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Synthesis and ^{19}F and ^{13}C NMR Studies of a Series of 4-Substituted Fluorocubanes: Resonance Dependence of ^{19}F Chemical Shifts in a Saturated System

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The substituent chemical shifts and the carbon−fluorine coupling constants of a range of 4-substituted cubyl fluorides in solvents of varying polarity are presented. Least squares regressional analysis of the data indicates that the fluorine probe, while being somewhat less sensitive to field effects as a result of the low polarizability of the cubane C−F bond, nevertheless responds in the "reverse" manner in agreement with precedents established in other alicyclic systems. The dependence of ^1J(CF) upon electronegativity has been interpreted as evidence for the occurrence of σ-induction over four bonds, the longest reported to date. Significantly, resonance parameters are found to be very important in describing the effect of substituents on both the fluorine chemical shifts and the magnitude of the one-bond and four-bond ^{13}C−^{19}F coupling constants. This represents one of the rare occasions that resonance effects have been observed in a fully saturated system in the ground state. A possible mechanism by which these resonance effects may be transmitted is presented.

Introduction

Considerable interest has recently been directed to developing an understanding of the transmission modes of substituent electronic and electrostatic effects in fully saturated systems. The use of ^{19}F NMR spectroscopy for studying the ground state has proven to be very rewarding,[1−4] although the results obtained employing the ^{19}F probe are frequently found to be different than those arising from reactivity studies.[5]

The effect of substituents upon fluorine shifts in bicyclic substrates such as bicyclo[2.2.2]octane (**1**)[1] and bicyclo[2.2.1]heptane (**2**)[2] has succumbed to rational analysis and has contributed greatly to an understanding in this area. Contrary to expectations, the field effect is seen[6] to perturb the ^{19}F probe in a "reverse" manner in these systems; i.e., upfield chemical shifts (shielding) are observed for electron-withdrawing substituents and downfield shifts for electron-donating substituents. Furthermore, studies employing system **1** have illustrated that substituent electronegativity effects can be transmitted over long distances via double hyperconjugation[1,7] (also referred to as σ-resonance, 2-fold hyperconjugation, and σ−σ hyperconjugation).

Although an analogous ^{19}F NMR investigation on fluorocubane has not been reported, three relevant studies into the effects of substituents in cubane employing reactivity probes have been described. Some years ago, Stock and his colleagues[8] examined the acidity of several 4-substituted cubanecarboxylic acids and concluded that substituent effects were transmitted solely by the direct field mode. More recently, Eaton[9] and Moriarity[10] have independently demonstrated that the cubyl cation can be generated from the triflate under solvolytic conditions much more readily than anticipated; the greatly enhanced thermodynamic stability of the cation was explained[9] on the basis of hyperconjugation. The rates of solvolysis of a range of 4-substituted cubyl triflates have also been examined.[9,10] In their most recent work on the effect of 4-trimethylmetalloidal substituents on the solvolytic behavior of cubyl triflate, Eaton and his associates[11] have convincingly demonstrated that the stability of the cubyl cation is increased by charge delocalization from the formal cationic to C4. However, the observed rate behavior was explained readily by invoking the field effect of the substituent only.

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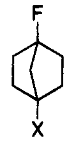

2

3

We now present a substituent effect study of the cubane system in which a ground state probe (the ^{19}F nucleus) is employed. Cubane offers an excellent carbon framework in which to investigate the consequences of bond geometry and strain on the mode of transmission of substituent effects. Thus, in fluorocubane **3** containing substituents at C4, for example, the substituent and probe are aligned linearly. Furthermore, the presence of any steric effect is essentially precluded, and, in

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⊗ Abstract published in *Advance ACS Abstracts,* July 15, 1995.

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[2] Adcock, W.; Abeywickrema, A. N.; Kok, G. B. *J. Org. Chem.* **1984**, *49*, 1387.

[3] Adcock, W.; Krstic, A. K. *Tetrahedron Lett.* **1992**, *33*, 7397.

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[9] Eaton, P. E.; Yang, C.-X.; Xiong, Y. *J. Am. Chem. Soc.* **1990**, *112*, 3225.

[10] Moriarty, R. M.; Tuladhar, S. M.; Penmasta, R.; Awasthi, A. K. *J. Am. Chem. Soc.* **1990**, *112*, 3228. Kevill, D. N.; D'Souza, M. J.; Moriarty, R. M.; Tuladhar, S. M.; Penmasta, R.; Awasthi, A. K. *J. Chem. Soc., Chem. Commun.* **1990**, 623.

[11] Eaton, P. E.; Zhou, J. P. *J. Am. Chem. Soc.* **1992**, *114*, 3118.

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addition, the rigidity of the system renders unlikely any substituent-induced structural changes. Cubane also possesses important similarities, as well as differences, to its well-studied bicyclo[2.2.2]octane relative. The similar internuclear distances and the colinear alignment of the probe and substituent in both systems means that the electrostatic influence of the field effect at the probe site should be of the same magnitude. However, because of the high s character of the carbon exocyclic bonding orbital in the carbon−fluorine bond in **3**[12] and the consequent decrease in its polarizability,[3] it is probable that cubyl fluorides would be less sensitive to the field effect than the bicyclo[2.2.2]octyl fluorides **1**.

The skew−bond relationship of the bridging bonds in cubane strongly suggests that double hyperconjugation should also be greatly diminished in this molecule, although the presence of multiple pathways (there are six equivalent routes between the substituent and probe in 1,4-disubstituted cubanes) means that double hyperconjugation cannot be ruled out *a priori*. Although most authors in the field agree that the σ-inductive mechanism is essentially ineffective beyond two carbon atoms,[13] the multiple pathways available in cubane and the greater polarizability of its C−C bonds as a result of their high degree of p character suggest that the possibility of detecting such long range σ-induction is more likely in **3** than in other aliphatic systems.

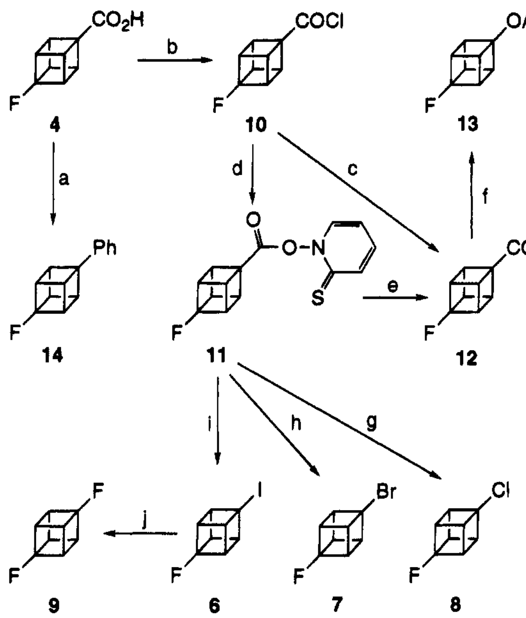
Results and Discussion

Syntheses. For the purposes of the ^{19}F NMR investigation, it was desirable that as wide a variety of 4-substituted fluorocubanes **3** as possible was available. The substituents were selected on the grounds that they cover a broad range of σ_F values (0.0−0.65) and that they included both σ- and π-donors and -withdrawers.

The substrates required for this study were all generated from 4-fluorocubanecarboxylic acid (**4**) by standard manipulation of the carboxyl group. We recently reported[12] on a procedure for the preparation of the fluoro ester **5**, the precursor to **4**; in the interim, we have found that a greatly increased yield (80%) of ester may be achieved by performing the reaction in a sealed vessel at a higher temperature (70−80 °C). This modification possesses the added advantage that it requires only 1 equiv of XeF_2 for complete consumption of the precursor iodo ester, compared with the 1.5 equiv found necessary[12] in the procedure using an open vessel.

As shown in Scheme 1, application of Barton ester methodology[14] to the derived carboxylic acid **4** delivered the halides **6−8** in good yield. 4-Iodocubyl fluoride (**6**) was also expeditiously prepared by treatment of the fluoro acid **4** with lead tetraacetate and iodine.[12] Fluorodeiodination of **6** with XeF_2 required more forcing conditions and gave 1,4-difluorocubane (**9**) in modest yield (60%). In this instance, $CFCl_3$ was employed as the solvent in order to facilitate isolation of the volatile difluoride. The sluggishness of 4-iodocubyl fluoride (**6**) toward fluorodeiodination relative to iodocubane can be ascribed to destabilization of the cationic intermediate in the former by the prescence of the electron-withdrawing fluorine substituent at C4.[11]

Scheme 1[a]



[a] (a) $Pb(OAc)_4$, C_6H_6, $h\nu$; (b) $SOCl_2$; (c) $LiCuMe_2$; (d) C_5H_4NSONa, DMAP; (e) MeCOCOMe, $h\nu$; (f) *m*-$ClC_6H_4CO_3H$; (g) CF_3CCl_3, $h\nu$; (h) $CF_3CHClBr$, $h\nu$; (i) CF_3CH_2I, $h\nu$; (i) XeF_2, sealed vessel, 80 °C.

4-Acetylcubyl fluoride (**12**) could be prepared by two methods (Scheme 1). In the first of these, **12** was obtained by treatment of the acid chloride **10** with lithium dimethylcuprate.[15] The alternative procedure is based on the known reaction of radicals with biacetyl to afford methyl ketones; such methodology plays a key role in the synthesis of bicyclo[1.1.1]pentane 1,3-diester,[16] and in the present work, irradiation of the Barton ester **11** in the presence of biacetyl was found to be an efficient route to **12**. For the conversion of 4-acetylcubyl fluoride (**12**) into 4-acetoxycubyl fluoride (**13**), exposing the crude product to Baeyer−Villiger oxidation was found to be expedient; this converted excess biacetyl to acetic anhydride which could be removed readily during the aqueous workup.

The lead tetraacetate-mediated arylation technique described by Moriarty[17] was successfully employed for the preparation of 4-phenylcubyl fluoride (**14**). In order to maximize yields in this reaction, it is important that the benzene solution be thoroughly deoxygenated prior to addition of the $Pb(OAc)_4$, otherwise the required product is contaminated by substantial amounts of the corresponding acetate. Isolation of the acetate is significant because its formation most likely involves oxidation of the intermediate cubyl radical to the corresponding cubyl cation which is then trapped by acetic acid; this observation supports the conclusion reached independently by Eaton[9] and Moriarty[10] that production of the cubyl cation is not as difficult as originally anticipated.

Reduction of the fluoro acid **4** with $LiAlH_4$ afforded the carbinol **15** which upon treatment with acetyl chloride in the presence of pyridine gave the acetoxymethyl derivative **16** without rearrangement. Scheme 2 also depicts the preparation of other nitrogen-containing functional groups from the amide **17**. Thus, dehydration

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(12) Della, E. W.; Head, N. J. *J. Org. Chem.* **1992**, *57*, 2850.

(13) Reynolds, R. F. *Prog. Phys. Org. Chem.* **1983**, *14*, 165 and references cited therein.

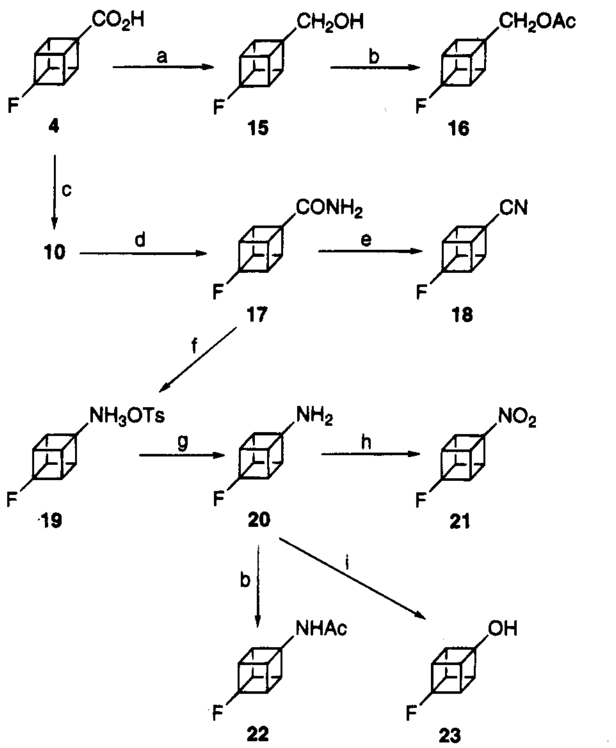
(14) (a) Della, E. W.; Tsanaktsidis, J. *Aust. J. Chem.* **1989**, *42*, 61. (b) Tsanaktsidis, J.; Eaton, P. E. *Tetrahedron Lett.* **1989**, *30*, 6967. (c) Della, E. W.; Taylor, D. K. *Aust. J. Chem.* **1991**, *44*, 881.

(15) Posner, G. H.; Whitten, C. E.; McFarland, P. E. *J. Am. Chem. Soc.* **1972**, *94*, 5106.

(16) Kasynski, P.; Michl, J. *J. Org. Chem.* **1988**, *53*, 4593.

(17) Moriarty, R. M.; Khosrowshahi, J. S.; Millar, R. S.; Flippen-Anderson, J.; Gilardi, R. *J. Am. Chem. Soc.* **1989**, *111*, 8943.

Scheme 2[a]

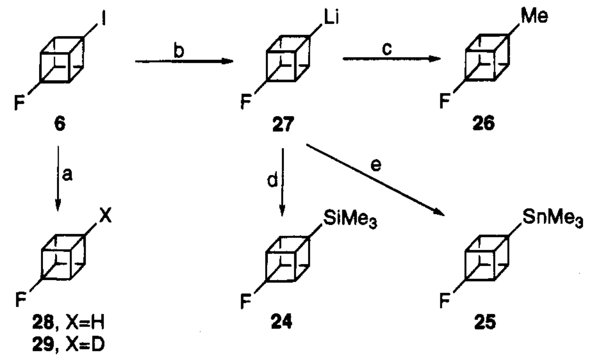


[a] (a) $LiAlH_4$; (b) AcCl, C_5H_5N; (c) $SOCl_2$; (d) NH_3 (aq); (e) $(CF_3CO)_2O$; (f) PhI(OH)OTs; (g) NaOH (aq); (h) m-$ClC_6H_4CO_3H$, $ClCH_2CH_2Cl$; (i) $NaNO_2$, H_2SO_4.

of 4-fluorocubanecarboxamide (**17**) was achieved with trifluoroacetic anhydride[18] and afforded the nitrile **18** in 73% yield. Hoffmann rearrangement of **17** was effected with (tosyloxy)hydroxyiodobenzene, as described by Moriarty and co-workers,[19] giving the ammonium tosylate salt **19** from which (4-fluorocubyl)amine (**20**) was readily obtained. Part of the latter was oxidized to the nitro compound **21** by *m*-chloroperbenzoic acid and the remainder converted into the acetamide **22**. Although Klunder and Zwanenburg[20] have reported the successful preparation of 4-bromocubanol by deamination of the corresponding amine, treatment of **20** under analogous conditions gave only a very small yield of 4-fluorocubanol (**23**). Again, the poor yield obtained in this transformation may be ascribed to the strongly destabilizing nature of the fluorine atom in reactions involving cationic intermediates as encountered above in the preparation of the difluoride **9**.

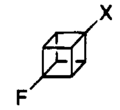
The silane **24** and the stannane **25** as well as 4-methylcubyl fluoride (**26**) were prepared as shown in Scheme 3 from 4-lithiocubyl fluoride (**27**), itself obtained by metallation of the fluoro iodide **6** with *tert*-butyllithium. Quenching the lithiated species **27** with trimethylsilyl or trimethylstannyl chloride[21] gave good yields of the metalloidal compounds **24** and **25**, respectively, and treatment with methyl triflate, as described previously[22] for the synthesis of methylcubane, gave the fluoride **26**. The stability of 4-lithiocubyl fluoride (**27**) is worthy of special mention in view of the behavior of related bridgehead dihalides toward *tert*-butyllithium. The bicyclic fluoro iodides **1**, $X = I$,[7a] and **2**, $X = I$,[23] for example, undergo rapid fragmentation when exposed to *tert*-butyllithium at low temperatures (ca. −80 °C), and both 1,4-diiodocubane and 1-bromo-4-iodocubane are converted into 1,4-dehydrocubane ("cubellane")[24] under these conditions. Even 1-chloro-4-iodocubane decomposes in a similar manner when treated at 0 °C with butyllithium.[24] Presumably, the species **27** is less inclined to undergo Grob fragmentation[25] as a result of the decreased nucleofugacity of fluorine bonded to a carbon of increased s character. The enhanced stability of **27** proved to be of considerable value because it led to much simpler syntheses of the derivatives **23**−**25** than otherwise may have been the case.

Scheme 3[a]



[a] (a) $Bu_3SnH(D)$, AIBN, $h\nu$; (b) t-BuLi, −80 °C; (c) MeOTf; (d) Me_3SiCl; (e) Me_3SnCl.

Preparation of fluorocubane (**28**), the reference compound for the ^{19}F SCS measurements, was achieved either by fluorodeiodination of iodocubane[12] or, more conveniently, by reduction of the fluoro iodide **6** with tributyltin hydride. The latter method was also employed for the synthesis of the corresponding deuteride **29**.



3

4, $X = CO_2H$
5, $X = CO_2Me$
6, $X = I$
7, $X = Br$
8, $X = Cl$
9, $X = F$
10, $X = COCl$
11, $X = CO_2NC_5H_4S$
12, $X = COMe$
13, $X = OAc$
14, $X = C_6H_5$
15, $X = CH_2OH$
16, $X = CH_2OAc$
17, $X = CONH_2$
18, $X = CN$
19, $X = NH_3OTs$
20, $X = NH_2$
21, $X = NO_2$
22, $X = NHAc$
23, $X = OH$
24, $X = SiMe_3$
25, $X = SnMe_3$
26, $X = Me$
27, $X = Li$
28, $X = H$
29, $X = D$

^{19}F Substituent Chemical Shifts. The fluorine substituent chemical shifts (SCS) for system **3** were measured under high dilution in a range of solvents and are displayed in Table 1. Some shifts for several substituents do not appear because of sample degradation in the more polar solvents; in particular, several samples were observed to degrade rapidly in trifluoroacetic acid.

A cursory examination of the data reveals that the fluorine probe is relatively insensitive to the effect of remote substituents; for example, the SCS in $CDCl_3$ span

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[19] Moriarty, R. M.; Khosrowshahi, J. S.; Awasthi, A. K.; Penmasta, R. *Synth. Commun.* **1988**, *11*, 1179.

[20] Klunder, A. J. H.; Zwanenburg, B. *Tetrahedron* **1972**, *28*, 4131.

[21] The parent compounds are also known: Della, E. W.; Patney, H. K. *Aust. J. Chem.* **1979**, *32*, 2243. Della, E. W.; Tsanaktsidis, J. *Organometallics* **1988**, *7*, 1178.

[22] Della, E. W.; Pigou, P. E. *J. Am. Chem. Soc.* **1984**, *106*, 1085.

[23] Adcock, W.; Gangodawila, H. *J. Org. Chem.* **1989**, *54*, 6040.

[24] Eaton, P. E.; Tsanaktsidis, J. *J. Am. Chem. Soc.* **1990**, *112*, 876.

[25] Grob, C. A. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 535.

Table 1. ^{19}F Substituent Chemical Shifts (SCS)[a–c] of the 4-Substituted Cubyl Fluorides 3

X	SCS			
	c-C_6H_{12}	$CDCl_3$	HFIP	TFA
NO_2	−2.50	−2.92	−4.70	−5.70
CN	−0.47	−0.80	−2.35	−3.25
COCl	−1.03	−1.27		
F	−2.20	−2.76	−4.50	−4.83
Cl	−2.62	−3.08	−4.45	−4.83
Br	−3.31	−3.82	−5.06	−5.22
I	−3.26	−3.62	−4.71	−5.22
OAc	−3.35	−3.66	−5.10	−5.75
$CONH_2$		−1.07		−4.00
CO_2H	−0.94	−1.19	−2.49	−4.37
OH	−2.51	−3.10		
COMe	−0.36	−0.64	−1.96	
CO_2Me	−0.95	−1.22	−2.39	−3.20
NH_2	−0.04	−0.38	−2.17	−3.85
Ph	−0.12	−0.02	−0.68	−0.80
CH_2OH	0.47	0.64	−0.40	
CH_2OAc	0.37	0.17	−0.54	−1.08
Me	0.54	0.50	−0.47	
$SiMe_3$	0.69	0.81	0.95	1.00
$SnMe_3$	−0.81	−0.77	−0.20	0.00
D[d]	0.052	0.054	0.020	

[a] Defined as the difference (in parts per million) between the ^{19}F chemical shift of the substituted compound and that of the parent (X = H). A positive sign implies deshielding (downfield shift). [b] Accurate to ±0.01 ppm. [c] X = H (relative to internal CF_3CCl_3) ($CDCl_3$) −57.69. [d] Accurate to ±0.001 ppm.

a somewhat narrower range (4.3 ppm) than that observed in both **1** (13.7 ppm)[1] and **2** (13.5 ppm)[2] in the same solvent. Furthermore, in the fluorobicyclo[2.2.2]octanes **1**, substituents with positive σ_F values lead, without exception, to upfield shifts of the ^{19}F signal. While this trend is generally true for the 4-substituted cubyl fluorides, it is noteworthy that (in C_6H_{12} and $CDCl_3$) substituents characterized by weak field effects are associated with positive (downfield) ^{19}F chemical shifts. A plausible explanation for this observation is that an additional interaction which opposes the field effect is occurring; otherwise, by analogy with the observed data in **1**,[1] all chemical shifts for substituents with positive σ_F values should be upfield. Finally, in accordance with observations in other studies, the shifts are seen to move progressively upfield in the more strongly hydrogen-bonding solvents.[1,2,4]

In order to provide a detailed assessment of the effect of the substituents, the data in Table 1 were subjected to a least squares linear regression analysis[26] along the lines described by Adcock[1,2] and Reynolds[13] using the general equation shown below.

$$^{19}\text{F SCS} = \varrho_F\sigma_F + \varrho_\chi\Delta\chi + \varrho_R\sigma_R + c$$

The substituent parameters employed by Adcock[1,2] have been used in this work in order to facilitate comparison between the results on related bicyclic and caged saturated systems. These include (i) the field effect (σ_F), as defined from data obtained from the p-fluorophenyl-4-substituted bicyclo[2.2.2]octanes.[1,2,27] Since these σ_F values have been measured in the ground state by ^{19}F NMR for fluorine attached to an sp^3 carbon in a wide variety of solvents, they are undoubtedly the most appropriate parameters defining the field effect of substituents for studies of saturated fluorides. Also included are (ii) electronegativity effects ($\Delta\chi$). The parameters determined by noncorrelative means from system **1**[2] were used in preference to those described by Inamato[28,29] so as to eliminate uncertainties concerning the ι values of several substituents.[1] Finally included are (iii) resonance effects (σ_R). The parameters defined from fluorobenzene derivatives,[30] which were selected by Adcock[1,31] to characterize the substituent effect on possible π-resonance interactions[32] that may have been operative in system **1**, were also employed for the analysis of the fluorocubanes **3**. Interestingly, a dependence of ^{19}F SCS on resonance effects was not observed[1] in the fluorobicyclo[2.2.2]octanes **1**, nor indeed have they been observed in any ground state aliphatic system to date. It has been pointed out[1] that, as the σ_R values have been derived from aromatic compounds, their applicability to a saturated system is valid if the relative magnitude of resonance effects is independent of the nature of the substrate. As more than one set of resonance parameters is required to define resonance effects in aromatic systems themselves, the application of any one particular set of resonance parameters to saturated compounds must be treated with caution at this stage.[33] With the above reservation, it should also be noted that, because resonance parameters, regardless of their type, reflect the ability of a substituent to accept (positive σ_R) or donate (negative σ_R) electron density via π-interaction, the nonlinearity between σ_R and either σ_F or $\Delta\chi$ is assured. Thus, if resonance interactions do exist for a particular aliphatic system, it is likely that the dependence could be determined by the use of any set of resonance constants; only the precision of the fit is likely to be affected.

The results of the correlations for all substituents were performed for the solvents C_6H_{12}, $CDCl_3$, and TFA and are presented in Table 2. It is noteworthy that a better fit was obtained when correlations for the two least polar solvents (C_6H_{12} and $CDCl_3$) were performed with exclusion of NH_2 and CN. Omission of these substituents may be justified if, as suggested, their σ_R values as defined from aromatic systems are inappropriate for describing their interaction with aliphatic systems.[33,34]

The amine **20** was found to be a deviant point in hexafluoroisopropanol (HFIP) as well, and its exclusion led to a dramatic improvement of fit. It is probable that the amine is protonated in HFIP; it was found, for

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(26) Regressional analyses performed with the MINITAB program. MINITAB release 7.2, IBM Risc System 6000 Version.

(27) Adcock, W.; Khor, T.-C. *J. Am. Chem. Soc.* **1978**, *100*, 7799.

(28) Inamato, N.; Masuda, S. *Tetrahedron Lett.* **1977**, 3287.

(29) All regressions (^{19}F SCS, Δ^nJ(CF) vs σ_F, $\Delta\chi$, and σ_R) have also been performed with Inamato's parameters $\Delta\iota$ (ref 28) ($\Delta\iota = \Delta\iota_X - \Delta\iota_H$). In general, correlations with $\Delta\chi$ were of marginally better precision than those obtained with $\Delta\iota$. Exclusion of the data for **18** from the correlations employing $\Delta\iota$ did lead to some improvement in fit as has been previously observed (ref 1). Exclusion of the data for **8** had no appreciable effect.

(30) Hanoch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

(31) The regressions of Adcock actually employed $\sigma_R{}^\circ$ values. These values are essentially the same as σ_R; see ref 35 and references therein.

(32) Hoffmann, R.; Imamura, A.; Hehre, W. J. *J. Am. Chem. Soc.* **1968**, *90*, 1499. Hoffmann, R.; Stohrer, W.-D. *J. Am. Chem. Soc.* **1972**, *94*, 779. Gleiter, R. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 696. Paddon-Row, M. N. *Acc. Chem. Res.* **1982**, *15*, 245.

(33) All regressions (^{19}F SCS, Δ^nJ(CF) vs σ_F, $\Delta\chi$, and σ_R) have also been performed with $\sigma_R{}^+$ values (ref 30). The precision of the fit did not vary significantly on application of these parameters. However, exclusion of certain strong π-donors from the correlations employing $\sigma_R{}^+$ as the resonance parameter led to greater improvements than were observed with σ_R on elimination of the same substituents. This observation is consistent with the notion that the resonance parameters for these substituents in particular require redefinition for use in aliphatic systems.

(34) Although generally regarded as a π-withdrawer, the CN group is also capable of stabilizing positive charge: Gassman, P. G.; Guggenheim, T. L. *J. Org. Chem.* **1982**, *47*, 3023 and refs 2 and 3 cited therein.

Table 2. Results of Correlative Analysis[a,b] of ^{19}F SCS of 4-Substituted Fluorocubanes 3 with σ_F, $\Delta\chi$, and σ_R

solvent	independent variables	ϱ_F[c]	ϱ_χ[c]	ϱ_R[c]	c[d]	r[e]	r^2	p_F[f]	p_χ[f]	p_R[f]	n[g]
c-C_6H_{12}	σ_F, $\Delta\chi$, σ_R	−5.74 (±1.70)	0.64 (±0.96)	3.66 (±1.60)	0.25 (±0.46)	0.75	0.56	0.005	0.517	0.038	18
	σ_F, $\Delta\chi$	−3.40 (±1.56)	−0.86 (±0.80)		0.13 (±0.52)	0.63	0.40	0.046	0.303		18
	σ_F	−4.14 (±1.40)			−0.08 (±0.48)	0.59	0.35	0.009			18
	σ_F, $\Delta\chi$, σ_R	−6.99 (±1.50)	1.10 (±0.78)	4.70 (±1.29)	0.20 (±0.36)	0.87	0.76	0.000	0.186	0.003	16[h,i]
	σ_F, $\Delta\chi$	−4.41 (±1.83)	−0.58 (±0.88)		0.11 (±0.50)	0.70	0.50	0.032	0.519		16[h,i]
	σ_F	−5.15 (±1.42)			0.31 (±0.48)	0.69	0.48	0.003			16[h,i]
$CDCl_3$	σ_F, $\Delta\chi$, σ_R	−7.58 (±1.77)	1.03 (±0.97)	4.20 (±1.46)	0.45 (±0.45)	0.82	0.67	0.001	0.304	0.012	19
	σ_F, $\Delta\chi$	−4.64 (±1.74)	−0.83 (±0.86)		0.31 (±0.54)	0.70	0.49	0.017	0.349		19
	σ_F	−5.55 (±1.47)			0.17 (±0.52)	0.68	0.46	0.001			19
	σ_F, $\Delta\chi$, σ_R	−9.13 (±1.36)	1.64 (±0.71)	5.41 (±1.06)	0.42 (±0.31)	0.93	0.86	0.000	0.037	0.000	17[h,i]
	σ_F, $\Delta\chi$	−5.88 (±2.00)	−0.44 (±0.96)		0.32 (±0.51)	0.76	0.58	0.011	0.652		17[h,i]
	σ_F	−6.50 (±1.45)			0.29 (±0.50)	0.75	0.57	0.000			17[h,i]
HFIP	σ_F, $\Delta\chi$, σ_R	−8.51 (±1.97)	−0.04 (±1.08)	5.47 (±1.93)	0.25 (±0.48)	0.91	0.83	0.001	0.970	0.016	15[i]
	σ_F, $\Delta\chi$	−5.87 (±2.18)	−1.74 (±1.14)		0.05 (±0.60)	0.84	0.70	0.020	0.150		15[i]
	σ_F	−8.13 (±1.68)			0.00 (±0.62)	0.80	0.64	0.000			15[i]
TFA	σ_F, $\Delta\chi$, σ_R	−6.17 (±2.75)	−1.26 (±1.63)	3.93 (±2.78)	−0.36 (±0.74)	0.89	0.79	0.052	0.458	0.192	14
	σ_F, $\Delta\chi$	−3.71 (±2.23)	−2.80 (±1.26)		−0.74 (±0.73)	0.86	0.74	0.128	0.051		14
	σ_F	−7.37 (±1.76)			0.47 (±0.84)	0.78	0.61	0.002			14

[a] General form of correlation equation: $^{19}\text{F SCS} = \varrho_F\sigma_F + \varrho_\chi\Delta_\chi + \varrho_R\sigma_R + c$. [b] SCS of **16** omitted from all correlations due to lack of substituent parameters; **29** also omitted. [c] Regression coefficients for individual terms plus or minus standard error of regression coefficient. [d] Intercept. [e] Multiple correlation coefficient. [f] p values. These values indicate the confidence level of the correlation and of the individual susceptibility terms. [g] Number of data points in correlation. [h] SCS of **18** omitted from data set. [i] SCS of **20** omitted from data set.

example, that **20** had to be excluded from the correlations in TFA, in which it certainly exists as the salt.

Since the precision of the correlations can only be described as moderate,[35] any conclusions describing ^{19}F SCS in terms σ_F, $\Delta\chi$, and σ_R must be treated with some reservation. Nevertheless, the trend of the correlations, as revealed by inspection of the magnitude of the various p values, indicates that the ^{19}F SCS in system **3** are best explained by a combination of field and resonance effects with, at best, a small dependence upon electronegativity. This is the first instance in which resonance effects have been identified in a fully saturated ground state system. It is gratifying to note that the correlations all successfully predict the shift for the parent **28** (SCS = 0).

The field susceptibility term (ϱ_F) in the correlations is negative in all cases which, according to the empirically derived relationship between the effect of σ-electron withdrawers and their upfield influence on SCS,[6] implies that σ-electron-withdrawing substituents located at the 4-position in fluorocubane serve to shield the fluorine nucleus. This observation is consistent with the observations made in both systems **1**[1] and **2**.[2] Bearing in mind the high s character of the exocyclic orbitals of cubane[36] and the consequent low polarizability this should impart to a cubane C−F bond[3] and because the magnitude of the field susceptibility is directly related to the polarizability of the C−F bond,[6] one would have intuitively expected the ϱ_F values to be smaller than those observed in either system **1** or **2**. In fact, the ϱ_F values are comparable in magnitude to those observed in **1**, a matter which is discussed in more detail below.

The resonance susceptibility term (ϱ_R) is positive in all cases which means that, in accordance with the current understanding of resonance effects in aromatic systems,[37] a π-donor (negative σ_R) will act to decrease the value of the SCS, i.e., to cause the shift to be upfield (shielded). The corollary is that resonance effects in aliphatic systems, as in aromatic substrates, serve to perturb the ($2p_X$ and $2p_Z$) π-electrons of the fluorine probe. The observation that the field and resonance effects sometimes reinforce and at other times oppose each other, depending on the resonance characteristics of the substituent, explains at least in part the small range of shifts observed in all solvents compared to that observed for systems **1**[1] and **2**[2] in which it was found unnecessary to include resonance effects. Further evidence for a resonance interaction can be gleaned from examination of the SCS of the substituents OAc and $CONH_2$, which possess identical σ_F values[1] and similar $\Delta\chi$ values ($\Delta\Delta\chi = 0.15$)[2] in $CDCl_3$. Thus, if the ^{19}F shifts were dependent only upon the σ_F and $\Delta\chi$ values, similar SCS for these groups should be observed regardless of whether the effects are in opposition. That the shifts are very different, considering the total range of SCS in this solvent, can be readily explained by the effects of the opposing mesomeric interactions of these two substituents.

Finally, as ϱ_χ is statistically unimportant, it implies that double hyperconjugative interactions[1,7] are unlikely in the cubane system. This is not surprising in view of the skew relationship of the intervening bonds and the resultant lack of overlap among the required orbitals.

In order to lend credence to the results obtained from this type of correlative analysis, it is normally considered desirable[1] to determine the field susceptibility parameter, ϱ_F, by noncorrelative means; this involves dividing the difference between the SCS of the two substituents by the difference between their σ_F values. For example, to separate field and electronegativity terms by noncorrelative means in system **1**, Adcock[1] employed the C_6H_5 and p-$NO_2C_6H_4$ substituents which have different σ_F values (0.13 and 0.33, respectively) but identical ι values. The ϱ_F values thus determined were in good agreement with those obtained by correlative means. It is noteworthy that application of this procedure to the 1-fluorobicyclo[2.2.1]heptanes **2** failed to support the correlative analysis; however, in this case, successful noncorrelative determination of the ϱ_F values was achieved by using CH_3 ($\sigma_F = 0.00$) and CH_2OH ($\sigma_F = 0.37$) which are suggested to possess similar electronegativity[38] and resonance parameters.[2]

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Table 3. ϱ_F Values for Systems 1,[a] 2,[b] and 3 as Determined by Correlative and Noncorrelative Means

	3		1		2	
solvent	$\varrho_F{}^c$	$\varrho_F{}^d$	$\varrho_F{}^c$	$\varrho_F{}^d$	$\varrho_F{}^c$	ϱ^{Fd}
c-C_6H_{12}	−3.52	−6.99	−3.13	−6.15	−3.60	−4.37
$CDCl_3$	−5.00	−9.13	−5.25	−8.97	−3.43	−5.39
HEFIP	−5.92	−8.51				
TFA	−7.35	−6.17	−17.6	−16.5	−14.1	−11.7

[a] See ref 1. [b] See ref 2. [c] Determined by noncorrelative means. [d] As determined from correlations.

The noncorrelative method employing CH_3 and CH_2OH was applied to the cubane system in an effort to shed further light upon what appeared to be anomalously large ϱ_F values obtained through the correlations. Unfortunately, the values obtained from these calculations, viz., $\varrho_F(C_6H_{12}) = 1.40$, $\varrho_F(CDCl_3) = -2.86$, and $\varrho_F(\text{HFIP}) = 0.33$, are obviously less representative of the true ϱ_F values than those presented in Table 2. Not only are they inconsistent in sign, but the most strongly hydrogen-bonding solvent in this group is associated with the smallest absolute ϱ_F value which contrasts strongly with conclusions from previous studies.[1,2] It is suggested that the inability of this method to successfully predict reasonable ϱ_F values in the fluorocubanes **3** may be attributed to two main factors. Firstly, the very small SCS and resulting inherent inaccuracies involved are exacerbated when the difference of the two SCS is taken. Secondly, because the correlations suggest that electronegativity is not an important interaction in the 1-fluorobicyclo[2.2.2]octanes **1**, the inability to reproduce reasonable ϱ_F values suggests that, unlike the situation encountered in aromatic compounds, the substituents have different resonance parameters in saturated substrates.

If the conclusion drawn from the correlations that the SCS in fluorocubanes are dominated by field and resonance effects is valid, then the problems cited above may be circumvented by selecting substituents which are more likely to possess identical σ_R values in aliphatic systems and whose SCS are sufficiently different that errors associated with the use of substituents whose ΔSCS is small is minimized. These criteria are fulfilled by the NO_2 and CO_2Me groups which are both π-electron withdrawers and which possess identical σ_R and $\sigma_R{}^+$ values.[30] In addition, the shifts for these two substituents are separated by at least 1.55 ppm (C_6H_{12}) which is considered reasonable in light of the narrow shift ranges.

Using the method of Adcock referred to above for these substituents yielded the noncorrelative values depicted in Table 3 (column 1). While these values do not agree with those determined from the correlations, they meet all expectations drawn from the correlative ϱ_F values of systems **1** and **2** and the expected low polarizability of the cubane C−F bond. The independently determined ϱ_F values all possess negative signs, signifying the reverse response[6] of the fluorine probe to field-induced perturbations of the σ C−F bond electron density as already established from correlative analysis. The values themselves are all consistently lower than those of both **1** and **2** for the same solvents. Furthermore, the increase in ϱ_F on progressing to more strongly HBD solvents, which serve to increase the polarizability of the C−F bond,[1] is smaller, although the relative increases are consistent with the other two systems. These last two observations are consistent with a "stiff" cubane C−F bond.

Table 4. Calculated Polar Field Contributions $(\varrho_F\sigma_F)^{a,b}$ to the ^{19}F SCS of the Fluorocubanes 3

	$\varrho_F\sigma_F$			
X	c-$C_6H_{12}{}^c$	$CDCl_3{}^d$	HFIP[e]	TFA[f]
NO_2	−2.23	−3.25	−4.08	−5.44
CN	−2.08	−2.80	−3.32	−5.22
COCl	−1.80	−2.45		
F	−1.37	−2.10	−2.66	−3.82
Cl	−1.52	−2.15	−2.55	−3.23
Br	−1.55	−2.20	−2.60	−3.23
I	−1.48	−2.10	−2.37	−2.94
OAc	−1.02	−1.65	−2.07	−3.31
$CONH_2$		−1.65		−5.07
CO_2H	−0.81	−1.60	−2.01	−3.23
OH	−0.81	−1.45		
COMe	−1.09	−1.40	−2.19	
CO_2Me	−0.77	−1.30	−1.78	−2.94
NH_2	−0.42	−0.95	−4.68	
C_6H_5	−0.53	−0.85	−1.12	−1.32
CH_2OH	−0.49	−0.50	−1.24	
Me	0.00	0.00	0.00	
$SiMe_3$	0.00	0.00	0.00	0.00
$SnMe_3$	0.00	0.00	0.00	0.00

[a] See the text for definition. [b] Contributions in ppm. [c] $\varrho_F = 3.52$. [d] $\varrho_F = -5.00$. [e] $\varrho_F = -5.92$. [f] $\varrho_F = -7.3$.

Table 5. Calculated Residual Contributions[a−c] to the ^{19}F SCS of the Fluorocubanes 3

	residuals			
X	c-C_6H_{12}	$CDCl_3$	HFIP	TFA
NO_2	−0.27	0.33	−0.62	−0.26
CN	1.61	2.00	0.97	1.97
COCl	0.77	1.18		
F	−1.39	−0.10	−1.84	−1.01
Cl	−1.10	−0.93	−1.90	−1.60
Br	−1.76	−1.62	−2.46	−1.99
I	−1.78	−1.52	−2.34	−2.28
OAc	−2.33	−2.64	−3.03	−2.44
$CONH_2$		0.58		−1.07
CO_2H	−0.13	0.41	−0.48	−1.14
OH	−1.70	−1.65		
COMe	0.73	0.76	0.23	
CO_2Me	−0.18	0.08	−0.61	−0.26
NH_2	0.38	0.57	−2.51	
C_6H_5	0.41	0.83	0.44	0.52
CH_2OH	0.96	1.14	0.84	
Me	0.54	0.50	−0.47	
$SiMe_3$	0.81	0.69	0.95	1.00
$SnMe_3$	−0.77	−0.81	−0.20	0.00

[a] ^{19}F SCS (observed) − polar field contribution ($\varrho_F\sigma_F$). [b] Contributions in ppm. [c] See Table 4 for polar field contributions.

By employing the independent ϱ_F and σ_F values, the polar (in this case, assumed to be field only) contribution to the SCS may be calculated, and thus, the residual contributions can be dissected out.[1,2] The results are presented in Tables 4 and 5.

The results of this noncorrelative analysis procedure support the hypothesis that the SCS of the cubane system are determined predominantly by a combination of field and resonance effects. The dissection generally predicts the π-donor or π-acceptor nature of most substituents in most solvents. There are however certain notable discrepancies, for many of which the residual contribution is small. That some substituents appear on the basis of the residual contributions to possess π-resonance characteristics diametrically opposed to that observed in aromatic compounds implies two possibilities: firstly, that the substituents do, in fact, behave differently in aliphatic systems or, secondly, that the basic assumption employed in the noncorrelative dissection, viz., that electronegativity effects are of insignificant importance,

Table 6. $^{19}F-^{13}C$ Coupling Constants[a] for the Carbons of the 4-Substituted Fluorocubanes 3

X	^1J(CF)[b]	Δ^1J(CF)	^2J(CF)	Δ^2J(CF)	^3J(CF)	Δ^3J(CF)	^4J(CF)	Δ^4J(CF)
H	329.4	0.0	24.35	0.0	4.85	0.0	13.54	0.0
NO_2	324.4	−5.0	26.95	2.60	6.20	1.35	18.32	4.78
CN	327.9	−1.5	26.51	2.16	5.49	0.64	15.75	2.21
COCl	328.4	−1.0	26.12	1.77	5.60	0.75	14.61	1.07
F	325.5	−3.9					27.10	13.56
Cl	324.3	−5.1	25.93	1.58	6.06	1.21	23.47	9.93
Br	324.7	−4.7	25.73	1.38	5.77	0.92	24.41	10.87
I	327.1	−2.3	25.27	0.92	5.31	0.46	23.80	10.26
OAc	322.5	−6.9	25.86	1.51	6.51	1.66	21.58	8.04
CO_2H	328.2	−1.2	25.59	1.24	5.42	0.57	13.64	0.10
NHCOMe	325.8	−3.6	25.70	1.35	6.10	1.25	18.20	4.66
COMe	328.9	−0.5	25.43	1.08	5.59	0.74	13.01	−0.53
CO_2Me	328.4	−1.0	25.51	1.16	5.49	0.64	13.55	0.01
NH_2	325.2	−4.2	25.20	0.85	6.45	1.60	17.08	3.54
C_6H_5	328.9	−0.5	25.00	0.65	5.62	0.77	13.92	0.38
CH_2OH	329.6	0.2	24.78	0.43	5.64	0.79	13.16	−0.38
CH_2OAc	328.5	−0.9	24.98	0.63	5.57	0.72	13.40	−0.14
Me	329.1	−0.3	24.45	0.10	5.61	0.76	13.44	−0.10
$SiMe_3$	334.1	4.7	23.85	−0.50	4.14	−0.71	11.09	−2.45
$SnMe_3$	334.0	4.6	23.50	−0.85	3.75	−1.10	13.14	−0.40

[a] Spectra were recorded in $CDCl_3$ solvent and are accurate to ±0.01 Hz. [b] Accurate to ±0.1 Hz.

Table 7. Results of Correlative Analysis[a,b] of Δ^nJ(CF) of 4-Substituted Fluorocubanes 3 with σ_F, Δ_χ, and σ_R

Δ^nJ(CF)	independent variables	ϱ_F[c]	ϱ_χ[c]	ϱ_R[c]	c[d]	r[e]	r^2	p_F[f]	p_χ[f]	p_R[f]	n[g]
Δ^1J(CF)	σ_F, $\Delta\chi$, σ_R	−8.26 (±2.35)	−3.88 (±1.30)	5.52 (±2.02)	2.88 (±0.59)	0.93	0.87	0.003	0.010	0.016	18
	σ_F, $\Delta\chi$	−4.67 (±2.32)	−6.11 (±1.22)		2.63 (±0.70)	0.89	0.80	0.063	0.000		18
	σ_F	−11.3 (±3.04)			1.70 (±1.06)	0.68	0.46	0.002			18
	σ_F, $\Delta\chi$, σ_R	−7.75 (±0.97)	−4.29 (±0.53)	5.76 (±0.85)	2.83 (±0.23)	0.99	0.98	0.000	0.000	0.000	16[h,i]
	σ_F, $\Delta\chi$	−4.78 (±1.83)	−6.15 (±1.05)		2.79 (±0.55)	0.93	0.87	0.021	0.000		16[h,i]
	σ_F	−10.7 (±2.80)			1.91 (±0.97)	0.71	0.51	0.002			16[h,i]
Δ^2J(CF)	σ_F, $\Delta\chi$, σ_R	2.93 (±0.33)	1.08 (±0.19)	0.64 (±0.29)	0.28 (±0.08)	0.98	0.97	0.000	0.000	0.048	17[h]
	σ_F, $\Delta\chi$	3.33 (±0.31)	0.86 (±0.17)		0.32 (±0.09)	0.97	0.95	0.000	0.000		17[h]
	σ_F	4.17 (±0.41)			0.18 (±0.14)	0.93	0.87	0.000			17[h]
Δ^3J(CF)	σ_F, $\Delta\chi$, σ_R	0.42 (±0.49)	1.19 (±0.27)	−0.87 (±0.43)	0.12 (±0.12)	0.91	0.83	0.405	0.010	0.065	17[h]
	$\Delta\chi$, σ_R		1.35 (±0.20)	−0.66 (±0.36)	0.18 (±0.11)	0.91	0.82		0.000	0.082	17[h]
	$\Delta\chi$		1.45 (±0.20)		0.15 (±0.11)	0.88	0.77		0.000		17[h]
Δ^4J(CF)	σ_F, $\Delta\chi$, σ_R	21.9 (±4.84)	−2.81 (±2.69)	−20.8 (±4.17)	−2.17 (±1.22)	0.88	0.78	0.000	0.314	0.000	18
	σ_F, σ_R	18.3 (±3.39)		−18.1 (±3.26)	−2.31 (±1.21)	0.88	0.77	0.000		0.000	18
	σ_F, $\Delta\chi$, σ_R	20.3 (±2.98)	−2.17 (±1.66)	−24.2 (±2.81)	−1.92 (±0.75)	0.96	0.92	0.000	0.217	0.010	16[i,j]
	σ_F, σ_R	17.5 (±2.13)		−22.4 (±2.50)	−2.01 (±0.77)	0.95	0.91	0.000		0.000	16[i,j]

[a] General form of correlation equation: $\Delta^nJ(CF) = \varrho_F\sigma_F + \varrho_\chi\Delta_\chi + \varrho_R\sigma_R + c$. [b] SCS of **16** omitted from all correlations due to lack of substituent parameters; **29** also omitted. [c] Regression coefficients for individual terms plus or minus standard error of regression coefficient. [d] Intercept. [e] Multiple correlation coefficient. [f] p values. These values indicate the confidence level of the correlation and of the individual susceptibility terms. [g] Number of data points in correlation. [h] ΔJ(CF) of **9** omitted from data set. [i] ΔJ(CF) of **13** omitted from data set. [j] ΔJ(CF) of **20** omitted from data set.

is not strictly valid. If the latter is true, then the independently calculated ϱ_F values will have associated with them a degree of error (due to the difference in $\Delta\chi$ between the NO_2 and CO_2Me substituents) that will be carried over into the calculated residual contributions. This in turn may be the cause of the anomalies observed in Table 5. As the Δ^1J(CF) values show a definite dependence on electronegativity (*vide infra*), the latter conclusion is the most likely.

In summary, when allowance is made for the fact that much of the above analysis is of an approximate and/or tentative nature in view of the average precision of the correlations, the weight of evidence nonetheless supports the unprecedented conclusion that substituent effects in cubane are dominated by both field and resonance effects.

$^{19}F-^{13}C$ Coupling Constants. Values of the carbon–fluorine coupling constants for the 4-X-substituted fluorocubanes in $CDCl_3$ are shown in Table 6, which also lists the differences between the coupling constants of the substituted and parent fluorocubanes for the four different types of carbon atoms of the cubane framework. A cursory examination of Table 6 reveals that, whereas one- and two-bond CF couplings do not show a large variation with a change of substituent, the three- and four-bond coupling constants appear to be more sensitive; the most spectacular changes occur in the case of ^4J(CF).

The coupling constants were dissected by means of a least squares regressional analysis, and the results are presented in Table 7. Despite the empirical observations above, the larger magnitude of the susceptibility parameters in the case of ^1J(CF) and ^4J(CF) indicates that the C1 and C4 positions are much more sensitive to the effect of substituents, although the relatively small range of ^1J(CF) values suggests an interesting and complex picture of the modes of substituent effect transmission in cubane. As the magnitude of r^2 and the p values suggest, values of ^1J(CF) correlate best with a combination of field, electronegativity, and resonance effects. Elimination of any one (or more) of these parameters from the correlations leads to a decrease in the precision of the fit. The correlations are improved significantly (r = 0.99) upon exclusion of the data for two π-donors, OAc and F. Similar anomalous behavior for some π-donors was also observed in the ^{19}F SCS study above, and it is suggested that the explanation offered there applies equally to the coupling data.

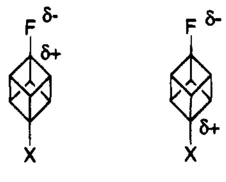
That Δ^1J(CF) responds systematically to variations in the electronegativity of the substituents has significant implications. Adcock[1] has indicated that variations in the hybridization of C1 in the bicyclo[2.2.2]octyl system may be attributed to structural and/or σ-inductive effects. Bearing in mind the high rigidity of the cubane framework and that it has not been necessary to invoke steric parameters to accurately describe the variations in ^1J(CF), one possibility is that the systematic dependence of Δ^1J(CF) on $\Delta\chi$ is the result of long range σ-induction.[39] Such a four-bond pathway (of which there are six available in **3**) represents the longest distance thus far encountered over which the σ-inductive effect has been seen to operate. By contrast, it is noteworthy that, in the bicyclo[2.2.2]octyl system (**1**) in which there are only three through-bond pathways between the substituent and C1 and in which the ^{19}F SCS are strongly influenced by an electronegativity effect via double hyperconjugation, the Δ^1J(CF) values are found to be insensitive to electronegativity effects.[1] The sign of the susceptibilty parameter, ϱ_χ, for Δ^1J(CF) in the cubyl fluorides is also in agreement with expectation.

In considering the resonance dependence of the ^1J(CF) couplings, attention is drawn to the positive sign of the susceptibility parameter (ϱ_R), which implies that π-donors (negative σ_R values) act to decrease the coupling constant by decreasing electron density at C1. It has already been shown above from ^{19}F chemical shift measurements that π-donors redistribute the π-electron density of the C−F bond in the direction of the fluorine nucleus (away from C1), and this redistribution satisfactorily explains the observed sign of ϱ_R at that carbon.

Coupling of fluorine to C2 shows a predominant dependence upon the field effect and, to a lesser extent, electronegativity; resonance effects appear to be unimportant at this site. Importantly, the correlation is of very good precision (r = 0.97) and accounts for 95% of the observed variations. Interestingly, fluorine coupling to C3 responds predominantly to electronegativity effects and shows essentially no dependence upon field effects; this is not surprising considering the angular dependence of this transmission mode.[40]

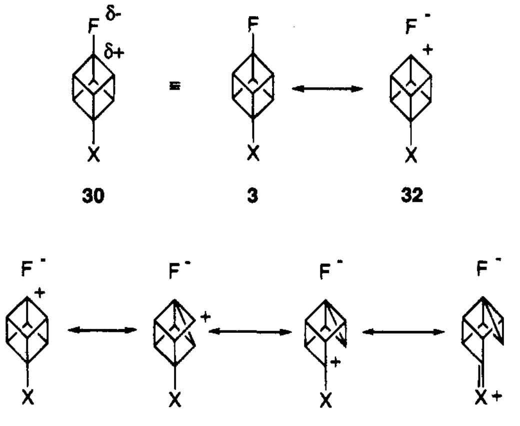
It was pointed out above that four-bond coupling shows the largest variation among the values of ^nJ(CF) observed in the set of 4-substituted fluorocubanes under examination, with the most spectacular effect displayed by the halogen atoms. As observed with ^1J(CF), coupling between fluorine and C4 also correlates best with exclusion of two π-donors, OAc and NH_2, both of which showed recalcitrant behavior in the earlier correlations, and this was ascribed to inaccuracies in their σ_R values when applied to aliphatic systems. It can be seen that the values of Δ^4J(CF) correlate primarily and very strongly with the field and resonance effects and show little dependence upon electronegativity effects.

For electron-withdrawing substituents at C4, the field effect is seen to lead to increased C−F coupling. This observation is best accommodated by considering charge density redistribution as shown in Figure 1; i.e., the contributor **31** must make a significant contribution to the ground state of **3**. However, a σ-electron-withdrawing substituent will disfavor **31**; hence, structure **30** is therefore correspondingly favored to delocalize charge away from C4, thus increasing the electron density at C4, in accordance with the sign of the ϱ_F value.



30 **31**

Figure 1.



30 **3** **32**

32 **33** **34** **35**

Figure 2.

The resonance interaction, which is extremely strong at this site ($\varrho_R = -22.4$) is seen to oppose the field effect. Accordingly, a π-donor must act to increase the electron density at C4 presumably by direct electron donation to stabilize the positive charge at C4 (Figure 1, structure **31**), thus increasing the value of ^4J(CF). That electronegativity appears to play no major role at C4 as determined from the correlations is unusual considering the proximity of the substituent and the probe.

The delocalization of the positive partial charge at C1 to C4 bears obvious similarites to the mechanism of delocalization of the full positive charge in the cubyl cation proposed by Eaton.[9,41] The analogous resonance structures for **3** are presented in Figure 2 (**32**−**35**). These resonance structures readily explain the delocalization of positive charge to C4 and thus the dependence and sign of the susceptibility parameters arising from the correlations at this site. These interactions also result in a concomitant increase in electron density at the fluorine nucleus and are thus in agreement with the correlations describing both the ^{19}F SCS and the Δ^1J(CF) couplings.

Summary and Conclusions. Correlative analysis of the ^{19}F chemical shifts and ^nJ(CF) couplings of a series of 4-substituted cubyl fluorides has been undertaken in an attempt to delineate the mechanism of transmission of substituent effects in the cubane system. In practice, although the correlations for the ^{19}F chemical shifts are, at best, fair, they nevertheless provide a clear indication of the relative importance of the contributions by field, resonance, and electronegativity effects; thus, both field and resonance effects are found to predominate with electronegativity playing a lesser role. Significantly,

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(39) Branch, G. E. K.; Charton, M. *The Theory of Organic Chemistry*; Prentice-Hall: New York, 1941; Chapter 6.

(40) Calculations employing the geometrical data calculated for cubane (ref 41) and the equation $E_z = \mu(2\cos\theta\cos\phi - \sin\theta\sin\phi)/r^3$ (ref 27) indicate that, for any particular substituent, the magnitude of the electric field component (E_z) at C1 and C2 is of very similar magnitude, making these two carbons directly comparable.

(41) Della, E. W.; Head, N. J.; Janowski, W.; Schiesser, C. H. *J. Org. Chem.* **1993**, *58*, 7876−7882.

electronegativity is seen to make a substantial contribution to changes in ^1J(CF) despite the fact that its effect is transmitted over such a long range via the σ-framework.

We believe that one of the most important discoveries of this study is the demonstration of the existence of strong resonance effects, which are shown to have an important influence on both the ^{19}F chemical shifts and the magnitude of the J(CF) couplings. As far as we are aware, this is the first occasion that resonance has been observed to operate in a fully aliphatic system.

Experimental Section

The synthesis and physical properties of methyl 4-iodocubane-1-carboxylate[12] and 1-bromocub-4-yl fluoride (7)[42] have been previously reported. Elemental analyses were carried out by the Australian Microanalytical Service, Melbourne.

Methyl 4-Fluorocubane-1-carboxylate (5). Improved Procedure. Xenon difluoride (1.17 g, 6.3 mmol) was added in one portion to a solution of methyl 4-iodocubane-1-carboxylate (1.8 g, 6.3 mmol) in CH_2Cl_2 (30 mL) in a glass pressure vessel. The vessel was quickly purged with argon and sealed. The mixture was stirred at room temperature for 5 min and then at 80 °C for 24 h. A standard workup afforded the fluoride **5** (0.93 g, 82%), whose spectral data were in accord with literature values.[12]

4-Fluorocubane-1-carboxylic Acid (4). A solution of the fluoro ester **5** (4.3 g, 24 mmol) in THF (100 mL) was treated with a solution of sodium hydroxide (2.5 g, 62 mmol) in methanol (25 mL) and the mixture stirred at room temperature for 1 h. The mixture was evaporated to dryness and the residue taken up in water (100 mL) which was extracted with dichloromethane (2 × 20 mL). The organic extracts were discarded, and the aqueous layer was acidified (to pH 1) with concd HCl. The acidified mixture was extracted with dichloromethane (1 × 100 mL, 3 × 20 mL), and the combined extracts were dried ($MgSO_4$) and evaporated. Sublimation of the residue (Kugelrohr, 90−100 °C/0.1 mm) gave the fluoro acid **4** (3.8 g, 96%): mp 159−161 °C; ^{1}H NMR δ 4.85−4.45 (m, 6H), 8.25 (bs, 1H); ^{13}C NMR δ 178.45 (d, ^5J(CF) = 7.21 Hz), 102.68 (d, ^1J(CF) = 328.1 Hz), 56.29 (d, ^4J(CF) = 13.64 Hz), 54.09 (d, ^2J(CF) = 25.59 Hz), 42.30 (d, ^3J(CF) = 5.42 Hz); MS *m/z* (relative intensity) 166 (2), 123 (21), 121 (100), 109 (21), 101 (68), 96 (60), 95 (33), 75 (54); HRMS calcd for $C_9H_9FO_2$ ($M0^{\bullet+}$ 166.0430, found 166.0427. Anal. Calcd for $C_9H_7O_2F$: C, 65.1; H, 4.2. Found: C, 64.7; H, 3.9.

1-Chloro-4-fluorocubane (8). Barton chlorodecarboxylation of the acid **4** (150 mg, 0.90 mmol) was achieved as described[14a] using 1,1,1-trichloro-2,2,2-trifluoroethane as solvent and chlorine atom donor. Standard workup and sublimation (Kugelrohr, 78 °C/5 mm) afforded 1-chloro-4-fluorocubane (**8**) (100 mg, 71%): mp 80.5−82.5 °C; ^{1}H NMR δ 3.68−4.65 (m); ^{13}C NMR δ 104.01 (d, ^1J(CF) = 324.34 Hz), 52.41 (d, ^2J(CF) = 25.93 Hz), 48.78 (d, ^3J(CF) = 6.06 Hz), 73.77 (d, ^4J(CF) = 23.47 Hz). Anal. Calcd for C_8H_8ClF: C, 61.4; H, 3.9. Found: C, 61.2; H, 4.1.

1-Fluoro-4-iodocubane (6). Method A: Barton Iododecarboxylation.[14b] A mixture of the fluoro acid **4** (100 mg, 0.60 mmol) and thionyl chloride (3 mL) was refluxed under nitrogen for 1.5 h and the excess thionyl chloride removed under vacuum (20 mm). The derived acid chloride was dissolved in CH_2Cl_2 (1.5 mL) and added dropwise under irradiation (300 W tungsten lamp) to a stirred suspension of sodium *N*-hydroxypyridine-2-thione (99 mg, 0.66 mmol), DMAP (cat), and CF_3CH_2I (0.3 mL, 3.0 mmol) in CH_2Cl_2 (10 mL). After 40 min, the reaction mixture was then subjected to standard workup and the residue sublimed (Kugelrohr, 95 °C/6 mm) to afford 1-fluoro-4-iodocubane (**6**) (105 mg, 70%): mp 99−101 °C; ^{1}H NMR δ 3.77−4.63 (m); ^{13}C NMR δ 103.92 (d, ^1J(CF) = 327.06 Hz), 56.44 (d, ^2J(CF) = 25.27 Hz), 37.80 (d, ^3J(CF) = 5.31 Hz), 49.50 (d, ^4J(CF) = 23.80 Hz); MS *m/z* (relative intensity) 127 (10), 120 (20), 101 (100), 96 (17), 75 (25); HRMS calcd for C_8H_8F (M − I)$^{\bullet+}$ 121.0454, found 121.0452. Anal. Calcd for C_8H_8FI: C, 38.7; H, 2.4. Found: C, 39.0; H, 2.4.

Method B: $Pb(OAc)_4/I_2$.[12] To a degassed solution of the acid **4** (1.0 g, 6.0 mmol) in benzene (120 mL) were added $Pb(OAc)_4$ (3.31 g, 7.44 mmol) and I_2 (3.6 g, 14.2 mmol). The resultant mixture was bought to reflux with irradiation (300 W), and after 3 h, the solution was cooled, filtered, washed with sodium metabisulfite solution (4 × 100 mL), and then dried ($MgSO_4$) and the bulk of the benzene removed by distillation through a packed column. The residue was sublimed under the conditions specified above, affording the iodide **6** (1.4 g, 90%) whose properties were in accord with those reported above.

1,4-Difluorocubane (9). Xenon difluoride (450 mg, 2.66 mmol) was added to a solution of the fluoro iodide **6** (440 mg, 1.77 mmol) in trichlorofluoromethane (10 mL) at 0 °C. The reaction vessel was purged with nitrogen, sealed, and heated at 70−80 °C overnight. A further portion of XeF_2 was added and the mixture again heated as described above. The resulting solution was diluted with trichlorofluoromethane (30 mL), washed with sodium metabisulfite solution (3 × 20 mL), and then dried ($MgSO_4$) and the solvent removed by careful distillation. Sublimation (25 °C/0.1 mm) of the residue into a cold trap (−100 °C) afforded 1,4-difluorocubane (**9**) (150 mg, 60%): mp 90 °C; ^{1}H NMR δ 4.10 (t, J(FH) = 6.1 Hz); ^{13}C NMR δ 104.45 (dd, ^1J(CF) = 325.4 Hz, ^4J(CF) = 27.3 Hz), 48.84 (dd, ^2J(CF) = 17.9 Hz, ^3J(CF) = 25.4 Hz); MS *m/z* (relative intensity) 139 (90), 127 (53), 119 (43), 114 (100), 101 (62), 95 (60); HRMS calcd for $C_8H_5F_2$ (M − H)$^{\bullet+}$ 139.0359, found 139.0340.

1-Acetyl-4-fluorocubane (12). Method A.[15] A mixture of the fluoro acid **4** (430 mg, 2.59 mmol) and thionyl chloride (10 mL) was refluxed for 2 h, after which excess thionyl chloride was removed. The derived acid chloride **10** was dissolved in ether (5 mL) and the solution added dropwise to a cold (−78 °C), stirred solution of lithium dimethylcuprate, prepared from treatment of CuI (1.48 g, 7.77 mmol) in ether (20 mL) with MeLi (10.4 mL, 1.5 M in pentane, 15.6 mmol) at 0 °C. After 20 min at −78 °C, the reaction was quenched with methanol (1.0 mL) and the mixture allowed to warm to room temperature before being added to an equal volume of water and filtered. The organic layer was washed with a further quantity of water (30 mL) and then dried ($MgSO_4$) and evaporated. Chromatography (silica gel; eluent, 5:1 pentane/ether) and recrystallization from pentane afforded the desired ketone **12** (172 mg, 40%): mp 88−90 °C; ^{1}H NMR δ 2.11 (s, 3H), 3.85−4.50 (m, 6H); ^{13}C NMR δ 102.85 (d, ^1J(CF) = 328.91 Hz), 53.55 (d, ^2J(CF) = 25.43 Hz), 42.31 (d, ^3J(CF) = 5.59 Hz), 64.44 (d, ^4J(CF) = 13.01 Hz), 206.03 (d, ^5J(CF) = 6.56 Hz), 24.65; MS *m/z* (relative intensity) 164 (12), 163 (16), 149 (24), 121 (100), 120 (53), 102 (65), 101 (100), 96 (87), 95 (63), 75 (87); HRMS calcd for $C_{10}H_9FO$ (M)$^{\bullet+}$ 164.0637, found 164.0617. Anal. Calcd for $C_{10}H_9FO$: C, 73.2; H, 5.6. Found: C, 73.0; H, 5.8.

Method B. Dicyclohexylcarbodiimide (782 mg, 3.61 mmol) was added to a solution of the acid **4** (600 mg, 3.61 mmol) and *N*-hydroxypyridine-2-thione (505 mg, 3.9 mmol) in $CHCl_3$ (30 mL) held at 0 °C and protected from light. The ensuing mixture was stirred overnight and then filtered, and the precipitate was washed with fresh $CHCl_3$ (10 mL). Evaporation of the solvent gave the thiohydroxamic ester **11** as a yellow solid which was treated with biacetyl (1.5 mL, 18 mmol) and CH_2Cl_2 (25 mL). The mixture was irradiated for 1 h under nitrogen and subjected to standard workup to afford the crude ketone **12** whose properties were in agreement with those of the sample above.

1-Acetoxy-4-fluorocubane (13). The crude ketone **12** obtained in method B was dissolved in CH_2Cl_2 (25 mL) and treated with solid $NaHCO_3$ (1.6 g, 19 mmol) and 80% *m*-chloroperbenzoic acid (3.1 g), and the mixture was then refluxed overnight. The organic layer was separated and treated in a similar fashion with fresh oxidant (×2), after which the mixture was washed with sodium sulfite (2 × 30 mL) and $NaHCO_3$ (30 mL). The organic layer was dried

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(42) Della, E. W.; Head, N. J.; Mallon, P.; Walton, J. C. *J. Am. Chem. Soc.* **1992** *114*, 10730.

($MgSO_4$) and evaporated to dryness at room temperature. Chromatography (Alumina, pH 10; eluent, 20% ether/pentane) of the residue and distillation of the eluted material (Kugelrohr, 80–90 °C/3.0 mm) afforded the desired acetate **13** (420 mg, 65%): mp ca. 25 °C; ^{1}H NMR δ 2.07 (s, 3H), 3.90–4.40 (m, 6H); ^{13}C NMR δ 169.2, 103.91 (d, ^1J(CF) = 322.54 Hz), 53.99 (d, ^4J(CF) = 25.41 Hz), 50.72 (d, ^2J(CF) = 25.92 Hz), 47.26 (d, ^3J(CF) = 6.51 Hz), 20.85 (OCOMe). Anal. Calcd for $C_{10}H_9O_2F$: C, 66.7; H, 5.0. Found: C, 66.3; H, 4.8.

1-Fluoro-4-phenylcubane (14). Following the procedure described by Moriarty et al.,[17] $Pb(OAc)_4$ (552 mg, 1.24 equiv) was added to a solution of the acid **4** (166 mg, 1.0 mmol) in thoroughly deoxygenated benzene (45 mL). The ensuing yellow solution was stirred at room temperature for 15 min and then irradiated (300 W tungsten lamp) under reflux for 3 h. The solution was cooled and filtered, and the filtrate was washed with benzene (2 × 20 mL). The combined extracts were evaporated to dryness, and the residue was taken up in chloroform (40 mL) which was washed with sodium bicarbonate solution (30 mL), dried ($MgSO_4$) and evaporated to dryness. The residue was chromatographed (silica gel; eluent, 5% EtOAc/hexane) to afford the desired fluoride **14** (150 mg, 70%): mp 69–72 °C; ^{1}H NMR δ 3.74–4.54 (m, 6H), 7.23 (bs, 5H); ^{13}C NMR δ 104.10 (d, ^1J(CF) = 328.91 Hz), 52.87 (d, ^2J(CF) = 25.00 Hz), 43.77 (d, ^3J(CF) = 5.62 Hz), 61.03 (d, ^4J(CF) = 13.92 Hz), 142.13 (d, ^5J(CF) = 6.23 Hz), 128.34, 126.06, 124.6. Anal. Calcd for $C_{14}H_{11}F$: C, 84.8; H, 5.9. Found: C, 84.5; H, 5.3.

1-(Hydroxymethyl)-4-fluorocubane (15). A solution of the fluoro acid **4** (200 mg, 1.2 mmol) in ether (4 mL) was added to a solution of $LiAlH_4$ (100 mg) in ether (10 mL) at reflux. The resultant mixture was stirred for 1.5 h and then the reaction quenched with water (0.2 mL), before the mixture treated sequentially with 15% NaOH (0.2 mL) and water (0.5 mL). The solution was then filtered, and the solids were washed with several portions of ether (total 40 mL). Desiccation ($MgSO_4$) and evaporation of the combined ether extracts afforded the fluorocarbinol **15** (160 mg, 88%) as colorless crystals. Sublimation (Kugelrohr, 100 °C/2 mm) gave pure **15** (155 mg): mp 95 °C; ^{1}H NMR δ 1.45 (s, 1H), 3.5–3.9, 4.0–4.45 (m, total 6H); ^{13}C NMR δ 101.09 (d, ^1J(CF) = 331.59 Hz), 62.36 (d, ^2J(CF) = 24.78 Hz), 38.71 (d, ^3J(CF) = 5.64 Hz), 58.86 (d, ^4J(CF) = 13.16 Hz), 62.46 (d, ^5J(CF) = 6.84 Hz); MS *m/z* (relative intensity) 152 (1.2), 133 (64), 121 (100), 115 (15), 109 (56), 101 (81), 96 (80); HRMS calcd for C_9H_9FO $(M)^{\bullet+}$ 152.0637, found 152.0631. Anal. Calcd for C_9H_9FO: C, 71.0; H, 6.0. Found: C, 71.1; H, 6.0.

1-(Acetoxymethyl)-4-fluorocubane (16). A solution of acetyl chloride (165 mg, 2.1 mmol) in pyridine (1.7 mL) was added to a solution of the carbinol **15** (105 mg, 0.69 mmol) in CH_2Cl_2 (2 mL). The mixture was stirred overnight under nitrogen before being diluted with CH_2Cl_2 (20 mL) and then washed repeatedly with water (6 × 20 mL). Desiccation ($MgSO_4$) and evaporation of the solvent followed by distillation (Kugelrohr, 100 °C/2 mm) of the residue afforded the acetate **16** as a colorless liquid (105 mg, 78%) which solidified upon standing: mp 47–48 °C; ^{1}H NMR δ 1.95 (s, 3H), 3.35–3.90 (m, 3H), 4.0–4.4 (m, 5H); ^{13}C NMR δ 171.15, 103.78 (d, ^1J(CF) = 328.52 Hz), 53.32 (d, ^2J(CF) = 24.98 Hz), 40.02 (d, ^3J(CF) = 5.57 Hz), 57.01 (d, ^4J(CF) = 13.40 Hz), 64.59 (d, ^5J(CF) = 7.07 Hz), 20.7; MS *m/z* (relative intensity) 151 (3), 135 (11), 134 (49), 133 (100), 121 (22), 109 (28), 101 (34), 96 (44); HRMS calcd for C_9H_8FO $(M - COMe)^{\bullet+}$ 151.0559, found 151.0586. Anal. Calcd for $C_{11}H_{11}FO_2$: C, 68.0; H, 5.7. Found: C, 67.8; H, 5.5.

4-Fluorocubane-1-carboxamide (17). A mixture of the fluoro acid **4** (500 mg, 3.0 mmol) and thionyl chloride (3.0 mL) was heated under reflux for 1.5 h. Excess thionyl chloride was removed, and the acid chloride **13** was dissolved in ether (3.0 mL). The solution was added dropwise to a well-stirred solution of aqueous ammonia (7 mL) at 0 °C, after which the mixture was stirred at room temperature for 1 h. The precipitated solids were collected by filtration and dried to a constant weight under vacuum to give the desired amide **17** (438 mg, 88%): mp >240 °C; ^{1}H NMR (100 MHz) δ 3.88–4.48 (m, 6H), 5.01–5.84 (br, 2H); MS *m/z* (relative intensity) 165 (4), 147 (9), 136 (15), 121 (100), 101 (67), 96 (53); HRMS calcd for $C_9H_{10}FNO$ $(M)^{\bullet+}$ 165.0590, found 165.0569. Anal. Calcd for C_9H_8FNO: C, 65.4; H, 4.9. Found: C, 65.2; H, 5.2.

4-Fluorocubane-1-carbonitrile (18). Trifluoroacetic anhydride (0.5 mL) was added to a vigorously stirred suspension of the amide **17** (127 mg, 0.78 mmol) in dioxane (3.5 mL) containing pyridine (0.3 mL) under nitrogen at 0 °C. The resultant solution was allowed to attain ambient temperature and then stirred overnight prior to the addition of pentane (15 mL). The pentane layer was washed with water (3 × 15 mL) and the aqueous solution back-extracted with ether (5 × 15 mL). The organic solutions were combined, dried ($MgSO_4$), and evaporated to dryness to afford the nitrile **18** (83 mg, 73%): mp 157–158 °C; ^{1}H NMR δ 3.87–4.61 (m); ^{13}C NMR δ 101.6 (d, ^1J(CF) = 327.93 Hz), 55.35 (d, ^2J(CF) = 26.51 Hz), 43.29 (d, ^3J(CF) = 5.39 Hz), 40.87 (d, ^4J(CF) = 15.75 Hz), 118.5 (d, ^5J(CF) = 8.40 Hz); MS *m/z* (relative intensity) 147 (46), 146 (54), 127 (29), 121 (71), 120 (66), 96 (100), 94 (36), 75 (35); HRMS calcd for C_9H_6N $(M)^{\bullet+}$ 147.0484, found 147.0491. Anal. Calcd for C_9H_6N: C, 73.5; H, 4.1. Found: C, 73.3; H, 4.4.

4-Fluorocuban-1-ylammonium Tosylate (19). Following the procedure described by Moriarty et al.,[19] a suspension of the fluoro amide **17** (350 mg, 2.1 mmol) in acetonitrile (21 mL) was added to a slurry of hydroxy(tosyloxy)iodobenzene[43] (831 mg, 2.1 mmol) in acetonitrile (20 mL). The ensuing mixture was stirred at room temperature for 1 min and then refluxed for 3 h, during which the reactants dissolved. At the end of the reflux period, a precipitate appeared which was collected at the pump and desiccated under high vacuum and identified as the salt **19** (342 mg, 52%): mp ca. 225 °C dec. Anal. Calcd for $C_{15}H_{16}O_3FNS$: C, 58.2; H, 5.2. Found: C, 58.1; H, 5.5.

4-Fluorocub-1-ylamine (20). The ammonium salt **19** (300 mg, 0.97 mmol) was treated with 10% sodium hydroxide solution (15 mL) and the mixture extracted with $CDCl_3$ (1 mL). The $CDCl_3$ extract provided the spectroscopic data for the amine **20**: ^{1}H NMR δ 3.33–4.32 (m, 6H), 1.83 (bs, 2H); ^{13}C NMR δ 46.13 (d, ^2J(CF) = 6.45 Hz), 49.92 (d, ^3J(CF) = 25.20 Hz), 71.75 (d, ^4J(CF) = 17.08 Hz), 104.91 (d, ^1J(CF) = 325.20 Hz).

1-Fluoro-4-nitrocubane (21). The chloroform extract above was evaporated to dryness at room temperature and the residue dissolved in dichloroethane. Oxidation of the amine **20** was effected by the procedure of Gilbert and Borden[44] by adding the dichloroethane solution dropwise to a refluxing suspension of *m*-chloroperbenzoic acid in dichloroethane. The resultant mixture was refluxed for a further 20 min and then washed sequentially with 1 M NaOH solution (3 × 25 mL) and 10% HCl (1 × 20 mL), before being dried ($MgSO_4$, K_2SO_4) and evaporated. Sublimation (Kugelrohr, 90 °C/3.5 mm) afforded the nitro compound **21** (84 mg, 52%): mp 137–138 °C; ^{1}H NMR δ 4.1–4.65 (m, featuring sharp signals at 4.36 and 4.45); ^{13}C NMR δ 102.43 (d, ^1J(CF) = 324.44 Hz), 52.29 (d, ^2J(CF) = 26.95 Hz), 47.39 (d, ^3J(CF) = 6.2 Hz), 87.70 (d, ^4J(CF) = 18.32 Hz); MS *m/z* (relative intensity) 120 (40), 109 (12), 101 (100), 95 (32), 89 (20), 83 (92). Anal. Calcd for $C_8H_6FNO_2$: C, 57.5; H, 3.6. Found: C, 57.2; H, 3.9.

4-Fluoro-1-acetamidocubane (22). A solution of acetyl chloride (57 mg, 0.73 mmol) in CH_2Cl_2 (1 mL) was added to a solution of the amine **20** (50 mg, 0.36 mmol) and pyridine (61 mg, 0.77 mmol) in CH_2Cl_2 (2 mL). The mixture was stirred at room temperature for 6 h, then diluted with CH_2Cl_2, and washed with 5% HCl solution (5 × 20 mL). The CH_2Cl_2 solution was dried ($MgSO_4$) and evaporated to dryness. The residue was recrystallized from ether, yielding the acetamide **22** (54 mg, 82%): mp 228 °C dec; ^{1}H NMR δ 2.25 (s, 3H), 4.15–4.65 (m, 6H), 6.30 (bs, 1H); ^{13}C NMR δ 23.12, 45.25 (d, ^3J(CF) = 6.10 Hz), 51.87 (d, ^2J(CF) = 25.6 Hz), 67.69 (d, ^4J(CF) = 18.2 Hz), 103.81 (d, ^1J(CF) = 325.8 Hz), 170.02; MS *m/z* (relative intensity) 179 (5), 165 (23), 136 (52), 121 (100), 96 (88); HRMS calcd for $C_{10}H_{10}FNO$ $(M)^{\bullet+}$ 179.0746, found 179.0740.

4-Fluorocuban-1-ol (23). Deamination of **19** was effected via the method of Klunder and Zwanenburg[20] in which $NaNO_2$

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(1.0 g, 14.5 mmol) was added in small portions over 2 h to a solution of the ammonium tosylate **19** (300 mg, 0.97 mmol) in 5% HCl (12 mL) . The solution was stirred at room temperature overnight before being saturated with NaCl and extracted with ether (3 × 25 mL). The ether extracts were washed with saturated sodium chloride solution (2 × 15 mL), dried ($MgSO_4$), and evaporated at 0 °C. The crude product was recrystallized from pentane to afford the alcohol **23** (36 mg, 27%): mp 58 °C; ^1H NMR δ 4.05–4.80 (m); MS *m/z* (relative intensity) 138 (1.3), 120 (71), 112 (54), 101 (100), 96 (37), 95 (24); HRMS calcd for C_8H_7FO $(M)^{\bullet+}$ 138.0481, found 138.0479.

1-Fluoro-4-(trimethylsilyl)cubane (24). The fluoro iodide **6** (350 mg, 1.41 mmol) in pentane/ether (3:2) was treated dropwise at −75 °C with a 1.7 M solution of *tert*-butyllithium in pentane (2.1 mL, 3.5 mmol). The mixture was allowed to stir at −75 °C for 10 min before the reaction was quenched with trimethylsilyl chloride (1 mL). The cold bath was removed and the solution allowed to warm to room temperature. The mixture was washed with water (3 × 20 mL) and then desiccated ($MgSO_4$) and concentrated by distillation through a packed column. Redistillation of the residue afforded the silane **24** as a colorless liquid (222 mg, 81%): ^1H NMR δ 3.50–4.10 (m, 3H), 4.15–4.68 (m, 3H), 0.0 (s, 9H); ^{13}C NMR δ 103.87 (d, $^1J(CF) = 334.1$ Hz), 56.78 (d, $^2J(CF) = 23.85$ Hz), 39.01 (d, $^3J(CF) = 4.14$ Hz), 49.82 (d, $^4J(CF) = 11.09$ Hz), −4.89. Anal. Calcd for $C_{11}H_{15}FSi$: C, 68.0; H, 7.8. Found: C, 67.7; H, 7.9.

1-Fluoro-4-(trimethylstannyl)cubane (25). The fluoro iodide **6** (300 mg, 1.2 mmol) was treated with *tert*-butyllithium as described above and the reaction quenched with a solution of trimethylstannyl chloride in 1:1 pentane/ether (2 mL) at −40 °C. The mixture was allowed to warm to room temperature and was then washed with water (3 × 30 mL) before being dried ($MgSO_4$) and concentrated to dryness by distillation through a packed column. The residue was chromatographed (silica gel; eluent, pentane) to afford the desired stannane **25** (299 mg) which was contaminated with a small quantity of fluorocubane. Removal of the latter under vacuum afforded an analytically pure sample of **25**: mp 74–75.5 °C; ^1H NMR δ 3.50–4.10 (m, 3H), 3.10–4.65 (m, 3H), 0.25 (s, 9H); ^{13}C NMR δ 103.65 (d, $^1J(CF) = 334.0$ Hz), 58.45 (d, $^2J(CF) = 23.50$ Hz), 43.40 (d, $^3J(CF) = 3.75$ Hz), 51.32 (d, $^4J(CF) = 13.14$ Hz), −13.77; MS *m/z* (relative intensity) 202 (30), 165 (65), 135 (24), 121 (87), 102 (100). Anal. Calcd for $C_{11}H_{15}FSn$: C, 46.4; H, 5.3. Found: C, 47.3; H, 5.1. The stannane **25** was found to be thermally unstable and had to be stored below 0 °C. As a result, the combustion data are unsatisfactory.

1-Fluoro-4-methylcubane (26). A 0.1 M solution of the iodide **6** (455 mg, 1.83 mmol) was treated with *tert*-butyllithium as described above, the reaction was quenched at −70 °C with methyl triflate (1.0 mL), and then the mixture was allowed to warm to room temperature. A solution of $NaHCO_3$ (10 mL) was added, and the two phases were stirred vigorously overnight. The organic layer was separated and washed with water (2 × 20 mL) before being dried ($MgSO_4$) and concentrated by distillation through a packed column. The residue was exposed to vacuum (0.1 mm), and the volatile components (157 mg) were collected in a cold trap (−100 °C). Analysis of the product (GC and ^1H and ^{13}C NMR) showed it to consist of a mixture of the title fluoride **26** and 2,2,3,3-tetramethylbutane in a ratio of 7.7:1: ^1H NMR ($CFCl_3$) δ 1.08 (s, 3H), 3.00–4.30 (m, 6H); ^{13}C NMR δ 104.93 (d, $^1J(CF) = 329.01$ Hz), 52.67 (d, $^2J(CF) = 24.45$ Hz), 42.39 (d, $^3J(CF) = 5.61$ Hz), 57.09 (d, $^4J(CF) = 13.44$ Hz), 19.48 (d, $^5J(CF) = 7.01$ Hz).

Fluorocubane (28). Tributyltin hydride (3.5 mL) and AIBN (several milligrams) were added to the iodo fluoride **6** (630 mg, 2.54 mmol), and the ensuing suspension was irradiated for 2 h under nitrogen at 0 °C. The mixture was then placed under vacuum (0.1 mm), and the volatile constituents were collected in a cold trap (−100 °C). Resublimation of the product (110 °C/2.5 mm) afforded fluorocubane (**28**) (273 mg, 88%) whose physical properties were in agreement with those reported.[12]

1-Deuterio-4-fluorocubane (29). Tributyltin deuteride (1 mL) and AIBN (several milligrams) were added to the fluoro iodide **6** (390 mg, 1.57 mmol), and the ensuing mixture was then irradiated for 2 h at room temperature. Isolation of the product was effected in the manner described above for the protio analog to give the deuteride **29** (179 mg, 93%): mp 115–116 °C; ^1H NMR δ 3.44–4.04 (m, 3H), 4.04–4.60 (m, 3H); ^{13}C NMR δ 103.69 (d, $^1J(CF) = 329.5$ Hz), 56.31 (d, $^2J(CF) = 24.32$ Hz), 39.86 (d, $^3J(CF) = 4.86$ Hz), 48.33 (dt, $^4J(CF) = 13.56$ Hz, $^1J(CD) = 24.11$ Hz).

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Supporting Information Available: ^{13}C NMR spectra of **9**, **22**, and **26** (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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