

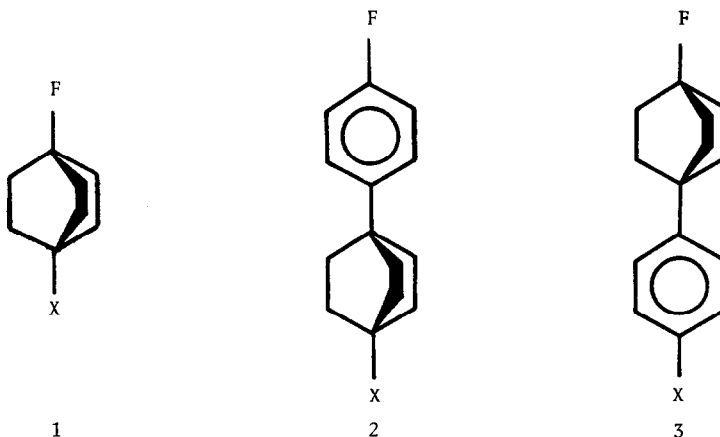
^{19}F SUBSTITUENT CHEMICAL SHIFTS (SCS) OF 4-SUBSTITUTED BICYCLO[2.2.2]OCT-1-YL FLUORIDES

William Adcock* and Anil N. Abeywickrema

School of Physical Sciences, The Flinders University of
South Australia, Bedford Park, S.A., 5042, AUSTRALIA.

Summary: The results of a linear multiple regression analysis indicate that the ^{19}F SCS of 4-substituted bicyclo[2.2.2]oct-1-yl fluorides are essentially a manifestation of electric field and electronegativity effects.

Herein we report ^{19}F substituent chemical shifts (SCS) of 4-substituted bicyclo[2.2.2]oct-1-yl fluorides (1) for a large number of substituents of diverse electronic type. The results are of



interest in connection with improving our understanding of two distinct phenomena : (1) substituent-induced ^{19}F chemical shifts which are in the opposite direction (reverse substituent dependence) to expectations based on the electron density parameter dominating the decisive paramagnetic contribution to ^{19}F chemical shifts^{1,2}. A previous study³ of system 1, which was limited to only two substituents ($X=\text{F}$ and COOEt), revealed that this model displays this unusual phenomenon; (2) the possibility of conjugative electronic transmission mechanisms in 1,4-disubstituted bicyclo[2.2.2]octyl derivatives^{4,5,6}. A molecular orbital description of this skeletal framework indicates that valence orbitals can be constructed with symmetry appropriate to the coupling of either π or σ orbitals of the substituent and probe site^{4,5,7}.

We have explored the relationship between the ^{19}F SCS of 1 listed in Table 1 and various substituent parameters (σ_{I} , ν , and $\sigma_{\text{R}}^{\text{O}}$) which are known to characterize electric field⁸, electronegativity^{8,9}, and resonance effects (π symmetry)¹⁰ respectively. In order to avoid likely solvent discrepancies in the known σ_{I} values of substituents and, in addition, to avoid using statistically refined values¹⁰ which may not be strictly applicable to model systems where the substituent is directly attached to an sp^3 hybridized carbon atom, we have employed a new σ_{I} scale for cyclohexane as solvent which were defined

Table 1

¹⁹F Substituent Chemical Shifts (SCS)^{a,b,c} of 4-Substituted Bicyclo[2.2.2]oct-1-yl Fluorides

Substituent (X)	SCS	Substituent (X)	SCS	Substituent (X)	SCS
NO ₂	-8.39	F	-8.90	NH ₂	-6.60
CN	-4.15	Cl	-6.97	N(CH ₃) ₂	-4.66
CF ₃	-5.08	Br	-5.94	NH.COCH ₃	-4.66
CHO	-3.09	I	-3.35	C ₆ H ₅	-3.37
COCH ₃	-4.15	OH	-8.06	CH ₃	-3.81
COOH	-4.75	OCH ₃	-6.40	Sn(CH ₃) ₃	3.67
COOCH ₃	-4.38	OCOCH ₃	-6.08		

a. Chemical shifts (ppm) relative to parent hydrocarbon (1, X=H) as internal standard. Accurate to ± 0.01 ppm. b. A positive sign implies deshielding. c. Solvent, cyclohexane.

Table 2

Results of Correlative Analysis^a

Independent Variables	ρ_I^b	ρ_I^b	ρ_R^b	c^c	r^d	S.E. ^e	F ^f	F _I ^f	F _I ^f	F _R ^f	n ^g
σ_I	-6.81			-3.00	0.457	2.43	4.76 ^h	4.76 ^h			20
	± 3.12										
σ_I, σ_R^o	-10.96		7.70	-0.77	0.750	1.86	10.96 ⁱ	17.28 ⁱ		13.78 ^j	20
	± 2.64		± 2.07								
$\sigma_I, \Delta I$	-3.56	-6.40		-0.72	0.880	1.33	29.29 ^k	3.98 ^l	42.79 ^k		20
	± 1.79	± 0.98									
$\sigma_I, \Delta I$	-6.15	-6.75		0.18	0.955	0.93	67.12 ^k	15.59 ^j	92.43 ^k		16 ^o
	± 1.56	± 0.70									
$\sigma_I, \Delta I, \sigma_R^o$	-7.39	-6.09	1.48	0.41	0.958	0.94	44.86 ^k	13.46 ^m	38.65 ^k	0.94 ⁿ	16 ^o
	± 2.01	± 0.98	± 1.52								

a. General form of correlation equation: $SCS = \rho_I \sigma_I + \rho_I \Delta I + \rho_R \sigma_R^o + c$. b. Regression coefficients for individual terms \pm standard error of regression coefficient. c. Intercept. d. Multiple correlation coefficient. e. Standard error of estimate. f. F test of variance for overall correlation and individual regression coefficients. Superscripts indicate confidence level (CL) of test. g. Number of data points in correlation. h. 95.0% CL. i. 99.9% CL. j. 99.8% CL. k. 99.99% CL. l. 90.0% CL. m. 99.5% CL. n. 60.0% CL. o. SCS of CN, CF₃, Cl, and CH₃ omitted from data set.

from the appropriate ^{19}F SCS of 1-X-4-(p-fluorophenyl)bicyclo[2.2.2]octanes (2)^{11,12}. It can be seen from the results of the correlative analysis set out in Table 2 that a combination of σ_{I} and ι gives the best fit of all the data (n=20). This particular correlation is significant at the 99.99% confidence level with a value of r^2 equal to 0.775. Thus, the correlation accounts for about 78% of the variations. Examination of the calculated SCS showed that a number of groups (CN, CF_3 , Cl and CH_3) deviate considerably from the experimental values. It is possible that the group electronegativities of these substituents maybe inadequately defined by their respective ι values and, hence, responsible for the deviations. Interestingly, other workers have suggested that the group electronegativity of CF_3 appears to be over-estimated by its ι value¹³. Whatever the reason, exclusion of these substituents gave a good correlation ($r=0.955$) of the SCS against a combination of σ_{I} and ι . The correlation is again at the 99.99% confidence level but now 91% ($r^2=0.912$) of the variations are accounted for. Moreover, the intercept is small, hence, the correlation satisfactorily predicts the SCS for the parent compound (X=H, SCS=0.00). When all three parameters (σ_{I} , ι , and $\sigma_{\text{R}}^{\text{O}}$) are included in the correlation, there is no statistically significant improvement in the fit due to the addition of $\sigma_{\text{R}}^{\text{O}}$ (note that the F test of the variance actually decreases)¹⁴.

Several significant conclusions maybe drawn from the statistical analysis. First, the ^{19}F SCS of 1 are determined predominantly by a blend of electric field and electronegativity effects. Furthermore, bearing in mind that $\Delta\iota$ values are numerically larger than the corresponding σ_{I} parameters, the relative magnitude of the susceptibility parameters (Table 2, ρ values) clearly establish the latter effect as the major factor. Compelling support for the validity of the statistical dissection is provided by an independent measure of ρ_{I} (-7.56 ± 0.40) for 1 from the ^{19}F SCS of 1-fluoro-4-para-substituted phenylbicyclo[2.2.2]octanes (3)¹⁵. Note that this value compares favourably with that listed in Table 2 ($\rho_{\text{I}} = -6.15 \pm 1.56$). Second, although theoretically possible, resonance effects involving orbitals of π symmetry appear not to be transmitted through the bicyclo[2.2.2]octyl skeletal framework. Third, a corollary of the previous conclusion is that the ^{19}F SCS of 1 are a manifestation of the σ electrons in the $2p_y$ orbital of fluorine being perturbed but not the π electrons in the $2p_x$ and $2p_z$ orbitals¹⁶. Interestingly, a similar perturbation of the local electronic environment of fluorine in meta- and para-substituted benzylfluorides also leads to large reverse ^{19}F SCS¹.

The origin of the electronegativity effect upon the ^{19}F chemical shifts of 1 is currently being probed by ^{13}C nmr. These details, together with the syntheses of 1, will be presented in a main paper.

References and Notes

1. W. Adcock and A.N. Abeywickrema, Tetrahedron Lett., 1809 (1979) and references therein.
2. R.T.C. Brownlee and D.J. Craik, Tetrahedron Lett., 1681 (1980) and references therein.
3. G.L. Anderson and L.M. Stock, J.Am.Chem.Soc., 91, 6804 (1969).
4. R. Hoffmann, Acc.Chem.Res., 4, 1 (1971); R. Gleiter, Angew.Chem.Internat.Edit., 13, 696 (1974).
5. R.B. Davidson and C.R. Williams, J.Am.Chem.Soc., 100, 2017 (1978) and references therein.
6. R.D. Topsom, Prog.Phys.Org.Chem., 12, 1 (1976).
7. (a) ^{19}F chemical shifts of arylfluorides are well known to be very sensitive to substituent-induced π electron perturbations^{7b}. Hence, given that the nature of the CF bond of alkylfluorides is believed to be similar (different only in degree of the contributing σ and π components)^{7c},

- the fluorine nucleus seems a most appropriate probe to test for this possible phenomenon.
- (b) W.J. Hehre, R.W. Taft, and R.D. Topsom, Prog.Phys.Org.Chem., 12, 159 (1976); (c) K.B. Wiberg, J.Am.Chem.Soc., 101, 2204 (1979); 102, 1229 (1980).
8. W.F. Reynolds, J.Chem.Soc., Perkin 2, 985 (1980) and references therein.
 9. N. Inamoto and S. Masuda, Tetrahedron Lett., 3287 (1977).
 10. J. Bromilow, R.T.C. Brownlee, V.O. Lopez, and R.W. Taft, J.Org.Chem., 44, 4766 (1979) and references therein.
 11. W. Adcock and T.C. Khor, J.Am.Chem.Soc., 100, 7799 (1978); W. Adcock and T.C. Khor, J.Org.Chem., 43, 1272 (1978); W. Adcock and G.L. Aldous, J.Organomet.Chem., (1980). In press; W. Adcock and A.N. Abeywickrema. Unpublished results.
 12. The σ_I parameters derived from the ^{19}F SCS ($\text{c-C}_6\text{H}_{12}$) of 2^{11} were scaled by setting σ_I for Br equal to 0.44^{10} .
 13. N. Inamoto, S. Masuda, K. Tori, and Y. Yoshimura, Tetrahedron Lett., 4547 (1978).
 14. A larger value of F implies a better overall correlation or a greater significance of an individual regression coefficient.
 15. (a) W. Adcock and T.C. Khor, J.Org.Chem., 42, 218 (1977) (b) The basis set of substituents (NO_2 , CN, $\text{C}(\text{CN})_3$, COOCH_3 , F, Br, OCH_3 , CH_3 , NH_2 , and $\text{N}(\text{CH}_3)_2$) for 3 was enlarged over that previously reported^{15a} in order to ensure a meaningful dissection of electronic effects by dual substituent parameter analysis (DSP equation)¹⁰. A good fit of the ^{19}F SCS ($\text{c-C}_6\text{H}_{12}$) was achieved ($\text{SCS} = -0.97\sigma_I - 0.64\sigma_R^0$; $n=10$; $\text{SD/RMS} = 12\%$; $\text{SD} = 0.06$) (c) Electric field effects for several substituents (NO_2 , CN, F, and Br) in 3 were estimated from $\rho_I\sigma_I$ for the DSP correlation. These values were then employed to calculate A for the Buckingham equation^{15d} ($\text{SCS} = \text{AE}_z$) by classical electrostatic calculations¹¹ (A (average) = -59.4×10^{-12} esu). A correlation of calculated SCS (AE_z) for 1 ($X=\text{NO}_2$, CN, F, Cl, Br and I) versus σ_I yields ρ_I (7.56 ± 0.40) for this system ($r=0.974$, $> 99.9\%$ CL). Because the $\rho_I\sigma_I$ term from the DSP correlation for 3 also manifests field-induced π polarization of the aromatic ring, the calculated ρ_I value for 1 is undoubtedly an overestimation. (d) A.D. Buckingham, Can.J.Chem., 38, 300 (1960).
 16. (a) It is noteworthy that CNDO/2 calculations^{16b} of some derivatives of 1 indicate that although substituents perturb the charge density of the $2p_y$ (σ) orbital, the charge density for both the $2p_x$ and $2p_z$ orbitals remains unchanged. (b) R.T.C. Brownlee and R.W. Taft, J.Am.Chem.Soc., 92, 7007 (1970).

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