

ambiguous identification of the true global minimum, practical considerations rule out such an approach in systems as complex as those studied here.

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- (32) The structure of tetracyclohexylethane, though gauche like **3**, is quite dissimilar in other respects (S. G. Baxter, unpublished results; Professor C. Rüchardt, personal communication).
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Substituent Effects in the Phenylbicyclo[2.2.2]octane Ring System by ^{19}F and ^{13}C NMR. The Nature of Aryl ^{19}F NMR Polar Field Effects¹

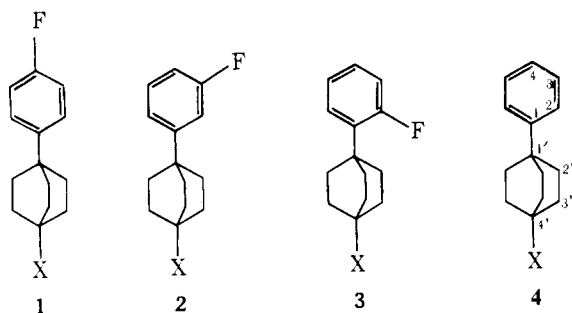
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Abstract: A number of bridgehead-substituted phenylbicyclo[2.2.2]octyl and (*o*-, *m*-, and *p*-) fluorophenylbicyclo[2.2.2]octyl derivatives have been synthesized and their ^{13}C and ^{19}F NMR spectra have been recorded. The substituent chemical shifts (SCS) of these stereochemically well-defined model systems permit, for the first time, a quantitative assessment of aryl NMR polar field effects in the complete absence of other electronic mechanisms. The results clearly establish field-induced π polarization (F_π) as an important mechanism of transmission of polar substituent effects. The relative magnitude of this effect at the meta and para positions of monosubstituted benzene derivatives is quantitatively defined. The dual nature of ^{19}F NMR polar field effects is confirmed and the two components (direct field (F_D) and field-induced π polarization (F_π)) determining this phenomenon are dissected. This enables the coefficient (A) of the Buckingham equation for linear electric field effects on $\text{C}_{\text{sp}^2}\text{-F}$ bonds to be calculated as well as the proportionality constant relating F_π determined ^{19}F and ^{13}C SCS. Unequivocal experimental evidence for reversed ^{19}F NMR polar field effects is also presented. Significant polar solvent shifts in the model systems are discussed.

Introduction

Although the difference of opinion^{2,3} concerning the nature of aryl ^{19}F NMR polar field effects has now been largely reconciled,^{4,5} the quantitative evaluation of the relative magnitude of the components (direct field (F_D) and field-induced π polarization (F_π) effects)⁶ determining this phenomenon is still a subject for deliberation. In order to shed further light on this question we decided to study the ^{19}F NMR spectra of three new model systems (1-X-4-(*p*-, *m*-, and *o*-fluorophenyl)bicyclo[2.2.2]octanes (**1**, **2**, and **3**, respectively)) in conjunction



with a ^{13}C NMR study of 1-X-4-phenylbicyclo[2.2.2]octanes (**4**).

The phenylbicyclo[2.2.2]octyl skeletal framework seemed eminently suited for this purpose for several reasons: (1) the skeletal framework allows the construction of stereochemically well-defined model systems in which the orientation (angle/distance factors) of the substituent relative to the probe center(s) is fixed; (2) the substituent (X) is effectively insulated

from the phenyl ring; thus a definitive experimental estimate of the effects of remote polar groups on aryl chemical shifts (^{19}F and ^{13}C) may be obtained in the complete absence of localized π -electron interactions (mesomeric and inductomesomeric effects); (3) the large number of bonds intervening between the probe (^{19}F or ^{13}C) and the substituent (X) ensures that σ induction is inoperative⁷; (4) substituent-induced structural changes and steric effects should be avoided; (5) no critical and tenuous assumptions regarding the relative sensitivity of sp^2 - and sp^3 -carbon-bound fluorine nuclei to electronic influences need be made when the data are compared with those from fully conjugated aryl fluorides;⁸ (6) an estimate of the relative magnitude of field-induced π polarization effects (F_π)^{4,5} at carbon centers C-4 and C-3 in system **4** by ^{13}C NMR, together with an estimate of the relative magnitude of ^{19}F NMR polar field effects ($F_D + F_\pi$) in systems **1** and **2**, may provide a reasonably quantitative disentanglement of direct field effects (F_D) in these systems. Hence A in the Buckingham equation ($\text{SCS} = AE_z$ where E_z is the direct field component along the CF bond)⁹ for linear electric field effects may then be unambiguously evaluated; (7) a consideration of orientational factors suggests that reversed ^{19}F NMR polar field effects should be observed in system **3**, a phenomenon previously sought after in other model aryl fluorides but to no avail;^{7b} (8) since the substituent dipole is aligned along the major axis of the ring system, the definition of the relative magnitude of F_π effects at C-4 and C-3 in system **4** should bear directly on similar polarization influences at the para and meta carbon positions of monosubstituted benzene derivatives.¹⁰ This is important since, although the latter system has been

Table I. Physical and Analytical Properties of the Phenylbicyclo[2.2.2]octane Systems (1, 2, 3, and 4)^a

system, X	mp, °C	anal. found (calcd), %		precursor
		C	H	
1, OMe	53.5–55.5	77.2 (76.9)	8.18 (8.17)	
2, OMe	46.5–47.5	76.9 (76.9)	8.09 (8.17)	
3, OMe	77.9–79.5	77.1 (76.9)	7.90 (8.17)	
4, OMe	38.5–39.5 (lit. ²² 37.5–38.5)			
1, OAc	108.5–110	73.6 (73.3)	7.37 (7.30)	OMe ^c
2, OAc	88.5–89.5	73.4 (73.3)	7.42 (7.30)	OMe ^c
3, OAc	107–108	73.1 (73.3)	7.14 (7.30)	OMe ^c
4, OAc	90–92	78.6 (78.7)	8.34 (8.25)	OMe ^c
1, OH	127–127.5	76.5 (76.3)	8.06 (7.78)	OAc ^d
2, OH	100.5–101.5	76.0 (76.3)	7.52 (7.78)	OAc ^d
3, OH	134.5–135.5	76.6 (76.3)	7.65 (7.78)	OAc ^d
4, OH	122.5–126 (lit. ²⁰ 122–123)			
2, F	65–68	75.8 (75.7)	7.18 (7.26)	OH ^e
3, F	140.5–141.5	75.9 (75.7)	7.40 (7.26)	OH ^e
1, Cl	109.5–111.5	70.7 (70.4)	6.78 (6.76)	OMe ^f
2, Cl	65–66.5	69.8 (70.4)	6.94 (6.76)	OMe ^f
3, Cl	65.5–71.5	70.9 (70.4)	6.76 (6.76)	OMe ^f
4, Cl	88.5–89.5 (lit. ²² 88.5–89.5)			
1, Br	115–118	59.0 (59.4)	5.63 (5.70)	OMe ²²
2, Br	99–99.5	59.7 (59.4)	5.58 (5.70)	OMe ²²
3, Br	78–78.5	59.5 (59.4)	5.80 (5.70)	OMe ²²
4, Br	108–108.5 (lit. ²⁰ 109–110)			OMe ²²
1, I	139.5–142	51.3 (50.9)	5.14 (4.88)	OMe ^g /OAc ^h
3, I	96–96.5	51.0 (50.9)	5.04 (4.88)	OMe ^g /OAc ^h
4, I	126–126.5	54.0 (53.9)	5.12 (5.49)	OMe ^g /OAc ^h
1, NHAc	193.5–194 (lit. ^b 189–191)	73.7 (73.5)	7.81 (7.71)	OH ⁱ
2, NHAc	211.5–215	73.3 (73.5)	7.48 (7.71)	OH ⁱ
3, NHAc	203.5–209.5 dec	73.5 (73.5)	7.53 (7.71)	OH ⁱ
4, NHAc	235–236.5 (lit. ^b 231.5–233)			OH ⁱ
1, NH ₂	82.5–83.5	76.9 (76.7)	8.10 (8.27)	NHAc ^j
2, NH ₂	73.5–77.5	76.3 (76.7)	7.62 (8.27)	NHAc ^j
4, NH ₂	62.5–64	83.0 (83.5)	9.20 (9.51)	NHAc ^j
1, NO ₂	107–108.5	67.0 (67.5)	6.85 (6.47)	NH ₂ ^k
2, NO ₂	104.5–107.5	67.2 (67.5)	6.34 (6.47)	NH ₂ ^k
4, NO ₂	105.5–107	73.0 (72.7)	7.38 (7.41)	NH ₂ ^k
1, CN	165.5–166.5	78.7 (78.6)	7.27 (7.03)	Br ^{20,21}
2, CN	110–110.5	78.8 (78.6)	7.19 (7.03)	Br ^{20,21}
4, CN	144.5–145 (lit. ²¹ 142–143)			Br ^{20,21}
2, NC	115.5–119.5	78.6 (78.6)	7.13 (7.03)	Br ^{20,21}
1, COOH	260–266	72.7 (72.6)	6.97 (6.90)	I ^l
4, COOH	258–274 dec (lit. ²¹ 289–291)			I ^l
1, COOEt	59.5–60.5	74.3 (73.9)	7.71 (7.66)	COOH ^m
4, COOEt	67.5–68.5	78.8 (79.0)	8.43 (8.58)	COOH ^m
1, COCH ₃	60.5–64.5	78.0 (78.0)	7.77 (7.77)	COOH ⁿ
4, COCH ₃	75.5–79.5	83.7 (84.2)	8.88 (8.83)	COOH ⁿ
3, Me	bp 120 °C (1 mm) <i>n</i> ^{22D} 1.5243	82.5 (82.5)	8.77 (8.77)	Br ¹⁶
1, CH ₂ OH	96.5–97.5	77.3 (76.9)	8.34 (8.17)	COOH ^o
1, CH ₂ Cl	76.5–78.5	71.6 (71.3)	7.27 (7.18)	CH ₂ OH ^p
1, CH ₂ CN	89.5–92.5	78.9 (79.0)	7.62 (7.46)	CH ₂ Cl ^q
1, SnMe ₃	82–83	55.6 (55.6)	7.11 (6.86)	Br ^r
3, SnMe ₃	62.5–65	55.4 (55.6)	6.91 (6.86)	Br ^r
4, SnMe ₃	71.5–72	58.3 (58.5)	7.61 (7.51)	Br ^r
1, H	58.5–59	82.0 (82.3)	8.34 (8.39)	Br ^{s,16}
2, H	45–46.5	82.3 (82.3)	8.45 (8.39)	Br ^{s,16}
3, H	48–51.5	82.0 (82.3)	8.46 (8.39)	Br ^{s,16}
4, H	80.5–83.5 (lit. ²¹ 78–80)			Br ²¹

^a A number of compounds (1, X = *i*-Bu, CHO, COBu-*t*, CONMe₂, C₆H₅, *p*-NO₂C₆H₄; 3, X = NH₂, NO₂; 4, X = ⁺NMe₃Cl⁻) were not purified for elemental analysis; however, their ¹H NMR and mass spectra were in accord with the assigned structures. These compounds were prepared from the appropriate precursors (Br, CH₂OH, COOH, COOH, Br, and C₆H₅, respectively) by known procedures. ^b E. I. du Pont de Nemours and Co., Bgd. Patent 664 913; *Chem. Abstr.*, **65**, 15268g (1966). ^c Ac₂O/BF₃·Et₂O: Z. Suzuki and K. Morita, *J. Org. Chem.*,

Table I (Continued)

32, 31 (1967). ^d NaOMe/MeOH: A. I. Vogel, "Practical Organic Chemistry", 3rd ed., Longman, London, 1956, p 249. ^e HF/C₆H₅N: G. Olah, M. Nojima, and I. Kerekes, *Synthesis*, 786 (1973). ^f AcCl/SnCl₄: Z. Suzuki and K. Morita, *J. Org. Chem.*, **32**, 31 (1967). ^g Ac₂O/55% aqueous HI: this study. ^h Me₂Si: T. L. Ho and G. Olah, *Angew. Chem., Int. Ed. Engl.*, **15**, 774 (1976); M. E. Jung and M. A. Lyster, *J. Am. Chem. Soc.*, **99**, 968 (1977). ⁱ MeCN/H₂SO₄: E. I. du Pont de Nemours and Co., Belgian Patent 664 913; *Chem. Abstr.*, **65**, 15268g (1966). ^j C₆H₅OH/48% aqueous HBr: H. R. Snyder and R. E. Heckert, *J. Am. Chem. Soc.*, **74**, 2006 (1952). ^k KMnO₄: N. Kornblum and W. J. Jones, *Org. Synth.*, **43**, 87 (1963). ^l *t*-BuLi/CO₂/H⁺: K. B. Wiberg, W. E. Pratt, and W. F. Bailey, *J. Am. Chem. Soc.*, **99**, 2297 (1977). ^m HMPA/NaOH/EtI: J. E. Shaw, D. C. Kunerth, and J. J. Sherry, *Tetrahedron Lett.*, 689 (1973). ⁿ MeLi: "Organic Reactions", Vol. 18, Wiley, New York, N.Y., 1970, Chapter 1. ^o BH₃/SMe₂: C. Lane, *Aldrichimica Acta*, **8**, 20 (1975). ^p Ph₃P/CCl₄: D. Brett, I. M. Downie, and J. B. Lee, *J. Org. Chem.*, **32**, 855 (1967). ^q NaCN/Me₂SO: L. Friedman and H. Shechter, *ibid.*, **25**, 877 (1960). ^r Me₃SnLi: C. Tamborski, F. E. Ford, and E. J. Sološki, *ibid.*, **28**, 237 (1963); G. S. Koerner, M. L. Hall, and T. G. Traylor, *J. Am. Chem. Soc.*, **94**, 7205 (1972). ^s R₃SnH/*hv*: H. G. Kuivila, *Synthesis*, 499 (1970); T. Y. Luh and L. M. Stock, *J. Org. Chem.*, **42**, 2790 (1977).

employed extensively as a model substrate for substituent effect studies, polarization of the phenyl ring as a result of polar influences remains ill defined owing to the difficulty of separating polar and mesomeric effects in unsaturated systems where the substituent is directly attached.

Herein we report the results of our study.

Experimental Section

General. Melting and boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer 237 spectrometer, whereas mass spectra were obtained with an AEI MS30 instrument generally operating at an ionizing potential of 70 eV.

Analytical vapor phase chromatographic data were obtained with a Varian 1740 gas chromatograph employing either a 10-ft 5% SE-30 on Chromosorb W 100/120 or a 10-ft Carbowax 20M on Chromosorb W 100/120 column.

Synthesis. Phenylacetone and *o*-, *m*-, and *p*-fluorotoluene were commercially available. *o*-,¹¹ *m*-,¹² and *p*-^{12,13} fluorophenylacetone were prepared and purified according to procedures described in the literature.¹⁴ The syntheses of some of the phenylbicyclo[2.2.2]octanes (**1** and **4**, X = F, Me, Et, *i*-Pr, *t*-Bu; **2**, X = Me, Et) have been reported elsewhere in connection with other studies.^{15,16} All other phenylbicyclo[2.2.2]octanes examined in this study are reported in Table I with physical properties and analytical data. The synthesis of the basic skeletal framework for the fluorine systems (**1**, **2**, and **3**, X = OCH₃) followed the procedure outlined below for 1-methoxy-4-phenylbicyclo[2.2.2]octane. Methods and references for functionalizing the bridgehead position in the phenylbicyclo[2.2.2]octanes are listed in the footnote to Table I. A full description of the synthetic procedures (yields, purification, etc.) of all compounds prepared for this study, together with ¹H NMR data, may be found elsewhere.¹⁷

1-Methoxy-4-phenylbicyclo[2.2.2]octane (4, X = OCH₃). Several attempts to decarboxylate 4-acetyl-4-phenylpentane-1,5-dicarboxylic acid¹⁸ to 4-acetyl-4-phenylcyclohexanone using a previously reported procedure¹⁹⁻²² proved unsatisfactory for large-scale preparations (1-2 mol of diacid). However, we have found that by adding barium hydroxide to the reaction mixture and by keeping the contact time during pyrolysis to a minimum, consistent yields (45-60%) of the cyclohexanone are obtained.

A mixture of 4-acetyl-4-phenylpentane-1,5-dicarboxylic acid¹⁸ (1-2 mol) and barium hydroxide (5% w/w of diacid) in excess acetic anhydride was heated to reflux. After 1 h, 80% of the acetic anhydride was removed by distillation before the reaction mixture was transferred to a Quickfit "Rotaflo" dropping funnel fitted to a two-neck round-bottomed flask. The flask was then evacuated (0.1 mm) and heated to 220 °C before the reaction mixture was introduced intermittently. The rate of addition was determined by the condensation of the pyrolysate in the receiver flask cooled in a dry ice/ethanol bath. After all the reaction mixture was added (~1 h for 1 mol of diacid), distillation was continued for a further 0.5 h. Redistillation of the pyrolysate afforded 4-acetyl-4-phenylcyclohexanone, bp 163-165 °C (2 mm). A sample was recrystallized from hexane, mp 80.5-82.5 °C (lit.^{19,22} 78, 81-82 °C).

The cyclohexanone was converted in good yield (93%) to 1-methoxy-4-phenylbicyclo[2.2.2]octan-2-one in the manner described by Morita and Kobayashi.²³ Wolff-Kishner reduction of the ketone as outlined by Zimmermann and McKelvey²² afforded 1-methoxy-4-phenylbicyclo[2.2.2]octane (**4**, X = OCH₃) almost quantitatively.

The preparation of the fluorine substituted derivatives (**1**, **2**, and **3**, X = OCH₃) followed similarly except for the final reductive step where the yields were much diminished (**1**, 31%; **2**, 60%; **3**, 76%).

Wolff-Kishner reduction of 1-methoxy-4-(*p*-fluorophenyl)-bicyclo[2.2.2]octan-2-one (190.9 g, 0.77 mol) afforded **1** (X = OCH₃, 55 g) after distillation with a large amount of solid residue remaining (111 g). Recrystallization of the residue gave white crystals: mp 74-75.5 °C; IR (cm⁻¹) 3405 (OH), 801, 819 (1,4-disubstituted benzene); ¹H NMR (CDCl₃) δ 1.48 (12 H, broad s), 2.63 (1 H, broad s), 3.12 (3 H, s), 3.42-4.13 (8 H, m), 6.62-7.24 (4 H, quartet); *m/e* 320. These data suggest that the compound is 1-(*p*-(2-(2-hydroxyethoxy)ethoxy)phenyl)-4-methoxybicyclo[2.2.2]octane. Anal. Calcd for C₁₉H₂₈O₄: C, 71.2; H, 8.81. Found: C, 71.3; H, 8.68.

Apparently this byproduct is formed as a result of a direct replacement of fluorine by a typical bimolecular aromatic nucleophilic substitution reaction. We are currently examining modifications of the Wolff-Kishner method as well as other reductive procedures in order to optimize the carbonyl to methylene conversion for the preparation of **1** and **2** (X = OCH₃).

Spectra. Most of the fluorine NMR spectra were measured with a Varian DP-60 spectrometer operating at 56.4 MHz under proton-coupled conditions, using solutions containing 5% (w/w) of the fluoro compound together with 3% (w/w) of 1,1,2,2-tetrachloro-3,3,4,4-tetrafluorocyclobutane (TCTFB) or 5% (w/w) of *p*-difluorobenzene as internal references. The Varian DP-60 instrument had been modified to obtain spectra in the HA mode which were calibrated using a Racal SA35 universal counter time. A dilution study on several compounds showed that the chemical shifts were not influenced by concentration effects at the levels employed. The largest change in chemical shift observed on dilution was 0.03 ppm.

Some of the ¹⁹F NMR spectra were obtained under proton-decoupled conditions in the pulse Fourier transform mode at 84.66 MHz with a Bruker 90 spectrometer. A pulse width of 1202 Hz was used and the data were collected into 16K/8K data points giving a resolution of better than 0.01 ppm. Each sample consisted of a mixture of the unsubstituted and substituted compound at a total concentration of less than 10% w/w.

The broad-band proton-decoupled ¹³C NMR spectra were recorded in the pulse Fourier transform mode on Bruker instruments operating at 67.89 (pulse width 15 000 Hz, 16K/8K data points, resolution of 0.03 ppm) and 22.625 MHz (pulse width 6024 Hz, 8K/4K data points, resolution of 0.07 ppm; after the instrument was upgraded, some data were collected into 16K/8K data points giving a resolution of 0.03 ppm) using *c*-C₆H₁₂/*c*-C₆D₁₂ (0.2 M) and DCCl₃ (0.5 M) solutions, respectively, with Me₄Si as an internal reference.

Results

The ¹³C substituent chemical shift (SCS) data for system **4** are tabulated in Table II. It should be noted that Toyne et al. have recently reported similar ¹³C chemical shift data in DCCl₃ for this system.²⁴ Although this study is concerned primarily with the aryl carbon centers, we have also listed the values for the bicyclooctyl ring essentially for the sake of completeness. Some of these latter data have already been discussed in connection with other work by us;⁸ however, we have nothing further to add except to point out that a least-squares regression analysis indicates that the ¹³C SCS for C-2', C-3', and C-4' correlate excellently (slope, ~1; *r* = 0.99-1.0) with similar data for the corresponding positions in 1-substituted bicyclo[2.2.2]octanes.²⁵ The analogous correlation for C-1' is somewhat poorer (*r* = 0.95).

Assignments followed unambiguously from the application of various routine techniques such as chemical shift, intensity, and substituent effect considerations as well as the fluorine

Table II. ^{13}C Substituent Chemical Shifts (SCS)^{a,b} of 1-X-4-Phenylbicyclo[2.2.2]octanes (**4**)

	C1	C2	C3	C4	C1'	C2'	C3'	C4'
					DCCl ₃ ^c			
Me	-0.39	-0.14	-0.07	0.07	0.46	0.65	7.22	3.44
Et	-0.29	-0.04	-0.04	0.00	0.75	0.43	4.52	6.27
<i>i</i> -Pr	-0.19	-0.04	-0.04	0.00	0.56	0.43	1.86	8.77
<i>t</i> -Bu	-0.22	-0.13	-0.04	0.00	0.07	0.43	-0.58	11.05
SnMe ₃	0.00	-0.07	0.00	0.00	-0.45	1.04	4.23	-2.47
F	-2.73	-0.26	0.13	0.52	0.13	1.35	4.93	69.92
Cl	-2.67	-0.39	0.06	0.46	-0.78	2.02	10.02	42.84
Br	-2.60	-0.52	0.00	0.46	-1.49	2.87	11.38	39.40
I	-2.08	-0.52	0.00	0.42	-2.63	3.61	14.37	21.29
OH	-1.95	-0.20	0.00	0.26	0.13	1.30	7.67	44.99
OMe	-1.88	-0.26	0.00	0.26	0.00	0.91	3.12	49.02
OAc	-2.21	-0.26	0.13	0.46	0.07	0.91	3.64	56.04
NHAc	-1.59	-0.13	0.13	0.40	0.20	0.33	4.49	26.98
NH ₂	-1.49	-0.20	-0.07	0.00	0.13	3.03	6.50	22.95
NO ₂	-3.51	-0.39	0.19	0.72	0.59	0.07	3.90	60.27
CN	-2.63	-0.36	0.22	0.68	-0.71	-1.39	3.42	2.96
COOEt	-1.36	-0.13	0.09	0.36	0.53	-0.42	2.21	35.53
COCH ₃	-1.52	-0.17	0.09	0.36	0.69	-0.48	1.53	20.54
					c-C ₆ H ₁₂ /c-C ₆ D ₁₂ ^d			
Me	-0.47	0.00	-0.02	0.00	<i>e</i>	0.68	7.27	<i>e</i>
Et	-0.28	0.03	0.03	0.00	0.85	0.57	4.60	5.99
<i>i</i> -Pr	-0.22	0.03	0.03	0.03	0.63	0.51	1.96	8.58
<i>t</i> -Bu	-0.20	0.00	0.03	0.03	0.00	0.49	-0.55	10.87
SnMe ₃	0.00	0.00	0.00	0.00	-0.10	1.08	4.30	-2.55
F	<i>e</i>	-0.19	0.25	0.54	<i>e</i>	1.48	5.03	<i>e</i>
Cl	-2.27	-0.25	0.22	0.54	-0.51	2.15	10.10	40.34
Br	-2.16	-0.27	0.25	0.57	-1.17	2.99	11.52	35.85
I	-1.56	-0.27	0.28	0.62	-2.26	3.81	14.73	16.78
OMe	-1.37	-0.08	0.11	0.24	0.19	1.11	3.18	47.92
NH ₂	-0.99	0.03	0.06	0.13	0.41	3.73	6.77	22.15
NO ₂	-3.06	-0.22	0.44	0.90	<i>e</i>	0.43	3.97	<i>e</i>
CN	<i>e</i>	-0.25	0.44	0.84	<i>e</i>	-0.93	3.86	<i>e</i>
COOEt	-1.04	0.03	0.17	0.32	0.66	-0.22	2.23	34.32
COCH ₃	-1.12	0.03	0.22	0.41	<i>e</i>	-0.14	1.68	19.99
					CD ₃ OD ^f			
NH ₃ ⁺ <i>g</i>	-2.97	-0.15	0.34	0.76				
NMe ₃ ⁺ <i>g</i>	-3.46	-0.20	0.32	0.89				
					CF ₃ CO ₂ H ^h			
NH ₃ ⁺	-4.88	-0.88	0.26	1.02				
NMe ₃ ⁺	-6.37	-0.97	0.39	1.23				

^a Defined as the difference (ppm) between the ^{13}C chemical shift of the substituted compound and that of the appropriate carbon in the parent hydrocarbon (X = H). Positive values indicate decreased shielding. ^b The carbon numbering system is as shown on the structural formula (**4**) in the Introduction. ^c X = H (DCCl₃, relative to Me₄Si): 150.58 (C1); 125.62 (C2); 128.09 (C3); 125.42 (C4); 34.13 (C1'); 32.18 (C2'); 26.59 (C3'); 24.58 (C4'). ^d X = H (c-C₆H₁₂/c-C₆D₁₂, relative to Me₄Si): 150.66 (C1); 125.73 (C2); 128.34 (C3); 125.73 (C4); 34.65 (C1'); 32.86 (C2'); 27.33 (C3'); 25.53 (C4'). ^e Not located. ^f X = H (CD₃OD, relative to Me₄Si): 151.78 (C1); 126.43 (C2); 128.92 (C3); 126.26 (C4). ^g Counterion. Cl⁻. ^h X = H (CF₃CO₂H, relative to the second low-field peak of CF₃ quartet): 34.52 (C1); 8.98 (C2); 11.20 (C3); 8.39 (C4).

substitution technique^{5,26} and off-resonance noise decoupling. The assignments for the bicyclooctyl ring carbon centers were greatly assisted by the data²⁵ for 1-substituted bicyclo[2.2.2]octanes and the additivity of C₆H₅ substituent effects in this ring system (C α , -9.64 ppm; C β , 5.57 ppm; C γ , -0.02 ppm; C δ , 0.09 ppm). Further, substitution at the bridgehead with F and (CH₃)₃Sn is manifested by characteristic ^{13}C - ^{19}F and ^{13}C - $^{117,119}\text{Sn}$ coupling constants. These data together with chemical shift information for centers not relevant to the problem at hand may be found elsewhere.¹⁷

The values listed in Table II for c-C₆H₁₂/c-C₆D₁₂, CH₃OD, CF₃CO₂H, and some for DCCl₃(Et, *i*-Pr, *t*-Bu, I, CN, COOEt, COCH₃) can be considered accurate to at least ± 0.06 ppm. The remaining data in DCCl₃ are accurate only to ± 0.14 ppm (see Experimental Section).

The probe temperature was 308 ± 3.0 K for all measurements except for those in CF₃CO₂H, which were run at 323 K owing to the limited solubility of the parent hydrocarbon (**4**,

X = H) in this solvent. Table III gives the ^{19}F SCS for systems **1**, **2**, and **3** in various solvents. These values can be considered accurate to at least ± 0.05 ppm. The values listed in parentheses were measured under proton-decoupled conditions with an accuracy of at least ± 0.01 ppm.

Discussion

The main assumption underlying the utilization of aryl ^{13}C and ^{19}F substituent chemical shifts (SCS) as sensitive monitors of substituent electronic effects is that they reflect ground-state charge density perturbations. Theoretical support for this premise has emerged based on the idea that the shifts are dominated by the paramagnetic term of the Ramsey equation.^{10,27,28} According to numerous correlations of aryl SCS (^{13}C and ^{19}F) with charge densities calculated by MO methods at various levels of sophistication in aromatic systems, the most important factor determining the chemical shift of carbon and fluorine in aryl systems is the π electron density on carbon

Table III. ^{19}F Substituent Chemical Shifts (SCS)^{a,b}

X	DMF	methanol	benzene	CH_2Cl_2	cyclohexane
1-X-4- <i>p</i> -Fluorophenylbicyclo[2.2.2]octanes (1) ^{c,g}					
Me	0.08 (0.07)		0.11	0.10	0.12 (0.09)
Et	(0.07)				(0.07)
<i>i</i> -Pr	0.06 (0.05)		0.10	0.06	0.08 (0.05)
<i>i</i> -Bu	0.09 (0.07)		0.14	0.05	0.11 (0.09)
<i>t</i> -Bu	0.06 (0.02)		0.11	0.05	0.03 (0.03)
Ph	0.29		0.40	0.50	0.44 (0.41)
SnMe_3	0.00		0.10	0.03	0.08 (0.02)
F	0.66	0.72	0.78	0.93	1.00 (1.04)
Cl	0.70	0.74	0.84	0.98	1.09 (1.14)
Br	0.71	0.75	0.85	1.00	1.17 (1.17)
I	0.66	0.68	0.81	0.87	1.11 (1.14)
OH	0.23	0.51	0.47	0.60	0.50 (0.60)
OMe	0.38	0.62	0.45	0.56	0.46 (0.52)
OAc	0.55	0.75	0.62	0.76	0.75 (0.76)
NHAc	0.28	0.52		0.59	
NH_2	0.14	0.48	0.30	0.33	0.26 (0.31)
NO_2	0.98	1.14	1.20	1.42	1.76 (1.72)
CN	0.77	0.97	0.98	1.20	1.49 (1.50)
COOH	0.34	0.40			
COOEt	0.44	0.60	0.44	0.54	0.49 (0.59)
CHO	0.46	0.62	0.66	0.78	0.76
COCH_3	0.43	0.62	0.51	0.59	0.60 (0.71)
$\text{COC}(\text{CH}_3)_3$	0.31				0.58 (0.59)
CONMe_2	0.30				0.45 (0.50)
CH_2OH	0.09		0.23	0.28	0.23 (0.26)
CH_2Cl	0.36		0.46	0.50	0.55 (0.61)
CH_2CN	0.41		0.55	0.67	0.86 (0.89)
$\text{C}(\text{OH})\text{Me}_2$	0.01		0.17	0.19	
$\text{C}(\text{Cl})\text{Me}_2$	0.30		0.38	0.41	0.42
<i>p</i> - $\text{NO}_2\text{C}_6\text{H}_4$	0.48		0.70	0.74	0.99 (1.03)
NH_3^+ ^d	2.18 (2.11)				
1-X-4- <i>m</i> -Fluorophenylbicyclo[2.2.2]octanes (2) ^{e,g}					
Me	-0.03 (0.00)				-0.02 (0.00)
Et	-0.03 (0.00)		-0.02	0.01	-0.02 (0.00)
F	0.23	0.37	0.27	0.46	0.58 (0.60)
Cl	0.29	0.44	0.33	0.53	0.64 (0.66)
Br	0.30	0.43	0.33	0.54	0.65 (0.69)
OH	0.04	0.19	0.17	0.26	0.34 (0.32)
OMe	0.11	0.12	0.15	0.24	0.26 (0.25)
OAc	0.20	0.35	0.21	0.36	0.51 (0.40)
NHAc	0.09	0.20		0.27	
NH_2	0.01	0.21	0.09	0.16	0.18 (0.13)
NO_2	0.40	0.61	0.49	0.74	0.97 (1.01)
NC	0.35	0.54	0.53	0.74	0.96
CN	0.37		0.40	0.66	0.90 (0.94)
NH_3^+ ^d	1.04 (1.10)				
1-X-4- <i>o</i> -Fluorophenylbicyclo[2.2.2]octanes (3) ^f					
Me	-0.17		-0.16	-0.18	-0.19 (-0.19)
SnMe_3	0.07		0.09	0.00	0.06 (0.05)
F	-0.55		-0.56	-0.55	-0.58 (-0.58)
Cl	-0.53		-0.57	-0.53	-0.57 (-0.58)
Br	-0.52		-0.57	-0.55	-0.56 (-0.57)
I	-0.55		-0.57	-0.56	-0.53 (-0.56)
OH	-0.41		-0.44	-0.45	-0.38
OMe	-0.44		-0.45	-0.49	-0.47 (-0.48)
OAc	-0.55		-0.54	-0.50	-0.54 (-0.53)
NHAc	-0.41			-0.44	
NH_2	-0.34		-0.38	-0.37	-0.36 (-0.33)
NO_2	-0.47		-0.57	-0.50	-0.61 (-0.61)
NH_3^+ ^d	-1.08				

^a Defined as the difference (ppm) between the ^{19}F chemical shift of the substituted compound and that of the parent compound (X = H). A positive sign implies deshielding. ^b Values in parentheses are from proton-decoupled spectra. ^c X = H (relative to TCTFCB): -316.4 (DMF), -310.9 (MeOH), -275.1 (C_6H_6), -319.2 (CH_2Cl_2), -238.8 Hz (c- C_6H_{12}). ^d Solvent, CF_3COOH . ^e X = H (relative to *p*-difluorobenzene): 326.5 (DMF), 331.1 (MeOH), 338.6 (C_6H_6), 326.7 (CH_2Cl_2), 346.4 Hz (c- C_6H_{12}). ^f X = H (relative to TCTFCB): 263.7 (DMF), 298.9 (C_6H_6), 288.5 (CH_2Cl_2), 329.4 Hz (c- C_6H_{12}). ^g Reference 65.

(Δq_π^{C}) and fluorine (Δq_π^{F}), respectively. Further, these two theoretical parameters have been shown to be linearly related to one another,^{4,10} which is the basis for the belief that π po-

larization of the aromatic system as reflected by ^{13}C SCS leads to a proportionate change in ^{19}F chemical shifts when fluorine is substituted for the ^{13}C nucleus as a probe. However, it is

Table IV. Results of Correlations of ^{13}C SCS (System 4) with Substituent Parameters

carbon no. ^a	solvent	DSP Analysis (SCS = $\rho_1\sigma_1 + \rho_R\sigma_R^0$)		SD ^b	<i>f</i> ^c	<i>n</i> ^d
		ρ_1	ρ_R			
C1	c-C ₆ H ₁₂ /c-C ₆ D ₁₂	-4.49	0.62	0.17	0.09	8
C1	DCCl ₃	-5.30	1.23	0.16	0.07	12
C2	c-C ₆ H ₁₂ /c-C ₆ D ₁₂	-0.39	0.08	0.09	0.48	9
C2	DCCl ₃	-0.73	0.21	0.09	0.28	12
C3	c-C ₆ H ₁₂ /c-C ₆ D ₁₂	0.66	0.12	0.04	0.13	9
C3	DCCl ₃	0.26	0.17	0.05	0.47	12
C4	c-C ₆ H ₁₂ /c-C ₆ D ₁₂	1.36	0.12	0.04	0.13	9
C4	DCCl ₃	1.15	0.12	0.05	0.11	12

	solvent	Least-Squares Analysis (SCS = $\rho_1\sigma_1 + \nu$)			<i>r</i> ^f	SD ^g	<i>n</i> ^d
		ρ_1	ν^e				
C1	c-C ₆ H ₁₂ /c-C ₆ D ₁₂	-4.35	-0.11	0.94	0.64	8	
C1	DCCl ₃	-3.91	-0.70	0.91	0.57	12	
C2	c-C ₆ H ₁₂ /c-C ₆ D ₁₂	-0.67	0.12	0.78	0.20	9	
C2	DCCl ₃	-0.61	-0.07	0.65	0.23	12	
C3	c-C ₆ H ₁₂ /c-C ₆ D ₁₂	0.75	-0.04	0.93	0.11	9	
C3	DCCl ₃	0.40	-0.08	0.68	0.14	12	
C4	c-C ₆ H ₁₂ /c-C ₆ D ₁₂	1.54	-0.09	0.96	0.16	9	
C4	DCCl ₃	1.21	-0.04	0.95	0.13	12	

^a Indicated on structural formula in Introduction. ^b The standard deviation of the fit. ^c The fit parameter, $f \equiv \text{SD}/\text{rms}$, where rms is the root mean square of the data points. Correlations of excellent precision are those for which $f \leq 0.1$. ^d The number of substituents in the data set. ^e Intercept. ^f Correlation coefficient. ^g The standard deviation of the slope.

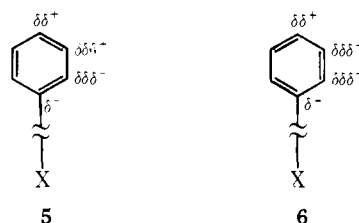
important to bear in mind that several major discrepancies from the theoretical work still remain unresolved. In particular, for both ^{13}C and ^{19}F SCS, it is found that no single shift/charge density relationship is able to correlate the meta and para positions of monosubstituted benzenes and fluorobenzenes.¹⁰ A similar situation prevails for the various conjugative dispositions of monosubstituted naphthalenes on correlation of the respective ^{13}C SCS against charge densities computed by INDO MO theory.^{5,29} Besides deficiencies in the various calculations, part of the problem appears to be the uncertain role σ charge densities play in determining aryl NMR shifts.^{10,27,28} In this connection, recent CNDO/2 calculations on very simple model systems,³⁰ which highlight the possible importance of σ bond polarizations in determining ^{13}C chemical shifts of π systems, are pertinent.

An important operational constraint in the utilization of ^{13}C and ^{19}F chemical shifts as charge density monitors is that the probe site be properly chosen so that comparisons of chemical shifts are confined to a closely related series of compounds and, at the same time, to those sites reasonably remote from the point of substitution such that steric, magnetic anisotropic, bond order, and neighboring group effects are unimportant. Hence ^{13}C and ^{19}F nuclei sited in the aryl ring of systems 1-4 are ideally located for assessing polar field effects on their chemical shifts, in the complete absence of other electronic mechanisms, provided that the hyperconjugative interaction between the phenyl and bicyclo[2.2.2]octyl moieties remains essentially invariant to bridgehead substitution. This latter requirement is clearly established by a study of the infrared spectra of several members of system 4 which indicates that the mesomeric parameters ($\sigma_R^0 = -0.17$)^{31a} remains constant within the limits of experimental error (± 0.01), as evidenced by the invariant intensity of the ν_8 vibrations.^{31b,c} However, it is important to note that the "anomalous" positive ^{19}F SCS for the alkyl groups in system 1 (Table III) have been attributed¹⁶ to a slight variation in σ_R^0 (less than 0.005) of the bicyclooctyl group as a result of small substituent-induced structural changes of the skeletal framework. These perturbations, however, are clearly very small; hence, the SCS may be confidently interpreted as being almost exclusively manifestations of polar phenomena.

A scrutiny of the ^{13}C SCS for system 4 listed in Table II

clearly indicates that the electric fields emanating from distant polar substituents (dipoles and poles) effect a significant redistribution of the π -electron density in the phenyl ring. The relationship between these data (Table II) and substituent polarity (σ_1 effect) has been explored by least-squares and multiparameter regression (DSP equation)³³ analysis. Best fit parameters (Table IV) were obtained by excluding SCS for those substituents (alkyl groups and Me_3Sn) which are obviously discordant with their generally accepted σ_1 values.^{33,34} Since the data for c-C₆H₁₂/c-C₆D₁₂ as solvent are much more accurate than those for DCCl₃ (see Experimental Section), the correlations for the former are more reliable and generally better than those for the latter. Hence further discussion concerning the quantitative aspects of the field-induced polarization will be confined essentially to the cyclohexane data. This is most appropriate on other grounds as well since only in cyclohexane as solvent can one be assured that intramolecular electric-field phenomena can be observed in the absence of reaction field effects.³⁵ Although Taft's dual substituent parameter (DSP) equation³³ is not strictly applicable to the model system in question, σ_R^0 values³³ being only valid for substituents directly attached to π systems, we have used it here with the idea in mind that any extraneous factors perturbing the ^{13}C (or ^{19}F , vide infra) chemical shifts should be "shunted" into the $\rho_R\sigma_R^0$ term, thus possibly providing a more accurate measure of the polar susceptibility parameter (ρ_1).

It can be seen from Table IV (c-C₆H₁₂/c-C₆D₁₂) that the correlations are quite reasonable for all carbon centers except C-2.³⁶ The ρ_1 values, together with the ^{13}C SCS data for the positive poles, +NH₃ and +NMe₃ (Table II; CH₃OD and CF₃CO₂H), indicate that the field-induced charge density perturbation in 4 may be schematically illustrated as in 5. This is in accord with a representation by Topsom et al.^{7b,37} for this



effect (F_π) on the monosubstituted phenyl ring system but not the pattern given in **6** by Reynolds et al.^{4,38} Both of these research groups carried out ^{13}C NMR studies of stereochemically nonrigid ω -substituted alkylbenzenes^{37b,39} which clearly identified the polarization at the terminal positions of the phenyl ring but left the situation for the "in-between" carbons, particularly C-2, in doubt. Reynolds et al. favored the polarization pattern in **6** rather than **5** because of the results of CNDO/2 calculated charge densities on ω -substituted alkylbenzenes³⁹ as well as on 1-ammonio-4-phenylbicyclo[2.2.2]octane³⁸ and other systems.⁴⁰

It is of interest to note the "anomalous" negative SCS (Table II) for the alkyl groups at C-1. These discrepancies together with the statistically significant ρ_R term for this position (Table IV) may be related to the small substituent-induced structural changes of the bicyclooctyl ring previously alluded to (vide supra).¹⁶ However, the possibility of hyperconjugative transfer of charge involving the bridging bond in bicyclo[2.2.2]octyl systems cannot be ignored.^{8,41} Note also the relatively large increase in the ^{13}C SCS at C-2 compared to the other carbon centers in going from CH_3OD to $\text{CF}_3\text{CO}_2\text{H}$ for $^+\text{NH}_3$ and $^+\text{NMe}_3$ (Table II). This could be evidence for the operation of pronounced reaction field effects³⁵ or other solvent aberrations at this position in polar solvents. Interestingly, the ratios of the SCS at C-4 for $^+\text{NH}_3$ and $^+\text{NMe}_3$ in CH_3OD and $\text{CF}_3\text{CO}_2\text{H}$ (0.85 and 0.86, respectively) are in precise agreement with the ratio of their σ_1 constants (1.08 ($^+\text{NH}_3$)/1.29 ($^+\text{NMe}_3$) = 0.84) determined using the β -fluoronaphthyl tag.⁴² The decreased SCS for these positive poles in CH_3OD ($\epsilon \approx 33$) compared to $\text{CF}_3\text{CO}_2\text{H}$ ($\epsilon \approx 8.6$) can be ascribed in part to the attenuation of electric fields in these systems by solvents with a relatively high dielectric constant (vide infra) as well as varying solvation factors.^{42b}

An interesting feature of the ^{13}C SCS data for system **4** (Table II) has been recently alluded to by Toyne et al.²⁴ If a linear relationship between ^{13}C SCS and π charge density is assumed, then the results suggest a nonzero net redistribution of π charge density. Toyne et al. considered several factors that may account for this observation including the possibility of a nonlinear relationship between SCS and charge densities. However, we must stress caution in comparing SCS for different carbon centers (tertiary and quaternary) since the shift/electron density constant may vary significantly. It is important to bear in mind that the chemical shift is a property of the interaction of the charge density with an external magnetic field and, thus, it depends not only on the value of the integrated charge density in the vicinity of the nucleus but also on the magnetic susceptibility of that charge density. Recently, Batchelor⁴³ presented linear electric field shift coefficients (carbon-13) for tertiary and quaternary aromatic carbon centers (1.6×10^{-11} and 3.6×10^{-11} esu, respectively), calculated by utilizing the Buckingham equation ($\text{SCS} = AE_z$; E_z is the electric field along the diad axes)^{9,44} for uniform field shifts in the framework of a bond polarizability model. Since the dipole moment (μ) of the substituent in **4** is directed along the main axis of the molecule, the SCS for C-1 and C-4 can be employed to provide an experimental estimate of these coefficients. For the two carbon centers, $E_z = 2\mu/r^3$ where r is the distance between the carbon centers and the center of the dipole moment of the substituent at the bridgehead. Using the SCS for Cl (Table II, cyclohexane), the A values for the tertiary and quaternary centers are 6.1×10^{-11} and 6.7×10^{-11} esu, respectively. Clearly, these results are in poor agreement with those of Batchelor.⁴³ This was not unexpected given the limitations of a bond polarizability model for aromatic systems and the use of a common shift/charge density constant. However, given the likelihood of a different shift/charge density constant for each different type of carbon center, the equivalent values for C-1 and C-4 must be considered fortuitous; otherwise it implies that the polarization of the phenyl ring is essentially localized!

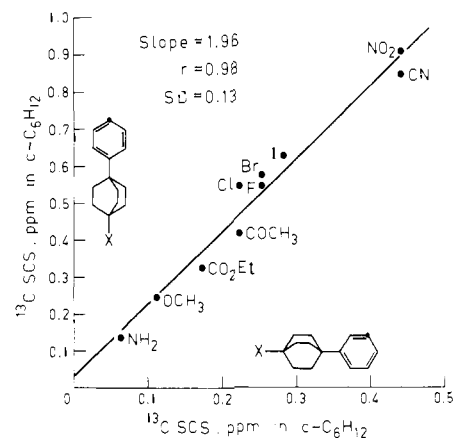


Figure 1. Plot of ^{13}C SCS (cyclohexane) of C-4 vs. C-3 for 1-X-4-phenylbicyclo[2.2.2]octanes (**4**).

ous; otherwise it implies that the polarization of the phenyl ring is essentially localized!

Bearing in mind the major thrust of this investigation, namely, quantitative delineation of ^{19}F NMR polar field effects, the most important result from the ^{13}C NMR study of system **4** is the estimation of relative polar field effects at C-4 and C-3. This ratio should provide a fairly good measure of relative π charge density changes (F_π effect) at these two centers for three reasons: (1) the ^{13}C probe is well behaved in these two dispositions to electric field perturbations as evidenced by the good correlations of the ^{13}C SCS with σ_1 (Table IV); (2) aryl ^{13}C chemical shifts are dominated by π charge density perturbations (vide supra); and (3) a consideration of orientational factors (angles/distances) and longitudinal σ -bond polarizabilities strongly suggests that σ charge density perturbations (Δq_σ^c) at both centers should be small and similar. Therefore, $(\Delta q_\pi^{C-4} + \Delta q_\sigma^{C-4})/(\Delta q_\pi^{C-3} + \Delta q_\sigma^{C-3}) \approx \Delta q_\pi^{C-4}/\Delta q_\pi^{C-3}$.

The ratio $(F_\pi(\text{C-4})/F_\pi(\text{C-3})) = \Delta q_\pi^{C-4}/\Delta q_\pi^{C-3}$ is readily obtained from the slope of a plot (Figure 1) of the appropriate SCS for these carbon centers or from the ratio of the appropriate ρ_1 parameters (Table IV; $\rho_1(\text{C-4})/\rho_1(\text{C-3}) = 2.06$). It is reasonable to assume that this ratio of F_π effects also holds in the para and meta position of monosubstituted benzenes (see Introduction). Thus, the correctness of the separation of polar effects by Taft's DSP treatment of ^{13}C SCS data¹⁰ from monosubstituted benzenes is upheld since $\rho_1(\text{para})/\rho_1(\text{meta}) \approx 2$, according to the results of a more recent definitive analysis.⁴⁵

The regression parameters for the correlative analyses between the ^{19}F SCS of **1**, **2**, and **3** (Table III) and substituent parameters (σ_1 and σ_R^0)^{10,34} are set out in Table V. The analyses for **1** were carried out using the SCS data (Table III) from Cl down to COCH_3 as well as CH_2Cl and CH_2CN , while for **2** and **3**, Me, Et, NC, F and Me, Me_3Sn , F were excluded, respectively. The substituents deleted from the basis sets either had SCS obviously not in accord with their σ_1 values^{33,34} or the inductive parameter is not reliably known. Substituents well known to exhibit strong specific substituent-solvent interactions (OH, NH_2 , COOH) are deleted from the correlations for DMF and CH_3OH . Overall, it can be seen (Table V) that the correlations are quite good for systems **1** and **2** given that some of the σ_1 values may be solvent dependent. However, unknown extraneous factors seem to be a problem with system **3** as indicated by the rather poor least-squares correlations, the statistically significant ρ_R values that emerge from the DSP treatment, and the inexplicable results for Me and Me_3Sn .⁴⁶ The "shunting" of these extraneous effects into the $\rho_R\sigma_R^0$ term (vide supra) is apparently successful based on the ^{19}F SCS (-1.08 ppm) of $^+\text{NH}_3$ ($\sigma_1 = 1.08$)⁴² in $\text{CF}_3\text{CO}_2\text{H}$, which in-

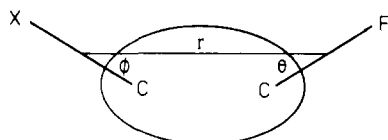


Figure 2. Diagram illustrating angle and distance factors for electric field calculations.

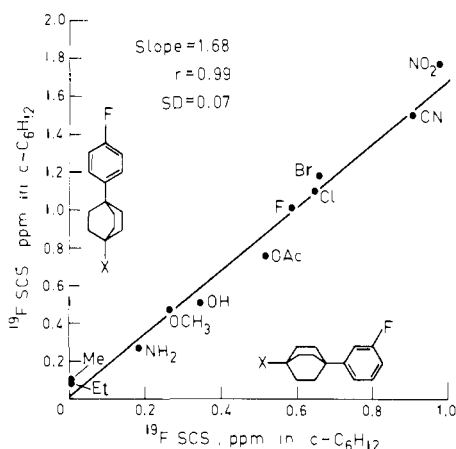


Figure 3. Plot of ^{19}F SCS (cyclohexane) of 1-X-4-(*p*-fluorophenyl)bicyclo[2.2.2]octanes vs. ^{19}F SCS (cyclohexane) of 1-X-4-(*m*-fluorophenyl)bicyclo[2.2.2]octanes.

indicates a ρ_1 value for **3** of -1.00 . This is in agreement with the magnitude of the ρ_1 values derived from the DSP analysis. It is possible that structural effects of the kind recently invoked to rationalize the "anomalous" ^{19}F SCS for the alkyl groups in **1**¹⁶ may also be manifested in the ^{19}F SCS for **3**.⁴⁷ Nevertheless, it seems unequivocal that the ^{19}F SCS data for **3** indicate the influence of reversed polar field effects ($F_D + F_\pi$)⁶ on ^{19}F chemical shifts.^{7b} We shall come back to this phenomenon later.

The direct field contribution (F_D) to the ^{19}F SCS of **1** and **2** can be estimated by dissecting out the field-induced π polarization component (F_π) which has been quantitatively defined in a relative manner for these systems (F_π (system **1**)/ F_π (system **2**) = 1.96) from the ^{13}C SCS (C-4 and C-3) of **4** (vide supra). This may be achieved in the following way. If the ^{19}F NMR polar field effect for any substituent in system **1** is equated to $F_D + F_\pi$, then the corresponding effect in **2** is equal to $x F_D + 0.51 F_\pi$ where $x = E_z$ (system **2**)/ E_z (system **1**); E_z is the component of the electric field acting along the carbon-fluorine bond direction and may be deduced by appropriate summation from the individual components of E which are readily derived.⁴⁸ An approximate and a more definitive expression for E_z are given in eq 1 and 2, respectively

$$E_z = \frac{2\mu \cos \theta}{r^3} \quad (1)$$

$$E_z^1 = \frac{\mu}{r^3} (2 \cos \theta \cos \phi - \sin \theta \sin \phi) \quad (2)$$

where μ is the dipole moment of the polar C-X bond from which the electric field originates, θ and ϕ are the angles between the CF and CX bond vectors, respectively, and a line of length r drawn between the midpoints of the CF and CX bonds (Figure 2). Therefore, ^{19}F NMR polar field effects in **1** relative to those in **2** may be expressed in the form $(F_D + F_\pi)/(x F_D + 0.51 F_\pi)$ and equated to the slope of the plot of ^{19}F SCS (cyclohexane) for **1** vs. those for **2** (Figure 3). Hence $(F_D + F_\pi)/(x F_D + 0.51 F_\pi) = 1.68$ and, therefore, direct field contributions (F_D) for **1** and **2** may be estimated. It should be noted that the ρ_1 values (Table V, cyclohexane) derived by DSP

Table V. Results of Correlations of ^{19}F SCS with Substituent Parameters

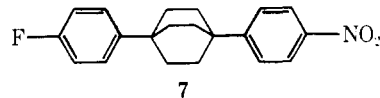
system	solvent	DSP Analysis (SCS = $\rho_1\sigma_1 + \rho_R\sigma_R^0$)			f^b	n^c
		ρ_1	ρ_R	SD ^d		
1	c-C ₆ H ₁₂	2.49	0.18	0.13	0.13	14
1	CH ₂ Cl ₂	2.19	-0.04	0.06	0.08	15
1	C ₆ H ₆	1.85	-0.03	0.07	0.10	14
1	CH ₃ OH	1.83	-0.06	0.06	0.08	11
1	DMF	1.50	0.02	0.05	0.09	13
2	c-C ₆ H ₁₂	1.49	0.14	0.05	0.07	8
2	CH ₂ Cl ₂	1.14	0.06	0.04	0.08	9
2	C ₆ H ₆	0.72	0.05	0.03	0.09	8
2	CH ₃ OH	0.96	0.18	0.04	0.10	6
2	DMF	0.63	0.11	0.03	0.11	7
3	c-C ₆ H ₁₂	-1.06	0.43	0.03	0.06	8
3	CH ₂ Cl ₂	-0.96	0.57	0.04	0.09	9
3	C ₆ H ₆	-1.04	0.49	0.04	0.08	8
3	DMF	-0.93	0.58	0.06	0.11	7

system	solvent	Least-Squares Analysis (SCS = $\rho_1\sigma_1 + \nu$)				n^c
		ρ_1	ν^d	r^e	SD ^f	
1	c-C ₆ H ₁₂	2.87	-0.17	0.96	0.24	14
1	CH ₂ Cl ₂	2.02	0.07	0.98	0.12	15
1	C ₆ H ₆	1.68	0.07	0.96	0.14	14
1	CH ₃ OH	1.42	0.18	0.98	0.10	11
1	DMF	1.46	0.01	0.97	0.12	13
2	c-C ₆ H ₁₂	1.63	-0.08	0.98	0.13	8
2	CH ₂ Cl ₂	1.20	-0.03	0.98	0.09	9
2	C ₆ H ₆	0.78	-0.03	0.98	0.07	8
2	CH ₃ OH	1.20	-0.13	0.97	0.14	6
2	DMF	0.83	-0.11	0.98	0.08	7
3	c-C ₆ H ₁₂	-0.53	-0.31	0.93	0.08	8
3	CH ₂ Cl ₂	-0.28	-0.39	0.71	0.10	9
3	C ₆ H ₆	-0.42	-0.36	0.88	0.09	8
3	DMF	-0.14	-0.44	0.33	0.18	7

^a The standard deviation of the fit. ^b The fit parameter, $f = \text{SD}/\text{rms}$, where rms is the root mean square of the data points. Correlations of excellent precision are those for which $f < 0.1$. ^c The number of substituents in the data set. ^d Intercept. ^e Correlation coefficient. ^f The standard deviation of the slope.

analysis for **1** and **2** provide a similar value (1.67) for relative polar field effects in these systems.

Before proceeding with electric field calculations on **1** and **2**, we felt that a reliable experimental estimate of the distance dependency of field effects in *real* molecules is warranted by expressions of uncertainty in the literature^{7a,49} concerning the exact inverse relationship (r^{-2} or r^{-3}). Until this study, such an unequivocal estimate could not be provided because of the lack of data from suitable model systems. This can be achieved here by comparing the difference between the ^{19}F SCS (Table III) of **7** (**1**, X = *p*-NO₂C₆H₄) and **1** (X = C₆H₅) with that of



1 (X = NO₂) for cyclohexane as solvent. The ratio is (0.55/1.76) = 0.313, implying a distance dependency law of $r^{-2.87}$. This result⁵⁰ attests to the validity of an inverse third power law (r^{-3} ; see eq 1 and 2) for all electric field calculations in the systems described here. The calculations summarized in Table VI were carried out using aliphatic bond dipole moments,⁵¹ standard structural parameters,⁵² as well as established structural information on the bicyclo[2.2.2]octyl skeletal framework.⁵³ Because the origin of the electric fields associated with the CX bonds has not been established, this is located at the bond center for C-F, C-Cl, C-Br, and C-I, while for NO₂, the assumed location is that given by Hamer and Reynolds.⁵⁴ The origin is considered at carbon for CN. The A values (Table VI) for the Buckingham equation (SCS = AE_z)^{9,44} for the

Table VI. Electric Field Calculations for Systems **1** and **2**

X	C-X, Å ^a	μ, D	1		2		1		2		¹⁹ F SCS, ppm ^f	1		
			$E_z \times 10^{-3}$, esu	$E_z \times 10^{-3}$, esu approx ^b	$E_z \times 10^{-3}$, esu exact ^c	$E_z(2)/E_z(1)$ ^d approx exact	% F_D ^e approx exact	% F_D ^e approx exact	$A \times 10^{12}$, esu approx exact					
F	1.38	1.96	7.08	6.70	7.35	0.946	1.04	19.6	16.1	31.1	28.1	1.00	27.7	22.7
C1	1.77	2.06	6.94	6.51	7.13	0.938	1.03	19.7	16.4	31.1	28.4	1.09	30.9	25.8
Br	1.94	2.18	7.13	6.63	7.26	0.930	1.02	20.3	16.7	31.7	28.6	1.17	33.3	27.4
I	2.13	2.04	6.47	5.98	6.54	0.924	1.01	20.6	17.0	32.0	28.9	1.11	35.3	29.2
NO ₂	2.09	3.63	11.58	10.71	11.76	0.925	1.02	20.7	16.7	32.1	28.6	1.76	31.5	25.4
CN	2.62	4.04	11.76	10.71	11.71	0.911	1.00	21.3	17.4	32.6	29.2	1.49	27.0	22.0
CN ^g	2.62	4.04	10.63	9.53	10.42	0.897	0.98	22.1	18.1				31.0	
						av		20.4	16.7	31.8	28.6		31.0	25.4

^a Dipole length. ^b Calculations using eq 1. ^c Calculations using eq 2. ^d $E_z(2)/E_z(1)$ equals x in the expression $(F_D + F_\pi)/(xF_D + 0.51F_\pi) = 1.68$ (see text). ^e Direct field contribution expressed as a percentage of total polar effect. ^f For cyclohexane as solvent (Table III). ^g Origin of electric field located 1.6 Å from bridgehead carbon.

effects of a uniform electric field on ¹⁹F chemical shifts are calculated using the direct field contribution to the observed ¹⁹F SCS (cyclohexane) of system **1**.

Several important conclusions follow from an examination of the results set out in Table VI. Firstly, it can be seen that the magnitude of the percent direct field contributions for **1** and **2** indicates unambiguously that field-induced π polarization is the dominant polar mechanism determining ¹⁹F SCS in these systems.³⁸ It is important to note that this conclusion is qualitatively demonstrated by the similarity between the pattern of ρ_1 values for the ¹⁹F SCS (Table V) and the corresponding ρ_1 values for the ¹³C SCS (Table IV), as well as by a comparison of the ¹⁹F and ¹³C SCS for the positive pole, +NH₃ (CF₃CO₂H, Tables II and III). The different blend of effects (F_D and F_π) determining the ¹⁹F SCS of **1** and **2** is further exemplified by the need for two separate least-squares correlative equations

$$^{19}\text{F SCS} = 1.83 \times ^{13}\text{C SCS} + 0.02$$

(**1** vs. **4** (C-4); cyclohexane;

$$n = 15; r = 0.99; \text{SD (slope)} = 0.07) \quad (3)$$

$$^{19}\text{F SCS} = 2.14 \times ^{13}\text{C SCS} + 0.04$$

(**2** vs. **4** (C-3); cyclohexane;

$$n = 6; r = 0.98; \text{SD (slope)} = 0.16) \quad (4)$$

when the data for **1** and **2** (Table III) are correlated against the corresponding ¹³C SCS for **4** (Table II, C-3 and C-4). However, if the F_D contribution to the ¹⁹F SCS of **1** and **2** is extracted so that the correlation is between SCS determined only by F_π , then it is found that a single relationship (eq 5 or 6) accommodates all the data (**1** and **2** vs. **4** (C-3 and C-4)). Two correlations are given since the % F_D contribution is slightly different (Table VI) depending on which equation (1 or 2) is employed in the field calculations.

$$^{19}\text{F SCS} = 1.37 \times ^{13}\text{C SCS} + 0.08$$

(cyclohexane; $n = 11$; $r = 0.98$; SD (slope) = 0.08) (5)

$$^{19}\text{F SCS} = 1.45 \times ^{13}\text{C SCS} + 0.08$$

(cyclohexane; $n = 11$; $r = 0.98$; SD (slope) = 0.08) (6)

Secondly, it can be seen that the coefficient (A) for the Buckingham equation is either 31.0×10^{-12} or 25.4×10^{-12} esu depending on the expression (eq 1 and 2) employed for calculating E_z . These values are in remarkably good agreement with recent determinations (34.0×10^{-12} or 27.0×10^{-12} esu) from an entirely different model system (4-substituted β,β -difluorostyrene) by Reynolds et al.⁴ and published while this work was in progress. The A value was employed by these workers,⁴ in conjunction with DSP ρ_1 values, to estimate the percent direct field contribution of the total ¹⁹F NMR polar field effect in para-substituted fluorobenzenes, 4-substituted

1-fluoronaphthalenes, and 10-substituted 9-fluoroanthracenes. Interestingly, these estimations differ significantly from those recently presented using a different approach.⁵ However, a recent analysis using a new DSP treatment⁴⁵ indicates that the ρ_1 values used by Reynolds et al.⁴ are in error. In a forthcoming paper,⁵⁵ we shall present an analysis of ¹⁹F NMR polar field effects in benzene and naphthalene employing the A coefficient derived in this work as well as the proportionality constant (eq 5 and 6) relating ¹⁹F and ¹³C SCS determined only by field-induced π polarization. By definition, A is a measure of the ease of distortion of the electron distribution along the CF bond; thus, the question arises whether it is the σ or potential π component of the bond that is the determining factor. According to CNDO/2 calculated charge densities on 4-substituted β,β -difluorostyrenes, Reynolds et al.⁴ have suggested that the direct field effect (F_D) is manifested predominantly by polarization of the CF σ bond with only minor polarization of the CF π bond. However, it is important to note that in a recent study by us¹⁶ of F_D effects on ¹⁹F chemical shifts in a model system in which structural constraints permit only polarization of the σ bond with no π electronic effects on fluorine (supported by CNDO/2 calculations), "anomalous" *upfield* shifts were observed. Hence, the unambiguous *positive* sign for A when fluorine is attached to an sp² hybrid carbon, as determined in this study and by Reynolds et al.,⁴ seems to implicate the π electrons, i.e., the minor polarization of the π component of the CF bond by F_D is the dominating factor. Hopefully, further light may be shed on this question by the application of more refined MO computational methods.

An important corollary of the determination of similar A values from the aforementioned different model systems is that field parameters evaluated from aliphatic systems for reasonably polar groups can be validly used in aromatic systems. This is in agreement with deductions from recent theoretical work by Reynolds et al.³² but contrary to another claim.⁵⁶

Although any quantitative analysis of the ¹⁹F SCS for system **3** is compromised by the influence of factors not directly polar in origin (vide supra), we believe that an understanding of the nature of ¹⁹F NMR polar effects here can be achieved by utilizing the A values (Table VI) and proportionality constants (eq 5 and 6) to calculate F_D and F_π contributions, respectively, to the ¹⁹F SCS. These values are listed in Table VII together with other pertinent and relevant information. Dipole lengths and aliphatic bond dipole moments employed in the calculations are given in Table VI. The most striking observation from the calculations summarized in Table VII is the very small direct field contribution (F_D) to the ¹⁹F SCS as calculated from the more definitive expression for E_z (eq 2). We have no explanation for this result except to point out that the assumptions inherent in the derivation of the equation may not hold for this system (**3**). Interestingly, the result is the same if a two-point charge model is employed to calculate E_z .⁵⁷

Table VII. Electric Field Calculations for System 3

X	$E_z \times 10^{-3}$, esu		F_D , ppm ^a		F_π , ppm ^b		^{19}F SCS (calcd) ^c		^{19}F SCS (obsd) ^d
	approx ^e	exact ^f	approx	exact	approx ^g	exact ^h	approx	exact	
F	-4.63	-0.45	-0.14	-0.01	-0.26	-0.28	-0.40	-0.29	-0.58
Cl	-4.67	-0.82	-0.15	-0.02	-0.34	-0.36	-0.49	-0.38	-0.58
Br	-4.84	-1.00	-0.15	-0.03	-0.37	-0.39	-0.52	-0.42	-0.57
I	-4.43	-1.06	-0.14	-0.03	-0.37	-0.39	-0.51	-0.42	-0.56
NO ₂	-7.91	-1.85	-0.25	-0.05	-0.30	-0.32	-0.55	-0.37	-0.61

^a Calculations using Buckingham equation ($\text{SCS} = AE_z$). ^b Calculated by multiplying the observed ^{13}C SCS (C-2) in system 4 (Table 11, cyclohexane) by the proportionality constants of eq 5 and 6. ^c $F_D + F_\pi$ (ppm). ^d Taken from Table 111 (cyclohexane). ^e Calculations using eq 1. ^f Calculations using eq 2. ^g Proportionality constant from eq 5. ^h Proportionality constant from eq 6.

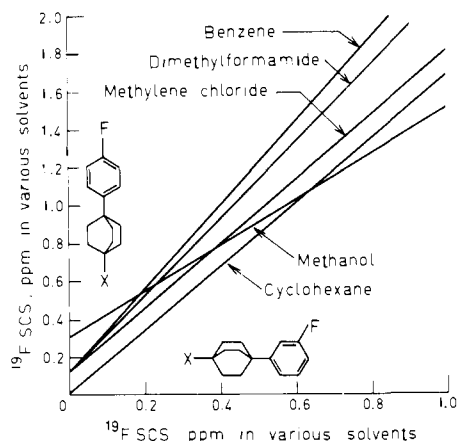


Figure 4. Plot of ^{19}F SCS of 1-X-4-(*p*-fluorophenyl)bicyclo[2.2.2]octanes vs. ^{19}F SCS of 1-X-4-(*m*-fluorophenyl)bicyclo[2.2.2]octanes for various solvents.

However, it can be seen that F_D contributions calculated with the approximate expression (eq 1) are significant and, moreover, lead to calculated ^{19}F SCS in rather good agreement with the observed values. Provided that this result is not fortuitous,⁵⁸ then, notwithstanding the operation of other factors perturbing ^{19}F SCS in 3 (vide supra), compelling evidence is provided for reversed direct field effects on ^{19}F chemical shifts.^{7b} It should be noted that similar reversed dipolar substituent effects observed in several chemical reactivity studies^{7b,59} have been tendered as cogent evidence for the existence of "through-space" rather than "through-bond" inductive effects.

The solvent effects displayed by systems 1 and 2, as reflected by their DSP derived ρ_1 values (Table V), are of interest in the light of a simple qualitative model proposed by Dayal and Taft⁶⁰ to account for ^{19}F NMR polar solvent shifts and the now established dual nature (vide supra) of aryl ^{19}F NMR polar shifts. According to Dayal and Taft,⁶⁰ the following three factors should be considered when rationalizing ^{19}F NMR polar solvent shifts. (1) An increase in the electron-withdrawing power of electronegative substituents ($\delta^+\text{C}-\delta^-\text{X}$) in polar solvents owing to greater separation of charge in the σ bonds as well as dispersion of the charge at the negative end of the dipole, which protrudes into the media, as a result of solvation. Obviously, both F_D and F_π contributions to the shift will be enhanced in polar solvents by this factor and, thus, ρ_1 should increase. (2) An increase in the effective dielectric constant owing to intrusion of the polar solvent into the cavity through which the major lines of force must pass.⁶¹ Besides the bulk dielectric constant of the solvent, this effect will also depend markedly on the shape of the cavity occupied by the model system in the media as well as the location of the probe site in the cavity with respect to the polar substituent. F_D contributions should be attenuated by this effect particularly in rod-like models (systems 1 and 2, and 4-substituted-4-fluorobiphenyls (8)⁶⁰) compared to disk or spherical-like models (para-substituted fluorobenzenes (9) and 10-substituted 9-

fluoroanthracenes (10)⁶⁰) as suggested by theory.⁶¹ However, the effect of this factor on F_π is not easy to assess even qualitatively. Intuitively, it might be expected to be small or even negligible when the substituent is directly attached to a fully conjugated aryl system (8, 9, and 10). The experimental evidence suggests that this is not the case for 1 and 2 as ρ_1 (DSP) for C-4 in system 4 is significantly larger for cyclohexane ($\epsilon \approx 2.0$) than for DCCl_3 ($\epsilon \approx 4.6$) (Table IV). Since the reverse order is expected on the basis of factor (1), this result implies a probable reduction of the F_π contributions in 1 and 2 by polar solvents. Interestingly, when the ^{13}C probe site is not located on the periphery at the remote end of the system but approximately in the center of the cavity (C-1 in 4), than the DSP ρ_1 ¹⁵ values (Table IV) indicate that F_π is enhanced in DCCl_3 compared to cyclohexane owing to the dominance of factor (1). (3) The polarization of the solvated C-F σ bond by the solvated X substituent will give rise to a C-F σ bond of 1 and 2 (X = polar substituent) which will be less polarized by the polar solvent than that of 1 and 2 (X = H). This factor will manifest itself in the observed polar shift by deshielding of F in 1 and 2 (X = polar substituent) compared to 1 and 2 (X = H).

Note (Table V) that the efficiency of transmission of ^{19}F NMR polar field effects in systems 1 and 2 is in the order cyclohexane > CH_2Cl_2 > benzene \sim MeOH > DMF and cyclohexane > CH_2Cl_2 > MeOH > benzene > DMF, respectively. These orders are clearly contrary to that observed for systems 9 and 10⁶⁰ but similar to the trends observed for 8 and other rod-shaped model systems.⁶⁰ Hence, in terms of the aforementioned model, factor (2) is dominant in determining the polar shifts of 1 and 2 as suggested by Dayal and Taft⁶⁰ for 8. The greater relative differential solvent shifts for 1 and 2 compared to 8 attests to the significantly smaller F_D contribution to the total ^{19}F NMR polar field effect in the latter system⁴ which is fully conjugated (vide infra). However, the reason why ^{19}F NMR polar field effects for 1 and 2 are also markedly attenuated in benzene ($\epsilon \approx 2.3$) compared to cyclohexane ($\epsilon \approx 2.0$) is not explicable. Clearly, the situation is complicated by many other factors (shape of the solvent molecules, reaction field effects, etc.)⁶² which are impossible to elucidate. The complexity of solvent effects in 1 and 2 is dramatically exemplified by the varying slopes of the linear regression lines, as well as the intercept for MeOH, shown in Figure 4, which represent the least-squares correlations of the ^{19}F SCS of 1 against those for 2 in the respective solvents. The disproportionate polar solvent shifts in 1 and 2 may be due, in part, to the different blend of F_D and F_π effects in these systems and the likelihood of factor (2) of the simple model (vide supra) being different for 1 and 2. It is important to note that if the DSP analysis can be considered to be successful in factoring out polar effects in system 3, then, in terms of the simple model, the similar ρ_1 values here (Table V) for the various solvents imply an almost exact cancellation of factors (1) and (3) by (2). Alternatively, ^{19}F NMR polar field effects here are essentially saturated!

Since the geometric relationship between the fluorine atom and the substituent for model system 1 is similar to the rela-

tionship between these groups in **8**,⁶⁰ a comparison of the polar susceptibility parameters (ρ_1^{15}) between these systems provides an assessment of the relative efficiency of conjugated structures and their unconjugated analogues for the propagation of aryl ¹⁹F NMR polar field effects. The appropriate parameters from a DSP analysis of ¹⁹F SCS from **8** are as follows:⁶⁰ $\rho_1 = 3.89$ (cyclohexane), $\rho_1 = 3.35$ (benzene), $\rho_1 = 3.17$ (DMF), $\rho_1 = 3.52$ (CH₂Cl₂), and $\rho_1 = 3.50$ (MeOH). Thus the fully conjugated system (**8**) is significantly more effective than the unconjugated analogue (**1**, Table V) for transmitting the σ_1 effect. A similar comparison between the ¹³C NMR ρ_1 value (acetone/DCCl₃, 2.00)⁴ for 4-substituted biphenyls (C-4) and that for C-4 in system **4** (DCCl₃, $\rho_1 = 1.15$) indicates that the enhancement in conjugated systems may be largely ascribed to the F_π contribution of the ¹⁹F NMR polar field effect. This conclusion is strongly corroborated by recent computational work.³⁸ However, there is also the possibility that the F_D component contributes to the enhancement in a minor way since calculations indicate the importance of the nature of the intervening molecular framework in transmitting direct field effects.³⁸ An interesting feature of the enhanced efficiency of ¹⁹F NMR polar field effects in the conjugated structure (**8**) compared to the unconjugated analogue (**1**) is its solvent dependency (ρ_1 (**8**)/ ρ_1 (**1**): 1.56 (cyclohexane); 1.81 (benzene); 2.11 (DMF); 1.61 (CH₂Cl₂); 1.91 (CH₃OH)). These solvent variations are probably the result of a different blend of F_D and F_π effects in **8** and **1** and, moreover, the different way in which factor (2) of the simple polar shift model (vide supra) effects F_D and F_π contributions in the two different model systems.⁶³

In conclusion, we would like to draw attention to two final points concerning the NMR substituent effect studies of **1**, **2**, and **4**. Firstly, the ¹⁹F chemical shifts of **1** and **2** (X = H) relative to fluorobenzene in cyclohexane (-5.66 and -0.66 ppm, respectively) may be substituted in the Taft equations⁶⁴ in order to obtain substituent parameters for the bicyclo[2.2.2]-octyl moiety ($\sigma_1 = -0.01$, $\sigma_R^0 = -0.17$). The value for the resonance parameter is in excellent agreement with that previously derived by the infrared technique ($\sigma_R^0 = -0.17$).^{31a} Secondly, the relatively large polar susceptibility parameters (ρ_1) observed for **1**, **2**, and **4** (C-4), particularly in cyclohexane, indicate that these systems may be usefully employed as sensitive model systems which are ideal for extending the scale of intrinsic polar effects (σ_1). In this connection, we have already used them¹⁶ to assess the polar effect of alkyl groups where these are attached to a sp³-hybridized carbon atom and, in future work, we will report on their application in the delineation of polar effects of other weak inductive groups (SiH₃, GeH₃, Si(CH₃)₃, Ge(CH₃)₃, Sn(CH₃)₃, Pb(CH₃)₃, etc.). An interesting result from the current study is that the σ_1 value for fluorine is calculated to be +0.40 from the ¹⁹F SCS of **1** and **2** in cyclohexane (Table III), which is clearly at odds with the currently accepted value (+0.50).³³ In retrospect, this is perhaps not surprising since the polar effect of fluorine has not been evaluated directly from the standard system, 4-substituted bicyclo[2.2.2]octyl-1-carboxylic acids,^{59a} but from other models in which electronegativity effects may be important.³² Interestingly, the order observed here for the polar effects (electron withdrawing) of halogen substituents (Cl ~ Br > F) is identical with that observed by Stock^{59a} from the ionization constants of dibenzobicyclo[2.2.2]octylcarboxylic acids.

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Iterative Force-Field Calculations of Cycloundecane, Cyclotridecane, and Cyclopentadecane

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Abstract: The conformations of cycloundecane, cyclotridecane, and cyclopentadecane have been investigated by iterative force-field calculations. Transition states linking the energy-minimum conformations were calculated for cycloundecane only. The known dynamic ^1H and ^{13}C NMR spectra of cycloundecane were analyzed in terms of the results of the force-field calculations of this hydrocarbon.

In recent years, X-ray diffraction studies, NMR spectroscopy, and strain energy calculations have provided considerable knowledge about the conformational properties of medium and large cycloalkanes and their derivatives. However, this knowledge is largely restricted to even-membered rings and rather little structural information is available for odd-membered saturated rings above cyclononane.

In this paper we present force-field calculations on the 11-, 13-, and 15-membered cycloalkanes. There is no direct structural information on these compounds, although the structure of cycloundecanone has been determined by X-ray diffraction methods.¹ NMR data^{2,3} on the three hydrocarbons show that dynamic NMR effects occur at temperatures somewhat lower than -140 °C. Therefore, conformational barriers of the order of 6 kcal/mol must exist in these compounds. However, the low-temperature ^1H and ^{13}C NMR spectra are complex and cannot be interpreted in the absence of additional information, such as provided by force-field calculations.

Some force-field calculations have already been carried out on the 11-, 13-, and 15-membered cycloalkanes. Dale^{4,5} has used a simple procedure to explore qualitatively or semi-quantitatively the energy-minimum conformations, as well as

the interconversion paths linking these conformations in medium- and large-ring cycloalkanes. Although refined force-field calculations have been carried out on one or two conformations of cycloundecane,^{6,7} this technique has not been applied in a systematic fashion to the ring systems discussed in the present work.

Results and Discussion

Strain energy (force-field or molecular mechanics) calculations were carried out with Boyd's iterative program MOL-BUILD.⁸ This program was modified to allow conformational changes to occur by driving the appropriate torsional angles as described by Wiberg and Boyd.⁹ Approximate coordinates for trial geometries were calculated by means of the program COORD¹⁰ with torsional angles obtained from Dreiding-Fieser molecular models. The exploration of pseudorotation paths involves the migration of a specific carbon atom (Figure 1) from a corner to an adjacent noncorner position (an elementary process^{4,5}), or sequences of such migrations. As a result of an elementary process, three torsional angles change by about 120° : ± 60 to ∓ 60 , ± 60 to 180 , and 180 to ± 60 , respectively.¹¹ One torsional angle passes through 0° and the other two pass through 120° , in a sequential rather than simultaneous fashion.