomer (**3**)			
	$^1J_{C_2F}$ (Hz)		δ C-2 (ppm)		$^1J_{C_2F}$ (Hz)		δ C-2 (ppm)	
H	178.46	(0.00)	95.53	(0.00)	178.46	(0.00)	95.53	(0.00)
NO_2	180.91	(2.45)	92.64	(−2.89)	181.28	(2.82)	92.06	(−3.47)
CN	180.66	(2.20)	92.75	(−2.78)	181.15	(2.69)	92.42	(−3.11)
COOH	179.69	(1.23)	94.01	(−1.52)	179.68	(1.22)	93.51	(−2.02)
$CONH_2$	179.30	(0.84)	94.28	(−1.25)	179.40	(0.94)	93.77	(−1.76)
$COOCH_3$	179.20	(0.74)	94.24	(−1.29)	179.20	(0.74)	93.67	(−1.86)
OH	178.71	(0.25)	94.14	(−1.39)	179.68	(1.22)	93.21	(−2.32)
OCH_3	179.69	(1.23)	93.99	(−1.54)	180.18	(1.72)	93.22	(−2.31)
$OCOCH_3$	179.69	(1.23)	93.69	(−1.84)	180.17	(1.71)	93.11	(−2.42)
F[c]	179.69	(1.23)	93.35	(−2.18)	180.78	(2.32)	92.60	(−2.93)
Cl[c]	180.30	(1.84)	93.09	(−2.44)	180.79	(2.33)	92.38	(−3.15)
Br[c]	180.42	(1.96)	92.91	(−2.62)	180.78	(2.32)	92.31	(−3.22)
I[c]	180.66	(2.20)	92.78	(−2.75)	181.15	(2.69)	92.30	(−3.23)
NH_2	178.80	(0.34)	94.71	(−0.82)	179.30	(0.84)	93.71	(−1.82)
$N(CH_3)_2$	178.70	(0.24)	94.94	(−0.59)	179.10	(0.64)	94.18	(−1.35)
CH_3	178.30	(−0.16)	95.62	(+0.09)	178.10	(−0.36)	94.78	(−0.75)
$C(CH_3)_3$ [d]	177.70	(−0.76)	95.04	(−0.49)	177.92	(−0.54)	95.94	(0.41)
CH_2OH	178.23	(−0.23)	95.30	(−0.23)	178.71	(0.25)	94.77	(−0.76)
C_6H_5 [c]	179.08	(0.62)	94.96	(−0.57)	178.96	(0.50)	94.23	(−1.31)
p-$NO_2C_6H_4$	179.44	(0.98)	94.28	(−1.25)	179.20	(0.74)	93.65	(−1.88)
p-CNC_6H_4	179.50	(1.04)	94.39	(−1.14)	179.10	(0.64)	93.75	(−1.78)
p-$COOCH_3C_6H_4$	179.50	(1.04)	94.82	(−0.71)	178.80	(0.34)	94.14	(−1.39)
p-FC_6H_4	179.00	(0.54)	94.95	(−0.58)	178.80	(0.34)	94.23	(−1.30)
p-BrC_6H_4	179.10	(0.64)	94.87	(−0.66)	178.80	(0.34)	94.16	(−1.37)
p-$CH_3OC_6H_4$	179.20	(0.74)	95.19	(−0.34)	179.10	(0.64)	94.44	(−1.09)
p-$NH_2C_6H_4$	177.73	(−0.73)	95.07	(−0.46)	178.71	(0.25)	94.32	(−1.21)
$Si(CH_3)_3$	178.22	(−0.24)	95.82	(+0.29)	178.22	(−0.24)	95.58	(+0.05)
$Sn(CH_3)_3$	178.71	(0.25)	95.34	(−0.19)	178.46	(0.00)	95.53	(0.00)

[a] Chemical shifts relative to central peak of $CDCl_3$ triplet set at 77.0 ppm.
[b] $\Delta\,^1J_{CF}$ and SCS in parentheses.
[c] Data taken from Ref. 9f.
[d] Data taken from Ref. 21.

the observed trend can be rationalized in terms of a competing anomeric effect[17] which involves the interaction of the nonbonding electron pair on oxygen with the σ^* orbital of the C—CH_2OH bond ($n_O \rightarrow \sigma^*_{C-CH_2OH}$).

Table 4. Results of correlation analyses[a] of ^{13}C chemical shifts of C-2 and $^1J_{C_2F}$ of systems 2 and 3 vs. polar field parameters (σ_F values)[b]

Dependent variable[c]	System	ρ_F [d]	c[e]	r[f]	n[g]
$\delta_{C\text{-}2}$	**2**	−5.56	95.75	0.96[h]	21
$\delta_{C\text{-}2}$	**3**	−5.76	95.22	0.94[h]	21
$^1J_{C_2F}$	**2**	4.49	178.12	0.92[h]	21
$^1J_{C_2F}$	**3**	5.50	178.13	0.93[h]	21

[a] General form of correlation equation: δ_C or $^1J_{CF} = \rho_F\sigma_F + c$.
[b] σ_F values taken from Refs 1 and 9a–d.
[c] Solvent, $CDCl_3$.
[d] Polar susceptibility parameter.
[e] Intercept.
[f] Correlation coefficient.
[g] Number of data points in correlation [see Table 3; excludes $C(CH_3)_3$ and *p*-SC_6H_4 where S = CN, $COOCH_3$, F, Br, CH_3O and NH_2].
[h] CL 99.99%.

By populating this antibonding orbital ($\sigma^*_{C-CH_2OH}$) it becomes less favourably disposed for interacting with the bridging ethano bonds (σ_{CC}) compared with $\sigma^*_{C-CH_3}$. Interestingly, the CH_2OH group is one of the so-called electrofugal substituents which display enhanced solvolysis rates in the bicyclo[2.2.2]octyl ring system compared with expectations based on field-inductive constants (σ_I^q).[18] These deviant results led Grob and coworkers[3] to postulate the concept of twofold or double hyperconjugation. The zero or near-zero values for the ^{19}F SCS of CH_3 and $C(CH_3)_3$ in **3** (Table 1) indicates that in this disposition their electronic influence is completely 'switched off,' which is in accord with the stereoelectronic requirement of double hyperconjugation and the weak polar field influences of alkyl groups ($\sigma_F = 0.02$–0.05).[1,9b,d]

Finally, it can be seen that the hyperconjugative influence of the *p*-SC_6H_4 groups, as measured by the residuals (^{19}F SCS $- \rho_F\rho_F$) of **2** (Table 2), is independent of the nature of the *para*-substituent (S). This is in complete accord with our previous deductions from the study of **1** (X = *p*-SC_6H_4).[8] It is an important observation in connection with our recent attempts at delineating the origin of the electronic factor governing

stereoselectivity of the reactions of 5-substituted(X)-2-adamantyl derivatives.[13]

^{19}F SCS of (*E*)- and (*Z*)-4-substituted(X)adamant-1-yl Fluorides (4 and 5, respectively)

The ^{19}F SCS of **4** and **5** in cyclo-C_6H_{12}, $CDCl_3$ and HFIP are given in Table 5. It can be seen that the SCS for the former are significantly larger than those of the latter. This pattern ($E > Z$) is similar to that observed above for the other set of model compounds (**2** and **3**). However, a notable distinction is that the differentials between the various substituents of **4** and **5** are considerably less than the corresponding values between **2** and **3**. The SCS of **4** for all three solvents correlate poorly ($r < 0.80$) against σ_F. By contrast, the shifts of **5** for all three solvents correlate very well against polar field constants [Eqns (4)–(6)]:

$$^{19}\text{F SCS} = -6.27\sigma_F + 0.14 \quad \text{(system 5, c-}C_6H_{12}\text{; } r = 0.96, n = 17) \tag{4}$$

$$^{19}\text{F SCS} = -8.36\sigma_F + 0.46 \quad \text{(system 5, } CDCl_3\text{; } r = 0.98, n = 18) \tag{5}$$

$$^{19}\text{F SCS} = -12.48\sigma_F + 0.20 \quad \text{[system 5, HFIP; } R = 0.98, n = 16 \text{ (excludes } NH_2)] \tag{6}$$

These results suggest that whereas the electrostatic field influence appears to be the only significant polar effect operating in the *Z*-series (**5**), an additional factor(s) is impacting in the *E*-series (**4**). Unfortunately, ^{19}F SCS data for the *p*-$NO_2C_6H_4$ and C_6H_5 substituents of **4** are not available, hence factorization by the non-correlative technique described above is not possible. However, the SCS of **4** correlate well against the corresponding values of **1** and **2** [Eqns (7) and (8), respectively]:

$$^{19}\text{F SCS (system 4)} = 0.86\ ^{19}\text{F SCS (system 1)} - 0.76 \quad (CDCl_3\text{; } r = 0.97, n = 17) \tag{7}$$

$$^{19}\text{F SCS (system 4)} = 1.17\ ^{19}\text{F SCS (system 2)} + 0.17 \quad (CDCl_3\text{; } r = 0.95, n = 17) \tag{8}$$

The obvious corollary is that the effects of double hyperconjugation are also significantly at play in **4** but is precluded from **5** on stereoelectronic grounds (see above). A significant point is that the marked variation of the ρ_F values of **5** with solvent [see Eqns (4)–(6)] strongly corroborates our previous conclusions[1,9f] that the solvent dependence of the ^{19}F SCS of **1** and **2** resides in the electrostatic field contribution. This must also be the case for **4**.

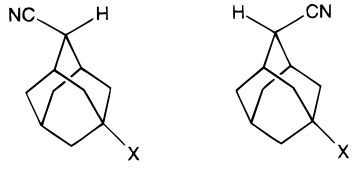
It should again be noted that the fluorine probe is not just mimicking perturbations at the adjacent carbon centre. This is evident by the fairly similar strong linear trends of the ^{13}C chemical shifts of C1 and $^1J_{CF}$ of both systems (**4** and **5**; see Table 6) against σ_F (Table 7). The situation, therefore, is similar to the trends noted above for **2** and **3** and further corroborates the general picture regarding the sensitivity of ^{19}F chemical shifts of alkyl fluorides to electron-delocalization effects.

A most noteworthy feature is the very much larger polar field susceptibility parameters (ρ_F values) for the fluorine probe of **5** [see Eqns (4)–(6); −6.27 (cyclo-C_6H_{12}), −8.36 ($CDCl_3$) and −12.48 (HFIP)] compared with those of **3** [see above; −0.50 (cyclo-C_6H_{12}), −1.38 ($CDCl_3$) and −4.44 (HFIP)]. By use of an expression for the component of the electric field (E_z) acting along the C—F σ-bond [Eqn (9)],[19] orientational factors suggest that the ρ_F values for **3** and **5** should be essentially the same.

$$E_z = \frac{\mu}{r^3}(2\cos\theta\cos\phi - \sin\theta\sin\phi) \tag{9}$$

where E_z is the electric field component acting along the C—F bond, μ is the dipole moment of the C—X bond, r is the distance between the origin of the dipole and the mid-point of the C—F bond and θ and ϕ are the angles between the CF and CX bond vectors, respectively.

We investigated this point further by examining the ^{13}C SCS of the cyano group in **6** and **7** (X = F, Cl, Br



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and I; see Table 8) and **2** and **3** [X = CN; ^{13}C SCS (**2**) = −0.88 ppm (CCl_4), −1.27 ppm ($CDCl_3$); ^{13}C SCS (**3**) = −0.69 ppm (CCl_4), −0.99 ppm ($CDCl_3$)]. A previous study in the bicyclo[2.2.2]octane ring system has shown that the ^{13}C SCS of the cyano group closely follows the field effect of substituents.[12] This is due to the dominant field-induced π polarization of the C≡N linkage. Hence it appears to be an ideal probe for examining the orientational factor, as determined from Eqn (9), in the two dispositions (2,5 or 1,4) of the adamantane ring (*E* and *Z*) without ambiguities associated with through-bond effects. It is pertinent then that the relative magnitude of the E_z values determined for C≡N in **6** and **7** (X = F, Cl, Br and I) and **2** and **3** (X = CN) by use of Eqn (9) (r being the length of the line drawn between the mid-point of the C—X bonds and the carbon in C≡N) parallel the relative magnitude of the ^{13}C SCS (**7** > **6**, **2** > **3** (X = CN), **6** (X = F) ≈ **2** (X = CN) and **7** (X = F) > 3 (X = CN)]. It should be noted that although the ^{13}C SCS are enhanced in $CDCl_3$ *vs.* CCl_4 (Table 8), this was expected since ρ_F values are increased by hydrogen bond donor solvents.[12] However, the appropriate relative values appear insensitive to the solvent.

Table 5. ^{19}F substituent chemical shifts (SCS)[a,b] of (E)- and (Z)-4-substituted(X) adamant-1-yl fluorides (**4** and **5**, respectively)

	E-isomer (**4**)			*Z*-isomer (**5**)		
X	c-C_6H_{12}	$CDCl_3$	HFIP	c-C_6H_{12}	$CDCl_3$	HFIP
NO_2	−9.28	−10.51	−13.91	−3.46	−4.45	−7.78
CN	−4.05	−5.19	−8.55	−3.00	−4.04	−7.07
COOH	−4.79	−5.45	−7.72	−1.62	−2.08	−3.96
$CONH_2$	−4.22	−5.41	−8.63	−1.34	−1.96	−4.48
$COOCH_3$	−4.35	−5.09	−8.01	−1.45	−1.86	−4.24
OH	−6.98	−7.77	−10.85	−1.38	−1.85	−4.45
OCH_3	−6.28	−6.98	−10.77	−1.58	−1.90	−4.99
$OCOCH_3$	−6.89	−7.75	−10.10	−2.18	−2.76	−4.74
F	−8.27[c]	−9.23[c]	−12.19[c]	−2.57[d]	−3.19[d]	−5.51[d]
Cl	−7.08	−7.98	−10.46	−2.77	−3.40	−5.34
Br	−6.70	−7.61	−9.95	−2.92	−3.57	−5.33
I	−5.69	−6.60	−8.75	−2.88	−3.57	−5.27
NH_2	−5.48	−6.30	−11.70	−0.63	−0.96	−6.33
CH_3	−3.21	−3.09	−3.06	0.12	0.20	0.14
CH_2OH	−2.60	−3.06	−4.84	0.00	−0.41	−2.20
$Si(CH_3)_3$	1.17	1.27[e]	—[i]	0.31	0.38[f]	0.30
$Sn(CH_3)_3$	1.85	1.93[g]	—[i]	0.42	0.38[h]	0.23
D	0.00	0.00	0.00	0.00	0.00	0.00

[a] See footnotes a, b and d in Table 1.
[b] X = H (relative to internal $CFCl_3$): δ −130.76 (c-C_6H_{12}) and −128.96 ($CDCl_3$).
[c] J_{FF} (Hz) = 4.64 (c-C_6H_{12}), 5.74 ($CDCl_3$) and 7.10 (HFIP).
[d] J_{FF} not observed.
[e] J_{SiF} = 3.90 Hz. Obtained from ^{29}Si NMR spectrum.
[f] J_{SiF} not observed.
[g] J_{SnF} (Hz) = 42.60 (c-C_6H_{12}) and 45.50 ($CDCl_3$). Obtained from ^{119}Sn NMR spectrum.
[h] J_{SnF} not observed.
[i] Compound decomposed.

Consequently, it seems reasonable to conclude that the aforementioned prediction of similar ρ_F values for **3** and **5** by Eqn (9) is valid. Hence, assuming reaction field effects and bulk dielectric influences are unimportant and, if not, then similar, we ascribe the observed large differences in the ρ_F values for **3** and **5** to the relative 'stiffness' of the C—F bond in the two systems, i.e. the electronic character of the C—F bond is fundamentally

Table 6. ^{13}C NMR parameters ($CDCl_3$)[a,b] for C-1 of systems **4** and **5**

	E-isomer (**4**)				*Z*-isomer (**5**)			
X	$^1J_{C_1F}$ (Hz)		δ C-1 (ppm)		$^1J_{C_1F}$ (Hz)		δ C-1 (ppm)	
H	183.59	(0.00)	92.47	(0.00)	183.59	(0.00)	92.47	(0.00)
NO_2	185.61	(2.02)	90.53	(−1.94)	185.58	(1.99)	90.29	(−2.89)
CN	185.55	(1.96)	90.07	(−2.40)	185.55	(1.96)	90.30	(−2.17)
COOH	184.00	(0.41)	91.58	(−0.89)	184.00	(0.41)	91.58	(−0.89)
$CONH_2$	184.00	(0.41)	91.84	(−0.63)	184.00	(0.41)	91.48	(−0.99)
$COOCH_3$	184.20	(0.61)	91.62	(−0.85)	184.20	(0.61)	91.62	(−0.85)
OH	184.08	(0.49)	91.55	(−0.92)	183.59	(0.00)	91.70	(−0.77)
OCH_3	184.40	(0.81)	91.92	(−0.55)	183.59	(0.00)	91.43	(−1.04)
$OCOCH_3$	185.10	(1.51)	91.00	(−1.47)	184.10	(0.51)	91.23	(−1.24)
F	185.06	(1.47)	91.07	(−1.40)	184.57	(0.98)	90.96	(−1.51)
Cl	185.10	(1.51)	90.57	(−1.90)	184.40	(0.81)	91.22	(−1.25)
Br	185.29	(1.70)	90.48	(−1.99)	184.37	(0.78)	91.29	(−1.18)
I	185.28	(1.69)	90.57	(−1.90)	184.57	(0.98)	91.46	(−1.01)
NH_2	183.97	(0.38)	91.77	(−0.70)	183.91	(0.32)	92.03	(−0.44)
CH_3	183.46	(−0.13)	92.32	(−0.15)	183.27	(−0.32)	92.78	(0.31)
CH_2OH	183.70	(0.11)	92.32	(−0.15)	183.70	(0.11)	92.49	(0.02)
$Si(CH_3)_3$	183.42	(−0.17)	92.68	(0.21)	183.28	(−0.31)	92.79	(0.32)
$Sn(CH_3)_3$	183.60	(0.01)	92.47	(0.00)	183.30	(−0.29)	92.74	(0.27)

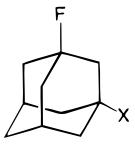
[a] Chemical shifts relative to central peak of $CDCl_3$ triplet set at 77.0 ppm.
[b] $\Delta\,^1J_{CF}$ and SCS in parentheses.

Table 7. Results of correlation analyses[a] of ^{13}C chemical shifts of C-1 and $^{1}J_{C_1F}$ of systems 4 and 5 vs. polar field parameters (σ_F values)

Dependent variable	System	ρ_F	c	r	n
$\delta_{C\text{-}1}$	**4**	−3.96	92.61	0.93	18
$\delta_{C\text{-}1}$	**5**	−3.87	92.77	0.96	18
$^{1}J_{C_1F}$	**4**	3.72	183.36	0.92	18
$^{1}J_{C_1F}$	**5**	3.27	183.16	0.91	18

[a] See footnotes to Table 4.

different when fluorine is attached to a secondary carbon compared with a tertiary carbon in the adamantane ring system. Our previous model system studies[1,8,9a,c,d] have revealed that the degree of direct electrostatic polarization of the C—F bond (field effect) is determined not only by the vector potential along its axis but also by the flexibility of the molecular framework of the substrate and the hydrogen-bond donor capacity of the solvent. Apparently the necessary structural adjustment at the carbon centre, which ensures that the C—F σ-bond is responsive to field-induced polarization, is more facile at a tertiary bridgehead carbon than a secondary methylene centre in the adamantane ring system. It is worth noting that the electrostatic field effect has been shown also to be a strong regulator of the ^{19}F SCS of 3-substituted(X)adamant-1-yl fluorides (**8**) [$\rho_F = -2.71$ (cyclo-C_6H_{12}), -5.31 ($CDCl_3$) and -12.22 (HFIP)].[9c] This model system is similar to **4** and **5** in that fluorine is also attached to a tertiary bridgehead centre. However, it should be noted that the ^{19}F SCS of **8** [^{19}F SCS (ppm) of $Si(CH_3)_3$ in **8**:



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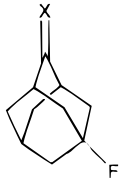

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Table 8. ^{13}C substituent chemical shifts (SCS)[a–c] of the cyano group of (E)- and (Z)-5-substituted(X)adamant-2-yl cyanides (**6** and **7**, respectively)

	E-isomer (**6**)		*Z*-isomer (**7**)	
X	CCl_4	$CDCl_3$	CCl_4	$CDCl_3$
F	−0.74	−1.14	−0.86	−1.26
Cl	−0.82	−1.19	−0.91	−1.26
Br	−0.76	−1.13	−0.94	−1.26
I	−0.55	−0.89	−0.84	−1.15
C_6H_5		−0.21		−0.33

[a] Chemical shifts (ppm) of C≡N of substituted compounds relative to the parent compound (X = H).
[b] X = H: δ 119.62 (relative to CCl_4 set at 95.4 ppm), 122.20 (relative to central peak of $CDCl_3$ triplet set at 77.0 ppm).
[c] ^{13}C SCS of cyano group of system **1** (X = CN): −1.39 ppm (CCl_4) and −1.76 ppm ($CDCl_3$; taken from Ref. 12).

0.66 (cyclo-C_6H_{12}), 0.92 ($CDCl_3$); these results were not previously reported (see Ref. 9c)] do not parallel those of **4** or **5** because the mix of electrostatic field and electron delocalization influences is different in each of these systems.

Based on orientational considerations [Eqn (9)], the ρ_F values for **4** and **5** should be approximately the same. Consequently, the shift differentials between **4** and **5** provide a measure of through-bond contributions to the ^{19}F SCS of **4** (Table 5). Except for the cyano substituent, which is endowed with a large polar field influence but a fairly feeble σ-electron-withdrawing effect, these differentials indicate that through-three-bond electron delocalization is the dominant factor regulating the shifts of **4**. In the main these are similar to those factored out for **2** (Table 2).

Finally, before closing the discussion on the ^{19}F SCS of **4** and **5**, there are three other points worthy of comment. First, it can be seen that no ^{2}H–^{1}H isotope effect on the ^{19}F chemical shifts of **4** (Table 5) was detected at 84.26 MHz. This is also the case for **2** (Table 1). However, proton-decoupled ^{19}F NMR spectra of the respective mixtures (**2**–**3** and **4**–**5**, X = D) recorded at 376.46 MHz revealed two signals, a singlet and a triplet, separated by 0.02 ppm in both cases. The upfield signal in each mixture was the triplet (due to long-range ^{2}H coupling, $^{5}J_{DF} = 0.61$ Hz) and because of the stereoelectronic requirement for five-bond coupling (see below) was assigned to the *E*-isomers (**2** and **4**). Based on $\gamma_{1_H}/\gamma_{2_H} = 6.5145$, $^{5}J_{HF}$ for **2** and **4** (X = H) is 4.0 Hz. It is significant to note that these isotopic shifts are significantly smaller than the ^{2}H–^{1}H isotope shift (−0.06 ppm) observed for **1**[20] whose origin has been ascribed to double hyperconjugation. The reduced number of bridging ethano bonds in **2** and **4** compared with **1** must be a contributing factor to the observed order. The latter structural feature is also largely responsible for $^{5}J_{HF}$ of **2** and **4** being less than the corresponding value for **1**[20] (4.0 *vs.* 5.6 Hz, respectively).

Second, it can be seen that five-bond long-range coupling constants ($^{5}J_{X,Y}$) are observed for **4** (see footnotes c, e and g in Table 5) but not for **5** (see footnotes d, f and h in Table 5). A similar distinction was noted previously between **2** and **3**.[9f] These results highlight that spin transmission information via the five-bond pathway is optimized when the bridging ethano bonds are in an antiperiplanar array with the C—X and C—F bonds. Finally, it is worth noting that the introduction of groups at the C-2 (or C-4, depending on the numbering system adopted) position via an sp^2-hybridized carbon (**9**, X = CH_2, O and NOH) has a marked effect on the ^{19}F chemical shift [^{19}F SCS (ppm): X = CH_2, −4.09 (c-C_6H_{12}), −4.49 ($CDCl_3$); X = NOH, −5.86 (c-C_6H_{12}), −7.23 ($CDCl_3$); X = O, −9.81 (c-C_6H_{12}), −11.85 ($CDCl_3$), −17.48 (HFIP)]. Although the insertion of an sp^2-hybridized carbon into the skeletal framework may induce a structural component to the perturbation, the well defined trend (X = O > NOH > CH_2) and the magnitude of the differentials clearly indicate strong regulation by an electronic effect also

(combined electrostatic field and electron delocalization influences). Unfortunately, there is no means by which factorization can be achieved.

CONCLUSIONS

The results of this model system study demonstrate further that fluorine is a sensitive and useful probe for monitoring polar effects in saturated systems. In particular, it is clear that ^{19}F chemical shifts of alkyl fluorides can be strongly regulated by both electrostatic field and through-bond electron delocalization influences of remote substituents. The former is a function not only of spatial factors (angles and distance) but also the 'stiffness' of the C—F σ-bond. The latter electronic mechanism clearly has specific stereoelectronic requirements which leads to 'on' and 'off' conformations.

Table 9. Exact mass data for mixtures of (E)- and (Z)-5-substituted(X)adamant-2-yl fluorides (2 and 3, respectively)[a]

X	Molecular formula	m/z (M^+) Calc.	m/z (M^+) Observed
NO_2	$C_{10}H_{14}NO_2F$	199.1655	199.1649
CN	$C_{11}H_{14}NF$	179.1110	179.1132
CO_2CH_3	$C_{12}H_{17}O_2F$	212.1213	212.1232
OCH_3	$C_{11}H_{17}OF$	184.1263	184.1263
$OCOCH_3$	$C_{12}H_{17}O_2F$	212.1213	212.1230
$N(CH_3)_2$	$C_{12}H_{20}FN$	197.1579	197.1555
CH_3	$C_{11}H_{17}F$	168.1303	168.1311
p-FC_6H_4	$C_{16}H_{18}F_2$	248.1376	248.1400
p-BrC_6H_4	$C_{16}H_{18}Br$	308.0576	308.0525
		310.0556	310.0532
p-$CH_3OC_6H_4$	$C_{17}H_{21}FO$	260.1576	260.1551
p-$CO_2CH_3C_6H_4$	$C_{18}H_{21}FO_2$	288.1525	288.1539
p-CNC_6H_4	$C_{17}H_{18}FN$	255.1423	255.1407

[a] Mixtures obtained (*Z*–*E*) by treating the corresponding alcohol mixtures with DAST (see text).

EXPERIMENTAL

Synthesis of Compounds

(*E*)- and (*Z*)-5-substituted(X)adamant-2-yl fluorides (2 and 3, respectively). Most of the additional new derivatives of **2** and **3** [X = NO_2, CN, $COOCH_3$, $OCOCH_3$, CH_3O, CH_3, $C(CH_3)_3$, $N(CH_3)_2$, *p*-CNC_6H_4, *p*-$COOCH_3C_6H_4$, *p*-FC_6H_4, *p*-BrC_6H_4, *p*-$CH_3OC_6H_4$ and *p*-$(CH_3)_2NC_6H_4$] were obtained as mixtures by treatment of the corresponding *E*/*Z* alcohol mixtures[13,21] with diethylaminosulphur trifluoride (DAST) as described previously.[9f] The fluoride mixtures were purified by chromatography (basic alumina; hexane–ethyl acetate). Their compositions (*E*/*Z* ratio) have been reported in connection with other studies.[13,21] Exact mass data for these

Table 10. Synthetic methods and exact mass data for mixtures of (E)- and (Z)-5-substituted (X)Adamant-2-yl fluorides (2 and 3, respectively)

X	Precursor	Synthetic method	Molecular formula	m/z (M^+) Calc.	m/z (M^+) Obs.
COOH	$COOCH_3$ [a]	1. KOH–C_2H_5OH–H_2O 2. 1 M HCl	$C_{11}H_{15}O_2F$	198.1056	198.1069
$CONH_2$	COOH	$SOCl_2$–NH_3	$C_{11}H_{16}FON$	197.1216	197.1243
CN	$CONH_2$	$(CF_3CO)_2O$–dioxane–pyridine[b]	$C_{11}H_{14}FN$	179.1100	179.1132
NH_2	$CONH_2$	OIC_6H_5–CH_3CN–HCOOH–H_2O[c]	$C_{10}H_{16}FN$	169.1266	169.1279
$N(CH_3)_2$	NH_2	HCHO–H_2O–H_2/Pd–C	$C_{12}H_{20}FN$	197.1579	197.1555
NO_2	NH_2	$KMnO_4$–acetone–H_2O–$MgSO_4$ [d]	$C_{10}H_{14}O_2FN$	199.1655	199.1649
CH_2OH	COOH	$BH_3 \cdot S(CH_3)_2$	$C_{11}H_{17}OF$	184.1263	184.1274
CF_3	NH_2	1. CF_3NO–CH_3OH, 70 °C 2. *hv*–$(CH_3)_3COH$[e]	$C_{11}H_{14}F_4$	222.1031	222.1010
OH	$OCOCH_3$ [f]	DMSO–KOH, 100 °C	$C_{11}H_{16}FO$	170.1106	170.1089
OCH_3	OH	1. NaH–THF 2. CH_3I, Δ	$C_{11}H_{17}FO$	184.1263	184.1263
D	Br[g]	(*n*-Bu)$_3$SnD–AIBN	$C_{10}H_{14}FD$	155.1221	155.1221

[a] Mixture obtained ($Z:E = 70:30$) by treating the corresponding alcohol mixture (Ref. 9f) with DAST (see text).
[b] Ref. 30.
[c] Ref. 31.
[d] Ref. 32.
[e] Ref. 33.
[f] Mixture obtained ($Z:E = 80:20$) by treating the corresponding alcohol mixture (Ref. 9f) with DAST (see text).
[g] See Ref. 9f.

Table 11. ^{13}C NMR chemical shifts (ppm)[a,b,c] of (E)-5-substituted(X)adamant-2-yl fluorides (2)

X	C-1,3	C-2	C-4,9	C-5	C-6	C-7	C-8,10	Other carbons			
H	32.85	95.62	35.76	26.90	37.25	27.24	31.49				
	(17.58)	(178.23)	(8.79)	(1.47)	(0.98)	(0.00)	(0.98)				
NO_2	33.48	92.64	38.53	83.20	40.44	28.58	29.55				
	(18.80)	(180.91)	(9.50)	(n/o)	(n/o)	(0.00)	(1.0)				
CN	31.54	92.75	38.15	29.24	39.45	25.95	29.57	124.00 (CN)			
	(19.53)	(180.66)	(9.77)	(n/o)	(n/o)	(0.00)	(0.98)	(2.93)			
CO_2H	32.12	94.10	36.80	39.62	38.15	26.68	30.19	183.58 (CO_2H)			
	(18.56)	(179.69)	(9.76)	(n/o)	(n/o)	(0.00)	(n/o)	(2.45)			
$CONH_2$	32.39	94.28	37.51	39.71	38.95	27.04	30.36	180.06 ($CONH_2$)			
	(18.80)	(179.30)	(9.77)	(n/o)	(n/o)	(0.00)	(n/o)	(2.00)			
CO_2CH_3	32.23	94.24	37.07	39.73	38.43	26.79	30.28	177.08 (CO)		51.65 (CH_3)	
	(18.56)	(179.20)	(9.28)	(n/o)	(n/o)	(0.00)	(0.98)				
OH	34.28	94.14	42.45	67.27	45.00	29.46	29.96				
	(19.04)	(178.71)	(9.28)	(n/o)	(n/o)	(0.00)	(n/o)				
OCH_3	33.93	93.99	38.22	70.69	40.25	29.07	30.19	48.07 (OCH_3)			
	(19.04)	(179.69)	(9.28)	(n/o)	(n/o)	(0.00)	(0.97)				
$OCOCH_3$	34.35	93.69	38.60	78.56	40.92	29.52	30.09	170.16 (CO)		22.50 (CH_3)	
	(19.54)	(179.69)	(9.77)	(n/o)	(n/o)	(0.00)	(n/o)				
NH_2	33.76	94.71	43.71	46.76	46.07	28.70	30.22				
	(18.60)	(178.80)	(9.40)	(n/o)	(n/o)	(0.00)	(0.90)				
$N(CH_3)_2$	33.44	94.94	36.00	37.25	38.25	28.36	30.73	52.95 (CH_3)			
	(18.50)	(178.70)	(9.50)	(n/o)	(n/o)	(0.00)	(n/o)				
CH_3	33.12	95.62	42.47	29.18	44.22	27.77	30.78	30.05 (CH_3)			
	(17.96)	(178.30)	(9.38)	(n/o)	(n/o)	(0.00)	(n/o)				
CH_2OH	32.43	95.30	36.94	33.77	38.60	27.05	30.93	72.47 (CH_2OH)			
	(19.04)	(178.23)	(9.27)	(n/o)	(n/o)	(0.00)	(0.97)				
C_6H_5	33.17	95.01	41.15	35.39	42.87	27.83	30.58	149.39 (i)	124.78 (o)	128.18 (m)	125.82 (p)
	(18.06)	(178.71)	(9.27)	(n/o)	(n/o)	(0.00)	(0.98)	(2.44)			
p-$NO_2C_6H_4$	32.89	94.38	40.82	36.15	42.53	27.55	30.32	156.90 (i)	125.87 (o)	123.40 (m)	146.08 (p)
	(19.04)	(179.69)	(9.30)	(n/o)	(n/o)	(0.00)	(0.98)	(1.96)			
p-CNC_6H_4	32.84	94.39	40.67	35.95	42.38	27.49	30.28	154.71 (i)	125.75 (o)	132.02 (m)	109.63 (p)
	(18.80)	(179.50)	(n/o)	(n/o)	(n/o)	(0.00)	(n/o)	(2.10)		118.90 (CN)	
p-$CO_2CH_3C_6H_4$	33.11	94.82	40.99	35.92	42.70	27.76	30.54	154.75 (i)	124.99 (o)	129.60 (m)	127.85 (p)
	(18.60)	(179.50)	(9.60)	(n/o)	(n/o)	(0.00)	(n/o)	167.06 (CO)		52.00 (CH_3)	
p-FC_6H_4	33.22	94.95	41.39	35.16	43.12	27.88	30.58	145.25 (i)	126.42 (o)	114.89 (m)	161.11 (p)
	(18.40)	(179.00)	(9.20)	(n/o)	(n/o)	(0.00)	(0.00)	(3.10)	(7.60)	(20.80)	(244.20)
p-BrC_6H_4	33.13	94.87	41.11	35.36	42.83	27.79	30.54	148.53 (i)	126.83 (o)	131.30 (m)	119.74 (p)
	(18.40)	(179.10)	(9.30)	(n/o)	(n/o)	(0.00)	(n/o)	(2.10)			
p-$NH_2C_6H_4$	33.12	95.07	41.22	34.44	42.98	27.77	30.50	139.54 (i)	125.37 (o)	114.84 (m)	144.00 (p)
	(18.56)	(177.73)	(8.79)	(n/o)	(n/o)	(0.00)	(n/o)	(1.96)			
p-$CH_3OC_6H_4$	33.30	95.19	41.46	34.89	43.20	27.95	30.68	141.81 (i)	125.87 (o)	113.59 (m)	157.67 (p)
	(18.30)	(179.20)	(9.30)	(n/o)	(n/o)	(0.00)	(n/o)	(2.10)		55.26 (CH_3)	

[a] Chemical shifts (ppm) for $CDCl_3$ solutions relative to Me_4Si. (n/o), not observed.
[b] ^{13}C–^{19}F coupling constants (Hz) are given in parentheses.
[c] Note that the carbon numbering system does not necessarily parallel the numbering system based on the IUPAC rules of nomenclature.

Table 12. ^{13}C NMR chemical shifts (ppm)[a] of (Z)-5-substituted(X)adamant-2-yl fluorides (3)

X	C-1,3	C-2	C-4,9	C-5	C-6	C-7	C-8,10	Other carbons			
H	32.85	95.62	31.49	27.24	37.25	26.90	35.76				
	(17.58)	(178.23)	(0.98)	(0.00)	(0.98)	(1.47)	(8.79)				
NO_2	34.39	92.06	34.72	83.32	40.44	28.26	33.55				
	(17.80)	(181.28)	(1.40)	(0.00)	(n/o)	(1.20)	(8.30)				
CN	31.65	92.42	33.74	29.31	39.34	25.61	33.67	124.28 (CN)			
	(17.58)	(181.15)	(1.46)	(0.00)	(n/o)	(1.47)	(8.30)				
CO_2H	32.40	93.51	32.36	39.62	38.15	26.37	34.34	183.72 (CO_2H)			
	(17.58)	(179.68)	(0.98)	(0.00)	(n/o)	(1.46)	(8.30)				
$CONH_2$	32.74	93.77	33.21	39.71	38.68	26.63	34.45	180.34 ($CONH_2$)			
	(17.60)	(179.40)	(n/o)	(0.00)	(n/o)	(1.50)	(8.60)				
CO_2CH_3	32.51	93.67	32.64	39.79	38.43	26.48	34.43	177.27 (CO)		51.54 (CH_3)	
	(17.57)	(179.20)	(n/o)	(0.00)	(n/o)	(1.46)	(8.30)				
OH	35.33	93.21	39.21	67.12	44.52	29.08	34.05				
	(17.58)	(179.68)	(0.97)	(0.00)	(n/o)	(1.47)	(8.79)				
OCH_3	34.98	93.22	34.57	70.56	40.57	28.76	34.27	47.63 (OCH_3)			
	(16.60)	(180.18)	(n/o)	(0.00)	(n/o)	(1.95)	(8.79)				
$OCOCH_3$	35.38	93.11	35.39	78.56	40.23	29.16	34.11	170.09 (CO)		22.50 (CH_3)	
	(18.07)	(180.17)	(n/o)	(0.00)	(n/o)	(1.47)	(8.30)				
NH_2	34.51	93.71	40.24	46.59	45.35	28.27	34.34				
	(17.30)	(179.30)	(n/o)	(0.00)	(n/o)	(1.50)	(8.30)				
$N(CH_3)_2$	34.21	94.18	31.58	38.00	37.13	28.07	34.77	52.87 (CH_3)			
	(17.51)	(179.10)	(n/o)	(0.00)	(n/o)	(1.30)	(8.80)				
CH_3	33.47	94.78	38.31	29.18	44.16	27.41	34.95	30.08 (CH_3)			
	(17.66)	(178.10)	(n/o)	(0.00)	(n/o)	(1.47)	(9.02)				
CH_2OH	32.77	94.77	32.88	33.77	38.47	26.69	35.07	73.01 (CH_2OH)			
	(17.58)	(178.71)	(0.98)	(0.00)	(n/o)	(1.47)	(8.79)				
C_6H_5	33.51	94.27	36.89	35.39	42.57	27.48	34.74	150.14 (i)	124.72 (o)	128.12 (m)	125.71 (p)
	(17.58)	(178.71)	(0.98)	(0.00)	(n/o)	(1.46)	(8.79)				
p-$NO_2C_6H_4$	33.23	93.74	36.57	36.15	42.22	27.19	34.43	157.61 (i)	125.80 (o)	123.40 (m)	146.02 (p)
	(17.58)	(179.20)	(0.97)	(0.00)	(n/o)	(1.47)	(8.30)				
p-CNC_6H_4	33.19	93.75	36.42	35.95	42.05	27.12	34.39	155.44 (i)	125.69 (o)	131.98 (m)	109.47 (p)
	(17.70)	(179.10)	(n/o)	(0.00)	(n/o)	(n/o)	(8.70)	119.00 (CN)			
p-$CO_2CH_3C_6H_4$	33.45	94.14	36.73	35.92	42.40	27.40	34.69	155.48 (i)	124.94 (o)	129.60 (m)	127.72 (p)
	(17.80)	(178.80)	(n/o)	(0.00)	(n/o)	(n/o)	(8.70)	167.13 (CO)		52.00 (CH_3)	
p-FC_6H_4	33.57	94.23	37.15	35.16	42.80	27.52	34.73	146.00 (i)	126.35 (o)	114.81 (m)	161.05 (p)
	(17.70)	(178.80)	(n/o)	(0.00)	(n/o)	(1.50)	(8.80)	(3.10)	(7.60)	(20.80)	(243.90)
p-BrC_6H_4	33.48	94.16	36.86	35.36	42.50	27.43	34.69	149.27 (i)	126.79 (o)	131.24 (m)	119.60 (p)
	(17.60)	(178.80)	(n/o)	(0.00)	(n/o)	(1.50)	(8.70)				
p-$NH_2C_6H_4$	33.44	94.32	37.00	34.44	42.63	27.38	34.64	140.41 (i)	125.37 (o)	114.84 (m)	144.00 (p)
	(17.57)	(178.71)	(n/o)	(0.00)	(n/o)	(n/o)	(8.78)				
p-$CH_3OC_6H_4$	33.65	94.44	37.22	34.89	42.87	27.60	34.84	142.62 (i)	125.80 (o)	113.55 (m)	157.58 (p)
	(17.70)	(179.10)	(n/o)	(0.00)	(n/o)	(n/o)	(8.60)	55.20 (CH_3)			

[a] See Footnotes a–c in Table 11.

mixtures are listed in Table 9. Several of the fluoride mixtures [**2** and **3**; X = NO_2, CN, CH_3O and $N(CH_3)_2$] were also obtained by standard functionalization procedures starting with the ester– and acetate–fluoride mixtures (**2** and **3**, X = $COOCH_3$ and $OCOCH_3$) as precursors (Table 10). Other fluoride mixtures (X = CF_3, CH_2OH, NH_2 and D) were obtained as indicated in Table 10.

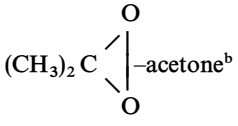
All the fluoride mixtures were unambiguously characterized by ^{13}C NMR (Tables 11 and 12). Spectral assignments followed unequivocally from the characteristic ^{13}C–^{19}F coupling constants in the adamantane skeletal framework[9c,22] and also by the chemical shift additivity method.[23]

(*E*)- and (*Z*)-1-substituted(X)adamant-1-yl fluorides (4 and 5, respectively). 1-Fluoroadamantane (**4** and **5**, X = H),[9c] 5-fluoroadamant-2-one (**9**, X = O),[9f] 2-methylene-5-fluoroadamantane (**9**, X = CH_2)[13] and (*E*/*Z*)-5-fluoroadamantan-2-ol (**4** and **5**, X = OH)[9f] were synthesized as described previously. (*E*)- and (*Z*)-1,4-difluoroadamantane (**4** and **5**, X = F) were available from our previous study (these compounds are equivalent to **2** and **3**, X = F).[9f] Several of the fluoride mixtures [**4** and **5**; X = NO_2, $COOCH_3$, $CONH_2$, CH_2OH, CH_3, NH_2, OCH_3, $OCOCH_3$, Cl, I, $Si(CH_3)_3$ and $Sn(CH_3)_3$] were obtained by standard functionalization procedures from the appropriate precursor (Table 13). These mixtures were all unambiguously characterized by ^{13}C NMR (Tables 14 and 15) as described above for systems **2** and **3**.

(*E*)- and (*Z*)-5-Fluoroadamantane-2-carboxylic acid (4 and 5, respectively, X = COOH). By use of the procedure of Farcasiu,[24] a solution of 5-fluoroadamant-2-one (**9** X = O; 2.0 g, 11.90 mmol) in dry DMSO (22 ml) was treated with dimethylsulphoxonium methylide [trimethylsulphoxonium iodide[25] (3.14 g, 14.30 mmol) and NaH (80%, 0.51 g, 17.16 mmol)]. A standard work-up followed by sublimation (70–100 °C/0.10 mmHg) afforded an *E*–*Z* mixture of the spirooxiranes as a white waxy solid (1.65 g, 76%). The epimers were shown by ^{13}C NMR to be in the ratio 34:66 (*E*:*Z*). This was confirmed by ^{19}F NMR and vapour-phase chromatography (VPC). Treatment of a mixture of the spirooxiranes (1.90 g, 10.43 mmol) in dry benzene (15 ml) with $BF_3 \cdot Et_2O$ (0.94 g, 6.60 mmol) gave a mixture of the carboxaldehydes (**4** and **5**, X = CHO) after a standard work-up. The crude aldehydes were then treated with a solution of Jones reagent[26] [H_2O (5 ml), H_2SO_4 (1.26 ml) and CrO_3 (1.53 g, 15.32 mmol)] to furnish, after sublimation (65–80 °C/0.20 mmHg), a mixture of the acids (**4** and **5**, X = COOH) as a white solid (1.30 g, 68%). Exact mass spectrum, calculated for $C_{11}H_{14}FCO_2H$ 198.1056, found 198.1095; ^{13}C NMR (Tables 14 and 15) indicated that the composition of the mixture was *E*:*Z* = 52:48.

(*E*)- and (*Z*)-2-Cyano-5-fluoroadamantane (4 and 5, respectively, X = CN). Following the procedure of van Leusen *et al.*[27] for the preparation of 2-cyanoadamantane, potassium *tert*-butoxide (1.67 g, 14.88 mmol) was added portionwise to a solution of the fluoro ketone (**9**, X = O; 1.0 g, 5.95 mmol) and (*p*-tolylsulfonyl)methyl isocyanide[28] (TosMIC; 1.74 g, 8.92 mmol, 1.5 mol equiv.) in 1,2-dimethoxyethane (21 ml) and absolute ethanol (600 μl) maintained at 5 °C. A standard work-up followed by sublimation (60 °C/0.5 mmHg) afforded the fluoro–cyanide mixture as a white solid (0.63 g, 59%). ^{13}C NMR (Tables 14 and 15) indicated that the composition of the mixture was *E*:*Z* = 50:50. Separation of

Table 13. Synthetic methods and exact mass data for mixtures of (E)- and (Z)-4-substituted(X)adamant-1-yl fluorides (**4** and **5**, respectively)

X	Precursor	Synthetic method	Molecular formula	*m*/*z* (M^+) Calc.	*m*/*z* (M^+) Obs.
$COOCH_3$	COOH	CH_2N_2–$(C_2H_5)_2O$	$C_{12}H_{17}FO_2$	212.1213	212.1243
$CONH_2$	COOH	$SOCl_2/NH_3$	$C_{11}H_{16}FNO$	197.1216	197.1210
CH_2OH	COOH	$BH_3 \cdot S(CH_3)_2$	$C_{11}H_{17}FO$	184.1263	184.1266
NH_2	$CONH_2$	$OIC_6H_5/CH_3CN/HCOOH/H_2O$[a]	$C_{10}H_{16}FN$	169.1267	169.1250
NO_2	NH_2	 –acetone[b]	$C_{10}H_{14}FNO_2$	199.1008	199.1024
OCH_3	OH	1. NaH–THF 2. CH_3I, Δ	$C_{11}H_{17}FO$	184.1263	184.1263
$OCOCH_3$	OH	1. NaH–THF 2. CH_3COCl, Δ	$C_{12}H_{17}FO_2$	212.1213	152.1027 ($M^{+\cdot} - CH_3COOH$)
Cl	COOH	1. NHTP[c]–CH_2Cl_2–DCC[d] 2. PTOC ester[e]–CCl_4–*hν*[f]	$C_{10}H_{14}ClF$	188.0768	188.0775
Br	COOH	1. NHTP[c]–CH_2Cl_2–DCC[d] 2. PTOC ester[e]–$CF_3CHClBr$–*hν*[f]	$C_{10}H_{14}BrF$	232.0263 234.0244	232.0260 234.0239
I	COOH	1. NHTP[c]–CH_2Cl_2–DCC[d] 2. PTOC ester[e]–CF_3CH_2I–*hν*[f]	$C_{10}H_{14}IF$	280.0126	280.0124
CH_3	**9**, X = CH_2	H_2/10% Pd–C–C_2H_5OH	$C_{11}H_{17}F$	168.1314	168.1318
$Si(CH_3)_3$	Br	$(CH_3)_3SiNa$–HMPA[f]	$C_{13}H_{23}FSi$	226.1553	226.1594
$Sn(CH_3)_3$	Br	$(CH_3)_3SnLi$–THF[f]	$C_{13}H_{23}FSn$	318.0806	303.0573 ($M^{+\cdot} - CH_3$)
D	Br	$(n\text{-}Bu)_3SnD$–AIBN	$C_{10}H_{14}FD$	155.1221	155.1224

[a] Ref. 31.
[b] Ref. 34.
[c] NHTP = *N*-hydroxy-2-thiopyridone.
[d] DCC = *N*,*N*-dicyclohexylcarbodiimide.
[e] Barton PTOC ester = *O*-acyl-*N*-hydroxy-2-thiopyridone. See Ref. 35.
[f] See Ref. 29 for method.

Table 14. ^{13}C NMR chemical shifts (ppm)[a,b] of (E)-4-substituted(X)adamant-1-yl fluorides (4)

X	C-3,5	C-4	C-2,9	C-1	C-8	C-7	C-6,10	Other carbons	
H	31.52	35.90	42.80	92.47	42.80	31.52	35.90		
	(9.77)	(1.95)	(17.09)	(183.59)	(17.09)	(9.77)	(1.95)		
NO_2	34.60	86.21	41.19	90.53	42.22	29.71	30.66		
	(9.96)	(n/o)	(19.62)	(185.61)	(17.81)	(9.90)	(1.81)		
CN	33.61	35.65	41.57	90.07	41.98	30.15	31.52	121.07 (CN)	
	(10.26)	(1.96)	(19.54)	(185.55)	(17.58)	(9.77)	(1.96)	(3.42)	
CO_2H	32.37	48.16	42.69	91.58	42.35	30.49	31.97	180.25 (CO_2H)	
	(10.30)	(n/o)	(18.10)	(184.00)	(n/o)	(9.80)	(n/o)		
$CONH_2$	33.47	48.39	42.93	91.84	42.51	30.57	31.68	176.07 ($CONH_2$)	
	(9.90)	(n/o)	(18.00)	(184.00)	(17.60)	(9.60)	(1.80)		
CO_2CH_3	32.56	48.18	42.75	91.62	42.38	30.56	31.97	173.48 (CO)	51.56 (CH_3)
	(10.30)	(1.70)	(18.20)	(184.20)	(n/o)	(9.80)	(1.90)	(2.90)	
OH	36.70	72.76	40.77	91.55	42.73	30.58	29.38		
	(10.25)	(1.46)	(18.58)	(184.08)	(17.09)	(9.77)	(2.44)		
OCH_3	33.64	81.47	40.80	91.92	42.74	30.61	29.85	55.63 (OCH_3)	
	(10.40)	(n/o)	(18.40)	(184.40)	(17.09)	(10.00)	(2.30)		
$OCOCH_3$	34.00	74.86	40.63	91.00	42.52	30.25	30.10	170.24 (CO)	21.22 (CH_3)
	(9.85)	(n/o)	(18.90)	(185.10)	(17.10)	(9.40)	(n/o)		
Cl	38.02	64.88	42.32	90.57	42.87	30.50	29.42		
	(9.80)	(n/o)	(18.80)	(185.10)	(17.00)	(9.80)	(n/o)		
Br	38.59	59.23	42.87	90.48	42.99	30.60	30.15		
	(9.94)	(n/o)	(18.73)	(185.29)	(17.11)	(9.65)	(1.95)		
I	39.95	40.35	43.24	90.57	43.11	30.79	31.54		
	(9.82)	(n/o)	(17.86)	(185.28)	(18.47)	(9.64)	(1.88)		
NH_2	37.33	54.16	42.10	91.77	43.07	30.84	29.17		
	(10.34)	(1.40)	(18.07)	(183.97)	(17.04)	(9.65)	(2.14)		
CH_3	36.32	37.60	43.88	92.32	43.46	31.40	29.59	18.58 (CH_3)	
	(10.13)	(n/o)	(16.98)	(183.46)	(17.15)	(9.57)	(2.16)		
CH_2OH	31.95	45.58	43.53	92.32	43.17	31.07	30.25	64.06 (CH_2OH)	
	(10.30)	(1.70)	(17.30)	(183.70)	(16.90)	(9.70)	(2.00)		
$Si(CH_3)_3$	32.67	35.83	45.86	92.68	42.64	31.35	33.29	−0.65 (CH_3)	
	(9.71)	(n/o)	(16.01)	(183.42)	(17.09)	(9.48)	(n/o)		
$Sn(CH_3)_3$	35.16	37.37	45.67	92.47	43.19	31.55	34.70	−9.46 (CH_3)	
	(8.99)	(1.81)	(15.76)	(183.60)	(17.21)	(9.36)	(2.04)		
			[59.53]					[319.07, 281.41]	

[a] See footnotes a–c in Table 11.
[b] ^{13}C–^{117,119}Sn coupling constants (Hz) in brackets.

the isomeric mixture was effected by HPLC (prepacked silica gel column) with 90% hexane–10% ethyl acetate as the eluent.

(*E*)-2-Cyano-5-fluoroadamantane (4, X = CN). M.p. 203–204 °C; ^{13}C NMR (Table 14); exact mass spectrum, calculated for $C_{11}H_{14}FN$ 179.1110, found 179.1109.

(*Z*)-2-Cyano-5-fluoroadamantane (*5*, X = CN). M.p. 190–192 °C; ^{13}C NMR (Table 15); exact mass spectrum, calculated for $C_{11}H_{14}FN$ 179.1110, found 179.1109.

(*E*)- and (*Z*)-2-Bromo-5-fluoroadamantane (4 and 5, respectively, X = Br). Following procedures recently described for the preparation of 1-bromo-3-chloroadamantane from 3-chloroadamantane-1-carboxylic acid,[29] a mixture of the fluoro acid (**4** and **5**, X = COOH; 250 mg, 1.26 mmol) was converted into the title compounds. Column chromatography (basic alumina; hexane as eluent) provided the mixture as a white solid (210 mg, 71%). ^{13}C NMR (Tables 14 and 15) indicated that the composition of the mixture was $E:Z = 25:75$. Separation of the isomeric mixture was effected by HPLC (prepacked silica gel column) with hexane as the eluent.

(*E*)-2-Bromo-5-fluoroadamantane (4, X = Br). M.p. 151–153 °C; ^{13}C NMR (Table 14); exact mass spectrum, calculated for $C_{10}H_{14}BrF$, 232.0263/234.0244; found, 232.0260/234.0239.

(*Z*)-2-Bromo-5-fluoroadamantane (5, X = Br). M.p. 158–159.5 °C; ^{13}C NMR (Table 15); exact mass spectrum, calculated for $C_{10}H_{14}BrF$, 232.0263/234.0244, found 232.0260/234.0239.

(*E*)- and (*Z*)-5-substituted(X)-2-cyanoadamantanes (6 and 7, respectively). The cyanide mixtures (X = Cl, Br, I and C_6H_5) were obtained from the corresponding 5-substituted(X) adamant-2-ones as described above for the fluorocyanides (**4** and **5**, X = CN). Separations of the isomeric mixtures (all 50:50 by ^{13}C NMR and VPC) were effected by HPLC (prepacked silica gel column) with 90% hexane–10% ethyl acetate as the eluent. The isomeric compounds were unambiguously identified by ^{13}C NMR. Spectral assignments followed from the chemical shift additivity method and from APT spectra.

(*E*)-1-Chloro-4-cyanoadamantane (6, X = Cl). M.p. 164–165 °C; ^{13}C NMR (Table 16); exact mass spectrum calculated for $C_{11}H_{14}ClN$, 197.0785/195.0815; found, 160.1133 ($M^{+\cdot}$ − Cl); calculated for ($M^{+\cdot}$ − Cl), 160.1126.

(*Z*)-1-Chloro-4-cyanoadamantane (7, X = Cl). M.p. 169–171 °C, ^{13}C NMR (Table 16); exact mass spectrum, calculated for $C_{11}H_{14}ClN$, 197.0785/195.0815; found, 160.1133 ($M^{+\cdot}$ − Cl); calculated for ($M^{+\cdot}$ − Cl), 160.1126.

(*E*)-1-Bromo-4-cyanoadamantane (6, X = Br). M.p. 154–156 °C; ^{13}C NMR (Table 16); exact mass spectrum, calculated for $C_{11}H_{14}BrN$, 241.0290/239.0310; found, 160.1133 ($M^{+\cdot}$ − Br); calculated for ($M^{+\cdot}$ − Br), 160.1126.

Table 15. ^{13}C NMR chemical shifts (ppm)[a,b] of (Z)-4-substituted(X)adamant-1-yl fluorides (5)

X	C-3,5	C-4	C-2,9	C-1	C-8	C-7	C-6,10	Other carbons	
H	31.52	35.90	42.80	92.47	42.80	31.52	35.90		
	(9.77)	(1.95)	(17.09)	(183.59)	(17.09)	(9.77)	(1.95)		
NO_2	33.66	86.61	37.59	90.29	42.22	29.95	35.31		
	(10.37)	(n/o)	(19.62)	(185.58)	(17.81)	(9.96)	(1.64)		
CN	33.91	35.42	38.47	90.30	41.96	29.93	34.90	120.95 (CN)	
	(10.25)	(1.96)	(19.53)	(185.55)	(17.58)	(9.77)	(1.96)		
CO_2H	32.81	47.87	39.03	91.58	42.30	30.65	36.21	180.19 (CO_2H)	
	(9.60)	(n/o)	(18.40)	(184.00)	(n/o)	(9.90)	(n/o)		
$CONH_2$	33.09	48.11	38.80	91.84	42.46	30.68	36.50	176.07 ($CONH_2$)	
	(10.40)	(n/o)	(18.40)	(184.00)	(16.70)	(9.60)	(1.80)		
CO_2CH_3	33.00	47.95	39.07	91.62	42.61	30.75	36.26	173.82 (CO)	51.56 (CH_3)
	(9.80)	(1.70)	(18.20)	(184.20)	(n/o)	(9.80)	(2.00)		
OH	37.93	72.07	36.32	91.70	42.57	30.09	34.61		
	(9.76)	(2.44)	(18.56)	(183.59)	(17.58)	(10.25)	(1.95)		
OCH_3	34.66	80.66	36.78	91.43	42.74	30.61	34.59	55.11 (OCH_3)	
	(9.77)	(n/o)	(18.06)	(183.59)	(17.09)	(10.00)	(1.96)		
$OCOCH_3$	35.32	74.26	37.04	91.23	42.39	30.25	34.53	170.19 (CO)	20.81 (CH_3)
	(9.40)	(n/o)	(18.60)	(184.10)	(17.70)	(9.40)	(n/o)		
Cl	39.42	64.67	36.34	91.22	42.72	29.93	36.37		
	(10.00)	(n/o)	(18.90)	(184.40)	(17.70)	(9.80)	(1.40)		
Br	40.08	59.23	37.01	91.29	42.91	30.00	37.00		
	(10.19)	(n/o)	(19.17)	(184.37)	(17.96)	(9.94)	(1.75)		
I	41.46	40.68	38.34	91.46	43.11	30.22	37.25		
	(10.29)	(n/o)	(19.10)	(184.57)	(18.47)	(9.87)	(1.75)		
NH_2	38.50	53.66	36.20	92.03	43.00	30.39	35.84		
	(9.48)	(1.95)	(17.91)	(183.91)	(17.38)	(9.87)	(2.00)		
CH_3	37.13	37.63	36.71	92.78	43.46	31.04	37.41	18.58 (CH_3)	
	(9.33)	(n/o)	(17.34)	(183.27)	(17.15)	(9.82)	(1.97)		
CH_2OH	32.59	45.34	37.40	92.49	43.23	31.54	37.03	63.83 (CH_2OH)	
	(9.30)	(1.70)	(17.60)	(183.70)	(17.20)	(9.80)	(1.90)		
$Si(CH_3)_3$	32.93	35.83	40.49	92.79	42.64	31.90	39.18	−0.95 (CH_3)	
	(9.65)	(n/o)	(17.18)	(183.28)	(17.09)	(9.64)	(n/o)		
$Sn(CH_3)_3$	35.70	37.54	41.78	92.74	43.19	31.85	39.00	−9.71 (CH_3)	
	(9.66)	(1.88)	(16.90)	(183.30)	(17.21)	(9.66)	(1.90)		
	[22.34]						[55.61]	[319.07, 281.41]	

[a] See footnotes a–c in Table 11.
[b] ^{13}C–$^{117,119}Sn$ coupling constants (Hz) in brackets.

(*Z*)-1-Bromo-4-cyanoadamantane (7, X = Br). M.p. 146–148 °C; ^{13}C NMR (Table 16); exact mass spectrum calculated for $C_{11}H_{14}BrN$, 241.0290/239.0310; found, 160.1133 ($M^{+\cdot}$ − Br), calculated for ($M^{+\cdot}$ − Br), 160.1126.

(*E*)-2-Cyano-5-iodoadamantane (6, X = I). M.p. 134–135 °C; ^{13}C NMR (Table 16); exact mass spectrum, calculated for $C_{11}H_{14}IN$, 287.0173; found, 160.1133 ($M^{+\cdot}$ − I), calculated for ($M^{+\cdot}$ − I), 160.1126.

(*Z*)-2-Cyano-5-iodoadamantane (7, X = I). M.p. 103–105 °C; ^{13}C NMR (Table 16); exact mass spectrum, calculated for $C_{11}H_{14}IN$, 287.0173; found, 160.1133 ($M^{+\cdot}$ − I); calculated for ($M^{+\cdot}$ − I), 160.1126.

Table 16. ^{13}C NMR chemical shifts (ppm)[a] of 2-cyano-5-substituted(X)adamantanes

Isomer	X	C-1,3	C-2	C-4,9	C-5	C-6	C-7	C-8,10	CN	Other carbons			
E- (6)	H	30.37	36.98	36.59	26.73	36.70	26.88	33.05	122.20				
	Cl	33.51	35.50	46.27	64.87	46.77	30.19	31.23	121.01				
	Br	34.16	35.48	47.70	60.90	48.24	30.97	31.21	121.08				
	I	34.44	35.52	50.63	42.87	51.24	31.34	31.26	121.31				
	C_6H_5	31.23	36.60	42.17	35.28	42.55	27.75	32.38	122.10	149.25 (i)	124.65 (o)	128.40 (m)	126.16 (p)
Z- (7)	H	30.37	36.98	33.05	26.88	36.70	26.73	36.59	122.20				
	Cl	33.73	35.22	43.00	65.06	46.75	29.96	34.61	120.95				
	Br	34.57	35.20	44.35	61.05	48.22	30.69	34.31	120.95				
	I	34.66	35.29	47.23	42.96	51.26	31.06	34.51	121.05				
	C_6H_5	31.31	36.36	38.77	35.51	42.29	27.58	35.88	121.97	149.34 (i)	124.76 (o)	128.37 (m)	126.12 (p)

[a] See footnotes a–c in Table 11.

(*E*)-2-Cyano-5-phenyladamantane (6, X = C_6H_5). M.p. 110–111 °C; ^{13}C NMR (Table 16); exact mass spectrum, calculated for $C_{17}H_{19}N$, 237.1517; found, 237.1517.

(*Z*)-2-Cyano-5-phenyladamantane (7, X = C_6H_5). M.p. 142–144 °C; ^{13}C NMR (Table 16); exact mass spectrum, calculated for $C_{17}H_{19}N$, 237.1517; found, 237.1517.

Spectra

Mass spectra were recorded on a Kratos MS25RF spectrometer. NMR spectra were recorded on JEOL FX-90Q and Gemini-300 spectrometers. The probe temperature of both instruments was 295 ± 2 K. The proton-decoupled ^{13}C NMR spectra were obtained on $CDCl_3$ solutions (*ca.* 0.5 M) with Me_4Si as an internal reference or with the central peak of the $CDCl_3$ triplet set at 77.0 ppm. For those spectra recorded at 22.53 MHz the data were collected into 16K/8K data points with spectral widths of 4000 and 2000 Hz (digital resolution 0.50 and 0.25 Hz, respectively). Spectral widths of 18 761.7 and 9718.2 Hz were employed for recordings at 75.462 MHz (64K/32K data points, digital resolution 0.60 and 0.30 Hz, respectively).

The ^{19}F NMR spectra were obtained under proton-decoupled conditions on very dilute solutions. Each sample consisted of the compound or mixture (*ca.* 1–2 mg) and the parent compound (X = H, *ca.* 1–2 mg) dissolved in 0.6–0.7 ml of the appropriate solvent. Most of the spectra were run at 84.26 MHz (16K/8K data points, spectral width 2000 Hz). Several were run at 282.328 MHz (64K/32K data points, spectral width 19 569 Hz). Isomer identification in the ^{19}F NMR spectra of the fluoride mixtures (**2**–**3** or **4**–**5**) was based on relative intensities, which were in accord with those determined by ^{13}C NMR. The methodology was previously validated for several mixtures by obtaining pure samples of the epimers.[9f]

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