Stereospecific Electronegative Effects. Part II.[1] Effects of Vicinal Substituents upon Geminal ^{1}H–^{19}F Spin–Spin Coupling Constants ($^2J_{HF}$) in Fluorocarbohydrates, Polyfluoro-1,4-dioxans, and Polyfluoro-1,4-oxathians

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A detailed study has been made of $^2J_{HF}$ values in the title compounds, and a simple additive method of calculating such coupling constants is reported. It seems probable that the approach could be of use in stereochemical and conformational studies of related molecules.

We have previously shown that the magnitudes of vicinal ^{1}H–^{19}F coupling constants ($^3J_{HF}$) in various fluorocarbohydrates are dependent upon a variety of structural features, some of which involve stereospecific substituent effects.[1] This is in accord with suggestions made elsewhere [2,3] and in a later publication [4] we were able to demonstrate the same sort of phenomenon very clearly for $^3J_{HF}$ in some ethane derivatives.

In Part I,[1] we reported the magnitudes of the values of $^2J_{HF}$ (presumably positive in sign by analogy with similar systems [5]), and noted that they varied within the range 47—53 Hz. At that time we were unable to comment further upon the cause of these variations, but it seemed probable that they arise from substituent effects due to groups which are vicinal with respect to the coupled nuclei; it is possible that such effects are stereospecific in nature and therefore of potential value as a structural tool, so it was decided to examine the available data in this light.

We have recently produced a successful qualitative picture of the origins of α- (*i.e.* geminal) substituent effects upon $^2J_{HF}$,[6] and since in the title compounds both α- and β- (*i.e.* vicinal) substituent effects are present it is possible to separate the two and examine only the latter.

DISCUSSION

Fluorocarbohydrates.—We confine our attention to pyranose systems of defined stereochemistry and conformation, since any attempt to rationalise vicinal substituent effects in non-rigid (*i.e.* conformationally inhomogeneous or mobile) systems is fraught with difficulty.[7] The vast majority of available data in this area concerns compounds in which the 'substituents' vicinal to the coupled ^{1}H and ^{19}F nuclei are oxygenated functions (including ring oxygen) or fluorine; we shall therefore be primarily concerned with this situation and later refer briefly to a wider range of substituents.

The approach is wholly empirical, and from a survey of the available data 'substituent contributions' to $^2J_{FH}$ have been deduced which behave additively; these may be defined as the observed effect upon $^2J_{HF}$ of replacing a hydrogen atom, which is in a vicinal relationship to the coupled H and F nuclei, with a substituent X. For X = OR (R = alkyl, Ac, Bz, H) or F, the substituent contributions have effectively the same magnitude and the only factor which apparently causes a variation is the geometrical disposition of X with respect to the coupled nuclei. As a basis for the calculation of $^2J_{HF}$ in a given situation, it is necessary to use a 'normal' or 'unperturbed' value of $^2J_{HF}$ for the fragment (A),

(A)

in which the substituents which are vicinal to H and F are hydrogen or alkyl (*i.e.* vicinal substituent effects are negligible).

For the unperturbed value of $^2J_{HF}$, we take the average observed value in a variety of 3α- and 3β-fluorosteroids in which C(2) and C(4) are unsubstituted; this is 50 ± 1 Hz.[8-10] The effect of replacing one of the

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[1] Part I, L. Phillips and V. Wray, *J. Chem. Soc.* (*B*), 1971, 1618.

[2] H. Booth, *Tetrahedron Letters*, 1965, 411.

[3] K. G. R. Pachler, *Tetrahedron Letters*, 1970, 1955.

[4] L. Phillips and V. Wray, *J.C.S. Perkin II*, 1972, 536.

[5] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, 'High Resolution N.M.R. Spectroscopy,' Pergamon, London, 1966, 1st edn., p. 888.

[6] M. H. Pendlebury, L. Phillips, and V. Wray, *J.C.S. Perkin II*, 1974, 787.

[7] J. W. Emsley, L. Phillips, and V. Wray, *Progr. N.M.R. Spectroscopy*, in the press.

[8] L. H. Knox, S. Berger, E. Verlade, D. Cuadriello, and A. D. Cross, *J. Org. Chem.*, 1964, **29**, 2187.

[9] J. L. Borgna and M. Mousseron-Canet, *Bull. Soc. chim. France*, 1970, 2210.

[10] J. C. Brial and M. Mousseron-Canet, *Bull. Soc. chim. France*, 1968, 3321.

carbon atoms, which is α to that bearing the coupled H and F nuclei, by oxygen (a situation which arises in 1-fluorocarbohydrates) may be assessed from the observed $^2J_{HF}$ value in compound (B); this is devoid of vicinal substituent effects, and is 51 Hz[11] so the contribution from α-oxygen is +1 Hz. Table 1 defines the additional parameters necessary to calculate $^2J_{HF}$ in compounds with oxygenated or fluorine substituents, and emphasises the importance of the stereochemical relationship between the centres of interaction.

TABLE 1

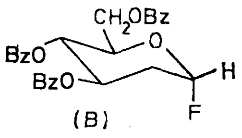
Parameters necessary for the calculation of $^2J_{FH}$ in fluorocarbohydrates, and polyfluoro-1,4-dioxans and -1,4-oxathians

$^2J_{HF}$ for the basic structure	50 Hz
Replacement of α-C by O	+1 Hz
Replacement of α-C by S	−4 Hz

Substituent effects for X (=O, OR, F) groups vicinal to H, F

Orientation of F	Orientation of X	
F Axial	X Equatorial	+1 Hz
F Equatorial	X Equatorial	
F Axial	O In ring (or S)	
F Equatorial	X Axial	−2 Hz
F Axial	X Axial	
F Equatorial	O In ring (or S)	

Application of these parameters, used additively, to the calculation of $^2J_{HF}$ in compounds which have been reported in the literature is summarised in Table 2. A comparison is made between the average of the observed $^2J_{HF}$ values for representative part-structures (considering only the substituents vicinal to H and F) and the calculated values. The agreement is satisfactory, with the root mean square (r.m.s.) deviation being ±1 Hz, and the method must be judged to be successful. Also included in Table 2 are calculated values for some situations which have not yet been described in the literature.



(B)

TABLE 2

Calculated and observed values of $^2J_{HF}$ for various local geometries in the chair form of pyranose-ring type fluorocarbohydrates

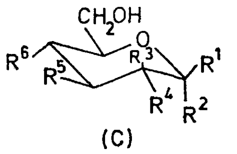
Site and orientation of fluorine	Site and orientation of substituent		Reference	$^2J_{HF}$/Hz calc.	Average $^2J_{HF}$/Hz obs.	Number of values from which average is taken
1e	2a		*a*—*c*	49	49·0,† 48·5 *	1,† 1 *
1a	2a		13, 14, 16, 18, 12, *d*—*h*			
1a	—		11, *e*, *f*	51	51·3 ‡	2
1e	2e		1, 11, *b*, *e*—*j*	52	52.0,† 51·7 *	11,† 1 *
1a	2e		1, 11, *d*—*l*		52·4,† 53·3 *	16,† 6 *
2e	1a	3a	*k*, *l*	44	45·1,† 45·3 *	2,† 3 *
2e	1a	3e	1, *k*, *l*	47	47·0,† 47·6 *	4,† 2 *
2e	1e	3a				
2a	1a	3a				
2e	1e	3e	1, *b*, *c*	50	50·3,† 49·0 *	2,† 1 *
2a	1a	3e	1, *b*, *k*, *l*		48·0,† 48·5 *	3,† 1 *
2a	1e	3a				
2a	1e	3e	1, *a*—*c*	53	51·4,† 49·0 *	2,† 1 *
3e	2a	4a		46		
3a	2a	4a	*h*		45·5 †	1 †
3e	2a	4e		49		
3e	2e	4a	*h*		47·5 †	2 †
3a	2a	4e				
3a	2e	4a				
3e	2e	4e	1, *h*, *k*, *m*—*o*	52	52·9 †	10 †
3a	2e	4e				
4e	3a			46		
4e	3e		1, *i*, *o*, *p*	49	49·9 †	5 †
4a	3a					
4a	3e		*q*	52	50·0 †	3 †

* Fluorine β-substituent. † Oxygenated β-substituent. ‡ No β-substituent.

[a] J. Adamson, A. B. Foster, L. D. Hall, and R. H. Hesse, *Chem. Comm.*, 1969, 309. [b] L. D. Hall, R. N. Johnson, A. B. Foster, and J. H. Westwood, *Canad. J. Chem.*, 1971, **49**, 118. [c] J. Adamson, A. B. Foster, L. D. Hall, R. N. Johnson, and R. H. Hesse, *Carbohydrate Res.*, 1970, **15**, 351. [d] L. D. Hall and J. F. Manville, *Canad. J. Chem.*, 1969, **47**, 19. [e] L. D. Hall and J. F. Manville, *Chem. and Ind.*, 1967, 468. [f] L. D. Hall and J. F. Manville, *Chem. Comm.*, 1968, 37. [g] L. D. Hall, J. F. Manville, and N. S. Bhacca, *Canad. J. Chem.*, 1969, **47**, 1. [h] L. D. Hall, R. N. Johnson, A. B. Foster, and J. H. Westwood, *Canad. J. Chem.*, 1971, **49**, 236. [i] A. D. Barford, A. B. Foster, J. H. Westwood, L. D. Hall, and R. N. Johnson, *Carbohydrate Res.*, 1971, **19**, 49. [j] E. M. Bessell, A. B. Foster, J. H. Westwood, L. D. Hall, and R. N. Johnson, *Carbohydrate Res.*, 1971, **19**, 39. [k] P. W. Kent, R. A. Dwek, and N. F. Taylor, *Tetrahedron*, 1971, **27**, 3887. [l] C. G. Butchard and P. W. Kent, *Tetrahedron*, 1971, **27**, 3457. [m] J. S. Brimacombe, A. B. Foster, R. Hems, J. H. Westwood, and L. D. Hall, *Canad. J. Chem.*, 1970, **48**, 3946. [n] A. B. Foster, R. Hems, and L. D. Hall, *Canad. J. Chem.*, 1970, **48**, 3937. [o] A. D. Barford, A. B. Foster, J. H. Westwood, and L. D. Hall, *Carbohydrate Res.*, 1969, **11**, 287. [p] A. B. Foster, R. Hems, and J. H. Westwood, *Carbohydrate Res.*, 1970, **15**, 41. [q] D. M. Marcus and J. H. Westwood, *Carbohydrate Res.*, 1971, **17**, 269.

[11] L. D. Hall and J. F. Manville, *Canad. J. Chem.*, 1967, **45**, 1299.

The application of the technique to a ' real ' situation is demonstrated in Table 3, where the data obtained by us previously [1] are compared with the values predicted for $^2J_{HF}$ by using the additivity relationships of Table 1.



(C)

The agreement is again excellent (±1 Hz; r.m.s.) and shows that the technique may be applied successfully in an experimental situation.

Substituents Other than X = OR *or* F.—Hall and Manville [12-14] have made a study of the effect of a variety of 2-substituents upon $^2J_{HF}$ in 1-fluorocarbohydrates. For completeness, their data are summarised in Table 4.

TABLE 3

Experimental and calculated values of $^2J_{HF}$ in fluorinated D-glucose and D-mannose derivatives (C) [1]

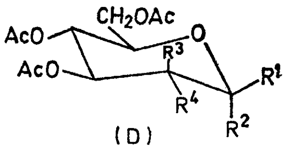
Structure (C)	$^2J_{HF}$/Hz Calc.	$^2J_{HF}$/Hz Obs.
$R^1 = R^3 = H, R^2 = F, R^4 = R^5 = R^6 = OH$	52	53·2
$R^1 = F, R^2 = R^3 = H, R^4 = R^5 = R^6 = OH$	52	52·0
$R^1 = R^3 = H, R^2 = R^5 = R^6 = OH, R^4 = F$	47	49·0
$R^1 = R^5 = R^6 = OH, R^2 = R^3 = H, R^4 = F$	50	50·0
$R^1 = R^3 = H, R^2 = R^4 = R^6 = OH, R^5 = F$	52	53·0
$R^1 = R^4 = R^6 = OH, R^2 = R^3 = H, R^5 = F$	52	52·0
$R^1 = R^3 = H, R^2 = R^4 = R^5 = OH, R^6 = F$	49	49·0
$R^1 = R^4 = R^5 = OH, R^2 = R^3 = H, R^6 = F$	49	49·5
$R^1 = R^4 = H, R^2 = R^5 = R^6 = OH, R^3 = F$	50	49·0
$R^1 = R^5 = R^6 = OH, R^2 = R^4 = H, R^3 = F$	53	52·0

The trends shown by these data confirm the generality of the observations made in Table 1 and show that the magnitude of substituent effects depends upon the electron-withdrawing power of the group. Thus, when the 1-F is axial, an axial 2-substituent causes $^2J_{HF}$ to *decrease* in the order I > Br > Cl > OR > F; an equatorial 2-substituent however causes $^2J_{HF}$ to *increase* in the same order. When the 1-F is equatorial, an axial 2-substituent *decreases* $^2J_{HF}$ (Cl > F) while an equatorial 2-substituent *increases* $^2J_{HF}$ in the order I < Br < Cl < OR < F.

TABLE 4

Effects of various 2-substituents upon $^2J_{HF}$ in some 1-fluorocarbohydrate derivatives (D) [12-14]

	(D; $R^1 = R^4 = H, R^2 = F, R^3 = X$)	(D; $R^1 = F, R^2 = R^4 = H, R^3 = X$)	(D; $R^1 = R^3 = H, R^2 = F, R^4 = X$)	(D; $R^1 = F, R^2 = R^3 = H, R^4 = X$)
X	$^2J_{HF}$/Hz	$^2J_{HF}$/Hz	$^2J_{HF}$/Hz	$^2J_{HF}$/Hz
F	48·0	48·5	53·3	51·7
OR	48·6		52·8	52·5
Cl	49·5	49·4	51·2	51·0
Br	50·2		51·5	50·3
I	51·7			50·5
H	51·4		51·4	



(D)

The rules summarised in Table 1 lead to some interesting conclusions. Irrespective of whether F is axial or equatorial, changing the substituent upon the adjacent carbon from an equatorial to an axial orientation results in a decrease (*ca.* −3 Hz) in $^2J_{HF}$. Conversely, unless the substituent is ' ring ' O (or S), changing the fluorine from an equatorial to an axial situation has little or no effect upon $^2J_{HF}$.

Examination of the data in Tables 2—4 shows that these statements are essentially true and provide a useful method of deciding between isomers in which the substituent is equatorial or axial, when $^2J_{HF}$ is available for both compounds. Table 5 illustrates the consequences of making these structural changes, using the data listed in the previous Tables.

There is some evidence in the steroid field that these conclusions may have wider application. Thus, on going from 2β-fluoro-3β-hydroxycholestane to the 3α-analogue, $^2J_{HF}$ decreases by 4 Hz; from 3β-fluoro-2β-hydroxycholestane to the 3α-analogue, however, $^2J_{HF}$ only changes by 0·5 Hz as expected.[15] Exceptions occur when the fluorine is involved in steric interactions, as in the 2β-orientation in steroids, and changing the orientation of fluorine may change $^2J_{HF}$ by up to 2 Hz. The statement concerning the effect of changing the orientation of the substituent seems to be without exception, however.

Application to Other Systems.—Burdon and Parsons [16] have used an empirical additivity method of calculating ^{19}F chemical shifts for the chair forms of polyfluorinated 1,4-dioxans and 1,4-oxathians in order to determine the structure and conformation of unknown derivatives. These workers point out that in both series it would be expected that there would be considerable deviation from the idealised geometry of cyclohexane-like chairs which we have assumed for the carbohydrate compounds. Nevertheless, it would be interesting to attempt to calculate the values of $^2J_{HF}$ in these compounds in order to examine the generality of the approach and if possible to shed further light upon some of the structural peculiarities (*e.g.* the adoption of flexible forms) suggested by Burdon and Parsons.

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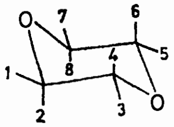
[12] L. D. Hall and J. F. Manville, *Canad. J. Chem.*, 1969, **47**, 361.
[13] L. D. Hall and J. F. Manville, *Canad. J. Chem.*, 1969, **47**, 379.
[14] L. D. Hall and J. F. Manville, *Chem. Comm.*, 1968, 37.
[15] J. Levisalles and M. Rudler-Chauvin, *Bull. Soc. chim. France*, 1971, 2073.
[16] J. Burdon and I. W. Parsons, *Tetrahedron*, 1971, **27**, 4553.

Polyfluoro-1,4-*dioxans*. Using the parameters listed in Table 1, $^2J_{HF}$ has been calculated for the structures and conformations suggested by Burdon and Parsons. The results are quoted in Table 6 [compounds (I)—(XV)] where they are compared with experiment; if an alternative structure is possible, whose calculated $^2J_{HF}$ values are in better agreement with experiment, this is also shown with the relevant parameters. The general level of agreement is surprisingly good, and if the result for J_{12} in compound (II) is ignored (see below) the r.m.s. deviation is ±2 Hz; for >70% of the data, the agreement is within ±1 Hz r.m.s. as obtained for the fluorocarbohydrates.



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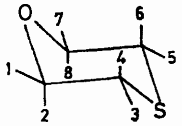
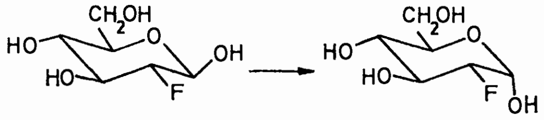


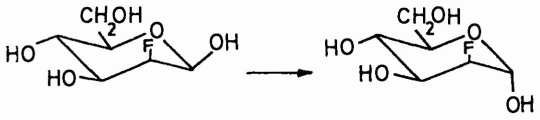
(F)

TABLE 5

The consequences upon $^2J_{HF}$ of changing the orientation of (*a*) the adjacent substituent and (*b*) the fluorine involved in coupling (Δ = difference in the two values)



(1)



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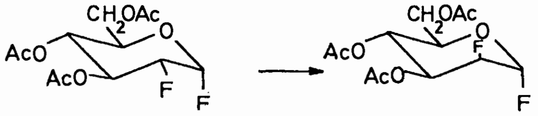

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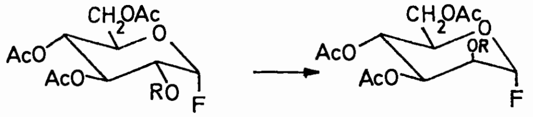
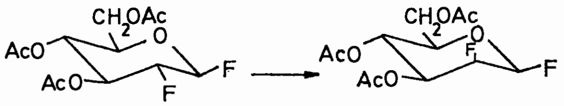


(4)



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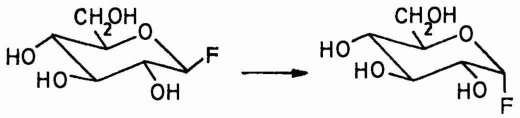

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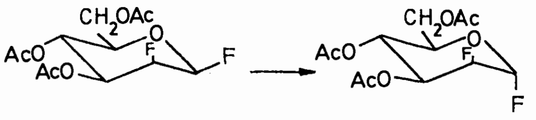

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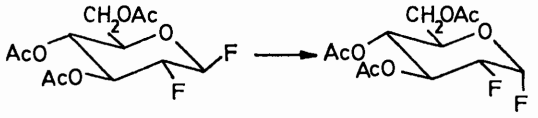

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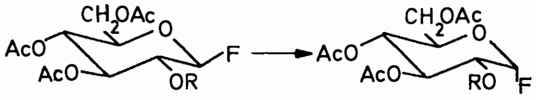

(9)

TABLE 5 (*Continued*)

Site and orientation of fluorine	Site and orientation of substituent		Δ^2J_{HF}/Hz
(*a*) Adjacent substituent			
1e	2e		−3·0
1e	2a		
1a	2e		−3·4
1e	2a		
2e	1a	3e	−2·1
2e	1a	3a	
2e	1e	3e	−1·7
2a	1a	3e	
2a	1e	3e	−4·4
2e	1e	3a	
3e	2e	4a	−2·0
3a	2a	4a	
Inversion (1)			−1·0
Inversion (2)			−3·0
Inversion (3)			−5·3
Inversion (4)			−4·2
Inversion (5)			−3·2
(*b*) Fluorine involved in coupling			
1e	2e		0·4
1a	2e		
4e	3e		0·1
4a	3e		
Inversion (6)			1·2
Inversion (7)			−0·5
Inversion (8)			1·6
Inversion (9)			0·3

For three compounds [(VII), (VIII), and (XII)] in Table 6, an alternative structure is indicated which gives better agreement with experimental $^2J_{HF}$ results. Application of the additivity method of Burdon and Parsons to the calculation of ^{19}F chemical shifts does not lead to even approximate agreement with experiment for the alternative structures for (VIII) and (XII), but for (VII) the alternative conformation actually gives slightly better results (r.m.s. 4·3 p.p.m. *cf.* 4·6 p.p.m.). Burdon and Parsons have suggested that this compound may exist as a flexible structure, but our alternative suggestion is clearly possible since it would not be possible to differentiate between the two by chemical means.

With the exception of these compounds, there is only one other in which even one of the calculated $^2J_{HF}$ values is in error by >3 Hz; this is $^2J_{12}$ in compound (II), which is quoted as 59 Hz compared with its calculated value of 47 Hz. The other three $^2J_{HF}$ in this compound are correctly estimated, and the value of 59 Hz is remarkably high; a search of the available literature fails to reveal another example of $^2J_{HF}$ in a six-membered ring which is as large as this, and values are almost invariably <54 Hz. Assuming that it has been correctly reported, this result must remain as a distinct anomaly.

Polyfluoro-1,4-*oxathians*. In order to calculate $^2J_{HF}$ in these compounds, it is necessary to have additional

TABLE 6

Experimental and calculated values of $^2J_{HF}$ in polyfluoro-1,4-dioxans and -1,4-oxathians [16]

Compound	Coupled nuclei	Structure (E) suggested in ref. 16								$^2J_{HF}$/Hz obs.	J_{HF}/Hz calc.	Possible alternative structure (E)								$^2J_{HF}$/Hz calc.
		R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8			R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8	
(I)	3, 4	F	F	H	F	H	H	H	H	52	51									
(II)	1, 2	F	H	H	F	H	F	H	H	59	47									
	3, 4									51	50									
	5, 6									53	53									
	7, 8									51	51									
(III)		H	F	H	F	H	F	H	F	53	50									
(IV)		{H	F	F	H	H	F	F	H} *	48	50									
		{F	H	H	F	F	H	H	F}											
(V)		H	F	H	F	F	H	F	H	53	50									
(VI)	1, 2	H	F	H	F	H	F	F	F	49	50									
	3, 4									49	50									
	5, 6									51	51									
(VII)	1, 2	H	F	H	F	F	H	F	F	51	50	F	H	F	H	H	F	F	F	50
	3, 4									51	50									50
	5, 6									53	48									51
(VIII)	1, 2	H	F	F	H	H	F	F	F	49	53	H	F	H	F	H	F	F	F	50
	3, 4									50	47									50
	5, 6									53	51									51
(IX)	1, 2	H	F	H	F	F	F	F	F	51	50									
	3, 4									51	50									
(X)		{H	F	F	H	F	F	F	F}	51	50									
		{F	H	H	F	F	F	F	F}											
(XI)		F	F	H	F	H	F	F	F	51	51									
(XII)	3, 4	{F	F	F	H	H	F	F	F}	47	50	F	F	F	H	F	H	F	F	48
	5, 6	{F	F	H	F	F	H	F	F}											
(XIII)		H	F	F	F	H	F	F	F	51	51									
(XIV)	1, 2	H	F	F	F	F	H	F	F	51	50									
	5, 6									51	50									
(XV)		F	F	H	F	F	F	F	F	51	51									
		Structure (F) suggested in ref. 16										Possible alternative structure (F)								
(XVI)	1, 2	F	H	H	F	H	F	F	F	47	47									
	3, 4									48	48									
	5, 6									48	46									
(XVII)	1, 2	H	F	H	F	H	F	F	F	47	50									
	3, 4									45	45									
	5, 6									45	46									
(XVIII)	1, 2	F	H	H	F	F	F	H	F	47	47	F	H	H	F	F	F	F	H	47
	3, 4									49	48									48
	5, 6									47	51									48
(XIX)	1, 2	H	F	H	F	F	F	F	H	49	50									
	3, 4									45	45									
	7, 8									50	48									
(XX)	1, 2	H	F	H	F	F	F	H	F	54	50									
	3, 4									49	45									
	7, 8									50	51									
(XXI)	1, 2	H	F	H	F	F	F	F	F	45	50	F	H	F	F	H	F	F	F	48
	3, 4									45	45									46
(XXII)	1, 2	{H	F	F	H	F	F	F	F}	47	50	F	H	H	F	F	F	F	F	47
	3, 4	{F	H	H	F	F	F	F	F}	47	45									48
(XXIII)	1, 2	H	F	F	F	H	F	F	F	51	51									
	5, 6									46	46									
(XXIV)	1, 2	{H	F	F	F	F	H	F	F}	51	50									
	5, 6	{F	H	F	F	H	F	F	F}	48	46									
(XXV)	1, 2	{H	F	F	F	F	F	F	H}	51	50									
	7, 8	{F	H	F	F	F	F	H	F}	51	50									
(XXVI)	1, 2	{F	F	H	F	F	H	F	F}	51	45									
	5, 6	{F	F	F	H	H	F	F	F}	51	45									
(XXVII)	3, 4	F	F	H	F	H	F	F	F	45	46									
	5, 6									45	46									
(XXVIII)	1, 2	H	F	F	F	F	F	F	F	50	51									
(XXIX)	3, 4	F	F	H	F	F	F	F	F	47	46									
(XXX)	1, 2	F	H	F	F	F	F	F	F	45	43									

* Structures enclosed in braces are equilibrating rapidly by conformational interconversion.

parameters to allow for the influence of the heterocyclic sulphur atom. Empirically, it is found that the best results are obtained if the parameters describing vicinal interactions of S are the same as quoted in Table 1 for heterocyclic oxygen; the effect of S which is α to the CHF group however is to reduce $^2J_{HF}$ by 4 Hz, and this is also quoted in Table 1.

Table 6 [compounds (XVI)—(XXX)] compares calculated values of $^2J_{HF}$ with experiment, and again the overall level of agreement is satisfactory, surprisingly so when one considers the probable distortions of the ring resulting from the presence of sulphur. The overall deviations from agreement result in an r.m.s. error of *ca.* 2·5 Hz, but since *ca.* 70% of the results lie within ±1 Hz r.m.s. of experiment the technique is still of potential value. For five compounds [(XVIII), (XX)—(XXII), and (XXVI)] the overall level of agreement is sufficiently poor to cause uncertainty as to the structure.

For (XVIII), (XXI), and (XXII) alternatives are suggested, but none of these leads to better agreement between calculated and observed chemical shifts.[16] For (XX) and (XXVI) we cannot suggest an alternative possibility; it should be commented however that the latter provides a clear anomaly with its extremely high value for $^2J_{HF}$ for a group adjacent to S (51 Hz *cf.* 45 Hz calculated).

In conclusion, we have demonstrated that the results obtained for fluorocarbohydrates in the pyranose form are capable of being applied in other areas. The vicinal substituent effects depend upon both the relative stereochemistry of the centres involved and upon the electronegativity of the substituent group. In the more complex systems, the calculations are not so precise as in the carbohydrates; they do, however, lead in several instances to alternative possible structures which are as acceptable as those proposed in the literature.[16]

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