Concerning the Origin of Substituent-Induced Fluorine-19 Chemical Shifts in Aliphatic Fluorides: Carbon-13 and Fluorine-19 Nuclear Magnetic Resonance Study of 1-Fluoro-4-phenylbicyclo[2.2.2]octanes Substituted in the Arene Ring

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Several 1-fluoro-4-(para-substituted phenyl)bicyclo[2.2.2]octanes have been synthesized and their NMR spectra (¹³C and ¹⁹F) recorded. The reverse ¹⁹F substituent chemical shifts (SCS) were found to correlate very well with substituent parameters (σ_{I} and σ_{R}^{0}) by using the dual substituent parameter (DSP) equation. Linear electric field effects for several substituents were estimated from the $\sigma_{I}\sigma_{I}$ term for the DSP correlation, and these were employed for calculating the coefficient (A) of the Buckingham equation (SCS = AE_z). The negative sign of the A value for linear electric field effects on C_{sp} -F bonds stands in contrast to the *positive* value for fluorine attached to sp² carbons. It was also found that the ¹⁹F SCS correlate extremely well with the corresponding ¹³C SCS of the bridgehead carbon (C1) attached to fluorine and with the changes in the one-bond carbon-fluorine spin-spin coupling constants ($\Delta^1 J_{CF}$). These results reveal that the phenomenon of reverse ¹⁹F SCS of aliphatic fluorides is a manifestation of dominant changes in fluorine σ -electron density. The origin of exalted ¹⁹F SCS of aliphatic fluorides in trifluoroacetic acid solution has been delineated.

Current theories concerning the electronic influence of remote substituents on ¹⁹F chemical shifts lead to the prediction that substituents which donate electrons to the local environment of the fluorine nucleus increase shielding and cause upfield shifts, while electron-withdrawing substituents deshield the fluorine nucleus and, therefore, effect downfield shifts. This so called "normal" situation is commonly encountered in aryl fluorides where the ¹⁹F substituent chemical shifts (SCS) due to remote substituents are believed to reflect primarily changes in fluorine π -electron density.^{1,2} In striking contrast, ¹⁹F SCS have been reported for several stereochemically well-defined aliphatic fluoride systems which are completely incompatible with the aforementioned expectations.^{3,4} For most of these systems, but not all,^{3d} the shifts are clearly in the opposite direction (reverse substituent dependence). This situation has led to considerable uncertainty concerning the relationship between aliphatic ¹⁹F SCS and the concomitant changes in the electron distribution about the fluorine atom.

Recently,⁵ on the basis of a study of substituent effects on ¹⁹F chemical shifts in a new model system (benzobicyclo[2.2.2]octen-1-yl fluorides), we tentatively proposed that reverse substituent behavior of ¹⁹F chemical shifts in aliphatic fluorides may be a manifestation of the dominant redistribution of the σ electrons in the CF bond (electrons in the 2p, orbital of fluorine). Moreover, as a corollary, we also suggested that since the relative extent of polarization of the σ (2p_v) and π (2p_x and 2p_z) electrons will depend significantly on the electronic structure of the bonds in the local vicinity of the fluorine atom, the chem-

(1) Hehre, W. J.; Taft, R. W.; Topsom, R. D. Prog. Phys. Org. Chem. 1976, 12, 159 and references cited therein.

(2) Reynolds, W. F.; Gibb, V. G.; Plavac, N. Can. J. Chem. 1980, 58, 839 and references cited therein.

(4) Adcock, W.; Khor, T. C. J. Org. Chem. 1977, 42, 218.
 (5) Adcock, W.; Abeywickrema, A. N. Tetrahedron Lett. 1979, 1809.

Table I. ¹⁹F SCS^{a-c} of 1-Fluoro-4-(para-substituted phenyl)bicyclo[2.2.2]octanes (1)

	¹⁹ F SCS						
х	cyclo- hexane	ben- zene	DCCl ₃	DMF	CF ₃ CO ₂ H		
NO ₂	-0.75	-0.65	-0.84	-0.47	-2.81		
CN	-0.67	-0.58	-0.74	-0.39	-2.61		
$C(CN)_3$	-0.81	-0.73	-0.90	-0.42			
COOCH ₃	-0.30	-0.26	-0.36	-0.25	-1.57		
OCH,	0.04	0.05	0.02	0.03	-0.53		
F	-0.34	-0.28	-0.32	-0.21	-0.48		
Br	-0.39	-0.34	-0.41	-0.28	-0.78		
NH ₂	0.21	0.18	0.17	0.31			
$N(CH_3)_2$	0.33	0.32	0.26	0.25			
CH,	0.09	0.09	0.06	0.06	0.19		
⁺ NH ₃					-2.39		
⁺ NH(CH ₃) ₂	2				-2.95		
$^{+}N(CH_3)_3$	-		-0.88 ^d		-3.24^{e}		

^a Defined as the difference (in parts per million) between the ¹⁹F chemical shift of the substituted compound and that of the parent compound (X = H). ^b A positive value implies deshielding. ^c Accurate to ± 0.01 ppm. ^d Counterion I⁻. ^e Counterion Cl⁻.

ical shift response of a fluorine nucleus in aliphatic systems to substituent effects may change from one system to another (i.e., chemical shifts may be either "normal" or "abnormal").

Since these ideas are without obvious theoretical basis, we decided to examine the question further by carrying out a more detailed investigation of the ¹⁹F SCS of the previously studied⁴ 1-fluoro-4-(para-substituted phenyl)bicyclo[2.2.2]octanes (1) and, in particular, to examine their



relationship with respect to pertinent ¹³C NMR parameters. Accordingly, we have synthesized a number of new derivatives of this system $[X = C(CN)_3 COOCH_3, OCH_3,$ $N(CH_3)_2$, CH_3] which, together with those previously reported (X = NO_2 , CN, F, Br, and NH_2),⁴ provide a basis set of substituents covering a wide range of electronic effects and have measured their ¹³C and ¹⁹F NMR spectra. The main virtues of the phenylbicyclo[2.2.2]octane ring

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^{(3) (}a) Bumgardner, C. L. J. Org. Chem. 1963, 28, 3225. (b) Baldwin,
J. E.; Fenoglio, D. J. J. Phys. Chem. 1966, 70, 227. (c) Béguin, C. Bull.
Soc. Chim. Fr. 1967, 4214. (d) Anderson, G. L.; Stock, L. M. J. Am.
Chem. Soc. 1969, 91, 6804. (e) Wahl, G. H.; Peterson, M. R. Ibid. 1970,
92, 7238. (f) Adcock, W.; Dewar, M. J. S.; Golden, R.; Zeb, M. A. Ibid.
1975, 97, 2198. (g) Dixon, E. A. Ph.D. Dissertation, University of Victoria,
Victoria, British Columbia, Canada, 1974. (h) Perkins, R. R.; Pincock,
P. F. Org. Magn. Bacon. 1975, 8, 165. (i) Remillow 1. Resumbles, P. T. R. E. Org. Magn. Reson. 1976, 8, 165. (i) Bromilow, J.; Brownlee, R. T. C.; Page, A. V. Tetrahedron Lett. 1976, 3055. (j) Brownlee, R. T. C.; Craik, D. J. Ibid. 1980, 1681. (k) Brownlee, R. T. C.; Craik, D. J. Aust. J. Chem. 1980, 33, 2555.

Table II. Results of Correlations of ¹⁹F SCS (System 1) with Substituent Parameters

solvent	ρΙ	ρ _R	SD ^b	f ^c	n^d
cyclohexane	-0.97	-0.64	0.06	0.12	10
benzene	-0.85	-0.59	0.04	0.11	10
DCCl,	-1.06	-0.62	0.06	0.11	10
DMF	-0.66	-0.44	0.04	0.13	8^e

^a General form of correlation equation: SCS = $\rho_{I\sigma_{I}} + \rho_{R}\sigma_{R}^{\circ}$. ^b The standard deviation of the fit. ^c The fit parameter, $f \equiv SD/rms$, where rms is the root mean square of the data points. Correlations of excellent precision are those for which $f \le 0.1$. ^d The number of substituents in the data set. e SCS of NH₂ and C(CN)₃ omitted from data set.

system as a rigid model for substituent-effect studies have been previously outlined,^{4,6-9} and these will not be reiterated here. Suffice it to state that for the current study it is important that the model is stereochemically welldefined and, moreover, that the substituent dipole and the CF bond are both aligned along the major axis of the ring system. Hence angles and distances are precisely defined.

Results and Discussion

¹⁹F SCS for system 1 in various solvents are listed in Table I. It can be seen from the regression parameters listed in Table II that these SCS correlate very well with substituent parameters $(\sigma_{\rm I} \text{ and } \sigma_{\rm R})^{10}$ on using the dual substituent parameter (DSP) equation.¹¹ Hence, these shift parameters may be considered to reflect electronic perturbations induced by the substituent as previously discussed.⁴ The most salient points to emerge from that discussion may be summarized as follows.

(1) The correlative equations show that both polar and resonance effects contribute to the ¹⁹F SCS. Structural constraints inherent in the model system suggests, therefore, that the net electric field at the probe nucleus is the resultant of fields associated with the substituent dipole (primary field) and the charges induced in the benzene ring by the substituent (secondary field). It is important to note that since the latter charges are due to both polar and resonance effects, the DSP dissection does not provide a distinct separation of the two contributing electric fields. Hence, the $\rho_1 \sigma_1$ term embodies the effects of the primary field as well as a contribution from the effects of field-induced π polarization of the aromatic ring.^{6,12,13}

(2) The negative susceptibility terms ($\rho_{\rm I}$ and $\rho_{\rm R}$) are indicative of reverse substituent dependence. Thus, the intrinsic response of fluorine in system 1 to intramolecular electrostatic fields is "abnormal".

If the linear electric field-induced ¹⁹F SCS of system 1 are due to CF σ bond polarization, it is logical to expect complementary charge density changes at the bridgehead carbon (C1) to which fluorine is attached. Moreover, it is reasonable to expect that these changes will be mirrored by the ¹³C SCS for this carbon center. It can be seen (Table III) that this is indeed the case and that there is an excellent correlation when these are plotted against the

(6) Adcock, W.; Khor, T. C. J. Am. Chem. Soc. 1978, 100, 7799.
(7) Adcock, W.; Khor, T. C. J. Org. Chem. 1978, 43, 1272.
(8) Adcock, W.; Aldous, G. L. J. Organomet. Chem. 1980, 201, 411.
(9) Adcock, W.; Aldous, G. L.; Kitching, W. J. Organomet. Chem.

1980, 202, 385. (10) Bromilow, J.; Brownlee, R. T. C.; Lopez, V. O.; Taft, R. W. J. Org.

Chem. 1979, 44, 4766. (11) (a) Wells, P. R.; Ehrenson, S.; Taft, R. W. Prog. Phys. Org. Chem.

1968, 6, 147. (b) Ehrenson, S.; Brownlee, R. T. C.; Taft, R. W. Ibid. 1973, 10, 1

(12) Reynolds, W. F.; Hamer, G. K. J. Am. Chem. Soc. 1976, 98, 7296 and references cited therein.

(13) Adcock, W.; Cox, D. P. J. Org. Chem. 1979, 44, 3004 and references cited therein.

Table III. ¹³C NMR Parameters for the Bridgehead Carbon (C1) of System 1^a

x	C1 SCS, ^b ppm	$^{1}J_{CF},$ Hz ^c	$\Delta^{1}J_{\mathrm{CF}},$ Hz^{d}
Н	0.00	183.35	0.0
NO,	-0.63	184.32	1.0
CN	-0.60	184.20	0.9
$C(CN)_{a}$	-0.64	184.40	1.1
COOCH,	-0.31	183.72	0.4
OCH,	-0.01	183.35	0.0
F	-0.19	183.60	0.3
Br	-0.28	183.84	0.5
NH.	0.13	183.11	-0.2
N(CH ₂)	0.18	183.10	-0.3
CH,	0.02	183.35	0.0

^a Solvent DCCl., ^b Defined as the difference between the ¹³C chemical shift of the substituted compound and that of the appropriate carbon in the parent hydrocarbon (X = H). Positive values indicate deshielding. Accurate to ± 0.02 ppm. ^c Accurate to ± 0.1 Hz. d Accurate to ±0.2 Hz.



Figure 1. Plot of ¹⁹F SCS vs. ¹³C SCS (C1) for system 1 in DCCl₃.

corresponding ¹⁹F SCS in DCCl₃ (Figure 1). In accordance with expectations from this linear relationship, the ¹³C SCS (C1) also correlate well (eq 1) with substituent parameters

¹³C SCS (C1) =
$$-0.78\sigma_{\rm I} - 0.47\sigma_{\rm R}^0$$
 (*n* = 10; SD =
0.07; SD/rms = 18%) (1)

on using the DSP equation.¹¹ Most importantly, the blend of the susceptibility parameters for this correlation ($\lambda =$ $\rho_{\rm R}/\rho_{\rm I} = 0.59$) is virtually identical with that observed for the corresponding correlation of the ¹⁹F SCS in DCCl₃ (Table II; $\lambda = 0.61$). Thus, it may be concluded that the ¹⁹F SCS of system 1 are a consequence of field-induced polarization of the CF σ bond and, therefore, are manifestations of changes in the σ electron density at fluorine. The fact that the SCS for fluorine and the adjacent carbon in system 1 have the same signs implies that a decrease



Figure 2. Plot of ¹⁹F SCS vs. $\Delta^1 J_{CF}$ for system 1 in DCCl₃.

in the fluorine σ -electron density leads to *upfield* shifts while an *increase* leads to *downfield* shifts.

Further compelling evidence for these conclusions follows from a consideration of the substituent-induced changes in the one-bond carbon-fluorine spin-spin coupling constants ($\Delta^1 J_{CF}$; Table III) of system 1. A recent study¹⁴ of a series of polycyclic bridgehead fluorides has shown that $\Delta^1 J_{\rm CF}$ reflects changes in the s character of the exocyclic orbital of the bridgehead carbon atom; i.e., changes in the Fermi contact term¹⁵ appear to be the dominant determinant. In this light, the trends in the ${}^{1}J_{CF}$ values of system 1 (Table III) are understandable in terms of changes in hybridization of the exocyclic orbital of C1 in response to σ -electron density changes due to field-induced polarization of the CF σ bond. For example, electron-withdrawing substituents (NO₂, CN, etc.) in system 1 polarize the CF σ bond such that σ -electron density increases at C1 with a concomitant decrease at fluorine. This leads to an increase in the s character of the exocyclic orbital of C1¹⁶ with a consequential increase in ${}^{1}J_{\rm CF}$ (i.e., $\Delta^{1}J_{CF}$ is positive). The converse situation holds for net electron-donating substituents (NH₂, N(CH₃)₂; Table III). Thus, the fact that there is a good correlation between the ¹⁹F SCS (DCCl₃) of system 1 and the corresponding $\Delta^1 J_{\rm CF}$ values (Figure 2) confirms that the former parameter is a manifestation of changes in fluorine σ -electron density.

It should be noted that the observation from this study that ${}^{1}J_{CF}$ responds significantly to intramolecular electrostatic field effects (through-space phenomena) suggests that its recent¹⁷ use as a probe of through-bond effects

Table IV. Electric Field Calculations for System 1

v	D ^a	C-X,	8 C	$10^{-3}E_{\rm CF}$	e e	$10^{12}A$,
л	μ, D	A	7, A	esu «	p Io I	esu
NO,	3.63	2.09	8.63	11.32	-0.63	-55.7
CN	4.04	2.61	9.18	10.44	-0.54	-52.0
F	1.96	1.35	8.26	6.97	-0.49	-69.6
Br	2.18	1.85	8.51	7.09	-0.43	-60.2

^a Dipole moment. ^b Dipole length. ^c Distance between origin of dipole and midpoint of the C-F bond. ^d $E_{CF} = 2\mu/r^3$. ^e $\rho_I = -0.97$ (c-C₆H₁₂; Table I). σ_I values were taken from ref 10.

 $(n-\sigma^* \text{ interactions})$ of dipolar substituents in the adamantane system is probably invalid.

An approximate estimate of the coefficient (A) for the Buckingham equation (SCS = AE_{2})¹⁸ may be obtained by utilizing electric field effects for several substituents (NO₂, CN, F, and Br) estimated from $\rho_{I}\sigma_{I}$ for the DSP correlation of the ¹⁹F SCS (Table II; $c-C_6H_{12}$). The calculations were carried out by utilizing structural and molecular parameters as previously indicated.⁶ Results are summarized in Table IV. It is important to note that the estimated average A value ($-59 \pm 8 \times 10^{-12}$ esu), which is applicable to fluorine attached to an sp³-hybridized quaternary carbon atom. represents an upper limit since the $\rho_{I}\sigma_{I}$ term of the DSP dissection must contain a contribution from the secondary field emanating from the aromatic π system (vide supra). The negative sign of the A value¹⁹ stands in stark contrast to the positive value for fluorine attached to sp² carbons $[A = (25-30) \times 10^{-12} \text{ esu}]^{2,6,12}$. The latter is considered to pertain to the π component of the C(sp²)-F bond. Since A is a formalized measure of the ease of distortion of the electron distribution along the CF bond, the significant A value for the $C(sp^3)$ -F bond contradicts the commonly held view that this bond is guite "stiff" and not readily polarized.²⁰ Interestingly, a comparison of some ¹³C SCS (DCCl₃, ppm) for the bridgehead carbon (C1) of (para-substituted phenyl)bicyclo[2.2.2]octanes (NO₂, -0.22; CN, -0.22; Br, -0.13),²¹ which are manifestations of field-induced polarization of the C(1)–H σ bond, with the corresponding values for system 1 (Table III) suggests that the C(sp³)-F bond is considerably more polarizable than a C(sp³)-H bond.²² This conclusion is based on the recent observation that the shift/charge density ratio of carbon is markedly decreased on replacing H by F.23

In our earlier report⁴ on system 1 we drew attention to the fact that the ¹⁹F SCS for ⁺NH₃ in CF₃CO₂H appeared enhanced compared to expectations based on its known substituent parameters. However, at the time, we were unable to offer a plausible explanation for the phenomenon.²⁴ In order to examine this apparent solvent effect

⁽¹⁴⁾ Della, E. W.; Cotsaris, E.; Hine, P. T. J. Am. Chem. Soc. 1981, 103, 4131.

⁽¹⁵⁾ Kowalewski, J. Prog. Nucl. Magn. Reson. Spectrosc. 1977, 11, 1.
(16) (a) Walsh, A. D. Discuss. Faraday Soc. 1947, 2, 18. (b) Bent, H.
A. Chem. Rev. 1961, 61, 275.

⁽¹⁷⁾ Duddeck, H.; Islam, R. Md. Tetrahedron 1981, 37, 1193.

⁽¹⁸⁾ Buckingham, A. D. Can. J. Chem. 1960, 38, 300.

^{(19) (}a) It is of interest to note that there has been some confusion in the literature concerning the sign of A for a C(sp³)-F bond^{19b,c}. (b) Petrakis, L.; Bernstein, H. J. J. Chem. Phys. **1963**, 38, 1562. (c) Yonemoto, T. Can. J. Chem. **1966**, 44, 223.
(20) (a) Dewar, M. J. S.; Squires, T. G. J. Am. Chem. Soc. **1968**, 90,

 ^{(20) (}a) Dewar, M. J. S.; Squires, T. G. J. Am. Chem. Soc. 1968, 90,
 (b) Dewar, M. J. S.; Kelemen, J. J. Chem. Phys. 1968, 49, 499.
 (21) Adcock, W.; Khor, T. C., unpublished work.

⁽²²⁾ The longitudinal bond polarizabilities of the C(sp³)-F and C-(sp³)-H bonds are 1.25×10^{-24} and 0.64×10^{-24} cm³, respectively: Le Févre, R. Adv. Phys. Org. Chem. 1965, 3, 50.

⁽²³⁾ Bromilow, J.; Brownlee, R. T. C.; Craik, D. J.; Sadek, M.; Taft,
R. W. J. Org. Chem. 1980, 45, 2429.
(24) (a) "Abnormal" ¹⁹F SCS have been reported^{24b} for some hy-

^{(24) (}a) "Abnormal" ¹⁹F SCS have been reported^{24b} for some hydroxy-substituted *n*-alkylfluorides and their esters in fluorotrichloromethane which are enhanced in trifluoroacetic acid solution. A tentative explanation for the solvent effect was advanced on the basis of the population of possible conformers. (b) Peterson, P. E.; Bopp, R. J.; Sheppard, W. A. J. Am. Chem. Soc. **1969**, *91*, 1251.

Table V.Polar Substituent Parameters (σ_I Values) Derived from the ¹⁹F SCS
of 1-X-4-(p-fluorophenyl)bicyclo[2.2.2]octanes (2)^a

X	cyclohexane ^b	lohexane ^b benzene ^c		DMF^{e}	$F^e CF_3CO_2H^f$	
C,H,	0.15	0.17	0.17	0.16	0.18	
p-NO ₂ C.H.	0.39	0.45	0.33	0.26	0.34	
F	0.39		0.42	0.40	0.52	
Cl	0.43		0.43	0.43	0.44	
Br	0.44		0.44	0.44	0.44	
Ī	0.42		0.42	0.40	0.40	

further, we have extended the ¹⁹F NMR measurements of system 1 in CF₃CO₂H to include a number of dipolar substituents as well as other nitrogen poles (Table I). Unfortunately, due to the unavailability of resonance parameters (σ_R^0 values) for many of the substituents in CF₃CO₂H, a meaningful DSP analysis of the results cannot be effected. However, it can be seen from the data listed in Table I for Br and CH₃, two groups whose substituent parameters are solvent independent,^{25,26} that the susceptibility parameters (ρ_I and ρ_R) for CF₃CO₂H as the solvent must be approximately twice those observed for cyclohexane (Table II). This conclusion is supported by the significant differential between the ¹⁹F SCS for the strongly polar ⁺N(CH₃)₃ group in DCCl₃ and CF₃CO₂H (Table I) which is far too large to be simply accounted for in terms of solvent-induced changes in the substituent constants.

Further exemplification of the significant solvent effect of CF₃CO₂H on the ¹⁹F SCS of system 1 can be obtained by viewing the model system as a 4-substituted 1-fluorobicyclo[2.2.2]octane. This allows new polar susceptibility parameters to be accurately determined for each solvent by dividing the appropriate ¹⁹F SCS for NO₂ in system 1 (Table I) by the *differential* between the appropriate $\sigma_{\rm I}$ values for C₆H₅ and p-NO₂C₆H₄ (Table V). The later values were derived from the ¹⁹F SCS of 1-X-4-(p-fluorophenyl)bicyclo[2.2.2]octanes (2)⁶⁻⁹ in the appropriate



solvent.²⁷ The polar susceptibility parameters determined in this way [$\rho_{\rm I}$ (c-C₆H₁₂) = -3.13; $\rho_{\rm I}$ (C₆H₆) = -2.32; $\rho_{\rm I}$ -(DCCl₃) = -5.25; $\rho_{\rm I}$ (DMF) = -4.70; $\rho_{\rm I}$ (CF₃CO₂H) = -17.56] strikingly demonstrate that field-induced shifts in these systems are substantially enhanced in CF₃CO₂H as the solvent.

The question arises, therefore, whether this marked solvent effect is a manifestation of a bulk medium effect (effective dielectric constant, reaction field effect, etc.) or a specific solute–solvent interaction. We believe the former can be discounted since in system 2, which is also a rodshaped model system and, therefore, sensitive to bulk medium effects,⁶ the polar susceptibility parameter actually decreases significantly in going from c-C₆H₁₂ to CF₃CO₂H (see footnote to Table V). In an attempt to shed light on the latter possibility, we have measured the ¹³C NMR spectra of several members of system 1 [X = NO₂, +NH₃, +NH(CH₃)₂, and +N(CH₃)₃] in CF₃CO₂H as the

Table VI. ¹³C NMR Parameters for the Bridgehead Carbon (C1) of System 1 in CF₃CO₂H

· · ·	•	<i>.</i>	
X	SCS, ppm ^{a, b}	$^{1}J_{\rm CF}$, Hz ^c	
H ^d	0.0	177.7	
NO,	-1.56	179.7	
⁺NH,	-1.21	178.7	
$^{+}NH(CH_{3})_{2}$	-1.56	178.7	
$^{+}N(CH_{3})_{3}$	-1.94	178.7	

^a See footnote *b* of Table III. ^b Accurate to ± 0.10 ppm. ^c Accurate to ± 1.0 Hz. ^d Relative to central peak of internal C₆D₆ (-27.91 ppm).

solvent. The pertinent parameters pertaining to the CF σ bond are listed in Table VI. A most trenchant result is that the enhanced ¹⁹F SCS (Table I) in CF_3CO_2H are clearly accompanied by a concomitant *increase* in the ^{13}C SCS of C1 as well as ${}^{1}J_{CF}$ (Table VI; cf. values for NO₂ with those listed in Table III). This strongly suggests that the exalted ¹⁹F SCS are manifestations of CF σ bond polarization. Hence, we believe that the ¹⁹F SCS of system 1 are markedly enhanced in trifluoroacetic acid solution because of strong hydrogen bonding interactions between the fluorine probe and the solvent. Such interactions have the tendency to increase the effective electronegativity of fluorine with a consequential increase in the p character of the exocyclic orbital of C1.¹⁶ This apparently leads to a marked increase in the longitudinal polarizability of the $C(sp^3)$ -F σ bond and, hence, a concomitant increase in the polar susceptibility parameter (ρ_1) . It should be noted that the proposed hybridization change of the exocyclic orbital of C1 in CF₃CO₂H is supported by the fact that ${}^{1}J_{CF}$ for system 1 (X = H) in CF_3CO_2H (177.7 Hz) is significantly less than that observed in $DCCl_3$ (183.35 Hz).

Further compelling evidence for strong hydrogenbonding interactions with fluorine attached to an sp³-hybridized carbon in trifluoroacetic acid solution is provided by the observed solvent effects on the polar inductive parameters ($\sigma_{\rm I}$ values)²⁸ of the halogens. These values have been determined from the ¹⁹F SCS of system 2²⁷ and are assembled in Table V. Note that in CF₃CO₂H as the solvent there is a significant *increase* in the $\sigma_{\rm I}$ value for fluorine. This stands in striking contrast to the values for the other halogens (Cl, Br, and I), which are apparently insensitive to the nature of the solvent. The increase in $\sigma_{\rm I}$ for fluorine in CF₃CO₂H is readily understood in terms of greater charge separation in the C–F bond as a consequence of strong hydrogen-bonding interactions.

It is of interest to note that the dramatic enhancement of the ¹⁹F SCS of aliphatic fluorides in trifluoroaceic acid solution stands in stark contrast to the situation observed with aryl fluorides.²⁵ For the latter systems, the changes in the ¹⁹F SCS in CF_3CO_2H can be attributed essentially

⁽²⁵⁾ Taft, R. W.; Price, E.; Fox, I. R.; Lewis, I. C.; Andersen, K. K.;
Davis, G. T. J. Am. Chem. Soc. 1963, 85, 709, 3146.
(26) Nelson, G. L.; Levy, G. C.; Cargioli, J. D. J. Am. Chem. Soc. 1972,

⁽²⁶⁾ Nelson, G. L.; Levy, G. C.; Cargioli, J. D. J. Am. Chem. Soc. 1912, 94, 3089.

⁽²⁷⁾ Since solvent effect studies have shown that Br is a "chemically" inert substituent,²⁵ scaling was achieved by setting σ_1 for this substituent equal to 0.44^{10} for each solvent.

^{(28) (}a) The polar inductive parameter (σ_1) provides a measure of the field effect (F) of a substituent^{9,28b} (b) Reynolds, W. F. J. Chem. Soc., Perkin Trans. 2 1980, 985 and references cited therein.

 Table VII.
 "'F SCS" of Benzobicyclo[2.2.2]octen-1-yl

 Fluorides (Systems 3 and 4)

		•	-	•			
		cyclohexane ^b		CF ₃ C	CO ₂ H		
	Х	3	4	3	4		
_	NO,	0.69	0.31	-2.88	-3.51		
	CN	0.09	-0.20	-3.20	-3.82		
	C(CN)	0.08	0.16				
	CÒOĆH,	0.52	0.07	-1.94	-2.55		
	COCH,	0.59	0.00	-2.18	-3.12		
	F	-0.04	0.79	-0.87	-0.57		
	Br	-0.18	0.46	-1.42	-1.12		
	NH.	-0.29	0.73				
	NHĆOCH,	0.04	-0.15	-2.39	-2.39		
	CH.	-0.07	0.11				
	⁺NΗ,	-0.25^{d}	-0.40^{d}	-2.81	-2.56		
	ر.						

^a See footnotes a-c of Table I. ^b X = H (relative to FCCl₃): -172.09 ppm (internal), -170.76 ppm (external). ^c Labile in CF₃CO₂H. ^d Solvent, DMF; counterion, Cl⁻.

to variations in the $\sigma_{\rm I}$ and $\sigma_{\rm R}^0$ values of the substituents.^{25,29} Thus, it appears that strong hydrogen bonding to fluorine in organic fluorides is extremely sensitive to the electronic character of the fluorine center. In this connection, because the phenomena appear to be related, it is worth noting that lanthanide shift reagents complex much more strongly with benzyl fluoride than fluorobenzene.³⁰

Finally, in view of the disclosures above that the ¹⁹F chemical shifts of bicyclo[2.2.2]oct-1-yl fluorides respond sensitively in the *reverse* direction to intramolecular electrostatic field effects, the recently reported ¹⁹F SCS (c-C₆H₁₂ as solvent) of 6- and 7-substituted 1-fluoro-4-methyl-1,2,3,4-tetrahydro-1,4-ethanonaphthalene (3 and 4, respectively)⁵ are of interest since, in general, they are



small and display no regular pattern of reverse substituent behavior (in order to facilitate comparison, these ¹⁹F SCS are reproduced in Table VII). This is exemplified by the fact that the SCS correlate poorly (eq 2 and 3) with sub-

SCS(system 3) =
$$0.37\sigma_{\rm I} + 0.97\sigma_{\rm R}^0$$
 (*n* = 10; SD = 0.26; SD/rms = 73%) (2)

SCS(system 4) =
$$0.34\sigma_{\rm I} - 1.10\sigma_{\rm R}^0$$
 (n =
10; SD = 0.27 ; SD/rms = 68%) (3)

stituent parameters ($\sigma_{\rm I}$ and $\sigma_{\rm R}^{0}$)¹⁰ on using the DSP equation.¹¹ The question arises, therefore, as to why a systematic trend of significant reverse ¹⁹F SCS is not observed in these systems as a result of field-induced polarization of the CF σ bond. Since we have shown that the susceptibility of the CF σ bond to electric field-induced polarization is enhanced in CF₃CO₂H as solvent, we decided to measure the ¹⁹F SCS of systems 3 and 4 in this solvent in an attempt to "unmask" the potential field influences. The results are listed in Table VII together with

Table VIII. $\Delta^{1}J_{CF}$ Values of Systems 3 and 4^{a-c}

	$\Delta^{1}\overline{J}_{C}$		
Х	3	4	
NO ₂	2.8	2.5	
CN C(CN),	2.0 2.9	2.0 2.9	
COOCH ₃	1.3	0.5	
COCH ₃ F	$1.3 \\ 0.5$	$1.3 \\ 0.5$	
Br	1.3	1.3	
NH ₂ NHCOCH.	-0.2	-0.2 1.3	
CH ₃	-0.2	-0.2	

^a Solvent DCCl₃. ^b Accurate to ± 0.7 Hz. ^c Taken from ref 34 (*correction*: ${}^{1}J_{CF} = 193.9$ Hz for 3 and 4, X = NO₂) and Adcock, W; Abeywickrema, A. N. *Aust. J. Chem.* 1980, 33, 181 (${}^{1}J_{CF} = 191.4$ Hz for 3 and 4, X = H).

the previously reported values in cyclohexane. It can be seen (Table VII) that the ¹⁹F SCS in CF_3CO_2H are large compared to those in c-C₆H₁₂, and, moreover, are all negative, indicating reverse substituent behavior. In addition, it can be seen that larger SCS are observed for those substituents whose field and resonance effects reinforce one another (NO₂, CN, COOCH₃, and COCH₃) than for those for which the two effects are opposed (F and Br). Hence, the electric field polarizing the CF σ bond has two components, a primary field [due to the dipole (or pole) associated with the substituent] and a secondary field (due to polar and resonance-induced charges in the benzene ring). The positive identification of an electric field contribution to the ¹⁹F SCS of systems 3 and 4 in CF₃CO₂H indicates that such a contribution, though smaller in magnitude, must also be manifest in the SCS observed in cyclohexane solution. Further support for this conclusion comes from the change in the one-bond carbon-fluorine coupling constants (${}^{1}J_{CF}$; Table VIII) which also characterizes field-induced polarization of the CF σ bond (vide supra). By employing the proportionality constant for the previously defined relationship between ¹⁹F SCS and $\Delta^1 J_{\rm CF}$ in system 1 (Figure 2), estimates of the potential electric field contribution to the ¹⁹F SCS of systems 3 and 4 can be obtained from the $\Delta^1 J_{CF}$ values. Hence, for example, field shifts of approximately -2.0 ppm can be estimated for the most powerful electron-withdrawing substituents $(NO_2 \text{ and } C(CN)_3)$. The fact that these substantial shifts are not observed in cyclohexane as the solvent (see Table VIII) suggests obscuration by an opposing factor. This additional factor, which leads to "normal" shifts, can probably be identified with perturbations of the fluorine π electrons which are coupled to the aromatic π system via the $\pi(cc)$ orbital of the interposing alkyl moiety.³¹

Conclusions

The relationship between ¹⁹F SCS of aliphatic fluorides and electron density on fluorine has been investigated. The results of the empirical analysis reveal that, in the absence of π -electron perturbations about fluorine, the ¹⁹F SCS of aliphatic fluorides reflect primarily changes in fluorine σ -electron density. Most significantly, since a decrease in σ -electron density leads to negative ¹⁹F SCS (upfield shift), this conclusion is not obviously reconciliable

⁽²⁹⁾ Adcock, W.; Alste, J.; Rizvi, S. Q. A.; Aurangzeb, M. J. Am. Chem. Soc. 1976, 98, 1701.

⁽³⁰⁾ Filippo, J. S.; Nuzzo, R. G.; Romano, L. J. J. Org. Chem. 1976, 41, 392.

^{(31) (}a) Adcock, W.; Abeywickrema, A. N. J. Org. Chem. 1982, 47, 779. (b) The perturbation of the fluorine π electrons in benzyl fluorides is not possible in that conformation where the CF bond is perpendicular to the plane of the benzene ring.^{31a}

Table IX. ¹³C Chemical Shifts^{*a*, *b*} for System 1

			chemical shift, ppm							
х	C1	C2	C3	C4	C _p	C _m	C _o	Ci	others	
H NO, CN C(CN) ₃	94.63 (183.8) 94.18 (185.0) 94.16 (185.0) 93.99 (184.4)	31.50 (19.1) 31.22 (20.3) 31.22 (20.3) 31.21 (19.6)	33.55 (10.3) 33.37 (9.2) 33.25 (11.1) 33.41 (10.3)	34.26 (2.9) 34.97 (no) ^c 34.86 (3.7) 34.77 (3.9)	147.84 (3.7) 155.63 (no) ^c 153.42 (3.7) 153.09 (no) ^c	125.36 126.45 126.37 128.01	$128.22 \\123.40 \\132.00 \\126.16$	125.94 146.32 109.93 122.70	118.84 (CN) 29.71 (C),	
COOCH ₃	94.34 (183.8)	31.37 (19.1)	33.40 (9.6)	34.74 (3.7)	153.30 (3.7)	125.52	129.58	127.96	107.77 (CN) 51.95 (CH ₃), 166.97 (CO)	
OCH ₃ F Br NH ₂ N(CH ₃) ₂ CH ₃	94.72 (183.1) 94.52 (183.1) 94.40 (185.0) 94.85 (183.1) 94.81 (183.1) 94.68 (183.1)	$\begin{array}{c} 31.57\ (19.1)\\ 31.46\ (20.3)\\ 31.36\ (20.3)\\ 31.60\ (19.1)\\ 31.63\ (19.1)\\ 31.60\ (19.1)\\ \end{array}$	33.79 (9.6) 33.74 (11.1) 33.45 (9.3) 33.76 (9.6) 33.71 (10.3) 33.66 (9.6)	33.66 (3.7) 33.90 (3.7) 34.09 (no) ^c 33.55 (no) ^c 33.31 (3.7) 33.96 (3.7)	140.02 (4.4) 143.56 (no) ^c 146.89 (3.7) 137.92 (3.7) 135.81 (3.7) 144.94 (3.7)	$126.33 \\ 126.94 \\ 127.30 \\ 126.17 \\ 125.94 \\ 125.29$	$113.56 \\ 114.85 \\ 131.24 \\ 114.99 \\ 112.55 \\ 128.96$	$157.77 \\ 161.22 \\ 119.81 \\ 144.34 \\ 148.86 \\ 135.43$	55.20 (CH ₃) 40.64 (CH ₃) 20.84 (CH ₃)	

^a Chemical shifts obtained in DCCl₃ as the solvent and referenced to SiMe₄. A positive value implies deshielding. ^b Coupling constants (J_{CF}, Hz) are listed in parentheses. ^c Not observed.

with current chemical shift theory.³²

Experimental Section

Synthesis of Compounds. 1-Fluoro-4-phenylbicyclo[2.2.2]octane (1, X = H) as well as its p-bromo, p-nitro, and p-amino derivatives $(1, X = Br, NO_2, and NH_2, respectively)$ were prepared according to procedures previously outlined.⁴ The p-cyano and p-fluoro derivatives (1, X = CN and F) as well as the benzobicyclo[2.2.2]octen-1-yl fluorides (systems 3 and 4) and the other phenylbicyclo[2.2.2]octane derivatives (2, X = F, Cl, Br, I, C₆H₅, and p-NO₂C₆H₄) were available from previous studies.^{45,6,33,34} The new derivatives of 1 were unambiguously characterized by ¹³C NMR (Table IX).

1-Fluoro-4-(p-carboxyphenyl)bicyclo[2.2.2]octane (1, X = COOH). A solution of n-butyllithium (11.9 mL of a 1.3 M solution in hexane, 0.0155 mol) was added dropwise to a stirred solution of the bromo derivative (1, X = Br, 4.0 g, 0.014 mol) in tetrahydrofuran (50 mL) maintained at -20 °C under N₂. After being stirred at the same temperature for a 10-min period, the solution was cooled to -90 °C and a rapid stream of dry carbon dioxide passed in for 30 min. The reaction mixture was then allowed to warm up to room tempeature before quenching with water. The resulting white slurry was shaken with a hot solution (80 °C) of 10% aqueous potassium hydroxide (150 mL) and then extracted with hot toluene $(2 \times 50 \text{ mL})$. The aqueous layer was separated, carefully acidified with concentrated hydrochloric acid, and allowed to cool to room temperature. After the mixture was allowed to stand for 4 h, the white precipitate was collected by vacuum filtration, air-dried, and sublimed. Recrystallization from a hexane-ethanol mixture afforded the acid as colourless leaflets: 2.4g (69%); mp 271-272 °C; mass spectrum, m/e 248 (M⁺). Anal. Calcd for C₁₅H₁₇FO₂: C, 72.56; H, 6.90. Found: C, 72.57; H, 7.23.

A sample of the carboxylic acid (0.5 g) was treated with diazomethane³⁵ to yield the methyl ester, which sublimed as a colorless solid (92% yield). Recrystallization from hexane afforded colorless needles: mp 113-114 °C; mass spectrum, m/e 262 (M⁺). Anal. Calcd for C₁₆H₁₉FO₂: C, 73.26; H, 7.30. Found: C, 73.50; H, 7.60.

1-Fluoro-4-(p-methylphenyl)bicyclo[2.2.2]octane (1, X = CH_3). The carboxylic acid was reduced with borane-methyl sulfide by following the procedure of Lane and co-workers.³⁶ After standard workup, the hydroxymethyl derivative $(1, X = CH_2OH)$ was recrystallized from hexane to afford fine colourless needles: 90% yield; mp 116.5–118 °C; mass spectrum, m/e 234 (M⁺). Anal. Calcd for C₁₅H₁₉FO: C, 76.89; H, 8.17. Found: C, 77.09; H, 8.35.

A sample of the alcohol was hydrogenated (45 psi) in the presence of 5% palladium on carbon in a Parr hydrogenator. A standard workup followed by recrystallization from aqueous ethanol and then hexane afforded colorless needles (75% yield) of the methyl compound (1, $X = CH_3$): mp 101–103 °C; mass spectrum, m/e 218 (M⁺). Anal. Calcd for C₁₅H₁₉F: C, 82.53; H, 8.77. Found: C, 82.78; H, 8.81.

1-Fluoro-4-[p-(tricyanomethyl)phenyl]bicyclo[2.2.2]octane $(1, X = C(CN)_3)$. Treatment of the alcohol $(1, X = CH_2OH)$ with phosphorus tribromide³⁷ afforded the bromomethyl derivative $(1, X = CH_2Br)$. Recrystallization from hexane afforded colorless needles: 78% yield; mp 102-103 °C; mass spectrum, m/e 298, 296 (M⁺). Anal. Calcd for C₁₅H₁₈BrF: C, 60.62; H, 6.10. Found: C, 60.66; H, 6.26.

The bromomethyl derivative was converted into the cyanomethyl compound (1, $X = CH_2CN$) according to a method outlined by Adams et al.³⁸ Recrystallization from hexane afforded colorless needles: 74% yield; mp 103-104 °C; mass spectrum, m/e 243 (M⁺). Anal. Calcd for C₁₆H₁₈FN: C, 78.98; H, 7.46. Found: C, 78.91; H, 7.59.

The nitrile $(1, X = CH_2CN)$ was converted into the tricyanomethyl compound (1, $X = C(CN)_3$) according to a procedure oulined by Williams and co-workers.³⁹ Recrystallization from hexane afforded colorless needles: 30% yield; mp 166-167 °C; mass spectrum, m/e 293 (M⁺). The sample was stored under nitrogen in the dark. Elemental analyses were not sought.

1-Fluoro-4-[p-(dimethylamino)phenyl]bicyclo[2.2.2]octane $(1, X = N(CH_3)_2)$. A mixture of the amine $(1, X = NH_2; 0.55)$ g, 0.0025 mol) and trimethyl phosphate⁴⁰ (0.24 g, 0.0017 mol) was warmed gently and, when the initial exothermic reaction had subsided, was heated at 190 °C for 2 h. After the mixture was cooled to 50 °C, a solution of sodium hydroxide (0.25 g) in water (1 mL) was added, and the resulting mixture was heated under reflux for a further 1 h. A workup in the usual manner afforded a brown solid. Sublimation followed by recrystallization from aqueous ethanol afforded colorless leaflets (0.41 g, 66%) of the dimethylamino derivative (1, X = N(CH₃)₂): mp 137-138 °C; mass spectrum, m/e 247 (M⁺). Anal. Calcd for C₁₆H₂₂FN: C, 77.69; H, 8.96. Found: C, 77.32; H, 8.87.

p-(4-Fluorobicyclo[2.2.2]oct-1-yl)phenyltrimethyl**ammonium Chloride** (1, $X = {}^{+}N(CH_3)_3Cl^{-}$). A mixture of the amine $(1, X = NH_2; 0.88 \text{ g}, 0.004 \text{ mol})$, methyl iodide (3.4 g, 0.024 mol)mol), anhydrous potassium carbonate (2.21 g, 0.016 mol), and dry acetone (5 mL) was heated under reflux for 72 h. A workup in the usual manner afforded the salt $(1, X = {}^{+}N(CH_3)_3I^{-})$ as a white solid (1.2 g, 77%). A portion of this compound (0.78 g, 0.002 mol) was placed on a column of Amberlite IRA-400 resin (25 g) and

⁽³²⁾ Ebraheem, K. A. K.; Webb, G. A. Prog. Nucl. Magn. Reson. Spectrosc. 1977, 11, 149 and references cited therein.

⁽³³⁾ Khor, T. C. Ph.D. Dissertation, The Flinders University of South Australia, 1978.

⁽³⁴⁾ Adcock, W.; Abeywickrema, A. N. Aust. J. Chem. 1981, 34, 1253. (35) Vogel, A. K. "Practical Organic Chemistry"; Longmans: London, 1970; pp 971-3.

⁽³⁶⁾ Lane, C. F.; Myatt, H. L.; Daniels, J.; Hopps, H. B. J. Org. Chem. 1974. 39. 3052.

⁽³⁷⁾ Gay, R. L.; Hauser, C. R. J. Am. Chem. Soc. 1967, 89, 2297. (38) Adams, R.; Thal, A. F. "Organic Syntheses"; Wiley: New York, (39) Williams, J. K.; Martin, E. L.; Sheppard, W. A. J. Org. Chem.

^{1966,} *31*, 919.

⁽⁴⁰⁾ Vogel, A. E. "Practical Organic Chemistry"; Longmans: London, 1970; pp 572-3.

eluted with methanol. Evaporation of the solvent afforded a white solid (1, $X = {}^{+}N(CH_3)_3Cl^-$; 0.48 g, 81%).

1-Fluoro-4-(p-methoxyphenyl)bicyclo[2.2.2]octane (1, X = OCH₃). (p-Methoxyphenyl)acetone was converted to 1methoxy-4-(p-methoxyphenyl)bicyclo[2.2.2]octan-3-one (a sublimed sample had a melting point of 89.5-91.5 °C) according to procedures previously outlined^{6,33} for the synthesis of 1-methoxy-4-phenylbicyclo[2.2.2]octan-3-one from phenylacetone. By use of the general procedure of Aquila,⁴¹ a solution of the ketone (52.0 g, 0.2 mol) and hydrazine hydrate (36.0 g, 0.72 mol) in triethylene glycol (160 mL) was heated under an atmosphere of nitrogen for 2 h at 100 °C. The temperature was then gradually raised to 165 °C during a 15-min period, and then the solution was allowed to cool to 50 °C. Meanwhile, a separate solution of potassium hydroxide (35.8 g, 0.64 mol) in triethylene glycol (100 mL) was also heated to 165 °C and allowed to cool to 50 °C. The two solutions were mixed and gradually heated to 185 °C with stirring under a nitrogen atmosphere, while the distillate was collected. After 4 h at this temperature, the mixture was cooled and poured on to a slurry of ice and water. After combination with the distillate, the solution was neutralized with concentrated hydrochloric acid and extracted with ether $(3 \times 250 \text{ mL})$. A standard workup followed by sublimation afforded 1-methoxy-4-(p-methoxyphenyl)bicyclo[2.2.2]octane as a colorless solid: 43.3 g (88%); mp 63-68 °C. A sample was recrystallized from aqueous methanol to afford colorless leaflets, mp 71-73 °C. Anal. Calcd for C₁₆H₂₂O₂: C, 78.01; H, 9.00. Found: C, 78.23; H, 8.95.

A portion of the crude compound was converted, via the acetate (mp 107–109 °C), to 1-hydroxy-4-(*p*-methoxyphenyl)bicyclo-[2.2.2]octane (mp 152–154 °C) by established procedures previously outlined.^{6,33} Recrystallization from a hexane/ethanol mixture afforded colorless needles, mp 158–158.5 °C. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.81; H, 8.88.

A mixture of 1-hydroxy-4-(p-methoxyphenyl)bicyclo[2.2.2]octane (1.16 g, 0.005 mol) and anhydrous hydrogen fluoride/ pyridine reagent^{4,42} (10 mL) was stirred for 48 h at room temperature. The resulting white slurry was poured onto ice and the solid collected by filtration. A VPC analysis of the crude dried product indicated the presence of a significant amount of the starting alcohol (10–15%). The crude product was chromatographed on alumina with pentane as the eluent. A pale yellow solid was obtained which afforded the fluoro derivative (1, X = OCH₃) as colorless plates (0.56 g, 48%) after sublimation and recrystallization from aqueous ethanol and then hexane: mp 86–87 °C; mass spectrum, m/e 234 (M⁺). Anal. Calcd for C₁₅H₁₉FO: C, 76.89; H, 8.17. Found: C, 77.19; H, 8.27.

(41) Aquila, H. Justus Liebigs Ann. Chem. 1969, 721, 220.
(42) Olah, G. A.; Nojima, M.; Kerekes, I. Synthesis 1973, 786.

General Information. Mass spectra were obtained on an AEI MS30 spectrometer using an ionizing energy of 70 eV. Vaporphase chromatographic analyses were performed on a Varian 1740 gas chromatograph with a 10-ft column of 5% SE-30 on 100/120 Chromosorb W. All melting points are uncorrected.

NMR Spectra. The broad-band proton-decoupled ¹³C NMR spectra were recorded in the pulse Fourier transform mode on a JEOL FX-90Q spectrometer operating at 22.53 MHz. The probe temperature was 295 ± 2 K. The data listed in Tables VI and IX were obtained from spectra recorded on CF₃CO₂H and DCCl₃ solutions (0.3–0.4 M) in 5-mm tubes with Me₄Si as an internal reference (spectral width 4000 Hz, 16K/8K data points, minimum digital resolution of 0.02 ppm). Those listed in Table III were measured on DCCl₃ solutions with the central peak of DCCl₃ as an internal reference (spectral width 1000 Hz, 16K/8K data points, minimum digital resolution of 0.12 Hz).

The ¹⁹F NMR spectral data listed in Tables I, V, and VII were obtained under proton-decoupled conditions in the pulse Fourier transform mode with a JEOL FX-90Q spectrometer operating at 84.26 MHz. A spectral width of 2000 Hz was used, and the data were collected into 8K/4K data points, giving a resolution of better than 0.01 ppm. Each sample consisted of a mixture of the unsubstituted (X = H, 1-2 mg) and substituted (1-2 mg) compounds dissolved in 0.5 mL of the appropriate solvent.

¹H NMR spectra were measured with a Varian A60 spectrometer.

Registry No. 1 (X = COOH), 81688-93-9; 1 (X = Br), 60526-64-9; 1 (X = COOCH₃), 81688-94-0; 1 (X = CH₂OH), 81688-95-1; 1 (X = CH_3), 81688-96-2; 1 (X = CH_2Br), 81688-97-3; 1 (X = CH_2CN), 81688-98-4; 1 (X = C(CN)₃), 81688-99-5; 1 (X = NH₂), 60526-67-2; 1 (X = N(CH₃)₂), 81689-00-1; 1 (X = $+N(CH_3)_3$) I⁻, 81689-01-2; 1 (X $(CH_3)_3$ Cl⁻, 81689-02-3; 1 (X = OCH₃), 81689-03-4; 1 (X = NO_2 , 60526-66-1; 1 (X = CN), 60526-65-0; 1 (X = F), 60526-63-8; 1 $(X = {}^{+}NH_3)$, 81689-04-5; 1 $(X = {}^{+}NH(CH_3)_2)$, 81689-05-6; 1 $(X = {}^{+}NH_3)$ H), 22947-58-6; 2 (X = H), 68756-28-5; 2 (X = C_6H_5), 68756-32-1; 2 $(X = p - NO_2C_6H_4)$, 68756-36-5; 2 (X = F), 60526-63-8; 2 (X = Cl), 61541-33-1; 2 (X = Br), 61541-34-2; 2 (X = I), 61541-35-3; 3 (X = NO₂), 72046-22-1; 3 (X = CN), 72046-23-2; 3 (X = $C(CN)_3$), 79963-25-0; 3 (X = COOCH₃), 72046-25-4; 3 (X = COCH₃), 72046-24-3; 3 (X = F), 72242-21-8; 3 (X = Br), 72046-26-5; 3 (X = NH₂), 72046-29-8; 3 (X = NHCOCH₃), 72046-28-7; 3 (X = CH₃), 72046-27-6; 3 (X = $^{+}NH_3$) Cl⁻, 81689-06-7; 3 (X = H), 74308-36-4; 4 (X = NO₂), 72046-30-1; 4 (X = CN), 72046-31-2; 4 (X = C(CN)₃), 79963-24-9; 4 $(X = COOCH_3)$, 72046-33-4; 4 (X = COCH₃), 72046-32-3; 4 (X = F), 72046-34-5; 4 (X = Br), 72046-35-6; 4 (X = NH_2), 72046-38-9; 4 (X = NHCOCH₃), 72046-37-8; 4 (X = CH₃), 72046-36-7; 4 (X = +NH₃) Cl⁻, 81689-07-8; (p-methoxyphenyl)acetone, 122-84-9; 1-methoxy-4-(p-methoxyphenyl)bicyclo[2.2.2]octan-3-one, 81689-08-9; 1-methoxy-4-(p-methoxyphenyl)bicyclo[2.2.2]octane, 81689-09-0; 1-acetyloxy-4-(p-methoxyphenyl)bicyclo[2.2.2]octane, 81689-10-3; 1hydroxy-4-(p-methoxyphenyl)bicyclo[2.2.2]octane, 81689-11-4.

Synthesis of 4-Substituted Bicyclo[2.2.2]oct-1-yl Fluorides

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The main details of the synthesis of a series of 4-substituted (X) bicyclo[2.2.2]oct-1-yl fluorides (1), which were required for substituent effect studies, are presented. The synthesis of most of these compounds [1, X = NO₂, CN, CONH₂, COCH₃, CHO, OCH₃, OCOCH₃, OH, F, Cl, Br, I, NH₂, N(CH₃)₂, NHCOCH₃, C₂H₅, *i*-C₃H₇, and Sn(CH₃)₃] has been accomplished from 4-fluorobicyclo[2.2.2]octane-1-carboxylic acid (1, X = COOH) in a straightforward fashion using fairly standard functionalization procedures. The key new precursor compound (1, X = COOH) was prepared from 4-methoxybicyclo[2.2.2]octane-1-carboxylic acid (7) which, in turn, was constructed from 4-acetyl-4-(ethoxycarbonyl)pimelic acid (2) in good yield. 1-tert-Butyl-4-fluorobicyclo[2.2.2]octane (1, X = C(CH₃)₃) was obtained from 7 via 1-tert-butyl-4-methoxybicyclo[2.2.2]octane. 1-Fluorobicyclo[2.2.2]octane (1, X = C₆H₅) were prepared by literature procedures.

In this paper we describe the syntheses and physical properties of a large number of 4-substituted bicyclo[2.2.2]oct-1-yl fluorides (1), most of which were previously unknown, which were required for the reasons indicated