Transmission of Polar Substituent Effects through the Bicyclo[2.2.2]octane Ring System as Monitored by ^{19}F NMR Shifts: A ^{19}F NMR Study of 10-Substituted 9-Fluorotriptycenes and 4-Substituted 4′-Fluorobibicyclo[2.2.2]octanes

William Adcock* and V. Sankar Iyer

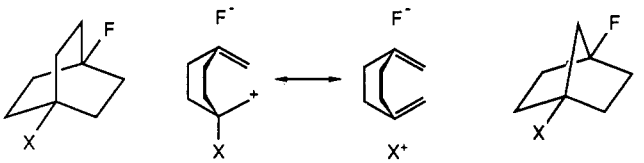
School of Physical Sciences, The Flinders University of South Australia, Bedford Park, S.A., Australia 5042

Received April 13, 1988

A series of 10-substituted 9-fluorotriptycenes (**5**) encompassing a wide range of substituents has been synthesized and characterized, and the ^{19}F chemical shifts have been measured in several solvents. Multiple linear regression analysis reveals no discernible relationship between the ^{19}F substituent chemical shifts (SCS) of **5** and polar substituent constants. Comparisons have been made between **5** and corresponding 4-substituted bicyclo-[2.2.2]oct-1-yl fluorides (**1**), which strongly corroborate the previous interpretation of the ^{19}F SCS of the latter system. In particular, the "through-bond" nature of the strong electronegativity effect (σ_χ) in **1** seems established. A more restricted series of 4-substituted 4′-fluorobibicyclo[2.2.2]octanes (**6**) have been acquired, and the pattern of shifts has been found to parallel polar field constants (σ_F values). In contrast to **1**, no evidence for a significant σ_χ effect is apparent in **6**. The pronounced sensitivity of **6** to electric field effects prompted its use in the determination of an unequivocal σ_F value for the CH_3 group.

Introduction

Recently, we reported that the ^{19}F substituent chemical shifts (SCS; charge density monitors) of 4-substituted bicyclo[2.2.2]oct-1-yl fluorides (**1**) seem dependent on both electrostatic field (σ_F effect) and electronegativity (σ_χ effect) effects.[1] The importance of the latter substituent factor as a long-range electronic influence is of considerable interest since recent analyses[2,3] of much chemical and physical data failed to delineate any definitive evidence for the transmission of substituent electronegativity effects beyond the first atom of attachment of the substituent.

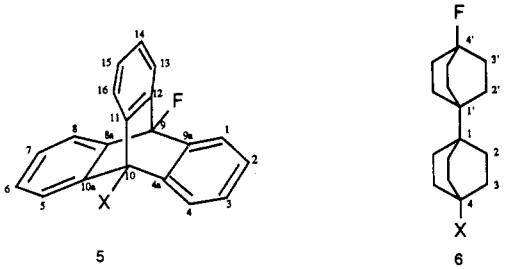


1 2 3 4

After canvassing several possible factors with respect to the origin of the electronegativity contribution to the ^{19}F SCS of **1**, we ascribed the phenomenon to a "through-three-bond" electron delocalization mechanism (TB-3 effect: a σ-resonance or $\sigma-\sigma$ hyperconjugative effect), which couples the C–X and C–F bond MO's through the intervening ethano σ bonds.[1] The prevailing orbital interactions governing this resonance effect have been attributed essentially to $\sigma_{CF}^*-\sigma_{CC}-\sigma_{CX}$. In valence bond terminology, the TB-3 effect in **1** may be denoted by canonical structures **2** and **3** (depicted for only one of the three ethano bonds). It is important to note that this proposal revives the concept of 2-fold hyperconjugation invoked by Grob et al.[4] to account for the fact that certain 4-substituted bicyclo[2.2.2]octyl nisylates appear to solvolyze faster than expectations based on σ_I^q values (derived from the pK_a values of 4-substituted quinuclidium perchlorates). Previously, based on theoretical calculations, Wenke and Lenoir[5] rejected the idea.

Subsequently, support for the proposed "through-bond" (TB) nature of the σ_χ effect in **1** came from a study of 4-substituted bicyclo[2.2.1]hept-1-yl fluorides (**4**).[6,7] The ^{19}F SCS of this system also revealed a significant electronegativity contribution but of *opposite* sign to that observed in **1**. Since the structural change of the intervening connective bonds between the bridgehead centers in proceeding from the bicyclo[2.2.2]octane (BCO) to the bicyclo[2.2.1]heptane system (BCH) is known to perturb significantly the blend of possible TB and "through-space" (TS) effects,[8] we[6,7] reasoned that the diametrically opposed σ_χ effects observed for **1** and **4** seem to make sense only in terms of antagonistic TB and TS contributions in **1** and **4**, respectively. It is of interest to note that, in the extreme, TB and TS interactions in **1** (X = Li)[9] and **4** (X = Li),[10] respectively, leads to facile loss of fluoride; the former yields 1,4-dimethylenecyclohexane while the latter gives the highly reactive [2.2.1]propellane.[10] The possible intermediacy of [2.2.2]propellane in the fragmentation of **1** (X = Li) was precluded by an appropriate trapping experiment.[9]

In the present paper we report ^{19}F SCS for 10-substituted 9-fluorotriptycenes (**5**) and 4-substituted 4′-fluorobibicyclo[2.2.2]octanes (**6**), which, as we shall see later, further strengthens the proposed "through-bond" nature of the electronegativity contribution to **1**. The bridgehead-bridgehead disubstituted triptycene system has been



5 6

(1) Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* **1982**, *47*, 2957.
(2) Reynolds, W. F. *J. Chem. Soc., Perkin Trans. 2* **1980**, 985. Reynolds, W. F. *Prog. Phys. Org. Chem.* **1983**, *14*, 165.
(3) Topsom, R. D. *Acc. Chem. Res.* **1983**, *16*, 292.
(4) Grob, C. A.; Rich, R. *Tetrahedron Lett.* **1978**, 663. Grob, C. A.; Rich, R. *Helv. Chim. Acta* **1979**, *62*, 2793.
(5) Wenke, G.; Lenoir, D. *Tetrahedron Lett.* **1979**, *20*, 2823.
(6) Adcock, W.; Abeywickrema, A. N.; Kok, G. B. *J. Org. Chem.* **1984**, *49*, 1387.
(7) Adcock, W.; Iyer, V. S. *Tetrahedron Lett.* **1984**, *25*, 5209.
(8) Stohrer, W. D.; Hoffmann, R. *J. Am. Chem. Soc.* **1972**, *94*, 779 and references cited therein.
(9) Adcock, W.; Iyer, V. S. *J. Org. Chem.* **1985**, *50*, 1538.
(10) Adcock, W.; Gangodawila, H.; Iyer, V. S. manuscript in preparation.

0022-3263/88/1953-5259$01.50/0

Table I. ^{19}F Substituent Chemical Shifts (SCS)[a-c] of 10-Substituted 9-Fluorotriptycenes (5)

X	SCS			
	c-C_6H_{12}	$CDCl_3$	DMF	CF_3CO_2H
NO_2	2.06	2.05	2.20	1.86
CN	0.43	0.51	0.69	0.32
COOH	1.68	1.64	1.47	1.71
$COOCH_3$	1.59	1.56	1.65	1.67
$COCH_3$	1.77	1.79	1.87	1.89
CHO	1.15	1.16	1.24	1.13
CH_2OH	0.83	0.78	0.66	0.87
COCl	2.09	2.04	1.58	*d*
OH	−0.31	−0.12	−0.17	0.08
F[e]	−0.13	−0.11	0.08	−0.34
Cl	0.55	0.53	0.72	0.35
Br	0.83	0.79	0.96	0.59
I	1.09	1.03	1.17	*d*
NH_2	−0.03	0.01	−0.07	0.76
CH_3	0.23	0.19	0.26	0.26
$Sn(CH_3)_3$[f]	0.97	0.89	0.98	*d*
D[g]	0.00	0.00	0.00	*d*

[a] Defined as the difference (in parts per million) between the ^{19}F chemical shift of the substituted compound and that of the parent compound (X = H). A Negative sign denotes shielding (upfield shift). [b] Accurate to ±0.01 ppm. [c] X = H (relative to internal $FCCl_3$): −208.12 (c-C_6H_{12}), −207.70 ($CDCl_3$), −206.13 ppm (DMF). [d] Not measured. [e] J_{FF} = 1.65 Hz, J_{CF} = 209.41 Hz. Obtained from ^{13}C satellites in the $^{19}F\{^1H\}$ spectrum ($CDCl_3$). [f] $^fJ_{^{117,119}Sn-^{19}F}$ not observed. [g] Accurate to ±0.002 ppm.

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

X	SCS			
	c-C_6H_{12}	$CDCl_3$	DMF	CF_3CO_2H
NO_2	−8.39	−9.89	−9.53	−17.45
CN	−4.15	−5.40	−4.79	−12.55
COOH	−4.75	−5.68	−4.93	−10.57
$COOCH_3$	−4.38	−5.29	−5.05	−10.19
$COCH_3$	−4.15	−5.11	−4.52	−10.56
CHO	−3.09	−4.10	−3.50	−9.92
CH_2OH[c]	−2.61	−3.27	−2.47	−6.59
COCl[c]	−5.01	−6.14	−5.01	*d*
OH	−8.06	−9.24	−7.47	−14.96
F	−8.90	−10.32	−10.19	−16.13
Cl	−6.97	−8.14	−8.07	−12.66
Br	−5.94	−7.07	−6.98	−11.50
I	−3.35	−4.29	−4.12	−8.22
NH_2	−6.60	−7.51	−6.28	−17.97
CH_3	−3.81	−3.92	−3.90	−4.08
$Sn(CH_3)_3$	3.67	3.83	3.94	*d*
D[e]	−0.059	−0.060	−0.058	*d*

[a] See footnotes *a* and *b* to Table I. [b] Taken from ref 1. [c] This study. [d] Not measured. [e] Taken from ref 7.

Table III. ^{19}F Substituent Chemical Shifts (SCS)[a,b] of Some 4-Substituted 4'-Fluorobibicylo[2.2.2]octanes (6)

X	SCS			
	c-C_6H_{12}	$CDCl_3$	DMF	CF_3CO_2H
F	−0.79	−1.00	−0.63	−2.59
Cl	−0.81	−1.00	−0.61	−2.22
Br	−0.84	−1.03	−0.64	−2.25
I	−0.81	−0.99	−0.61	−2.08
CH_3	−0.10	−0.08	−0.07	−0.12

[a] See footnotes *a* and *b* to Table I. [b] X = H (relative to internal 1 (X = H): −2.28 (c-C_6H_{12}), −2.35 ($CDCl_3$), −2.38 (DMF), −1.97 ppm (CF_3CO_2H).

previously employed as a model substrate for the study of polar substituent effects.[11] In that case a carboxyl group (energy monitor) was utilized as the probe, and the trends of the dissociation constants were shown to be satisfactorily accommodated by a field-effect model. To the best of our knowledge, the bibicyclo[2.2.2]octane system has never before been used for such studies but has been recently employed as a saturated spacer or linker group in other connections.[12-14] Both systems, being geometrically rigid polycyclic alkanes, appear to be ideal for providing NMR chemical shift information unencumbered by various phenomena (proximity, magnetic anisotropic, and stereochemical effects), which are well-known to obscure chemical shift/electron density relationships.

Results and Discussion

Fluorotriptycenes (5). The ^{19}F SCS for system **5** in c-C_6H_{12}, $CDCl_3$, DMF, and CF_3CO_2H are assembled in Table I. In order to facilitate comparisons, the previously reported corresponding values of system **1** are listed in Table II. Before drawing comparisons between these data, it is instructive to take note of several significant features of **5**. These are as follows: (i) Compound **5** may be viewed formally as a benzannelated derivative of **1**. (ii) The geometric relationship between the substituent and fluorine probe in **5** is virtually identical with that in **1**. Hence, angle and distance considerations suggest similar electrostatic field and "back-lobe or TS" influences on the probe in both systems. A major difference between these model systems is that the BCO skeletal framework of **5** is much more rigid than that of **1**. (iii) The C–F σ-bond of **5** is structurally precluded from hyperconjugation with the adjacent π-systems. This situation is highlighted by the fact that long-range five-bond coupling ($^5J_{CF}$) between fluorine and appropriate aryl carbons (C3,6,15), essentially a π-electron-transmitted coupling in benzylic systems,[15,16] is not observed in **5** (Table IV). (iv) Although it is possible that field-induced π-polarization of the benzene rings may perturb the electronic environment of the fluorine nucleus, it should be remembered that such an effect would be proportional to σ_F^2.

A cursory examination of the ^{19}F SCS (Tables I and II) reveals that there is a significant and striking difference between the two sets of SCS.[17] The overall situation is exemplified by the fact that whereas multilinear regression analysis indicates that the ^{19}F SCS of **1** can be described to a fair degree of accuracy by a linear two-parameter equation (SCS = $\rho_F\sigma_F + \rho_X\sigma_X + c$),[1] a similar analysis[18] reveals that the shift parameters of **5** cannot be fitted to the same model or one just involving a single parameter ($r^2 < 0.40$). It should be noted that this analysis conflicts with claims that ^{19}F SCS for a limited number of acety-

(11) Bowden, K.; Parkin, D. C. *Can. J. Chem.* **1969**, *47*, 177.
(12) Zimmerman, H. E.; Goldman, T. D.; Hirzel, T. K.; Schmidt, S. P. *J. Org. Chem.* **1980**, *45*, 3933.
(13) Beratan, D. N. *J. Am. Chem. Soc.* **1986**, *108*, 4321 and references cited therein.
(14) Reiffenrath, V.; Schneider, F. *Z. Naturforsch., A: Phys. Phys. Chem., Kosmophys.* **1981**, *36A*, 1006.
(15) Adcock, W.; Abeywickrema, A. N. *Aust. J. Chem.* **1980**, *33*, 181.
(16) Schaefer, T.; Peeling, J.; Sebastian, R. *Can. J. Chem.* **1985**, *63*, 3219.
(17) (a) A *decrease* in σ-electron density leads to *negative* ^{19}F SCS (*upfield* shift) in system 1.[17b] The converse situation holds for an *increase* in σ-electron density.[17c] (b) Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* **1982**, *47*, 2945. (c) On the basis of theoretical studies, it has been suggested that an *increase* in the total electronic population is accompanied by a downfield shift (sp^3C, carbonyl C, and dialkyl ether O atoms) when the increase in charge is dictated by the σ population (Fliszár, S.; Cardinal, G.; Bêraldin, M. T. *J. Am. Chem. Soc.* **1982**, *104*, 5287.
(18) (a) Dipolar field parameters (σ_F values) defined from the ^{19}F SCS of 1-X-4-(*p*-fluorophenyl)bicyclo[2.2.2]octanes (**8**) are available for all the substituents in Table I except for COCl, which was specifically measured for this study. σ_F values derived for COCl from the ^{19}F SCS (ppm) of **8** (1.39 (c-C_6H_{12}), 1.27 ($CDCl_3$), 0.64 (DMF)) are 0.51 (c-C_6H_{12}), 0.49 ($CDCl_3$), and 0.40 (DMF). See ref 1 for appropriate ρ_F values for **8**. (b) See also ref 34 in ref 6.

Table IV. ^{13}C NMR Chemical Shifts[a-c] of 10-Substituted 9-Fluorotriptycenes (5)

X	chemical shift, ppm								
	C1,8,13	C2,7,14	C3,6,15	C4,5,16	C4a,10a,11	C8a,9a,12	C9	C10	others
H	118.98	125.25	125.77	123.11	142.27	143.36	98.84	52.45	
	(5.37)			(2.93)	(6.35)	(20.02)	(207.03)	(2.44)	
NO_2	118.82	126.86	126.38	121.50	137.57	141.88	96.90	94.84	
	(5.86)			(3.91)	(6.35)	(20.99)	(207.53)	(3.42)	
CN	119.40	126.88	126.44	121.46	137.78	141.71	97.52	52.45	115.35 (CN)
	(5.85)			(2.93)	(5.86)	(21.00)	(208.50)	(2.45)	
$COOCH_3$	118.74	125.82	125.82	123.25	140.45	143.55	97.74	60.51	52.03 (CH_3)
	(6.72)			(2.45)	(6.10)	(20.14)	(205.69)	(2.44)	169.86 (CO)
$COCH_3$	118.93	125.74	125.74	123.26	140.42	144.31	97.73	64.76	32.86 (CH_3)
	(6.70)			(3.06)	(6.10)	(20.14)	(205.07)	(2.44)	205.84 (CO)
CHO	119.35	125.90	125.90	121.90	139.76	143.85	97.87	59.41	199.71 (CO)
	(6.59)			(2.94)	(5.87)	(20.52)	(206.62)	*d*	
CH_2OH	118.91	125.34	125.77	121.64	145.39	143.90	*d*	53.22	60.78 (CH_2OH)
	(6.35)			(2.44)	(6.35)	(20.99)		(1.91)	
OH	118.45	125.45	125.71	119.06	143.64	142.01	97.46	79.35	
	(5.37)			(2.93)	(6.84)	(20.51)	(207.52)	(2.93)	
F	118.71	125.99	125.99	118.71	140.69	140.69	97.18	97.18	
	(5.38)			(5.38)	(21.24)	(21.24)	(208.74)	(208.74)	
	(3.91)			(3.91)	(6.59)	(6.59)	(3.66)	(3.66)	
Cl	118.27	126.25	125.98	121.12	141.43	141.90	97.26	72.90	
	(5.86)			(2.44)	(6.35)	(20.99)	(207.52)	(2.93)	
Br	118.25	126.33	126.03	123.28	141.54	141.84	97.36	68.76	
	(5.86)			(2.93)	(6.35)	(20.02)	(207.03)	(2.93)	
I	118.17	126.59	126.18	127.58	142.56	141.53	97.81	56.36	
	(5.86)			(2.44)	(5.86)	(20.50)	(206.54)	(2.93)	
NH_2	118.54	125.40	125.68	118.95	144.09	143.13	97.68	63.10	
	(5.37)			(2.44)	(6.35)	(20.51)	(206.55)	(3.40)	
CH_3	118.51	125.08	125.53	120.32	144.40	144.36	98.30	48.30	12.83 (CH_3)
	(5.85)			(3.42)	(6.35)	(19.53)	(205.57)	(1.95)	
$Sn(CH_3)_3$[d]	119.30	125.01	125.50	124.84	145.65	145.95	98.64	51.83	-6.75 ($Sn(CH_3)_3$)
	(7.33)			(3.06)	(6.11)	(19.53)	(204.46)	(1.83)	[325.32]
									[341.19]
D	119.0	125.27	125.79	123.08	142.24	143.38	99.51	52.47	
	(5.37)			(2.93)	(5.86)	(20.02)	(206.67)	(2.44)	

[a] Chemical shifts for $CDCl_3$ solution relative to Me_4Si. Accurate to ±0.04 ppm. Positive shifts indicate decreased shielding. [b] $^{13}C-^{19}F$ coupling constants (in hertz) are given in parentheses. [c] The number of the ring carbon atoms is shown in structure **5**. [d] $^{13}C-^{117,119}Sn$ coupling constants (in hertz) are given in brackets. [d] Not observed.

lene-bridged 10-substituted 9-fluoroanthracenes, a model system similar to **5** but possessing less symmetry, accurately portray the influence of remote dipolar groups.[19] This contrast in results highlights the need for a set of substituents encompassing a diverse range of electronic type.

A careful scrutiny of the data in Table I suggests that it is just not simply a case of the ^{19}F chemical shifts of **5** not responding systematically to the polar effects of the substituents but one in which the fluorine monitor appears to be "switched off" entirely as an electronic probe. The latter conclusion follows from the very small ^{19}F SCS for *fluorine* and *cyano* in **5** (Table I), both powerful inductive substituents but sterically very small. Superficially, the apparent random variations of the ^{19}F SCS of **5** seem more in line with the relative steric sizes of some of the groups. In this connection it is worth noting that the possibility of a remote buttressing effect being transmitted between the bridgehead positions in triptycene has recently been mooted.[20] Although the ^{19}F SCS of **5** correlate poorly against available steric parameters,[21] it should be borne in mind that the steric requirements of substituents depend crucially on the particular substrate in question.[22] The "pocket" for the substituent at the bridgehead position of triptycene is quite unique and not necessarily simulated in the available model substrates.

We believe that there are two main reasons for the extraordinary difference in behavior of fluorine as an electronic probe in systems **1** and **5**. Firstly, the electrostatic field contribution ($\rho_F\sigma_F$) to the ^{19}F SCS of alkyl fluorides has been shown to have its origin in the polarization of the C–F σ-bond.[17b] This leads to changes in hybridization of the exocyclic orbital of the bridgehead carbon attached to fluorine in response to the consequential electron density changes. In addition, it has been shown that the polar field effect is markedly enhanced in powerful hydrogen-bond donor solvents (HBD) due to strong hydrogen-bonding interactions with the fluorine probe increasing the polar susceptibility parameter (ρ_F).[1,17b] Hence, in the light of this knowledge it can be envisaged that ρ_F will decrease and be less perturbed by HBD solvents as the C–F σ-bond becomes "stiffer" with increasing rigidity of the skeletal framework of the model substrate. Apparently, in the case of system **5** the C–F σ-bond is so "stiff" that $\rho_F \approx 0$. This is dramatically confirmed by the absence of any obvious exaltation of the ^{19}F SCS of **5** in CF_3CO_2H (Table I), which stands in stark contrast to the corresponding shifts of **1** (Table II).[1,17b]

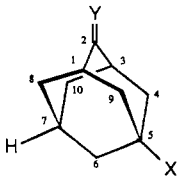
Changes in the one-bond carbon–fluorine spin–spin coupling constants (Δ^1J_{CF}) also manifest electrostatic field polarization of the C–F σ-bond.[1,17b] Hence, in the light of the analysis of the ^{19}F SCS, its not surprising that whereas a good correlation exists between Δ^1J_{CF} for **1** vs σ_F^1 no discernible relationship exists for the corresponding values of **5** (see Table IV). Interestingly, physical and chemical properties are available[23] to suggest that the bicyclo-

(19) Anderson, G. L.; Stock, L. M. *J. Am. Chem. Soc.* **1969**, *91*, 6804.
(20) Imashiro, F.; Takegoshi, K.; Terao, T.; Saika, A. *J. Phys. Chem.* **1982**, *86*, 3306.
(21) (a) Charton, M. *J. Org. Chem.* **1969**, *91*, 615. (b) Bott, G.; Field, L. D.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618 and references cited therein.
(22) Hounshell, W. D.; Iroff, L. D.; Iverson, D. J.; Wroczynski, R. J.; Mislow, K. *Isr. J. Chem.* **1980**, *20*, 65.

[2.2.1]heptane and triptycene systems exhibit similar angular strains at the respective bridgeheads. This similarity is also mirrored by the $^1J_{CF}$ values for the parent systems (X = H) of **4** and **5** ($CDCl_3$: 207.6[6] and 207.03 Hz (Table IV), respectively). It is noteworthy then that significant ρ_F values have been identified for the ^{19}F SCS of **4**[6] but not **5**, which indicates some flexibility in the structure of the former system. Structural evidence is available to support this deduction.[24]

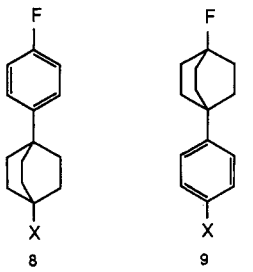
Secondly, since a description in qualitative MO terms of the TB-3 effect (see above) suggests that the extent of delocalization of electrons from the neighboring antiperiplanar C–C bonds into the σ^* orbital of the C–F bond is pertinent, the orbital energy gap (ΔE)[25] between σ_{CC} and σ_{CF}^* is expected to be a dominant factor governing the σ_χ effect. Thus, benzannelation of the ethano bonds of **1** to give **5** should reduce the influence of this polar transmission mechanism considerably since an increase in the s character of the two hybrid orbitals forming the bridging σ bonds (σ_{CC}) increases ΔE.[25] The effect of this structural modification is apparently so pronounced that the ^{19}F SCS of **5** show no dependency on σ_χ whatsoever. It should be noted that the relative extent to which the bridgehead bonds in **1** and **5** are coupled is dramatically reflected by the relative magnitude of some long-range five-bond spin–spin coupling constants (($CDCl_3$, Hz): $^5J_{^1H-^{19}F}$ = 5.6 (1)[26] vs 0.00 (5);[27] $^5J_{^{119}Sn-^{19}F}$ = 74.47 (1)[28] vs 0.00 (5); $^5J_{^{19}F-^{19}F}$ = 19.0 (1)[1] vs 1.65 (5); $^5J_{^{13}C-^{19}F}$ = 5.1 (1)[29] vs 0.00 (5)).

Clearly, the findings disclosed herein concerning **5** strengthen our previous analysis and interpretation of the ^{19}F SCS of **1**.[1] In particular, the "through-bond" nature of the σ_χ effect in **1** seems confirmed. We are currently examining the importance of this polar mechanism in connection with the solvolytic rates of some 4-substituted bicyclo[2.2.2]oct-1-yl derivatives as well as the ^{19}F SCS of 5-substituted adamant-2-yl fluorides. The latter study may bear significantly on the origin of the electronic effect responsible for tuning the π-faces of 2,5-(or 1,4-)disubstituted adamantanes (**7**, Y = O or CH_2) with respect to nucleophilic and electrophilic addition reactions.[30]



7

Fluorobibicyclo[2.2.2]octanes (6). The ^{19}F SCS of system **6** for a limited number of substituents in various solvents are set out in Table III. It can be seen that the shift patterns for the *halogens* are practically identical with those expected from the dipolar field parameters (σ_F) defined from the ^{19}F SCS of 1-X-4-(*p*-fluorophenyl)bicyclo[2.2.2]octanes (**8**) in the same solvents,[1] i.e. in general



8 9

the order is F ~ Cl ~ Br ~ I except for CF_3CO_2H where the order is F > Cl ~ Br > I.[1,17b] Any significant perturbation of the shifts by an electronegativity effect (σ_χ) would have generated a consistently different pattern, namely, F > Cl > Br > I for all solvents. Thus, as expected on the basis of the TB-3 mechanism (see Introduction), the σ_χ effect is not transmitted beyond one BCO ring. Previously, we scaled the σ_F parameters defined from the ^{19}F SCS of **8** by setting the value for Br equal to 0.44.[1] By use of this constant, polar susceptibility parameters (ρ_F) can be determined for **6** (ρ_F = −1.91 (c-C_6H_{12}), −2.34 ($CDCl_3$), −1.46 (DMF), −5.11 (CF_3CO_2H)), which quantify the high sensitivity of this system to substituent field effects. The origin of the striking solvent effect for CF_3CO_2H (exalted ρ_F value) has been previously discussed in connection with our studies of **1**[1,17b] and need not be reiterated here.

It is of interest to draw a comparison between the ρ_F values for **6** and those for 1-fluoro-4-(*p*-substituted phenyl)bicyclo[2.2.2]octanes (**9**) (ρ_F = −0.97 (c-C_6H_{12}), −1.06 ($CDCl_3$), −0.66 (DMF))[17b] since both systems are structurally similar with respect to the geometric relationship between the fluorine probe and the substituent. Surprisingly, the susceptibility parameters for **6** are twice as large as those for **9**! This result clearly conflicts with expectations that the σ_F effect should be transmitted more efficiently in **9** as a result of field-induced π-polarization of the benzene ring.[2] The possibility that the reason for this puzzling result resides in the effective dielectric constant term (ϵ)[31] of the electric field expression is precluded by the fact that the attenuation of ρ_F on proceeding from **6** to **9** seems independent of the bulk dielectric constant of the solvent (see results above).

A further puzzling feature worth noting is that the ρ_F values for **1** (−3.13 (c-C_6H_{12}), −5.25 ($CDCl_3$), −4.70 (DMF), −17.56 (CF_3CO_2H),[1,17b] which were previously derived from the data of *p*-$NO_2C_6H_4$ and C_6H_5 (a methodology that has been subsequently substantiated),[28,32] are drastically discordant with predictions based on the corresponding values of **6** (see above) and distance dependency considerations ($E_z \propto 1/r^3$).[33] According to the latter expression, ρ_F values for **1** should be ca. 8 times greater than those for **6**!

We believe that since the magnitude of ρ_F for saturated fluorides depends importantly on the ability of the carbon atom attached to the fluorine probe to undergo structural readjustment in response to longitudinal polarization of the CF σ-bond,[17b] both the aforementioned apparent anomalies may simply mirror the relative extent to which the BCO and phenyl groups in **6** and **9**, respectively, are

(23) Skvarchenko, V. R.; Shalaev, V. K.; Klabunovskii, E. I. *Russ. Chem. Rev.* **1974**, *43*(11), 951 and references cited therein.
(24) The bridgehead positions in 1,4-dichlorobicyclo[2.2.1]heptane are both flattened relative to the parent unsubstituted bicyclo[2.2.1]heptane (Chiang, J. F.; Wilcox, C. F.; Bauer, S. H. *J. Am. Chem. Soc.* **1968**, *90*, 3149).
(25) Dewar, M. J. S.; Dougherty, R. C. *The PMO Theory of Organic Chemistry*; Plenum: New York, 1975.
(26) (a) See ref 9 in ref 7. (b) Barfield, M.; Della, E. W.; Pigou, P. E.; Walter, S. R *J. Am. Chem. Soc.* **1982**, *104*, 3459.
(27) No discernible coupling was observed at 399.65 MHz. We thank Dr. W. Kitching for access to the high-field Bruker spectrometer at the University of Queensland.
(28) Adcock, W.; Gangodawila, H.; Kok, G. B.; Iyer, V. S.; Kitching, W.; Drew, G. M.; Young, D. *Organometallics* **1987**, *6*, 156.
(29) Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* **1982**, *47*, 2951.
(30) (a) Cheung, C. K.; Tseng, L. T.; Lin, M.-H.; Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598. (b) Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 5874.
(31) Ehrenson, S. *J. Phys. Chem.* **1977**, *81*, 1520 and references cited therein.
(32) Adcock, W.; Abeywickrema, A. N.; Iyer, V. S.; Kok, G. B. *Magn. Reson. Chem.* **1986**, *24*, 213.
(33) Adcock, W.; Khor, T. C. *J. Am. Chem. Soc.* **1978**, *100*, 7799 and references cited therein.

able to anchor the BCO skeletal framework to field-induced distortions at the appropriate bridgehead carbon. The ρ_F parameters for **6** and **9** (see above) suggest that the CF σ-bond in the latter system is "stiffer" than that in the former as a result of this substituent-induced structural factor.

Finally, we report that the discovery that **6** is very sensitive to polar-field phenomena prompted us to utilize this model system for the determination of an unequivocal σ_F value for the *methyl* group attached to a sp^3 carbon. There is conflict in the literature concerning the sign of this parameter,[34] however, the commonly held view is that it is *negative* (apparently electron donating). It can be seen (Table III) that the ^{19}F SCS for CH_3 in **6** are *negative* and, therefore, σ_F for this substituent must be *positive*. Interestingly, this is in accord with results from **8**[34b,35] and other 1,4-disubstituted bicyclo[2.2.2]octanes[36] where the NMR probe (^{19}F or ^{13}C) is an integral part of an unsaturated system. However, the results for the latter systems were considered equivocal because of the possible substituent-induced perturbation of the resonance effect of the BCO group. By use of the ρ_F values for **5** (see above), σ_F values for CH_3 can be calculated (0.05 (c-C_6H_{12}), 0.03 ($CDCl_3$), 0.05 (DMF), 0.02 (CF_3CO_2H) from the appropriate ^{19}F SCS (Table III). It must be emphasized, however, that for statistical purposes the σ_F value for CH_3 can be assumed to be zero without significant error as previously suggested.[1]

Experimental Section

Melting and boiling points are uncorrected. Distillations were generally carried out with a Kugelrohr apparatus (Büchi: GKR-50). Hence, boiling points quoted pertain to this equipment. Analytical vapor-phase chromatographic (VPC) analyses were performed on a Varian 1740 gas chromatograph with use of a 10-ft column of 5% SE-30 on 100–120 Chromosorb W. The broad-band proton-decoupled ^{13}C 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 spectra were obtained on $CDCl_3$ solutions (ca. 0.5 M) in 5-mm tubes with Me_4Si as an internal reference (spectral widths 2000/4000/5000 Hz, 16K–8K data points minimum digital resolution of 0.25/0.5/0.6 Hz). The ^{19}F NMR spectra were obtained under proton-decoupling conditions in the pulse Fourier transform mode with the aforementioned spectrometer operating at 84.26 MHz. Spectral widths of 2000 and 1000 Hz, respectively, were used, and the data were collected into 16K/8K data points giving a digital resolution of 0.24 and 0.12 Hz, respectively. For the fluorotriptycenes, each sample consisted of the substituted compound (<1 mg) and the parent system (X = H; <1 mg) in 0.5 mL of the appropriate solvent. However, for the fluorobibicyclo-[2.2.2]octanes, which were all obtained as mixtures except for 4,4′-difluoro-1,1′-bibicyclo[2.2.2]octane, the latter compound was employed as the internal reference.

Preparation of Fluorotriptycenes (5). 9-Fluorotriptycene (5, X = H). 9-Acetoxytriptycene was prepared by the addition of benzyne to 9-acetoxyanthracene[37] (7.0 g, 0.029 mol) via the procedure of Friedman and Logullo.[38] Recrystallization from hexane gave colorless prisms (5.0 g, 54.3%): mp 255–257 °C; ^1H NMR ($CDCl_3$) δ 2.66 (3 H, s, CH_3), 5.43 (1 H, s, CH), 7.00–7.56 (12 H, m, Ar); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 121.22 (C1, 8, 13), 124.66 (C2, 7, 14), 125.52 (C3, 6, 15), 123.25 (C4, 5, 16), 142.34 (C4a, 10a, 11), 143.07 (C8a, 9a, 12), 86.71 (C9), 53.22 (C10), 168.62 (CO), 21.62 (CH_3).

A solution of 9-acetoxytriptycene (5.0 g, 0.016 mol), 95% ethanol (100 mL), and potassium hydroxide (20.0 g of 85% pellets) was heated under reflux with vigorous stirring for 3 h. After cooling, the reaction mixture was added to ice–water and then extracted with dichloromethane. Drying and removal of the solvent followed by sublimation of the crude residue afforded 9-hydroxytriptycene as a pale yellow solid (3.5 g, 81.3%). A sample was purified by recrystallization from methanol: mp 236–238 °C (lit.[39] mp 245.0–246.5 °C); ^1H NMR ($CDCl_3$) δ 3.40 (1 H, s, OH), 5.46 (1 H, s, CH), 7.06–7.20 (6 H, m, Ar), 7.30–7.73 (6 H, m, Ar); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 118.94 (C1, 8, 13), 125.03 (C2, 7, 14), 125.39 (C3, 6, 15), 123.14 (C4, 5, 16), 143.64 (C4a, 10a, 11), 145.78 (C8a, 9a, 12), 80.72 (C9), 52.74 (C10).

A solution of 9-hydroxytriptycene (3.5 g, 0.013 mol) in a minimum quantity of anhydrous dichloromethane was placed in a stainless steel autoclave (300 mL) and treated with sulfur tetrafluoride (**CAUTION**: toxic)[40] in the manner previously outlined for the preparation of 1-fluoro-4-methyl-1,2,3,4-tetrahydro-1,4-ethanonaphthalene.[41] A workup following the usual precautions, followed by column chromatography (aluminium oxide; petroleum ether (40–60 °C) as eluant) and sublimation, afforded 9-fluorotriptycene (**5**, X = H) as a white solid (3.0 g, 84.7%). An analytical sample was obtained by recrystallization from hexane: mp 250–252 °C; ^1H NMR ($CDCl_3$) δ 5.43 (1 H, s, CH), 6.96–7.30 (6 H, m, Ar), 7.40–7.73 (6 H, m, Ar); ^{13}C NMR (see Table IV). Anal. Calcd for $C_{20}H_{13}F$: C, 88.21; H, 4.81. Found: C, 87.56; H, 5.02.

9-Bromo-10-fluorotriptycene (5, X = Br). 9,10-Dibromotriptycene[42] was prepared by the addition of benzyne to 9,10-dibromoanthracene[43] (5.0 g, 0.015 mol) via the procedure of Friedman and Logullo.[38] Sublimation of the crude product afforded a pale yellow solid (4.2 g, 48.5%). A sample was purified by recrystallization from a chloroform/methanol mixture (1:1 v/v): mp 295–300 °C (lit.[42] mp 315–316 °C); ^1H NMR ($CDCl_3$) δ 7.13–7.36 (6 H, m, Ar), 7.76–8.00 (6 H, m, Ar); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 123.38 (Cl, 8, 13, and C4, 5, 16), 126.44 (C2, 7, 14 and C3, 6, 15), 142.67 (C4a, 10a, 11 and C8a, 9a, 12), 70.67 (C9, 10).

By use of the lithiation procedure of Kawada and Iwamura,[44] a solution of 9,10-dibromotriptycene (10.0 g, 0.024 mol) in benzene/diethyl ether (100 mL; 1:2 v/v) was treated with ca. 1.6 equiv of *n*-butyllithium (36 mL of 1 M solution in hexane; 0.038 mol) at 0 °C under an atmosphere of dry nitrogen. The reaction mixture was stirred at this temperature for 30 min and then for a further 1 h after removal of the cold bath. The resulting suspension of 9-bromo-10-triptycyllithium was then added slowly through a cannula to a vigorously stirred ethereal solution of molybdenum pentoxide/pyridine/hexamethylphosphoramide complex[45] (MoOPH; 22.2 g, 0.048 mol) at −78 °C under an atmosphere of nitrogen. After being stirred for an hour at this temperature, the reaction mixture was allowed to warm up to 0 °C before water (300 mL) was added, and the mixture was stirred for a further 1 h at room temperature before being thoroughly extracted with chloroform (4×). The combined extract was washed

(34) (a) Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3095 and references cited therein. (b) Adcock, W.; Khor, T. C. *J. Org. Chem.* **1978**, *43*, 1272 and references cited therein. (c) Taft, R. W.; Taagepera, M.; Abboud, J. L. M.; Wolk, J. F.; De Frees, D. J.; Hehre, W. J.; Bartmess, J. E.; McIver, R. T. *J. Am. Chem. Soc.* **1978**, *100*, 7765. (d) Fischer, A.; King, M. J.; Robinson, F. R. *Can. J. Chem.* **1978**, *56*, 3072 and references cited therein. (e) Reynolds, W. F.; Gomes, A.; Moron, A.; MacIntyre, D. W.; Tanin, A.; Hamer, G. K.; Peat, I. R. *Can. J. Chem.* **1983**, *61*, 2376 and references cited therein. (f) Caldwell, G.; McMahon, T. B.; Kebarle, P.; Bartmess, J. E.; Kiplinger, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 80.

(35) Adcock, W.; Aldous, G. L.; Kitching, W. *J. Organomet. Chem.* **1980**, *202*, 385.

(36) (a) Adcock, W.; Kok, G. B. *J. Org. Chem.* **1985**, *50*, 1079. (b) Adcock, W.; Butt, G.; Kok, G. B.; Marriott, S.; Topsom, R. D. *J. Org. Chem.* **1985**, *50*, 2551.

(37) Barnett, E. DeB.; Matthews, M. A. *J. Chem. Soc.* **1923**, *123*, 380.

(38) Friedman, L.; Logullo, F. M. *J. Am. Chem. Soc.* **1963**, *85*, 1549. Friedman, L.; Logullo, F. M. *J. Org. Chem.* **1969**, *34*, 3089.

(39) Imashiro, F.; Hirayama, K.; Terao, T.; Saika, A. *J. Am. Chem. Soc.* **1987**, *109*, 729.

(40) Boswell, G. A.; Ripka, W. C.; Scribner, R. M.; Tullock, C. W. *Org. React. (N.Y.)* **1974**, *21*, 1.

(41) Adcock, W.; Abeywickrema, A. N. *Aust. J. Chem.* **1981**, *34*, 1253.

(42) Bohm, H.; Kalo, J.; Yarnitzky, C. H.; Ginsburg, D. *Tetrahedron* **1974**, *30*, 217. Markyl, G.; Mayr, A. *Tetrahedron Lett.* **1974**, *20*, 1817.

(43) Heilbron, I. M.; Heaton, J. S. *Organic Synthesis*; Wiley: New York, 1943; Collect. Vol. I, p 207.

(44) Kawada, Y.; Iwamura, H. *J. Org. Chem.* **1981**, *46*, 3357. Kawada, Y.; Iwamura, H. *J. Am. Chem. Soc.* **1983**, *105*, 1449.

(45) Mimoun, H.; de Roch, S.; Sajus, L. *Bull. Soc. Chim. Fr.* **1969**, *5*, 1481. Lewis, N. J.; Gabhe, S. Y. *Aust. J. Chem.* **1978**, *31*, 2091. Lewis, N. J.; Gaghe, S. U.; de la Mater, M. R. *J. Org. Chem.* **1977**, *42*, 1479.

Table V. ^{13}C NMR Chemical Shifts[a,b] of Some 4-Substituted 4′-Fluorobibicyclo[2.2.2]octanes (6)

X	chemical shift, ppm							
	C1	C2	C3	C4	C1′	C2′	C3′	C4′
H	33.71	24.77	26.00	23.1	34.49	26.52	31.23	94.51
	(3.42)				(3.41)	(9.76)	(18.56)	(183.23)
F	34.10	26.59	31.02	94.14	34.10	26.59	31.02	94.14
	(3.42)	(9.77)	(19.04)	(184.08)	(3.42)	(9.77)	(19.04)	(184.08)
Cl	33.25	27.41	36.23	67.15	34.14	26.48	31.00	94.06
	(3.42)				(3.42)	(9.77)	(19.04)	(183.84)
Br	32.56	28.32	37.66	63.93	34.14	26.42	30.98	94.03
	(3.42)				(3.41)	(9.76)	(20.02)	(183.85)
I	31.55	29.10	40.74	45.92	34.68	26.34	30.94	94.12
	(3.42)				(3.42)	(10.26)	(19.04)	(184.09)
CH_3	34.24	25.61	33.57	27.15	34.50	26.59	31.21	94.51
	(3.42)				(3.41)	(9.77)	(18.56)	(183.11)

[a] See footnotes *a* and *b* to Table IV. [b] The numbering of the ring carbon atoms is shown in structure **6**.

with 5% hydrochloric acid, 10% aqueous sodium carbonate, and then finally with water. The extract was then dried, and the solvent was removed to afford a viscous liquid, which solidified on standing. Chromatography on a column of silica gel gave first of all a fraction consisting mainly of 9-bromotriptycene (petroleum ether (40–60 °C) as eluant), and then a second fraction of HMPA (petroleum ether/chloroform mixture (80:20 v/v) as eluant), and finally 9-bromo-10-hydroxytriptycene (chloroform as eluant), which was sublimed to afford a white solid (5.1 g, 60%). A sample was crystallized from a hexane/chloroform mixture (1:1 v/v): mp 245–248 °C; ^1H NMR ($CDCl_3$) δ 3.46 (1 H, s, OH), 7.13–7.33 (6 H, m, Ar), 7.56–7.73 (6 H, m, Ar); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 123.41 (C1, 8, 13), 125.73 (C2, 7, 14), 126.20 (C3, 6, 15), 118.30 (C4, 5, 16) 144.38 (C4a, 10a, 11) 142.91 (C8a, 9a, 12), 69.84 (C9), 79.38 (C10).

A solution of 9-bromo-10-hydroxytriptycene (5.0 g, 0.014 mol) in anhydrous dichloromethane (25 mL) was treated with sulfur tetrafluoride as indicated above for the preparation of 9-fluorotriptycene (**5**, X = H). A workup following the usual precautions, followed by column chromatography (silica gel; petroleum ether (40–60 °C) as eluant) and sublimation afforded 9-bromo-10-fluorotriptycene (**5**, X = Br) as a white solid (3.9 g, 80%): mp 255–258 °C; ^1H NMR ($CDCl_3$) δ 7.1–7.33 (6 H, m, Ar), 7.6–8.0 (6 H, m, Ar); ^{13}C NMR (see Table IV). Anal. Calcd for $C_{20}H_{12}BrF$: C, 68.37; H, 3.41. Found: C, 68.11; H, 3.88.

Several preparations (5 × 1) of this important precursor compound (**5**, X = Br; see Table VI) revealed that the yield and purity varied markedly with the quality of the commercial grade sulfur tetrafluoride. Except for one batch, all others were contaminated with 9-bromo-10-chlorotriptycene, which was readily identified by ^{13}C NMR spectroscopy (see spectrum below in the preparation of 9-chloro-10-fluorotriptycene). A preparation in the absence of solvent suggests that a contaminant in the sulfur tetrafluoride (possibly sulfur dichloride) is responsible for the formation of the byproduct. Since the chloro–bromo impurity is difficult to remove from the precursor compound (**5**, X = Br) and, moreover, since its presence does not interfere with the final ^{19}F NMR measurements, functionalization was generally carried out on the crude product (see Table VI).

9-Chloro-10-fluorotriptycene (5, X = Cl). 9-Bromo-10-chlorotriptycene was prepared by the addition of benzyne to 9-bromo-10-chloroanthracene[46] (10 g, 0.03 mol) via the procedure of Friedman and Logullo.[38] Chromatography (aluminum oxide; petroleum ether (40–60 °C) as eluant) of the crude product afforded a colorless solid (5.5 g, 50%): mp 287–289 °C; ^1H NMR ($CDCl_3$) δ 7.2–7.4 (6 H, m, Ar), 7.83–8.06 (6 H, m, Ar); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 123.34 (C1, 8, 13), 126.31 (C2, 7, 14), 126.38 (C3, 6, 15), 120.98 (C4, 5, 16), 142.65 (C4a, 10a, 11), 142.78 (C8a, 9a, 12) 70.12 (C9), 74.02 (C10).

9-Bromo-10-chlorotriptycene (5 g, 0.013 mol) was converted into 9-chloro-10-hydroxytriptycene according to the methods outlined above for the preparation of the corresponding bromo derivative. Chromatography followed by sublimation afforded a white solid (2.5 g, 63%): mp 238–240 °C; ^1H NMR ($CDCl_3$) δ 3.43 (1 H, broad s, OH), 7.13–7.26 (6 H, m, Ar), 7.60–7.93 (6 H, m, Ar); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 121.16 (C1, 8, 13), 125.64 (C2, 7, 14), 126.03 (C3, 6, 15), 118.27 (C4, 5, 16), 144.52 (C4a, 10a, 11), 142.70 (C8a, 9a, 12), 73.48 (C9), 79.29 (C10).

A solution of 9-chloro-10-hydroxytriptycene (2.0 g, 0.006 mol) in anhydrous dichloromethane (15 mL) was treated with sulfur tetrafluoride as indicated above for the preparation of 9-fluorotriptycene (5, X = H). A similar workup, followed by sublimation, afforded 9-chloro-10-fluorotriptycene (**5**, X = Cl) as a white solid (1.3 g, 70.6%): mp 230–235 °C; ^1H NMR ($CDCl_3$) δ 7.13–7.33 (6 H, m, Ar), 7.60–7.93 (6 H, m, Ar); ^{13}C NMR (see Table IV) indicated that the compound was contaminated with 9,10-dichlorotriptycene (ca. 5–10%). See the latter part of the description above of the synthesis of the bromo–fluoro compound (**5**, X = Br) regarding the likely origin of this impurity.

9-Fluoro-10-methyltriptycene (5, X = CH_3). 9-Methyl-10-methoxytriptycene was prepared by the addition of benzyne to 9-methyl-10-methoxyanthracene[47] (9 g, 0.041 mol) via the pro-

Table VI. Synthetic Methods, Yields, and Physical Properties of 10-Substituted 9-Fluorotriptycenes (5)

5, X =	precursor	method	yield, %	mp, °C
D	5, X = Br	(1) *n*-BuLi/0 °C/1 h;[44] (2) D_2O	60[a]	251–253
OH	5, X = Br	(1) *n*-BuLi/0 °C/1 h;[44] (2) MoOPH[45,b]	62	158–163
F	5, X = OH	SF_4[39,b]	74	258–263
I	5, X = Br	(1) *n*-BuLi/0 °C/1 h;[44] (2) C_6H_5I/24 h	43	206–212
COOH	5, X = Br	(1) *n*-BuLi/0 °C/1 h;[44] (2) CO_2/HCl	59	<300
$COOCH_3$	5, X = COOH	$CH_2N_2/O(C_2H_5)_2$	100	174–179
$COCH_3$	5, X = COOH	$CH_3Li/O(C_2H_5)_2$/ $(CH_3)_3SiCl$[49]	80	184–189
CH_2OH	5, X = COOH	$H_3BS(CH_3)_2$[c]	90	234–238
CHO	5, X = CH_2OH	$C_5H_5NHCrO_3Cl$[d]	69	205–208
CN	5, X = CHO	(1) NH_2OH; (2) $(CH_3CO)_2O$[e]	67	222–227
NH_2	5, X = COOH	(1) $SOCl_2$/reflux/1 h; (2) NaN_3;[f] (3) KOH/C_2H_5OH[f]	94	204–209
NO_2	5, X = NH_2	*m*-$ClC_6H_4CO_3H$/ CH_2Cl_2[g]	90	234–239
$Sn(CH_3)_3$	5, X = Br	$(CH_3)_3SnLi$/THF[h]	49	170–176

[a] Ca. 70% deuterium incorporation by ^1H NMR. [b] See the Experimental Section for synthesis of **5**, X = Br. [c] Brown, H. C.; Rao, C. G.; Kulkarni, S. V. *Synthesis* **1979**, 704. [d] Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, *31*, 2647. Cheng, V. S.; Liu, W. L.; Chen, S. *Synthesis* **1980**, 223. [e] Kornfeld, E. C.; Barney, P.; Blankley, J.; Paul, W. *J. Med. Chem.* **1965**, *8*, 342. [f] Bartlett, M. J.; Rayan, M. J.; Cohen, S. G. *J. Am. Chem. Soc.* **1942**, *64*, 2649. Bartlett, P. D.; Greene, F. D. *Ibid.* **1954**, *76*, 1088. [g] Applequist, D. E.; Renken, T. L.; Wheeler, J. W. *J. Org. Chem.* **1982**, *47*, 4985. [h] Tamborski, C.; Ford, F. E.; Soloski, E. J. *J. Org. Chem.* **1963**, *28*, 237.

(46) (a) Nonhebel, D. C. *J. Chem. Soc.* **1963**, 1216. (b) Mosnain, D.; Nonhebel, D. C. *Tetrahedron* **1969**, *25*, 1591.

cedure of Friedman and Logullo.[38] Sublimation afforded the former compound as a white solid (3.5 g, 28.6%): mp 248–253 °C; ^{1}H NMR ($CDCl_3$) δ 2.36 (3 H, s, CH_3), 4.4 (3 H, s, OCH_3), 7.0–7.23 (6 H, m, Ar), 7.33–7.83 (6 H, m, Ar); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 120.94 (C1, 8, 13), 124.94 (C2, 7, 14), 124.71 (C3, 6, 15), 120.42 (C4, 5, 16), 146.42 (C4a, 10a, 11), 146.16 (C8a, 9a, 12), 48.17 (C9), 87.16 (C10), 57.53 (OCH_3), 13.44 (CH_3).

A mixture of 9-methyl-10-methoxytriptycene (2 g, 0.0067 mol), 48% aqueous hydrobromic acid (50 mL) and acetic anhydride (50 mL) was refluxed for 3 days. After cooling, the reaction mixture was poured into water, and the resulting precipitate was collected by filtration. Sublimation afforded 9-hydroxy-10-methyltriptycene as a white solid (1.5 g, 78.8%): mp 253–256 °C; ^{1}H NMR ($CDCl_3$) δ 2.56 (3 H, s, CH_3), 3.56 (1 H, broad s, OH), 7.16–7.40 (6 H, m, Ar), 7.50–7.86 (6 H, m, Ar); ^{13}C NMR ($CDCl_3$) δ 118.49 (C1, 8, 13), 124.93 (C2, 7, 14), 125.21 (C3, 6, 15), 120.42 (C4, 5, 16), 145.77 (C4a, 10a, 11), 146.88 (C8a, 9a, 12), 79.94 (C9), 48.13 (C10), 13.08 (CH_3).

A solution of 9-hydroxy-10-methyltriptycene (0.5 g, 0.0017 mol) in anhydrous dichloromethane (10 mL) was treated with sulfur tetrafluoride as indicated above for the preparation of 9-fluorotriptycene (**5**, X = H). A similar workup, followed by column chromatography (silica gel) and sublimation, afforded 9-fluoro-10-methyltriptycene (**5**, X = CH_3) as a white solid (0.3 g, 62.5%): mp 221–230 °C; ^{1}H NMR ($CDCl_3$) δ 2.40 (3 H, s, CH_3), 7.06–7.46 (6 H, m, Ar), 7.60–7.96 (6 H, m, Ar); ^{13}C NMR (see Table IV) indicated that the compound was contaminated with 9-chloro-10-methyltriptycene (ca. 5%). See the latter description above of the synthesis of the bromo–fluoro compound (**5**, X = Br) regarding the likely origin of this impurity.

Summarized details of the synthetic methods, yields, and physical properties of the remaining derivatives of **5** are listed in Table VI. All were unambiguously characterized by ^{13}C NMR (Table IV). Assignments for these compounds followed unequivocally from the characteristic ^{13}C–^{19}F coupling constants in the triptycene skeletal framework. Standard assignment procedures such as chemical shift and intensity were also important. ^{13}C SCS data for 1-substituted 4-methyl-1,2,3,4-tetrahydro-1,4-ethanonaphthalenes[48] played an important role in distinguishing between C2,7,14 and C3,6,15.

Preparation of Fluorobibicyclo[2.2.2]octanes (6). 1-Acetyl-4-methoxybicyclo[2.2.2]octane. By use of the procedure of Rubottom et al.,[49] an ethereal solution of methyllithium (150 mL of 0.8 M solution, 0.12 mol) was added over a period of 5 min to a well-stirred solution of 4-methoxybicyclo[2.2.2]octane-1-carboxylic acid[29] (5 g, 0.027 mol) in anhydrous diethyl ether (100 mL) kept at 0 °C under an atmosphere of nitrogen. After the reaction mixture was stirred at this temperature for a further 3 h, freshly distilled chlorotrimethylsilane (40 mL, 0.3 mol) was added to the solution, and the mixture was then allowed to warm up to room temperature. A standard workup followed by Kugelrohr distillation (85 °C/0.1 mmHg) afforded the title compound as a colorless oil (4.5 g, 92%): ^{1}H NMR ($CDCl_3$) δ 1.8 (12 H, s, CH_2CH_2), 2.1 (3 H, s, $COCH_3$), 3.2 (3 H, s, OCH_3); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 44.23 (C1), 28.76, (C2), 28.58 (C3), 73.51 (C4), 49.11 (OCH_3), 212.16 (CO), 25.22 ($COCH_3$). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.50; H, 9.89. Found: C, 72.79; H, 10.23.

1-Acetoxy-4-methoxybicyclo[2.2.2]octane. A solution of 1-acetyl-4-methoxybicyclo[2.2.2]octane (3 g, 0.016 mol) in anhydrous chloroform (5 mL) was added slowly to a solution of *m*-chloroperbenzoic acid (8 g, 0.046 mol) in chloroform (50 mL).[29] The reaction mixture was stirred at room temperature until VPC analyses indicated that conversion was complete (ca. 2 days). A standard workup, followed by Kugelrohr distillation (80 °C/0.2 mmHg) afforded the title compound as a colorless oil (2.5 g, 80%): ^{1}H NMR ($CDCl_3$) δ 3.2 (3 H, s, OCH_3), 1.8–2.16 (15 H, s, CH_2CH_2 and $COCH_3$). ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 78.55 (C1), 29.69 (C2), 30.12 (C3), 71.81 (C4), 49.43 (OCH_3), 170.30 (CO), 22.35 ($COCH_3$). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.66; H, 9.09. Found: C, 66.31; H, 8.88.

1,4-Diiodobicyclo[2.2.2]octane was prepared from 1-acetoxy-4-methoxybicyclo[2.2.2]octane (2 g, 0.01 mol) by treatment with freshly distilled hydriodic acid in the same manner as previously described for its preparation from 1-iodo-4-methoxybicyclo[2.2.2]octane.[28] Sublimation afforded the diiodide as a white solid (3.3 g, 91.2%), which was recrystallized from a hexane/ethanol mixture: mp 239–240 °C (lit.[12] mp 239–240.5 °C).

1-Iodo-4-methoxybicyclo[2.2.2]octane. 1,4-Diiodobicyclo[2.2.2]octane (22.0 g, 0.067 mol) was converted into 1-acetoxy-4-iodobicyclo[2.2.2]octane (15.0 g, 76.2%; mp 127–128 °C (lit.[12] mp 128.6–129.2 °C)) and then 4-iodobicyclo[2.2.2]octan-1-ol (11.2 g, 87.1%; mp 160–161 °C (lit.[12] mp 162–162.2 °C)) according to methods outlined by Zimmerman et al.[11] Via a method described by the same workers,[12] the iodo alcohol was converted to the title compound, which was sublimed (14.2 g, 90.4%) and recrystallized from a hexane/ethanol mixture (1:1 v/v): mp 71–72 °C (lit.[12] mp 79.6–79.8 °C).

It should be noted that 1-iodo-4-methoxybicyclo[2.2.2]octane[28] can be synthesized directly from 4-methoxybicyclo[2.2.2]octane-1-carboxylic acid by decarboxylative iodination with *tert*-butyl hypoiodite as reagent. However, the yield is poor (ca. 25%), and the method is not readily amenable to a suitable large-scale preparation.

4,4′-Dimethoxy-1,1′-bibicyclo[2.2.2]octanes. By use of the procedure of Zimmerman et al.,[12] 1-iodo-4-methoxybicyclo[2.2.2]octane (12 g, 0.045 mol) was treated with magnesium (17 g, 0.67 mol) and anhydrous nickel chloride (8 g, 0.061 mol) in diethyl ether (450 mL). After workup as described by the aforementioned workers, a crude product was obtained consisting of 1-methoxybicyclo[2.2.2]octane and the title compound (1.5:1.0 by GLC analysis). The former compound was removed by careful distillation (3.8 g, 60.8%), and the residue was sublimed and recrystallized from hexane to afford the dimer as colorless needles (4.2 g, 33.5%): mp 163–165 °C (lit.[12] mp 168.1–168.5 °C); ^{1}H NMR ($CDCl_3$) δ 1.53 (24 H, s, CH_2CH_2), 3.2 (6 H, s, OCH_3); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 33.98 (C1,1′), 26.05 (C2,2′), 29.30 (C3,3′), 73.27 (C4,4′), 48.95 (OCH_3).

4-Hydroxy-4′-iodo-1,1′-bibicyclo[2.2.2]octane. By use of the procedure of Zimmerman et al.,[12] 4,4′-dimethoxy-1,1′-bibicyclo[2.2.2]octane (3.0 g, 0.011 mol) was treated with 57% aqueous HI (60 mL) in benzene (240 mL). Workup as described followed by recrystallization from a hexane/ethanol mixture afforded the title compound (3.1 g, 79.7%): mp 190–192 °C (lit.[12] mp 195.3–195.8 °C); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 34.61 (C1), 26.20 (C2), 33.80 (C3), 68.99 (C4), 31.60 (C1′), 29.15 (C2′), 40.85 (C3′), 46.47 (C5′).

4,4′-Difluoro-1,1′-bibicyclo[2.2.2]octane (6, X = F). By use of the procedure of Suzuki and Morita,[50] a solution of 4,4′-dimethoxy-1,1′-bibicyclo[2.2.2]octane (4.2 g, 0.017 mol) in acetic anhydride (10 mL) was treated with 2–4 drops of boron trifluoride etherate and stirred at room temperature until VPC analyses indicated that all the starting material had been consumed (ca. 60 h). The reaction mixture was poured onto ice/water and extracted with ether (3 × 1). The combined extract was washed with saturated sodium bicarbonate solution and dried, and the solvent was removed. Sublimation afforded 4,4′-diacetoxy-1,1′-bibicyclo[2.2.2]octane as a white solid (4.3 g, 85%): mp 224–226 °C; ^{1}H NMR ($CDCl_3$) δ 1.66–1.96 (24 H, m, CH_2CH_2), 2.00 (6 H, s, $OCOCH_3$); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 33.99 (C1,1′), 26.05 (C2,2′), 29.85 (C3,3′), 80.18 (C4,4′), 170.41 (CO), 22.46 ($COCH_3$).

A mixture of the diacetoxy compound (4.0 g, 0.011 mol), sodium methoxide (1.3 g), and absolute methanol (20 mL) was heated under reflux for 5 h.[29] A standard workup followed by sublimation and recrystallization from hexane afforded 4,4′-dihydroxy-1,1′-bibicyclo[2.2.2]octane as a white solid (2.7 g, 90%): mp 230–233 °C; ^{1}H NMR ($CDCl_3$) δ 0.86–1.23 (12 H, m, CH_2CH_2), 1.53–1.80 (12 H, m, CH_2CH_2) 3.73 (2 H, broad s, OH); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 34.11 (C1,1′), 26.08 (C2,2′), 33.98 (C3,3′), 69.15 (C4,4′).

A solution of the dihydroxy compound (2.5 g, 0.01 mol) in anhydrous dichloromethane (15 mL) was treated with sulfur tetrafluoride in the manner previously outlined for the preparation of methyl 4-fluorobicyclo[2.2.2]octane-1-carboxylate.[29] A workup following the usual precautions, followed by sublimation and

(47) Meyer, K. H.; Schlosser, H. *Annalen.* **1920**, *420*, 126.
(48) Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* **1982**, *47*, 779.
(49) Rubottom, G. M.; Kim, C. W. *J. Org. Chem.* **1983**, *48*, 1550.
(50) Suzuki, Z.; Morita, K. *J. Org. Chem.* **1967**, *32*, 31.

recrystallization from a hexane/ethanol (1:1 v/v) mixture, afforded 4,4′-difluoro-1,1′-bibicyclo[2.2.2]octane (**6**, X = F) as a white microcrystalline solid (2.3 g, 90.6%): mp 278–280 °C; ^{1}H NMR ($CDCl_3$) δ 1.63 (24 H, s, CH_2CH_2); ^{13}C NMR (see Table IV). Anal. Calcd for $C_{16}H_{24}F_2$: C, 75.59; H, 9.45. Found: C, 75.29; H, 9.84.

Preparation of Some 4-Substituted 4′-Fluoro-1,1′-bibicyclo[2.2.2]octanes as Mixtures (6, X = H, Cl, Br, I, and CH_3). Initially, we set out to prepare 4-iodo-4′-fluoro-1,1′-bicyclo[2.2.2]octane (**6**, X = I) as an appropriate precursor for synthesizing a fairly extensive series of system **6**. However, this goal was thwarted when an attempt to prepare this compound in quantity by treatment of 4-hydroxy-4′-iodo-1,1′-bibicyclo[2.2.2]octane with sulfur tetrafluoride at room temperature in the usual manner afforded the difluoro derivative (**6**, X = F) almost quantitatively. At this stage of our investigation, a cost–benefit analysis led us to restrict our efforts to a more limited range of compounds obtainable as mixtures from the readily available difluoro compound (**6**, X = F).

By use of the procedure of Olah et al.,[51] 4,4′-difluoro-1,1′-bicyclo[2.2.2]octane was treated with ca. 1 equiv of iodotrimethylsilane to afford a mixture containing 4-iodo-4′-fluoro-1,1′-bibicyclo[2.2.2]octane (**6**, X = I; ca. 32%), 4,4′-diiodo-1,1′-bibicyclo[2.2.2]octane (ca. 4%), and unreacted starting material (ca. 64%). Samples of the sublimed mixture were then treated appropriately with Li/*t*-BuOH/THF,[52] ICl,[53] or Br_2[54] to provide mixtures containing the parent system (**6**, X = H), the chloro–fluoro (**6**, X = Cl) and bromo–fluoro (**6**, X = Br) derivatives, respectively. Treatment of the difluoro precursor (**6**, X = F) with a limited quantity of trimethylaluminium as previously described[34b] gave a mixture containing the methyl–fluoro derivative (**6**, X = CH_3), 4,4′-dimethyl-1,1′-bibicyclo[2.2.2]octane, and unreacted starting material. All the aforementioned mixtures were unambiguously characterized by VPC analysis and ^{13}C NMR (Table IV). Spectra assignments for the various compounds were facilitated by the characteristic ^{13}C–^{19}F coupling constants in the bicyclo[2.2.2]octane ring system as well as by the fact that, except for bridgehead positions, additivity of substituent effects on chemical shifts work very well for 1,4-disubstituted bicyclo[2.2.2]octanes. The availability[55] of authentic samples of 1,1′-bibicyclo[2.2.2]octane (mp 234–236 °C; ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 34.06 (C1,1′), 24.75 (C2,2′), 26.18 (C3,3′), 23.79 (C4,4′)) and 4,4′-dimethyl-1,1′-bibicyclo[2.2.2]octane (mp 182–184 °C (lit.[56] mp 184–185 °C); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 34.48 (C1,1′), 25.59 (C2,2′), 33.55 (C3,3′), 27.16 (C4,4′), 28.14 (CH_3)) allowed ^{13}C NMR spectra to be calculated for all the appropriately substituted bibicyclo[2.2.2]octanes. These agreed well with all the observed spectra.

Registry No. **5** (X = H), 116263-68-4; **5** (X = Br), 116263-70-8; **5** (X = Cl), 116263-73-1; **5** (X = CH_3), 116263-76-4; **5** (X = NO_2), 116263-86-6; **5** (X = CN), 116263-87-7; **5** (X = COOH), 116263-88-8; **5** (X = $COOCH_3$), 116263-89-9; **5** (X = $COCH_3$), 116263-90-2; **5** (X = CHO), 116263-91-3; **5** (X = CH_2OH), 116263-92-4; **5** (X = COCl), 116263-93-5; **5** (X = OH), 116263-94-6; **5** (X = I), 116263-95-7; **5** (X = NH_2), 116263-96-8; **5** (X = $Sn(CH_3)_3$), 116263-97-9; **5** (X = D), 116278-40-1; **6** (X = F), 116263-80-0; **6** (X = I), 116263-81-1; **6** (X = Cl), 116263-83-3; **6** (X = H), 116263-82-2; **6** (X = CH_3), 116263-84-4; **6** (X = Br), 116263-85-5; 9-acetoxytriptycene, 97733-14-7; 9-hydroxytriptycene, 73597-16-7; 9,10-dibromoanthracene, 523-27-3; 9,10-dibromotriptycene, 795-42-6; 9-bromo-10-hydroxytriptycene, 116263-69-5; 9-bromo-10-chloroanthracene, 22273-72-9; 9-bromo-10-chlorotriptycene, 116263-71-9; 9-chloro-10-hydroxytriptycene, 116263-72-0; 9-methyl-10-methoxyanthracene, 21992-33-6; 9-methyl-10-methoxytriptycene, 116263-74-2; 9-hydroxy-10-methyltriptycene, 116263-75-3; 1-acetyl-4-methoxybicyclo[2.2.2]octane, 116263-77-5; 4-methoxybicyclo[2.2.2]octane-1-carboxylic acid, 773-34-2; 1-acetoxy-4-methoxybicyclo[2.2.2]octane, 116263-78-6; 1,4-diiodobicyclo[2.2.2]octane, 10364-05-3; 1-iodo-4-methoxybicyclo[2.2.2]octane, 74467-18-8; 1-acetoxy-4-iodobicyclo[2.2.2]octane, 74467-16-6; 4-iodobicyclo[2.2.2]octan-1-ol, 74467-17-7; 4,4′-dimethoxy-1,1′-bibicyclo[2.2.2]octane, 74467-39-3; 4-hydroxy-4′-iodo-1,1′-bibicyclo[2.2.2]octane, 74467-40-6; 4,4′-diacetoxy-1,1′-bibicyclo[2.2.2]octane, 116278-39-8; 4,4′-dihydroxy-1,1′-bibicyclo[2.2.2]octane, 116263-79-7.

(51) Olah, G. A.; Narang, S. C.; Field, L. D. *J. Org. Chem.* **1981**, *46*, 3727.
(52) Chapman, N. B.; Sotheeswaran, S.; Toyne, K. J. *J. Org. Chem.* **1970**, *35*, 917.
(53) Kauer, J. C. *Prepr. Div. Pet. Chem., Am. Chem. Soc.* **1970**, *15*, B14–B18.
(54) Wiberg, K. B.; Pratt, W. E.; Matturro, M. G. *J. Org. Chem.* **1982**, *47*, 2720.
(55) Adcock, W.; Kok, G. B., unpublished work.
(56) Adam, W.; Mazenod, F.; Nishizawa, Y.; Engel, P. S.; Baughman, S. A.; Chae, W. K.; Horsey, D. W.; Quast, H.; Seiferling, B. *J. Am. Chem. Soc.* **1983**, *105*, 6141.

Conformational Transmission in Nucleotides Containing Trigonal Bipyramidal Phosphorus as the Internucleoside Linkage

Leo H. Koole,* Marcel H. P. van Genderen, and Henk M. Buck

Department of Organic Chemistry, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands

Received April 29, 1988

A set of nucleotide analogues containing a stable trigonal bipyramidal phosphorus (P^V TBP) moiety (**5**–**11**) has been developed, and their conformational properties were studied with 300- and 500-MHz ^{1}H NMR. In the solvent acetone-d_6, it is found that the conformation of the model compounds is determined by a hydrogen bond between the backbone atom $O_{5'}$ and the base proton H_6 (pyrimidine base) or H_8 (purine base), resulting in a preference for the standard gauche(+) conformation around the $C_{4'}$–$C_{5'}$ bond. In the hydrogen bond disrupting solvent DMSO-d_6, the P^V TBP nucleotides **5**–**8** clearly show conformational transmission, i.e., a preference for the unusual gauche(−) (g^-) rotamer around the $C_{4'}$–$C_{5'}$ bond is found. This structural distortion opposes stacking of the bases, as is confirmed by the observation that the preference for g^- is strongest for **7** and **8**, in which stacking is eliminated. The present results provide support to our earlier proposition that formation of P^V TBP locations in DNA can lead to a marked change of the secondary structure (Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1980**, *99*, 181).

In the past years we developed and firmly established a concept for conformational transmission in a variety of trigonal bipyramidal phosphorus (P^V TBP) compounds.[1] It was shown that the construction of specific ligands

0022-3263/88/1953-5266$01.50/0