The Dependence of Vicinal Proton–Proton Coupling Constants on Dihedral Angle and Substituents

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Extended Hückel theory molecular orbital calculations of the vicinal proton–proton coupling constants in 1,1- and 1,2-difluoroethanes are presented and compared with experimental results. Equations, describing the angular dependence of vicinal couplings in substituted CH–CH fragments, are formulated on the basis of the MO calculations. Empirical parameters for these equations are derived from a least-squares treatment of a large number of experimental coupling constants.

THE Karplus equation,[1] which relates the vicinal coupling constants to the dihedral angle between the coupling protons, is a relation used very frequently in proton magnetic resonance studies of the structure and conformation of organic compounds. More recent investigations have indicated that this equation, originally derived for the unperturbed ethane molecule, is inadequate for substituted CH–CH fragments. It fails, for instance, to account for any of the following observations: (1) the dependence of vicinal couplings on the relative positions of the coupling protons and a substituent;[2] (2) the increase of vicinal couplings with increasing electronegativity of the substituent in certain arrangements (*e.g.*, the *gauche* coupling in the *trans*-rotamer of 1,2-dihalogenoethanes[3]); and (3) the variation of $3N/2 + L/2$, a parameter obtained from an analysis of the ^{1}H n.m.r. spectra of 1,2-disubstituted ethanes, with solvent and temperature.[4]

Recent MO calculations of vicinal coupling constants in some substituted ethanes have yielded detailed information on the effects of substituents. In particular, those experimentally observed trends at variance with the Karplus equation have been borne out by extended Hückel theory (EHT)[5] as well as self-consistent field (SCF)[6] MO calculations. Additivity of the substituent effects has been assumed in a comparison of the experimental and theoretical results.[5b] Further EHT MO calculations for the difluoroethanes, which test this assumption and lead to equations describing the angular dependence of vicinal couplings in substituted CH–CH fragments, are presented here.

HMO Calculations of Coupling Constants.—Method of calculation and results. MO calculations of the vicinal proton–proton coupling constants in 1,1- and 1,2-difluoroethane have been performed for a series of conformations, the H–H dihedral angle being varied in steps of 20°. The calculations are based on the linear combination of atomic orbitals LCAO-MO theory of coupling constants as formulated by Pople and Santry.[7] MO Coefficients and one-electron orbital energies have been obtained from extended Hückel theory calculations as suggested by Fahey *et al.*[8] Tetrahedral bond angles have been assumed throughout and standard bond lengths have been used (C–C = 1·54, C–H = 1·09, C–F = 1·36 Å). Full details of the calculations are in ref. 5*b*.

The calculated vicinal proton–proton coupling constants for difluoroethanes are in Table 1. Their angular dependence and the definition of the two different H–H couplings in 1,2-difluoroethane are shown in Figure 1.

TABLE 1

The calculated vicinal proton–proton coupling constants in 1,1- and 1,2-difluoroethane as function of the dihedral H–H angle

	CH_3–CHF_2	CH_2F–CH_2F	
ϕ	J/Hz	J/Hz	J'/Hz
0	4·25	5·01	4·56
20	3·74	4·34	5·14
40	2·49	2·87	4·50
60	1·10	1·21	2·84
80	0·23	0·23	0·97
100	0·46	0·47	−0·06
120	1·88	2·05	0·47
140	3·91	4·43	2·47
160	5·67	6·57	4·85
180	6·36	7·56	6·80
200	5·67	6·57	7·44
220	3·91	4·43	6·51
240	1·88	2·05	4·33
260	0·46	0·47	1·87
280	0·23	0·23	0·45
300	1·10	1·21	0·28
320	2·49	2·87	1·26
340	3·74	4·34	3·00
360	4·25	5·01	4·56

Angular dependence. The dihedral angle dependence of the calculated coupling constants in monosubstituted ethanes $CH_3{\cdot}CH_2{\cdot}X$ has been expressed by equation (1).[5b]

$$J_X = A_X + B_X \cos\phi + C_X \cos 2\phi + D_X \sin\phi + E_X \sin 2\phi \quad (1)$$

The coupling constants for the difluoroethanes in Table 1 have also been fitted to equation (1) by least-squares techniques. The resulting constants K_X $(= A_X \ldots E_X)$ and the corresponding r.m.s. errors are in Table 2. The values for ethane and fluoroethane[5] have been included for comparison. The signs of the D and E values depend on the relative positions of the coupling protons and the substituent. These may be defined in terms of the

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[6] G. E. Maciel, J. W. McIver, jun., N. S. Ostlund, and J. A. Pople, *J. Amer. Chem. Soc.* 1970 **92**, 4497.

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[8] R. C. Fahey, G. C. Graham, and R. L. Piccioni, *J. Amer. Chem. Soc.*, 1966, **88**, 193.

angle $\phi_{\alpha X}$ as follows (Figure 2). The angle $\phi_{\alpha\beta}$ is taken as positive, independent of its sense of rotation, and $\phi_{\alpha X}$ is measured in the same direction as $\phi_{\alpha\beta}$. The D and E values in Table 2 correspond to an arrangement with $\phi_{\alpha X} = 120°$. Their signs have to be reversed if $\phi_{\alpha X} = 240°$ [Figure 2(b)].

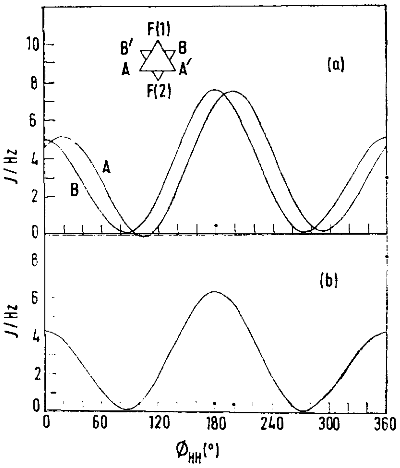
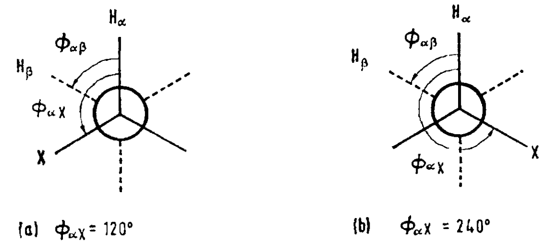


FIGURE 1 Calculated vicinal proton couplings as a function of the dihedral angle ϕ_{HH}; (a) 1,2-difluoroethane; A, $J' = J_{AB'}$; B, $J = J_{AB}$; (b) 1,1-difluoroethane

TABLE 2

Constants for equation (1)

Compound	$\Sigma\Delta N_X$	A	B	C	D	E	R.m.s.
$CH_3 \cdot CH_3$	0	4·21	−1·30	4·06	0	0	0·08
$CH_3 \cdot CH_2F$	1·85	3·68	−1·21	3·35	−0·20	1·12	0·08
$CH_3 \cdot CHF_2$	3·70	2·75	−0·98	2·55	0	0	0·08
$CH_2F \cdot CH_2F$ (J)	3·70	3·16	−1·12	3·03	0	0	0·22
(J')	3·70	3·21	−1·06	2·51	−0·35	1·85	0·12



(a) $\phi_{\alpha X}$ = 120° (b) $\phi_{\alpha X}$ = 240°

FIGURE 2

The angle dependence of the two couplings in 1,2-difluoroethane appears very similar except for a phase shift [Figure 1(a)]. This suggests an alternative formulation (2) of the angle and substituent dependence.

$$J_X = A_X' + B_X' \cos(\phi + \varepsilon_X) + C_X' \cos 2(\phi + \varepsilon_X) \quad (2)$$

Equations (1) and (2) are closely related and interconversion of the constants is straightforward. The phase shift ε_X is obtained from either $\tan \varepsilon_X = -D_X/B_X$ or $\tan 2\varepsilon_X = -E_X/C_X$. The other constants in equation (2) can be calculated from $A_X' = A_X$, $B_X' = B_X/\cos \varepsilon_X$, and $C_X' = C_X/\cos 2\varepsilon_X$.

Dependence on substitution. For monosubstituted ethanes the constants in equation (1) are related linearly to the electronegativity of the substituent.[5b] The corresponding values for the difluoroethanes fit well into these linear relations (Table 2). Deviations are observed for the A value of 1,1-difluoroethane and the C value of J in 1,2-difluoroethane.

The linear correlations are equally consistent when equation (2) is used (Figure 3), the exceptions being the A' and C' values of 1,1-difluoroethane. The phase shifts ε_X are also linear functions of $\Sigma\Delta N_X$. [ΔN_X Is the electronegativity difference between a substituent X and hydrogen ($\Delta N_X = N_H - N_X$) and the sum is taken over all substituents on a particular CH–CH fragment.] The deviations from linearity at small values of $\Sigma\Delta N_X$ are attributed to the fact that ε_X is obtained from the ratio of two small numbers (in particular those obtained from D_X/B_X).

The linear dependence of the constants K_X on the sum of the electronegativity differences of the substituents, as evident in Table 2 and Figure 3, allows the inclusion of the substituent effects into equations (1) and (2) in an explicit form (3). K_H Denotes the respective constants

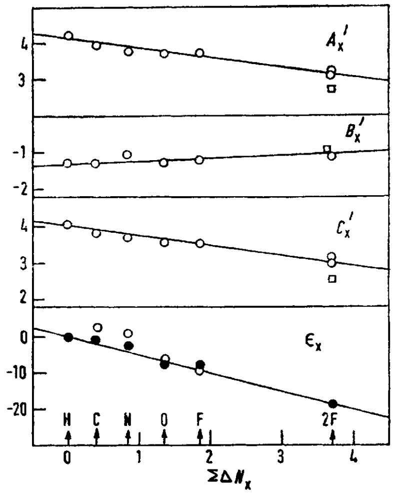


FIGURE 3 Constants for equation (2) as a function of the electronegativity of the substituents [□ 1,1-difluoroethane; ε_X obtained from either B_X/D_X (○) or C_X/E_X (●)]

$$K_X = K_H - k\Sigma\Delta N_X \quad (3)$$

in ethane, D_H, E_H, and ε_H are zero, and the various contributions to D_X, E_X, as well as ε_X, have to be added or subtracted in accordance with the sign convention defined above. (In practice the sign is best transferred to ΔN_X such that $D_X = -d\Sigma'\Delta N_X$, $E_X = -e\Sigma'\Delta N_X$, and $\varepsilon_X = -\varepsilon\Sigma'\Delta N_X$, where Σ' could contain various positive and negative contributions.) In 1,1-difluoroethane for instance the sine terms and ε_X vanish ($D_{F(1)} = -D_{F(2)}$; $E_{F(1)} = -E_{F(2)}$; $\varepsilon_{F(1)} = -\varepsilon_{F(2)}$). 1,2-Difluoroethane has two different couplings as defined in Figure 1(a), one of these being symmetrical about $\phi = 180°$ (J; sine terms and phase shift vanish), the other one being asymmetrical (J'; $D_X = -2d\Delta N_F$, $E_X = -2e\Delta N_F$; $\varepsilon_X = -2\varepsilon\Delta N_F$).

Empirical Correlations.—Coupling constants in fluoroethanes. The qualitative correspondence between coupling constants calculated by the LCAO–MO method in conjunction with the extended Hückel theory and experimental values has been discussed.[5b] The results for the difluoroethanes agree equally well with experimental trends. An approximately linear decrease of the average vicinal coupling constant with increasing fluorine substitution is found experimentally and theoretically in the series ethane, fluoroethane, and 1,1-difluoroethane (Table 3). The observed coupling constants in 1,2-difluoroethane are weighted averages over unequally populated rotational isomers. Values reported for the individual isomers make use of a complex formula describing the solvent–solute interactions in a classical fashion.[2c] The results have to be interpreted with caution because of the approximations inherent in the classical theory, the uncertainty in the energy difference between the rotational isomers, and the lack of information on the exact geometry of the *gauche* conformation. There is, nevertheless, a good correspondence in the relative magnitudes of the various observed and calculated coupling constants (Table 3).

TABLE 3

Calculated and observed couplings (Hz) for fluoroethanes

Compound	$CH_3{\cdot}CH_3$	$CH_3{\cdot}CH_2F$	$CH_3{\cdot}CHF_2$	$CH_2F{\cdot}CH_2F$ *					
Coupling	J_{av}	J_{av}	J_{av}	J_g	J_t	J_{av}	J_g'	$J_g' + J_t'$	J_{av}'
Calc.	4·21	3·68	2·75	0·65	7·56	2·95	2·84	6·65	3·17
Obs.	8·0	6·9	4·5	1·4	11·2	4·7	6·2	11·2	5·8
J_{obs}/J_{calc}	1·90	1·87	1·64	2·15	1·48	1·59	2·18	1·69	1·83

* A dihedral angle of 70° has been assumed for the *gauche* conformers.

TABLE 4

Empirical constants derived for equation (3)

Constant	*A*	*B*	*C*	*a*	*b*	*c*	*d*	*e*	R.m.s.
Equation (1)	7·48	−2·03	4·60	0·74	−0·17	0·23	−0·06	−0·62	0·65
Equation (2)	7·49	−1·62	4·84	0·76	0·05	0·30			0·67

The calculated *A* values, which correspond to the average coupling constants in substituted ethanes with three conformations of equal energy, are lower for 1,1-difluoroethane than for the 1,2-isomer. There is some, yet not unequivocal, experimental support for this trend in a number of disubstituted ethanes.[9]

Angle and substituent dependence. A second important feature, which has been borne out by the MO calculations, is the dependence of the substituent effect on the relative positions of the coupling protons and the substituent. This could not be accounted for by a relation as simple as the original Karplus equation. It is therefore of interest to investigate whether equations (1) or (2), incorporating empirically determined parameters, would give a better description of the angular dependence of vicinal couplings in substituted CH–CH fragments.

Selection of compounds. A large number of experimental values of vicinal proton couplings have been selected from the literature and have been subjected to a least-squares treatment in order to determine the parameters in equations (1) and (2). Care has been taken to choose only coupling constants obtained from a proper analysis of the ^1H n.m.r. spectrum. The compounds included substituted ethanes and alicyclic as well as heterocyclic five- and six-membered ring compounds of various types. Certain assumptions had to be made to enable treatment of the data because of the limited knowledge on the exact conformations and dihedral and bond angles.

The substituted ethanes included compounds with three equivalent rotational isomers as well as 1,2-disubstituted ethanes. The coupling constants for the second set had either been derived from an analysis of their solvent-dependence, in which case only reliable results for the predominant rotamer have been used, or had been obtained from compounds with bulky substituents such that the presence of the *trans*-conformer only could be assumed.

The five-membered ring compounds included bicyclo[2.2.1]heptenes with a rigid carbon skeleton and an eclipsed CH_2–CHX moiety. Other five-membered rings have been assumed to undergo pseudorotation, the dihedral angle between *cis*- and *trans*-proton pairs being $0° \pm \phi_{max.}$ and $120° \pm \phi_{max.}$, respectively. All angles between the limiting values have been given equal probability. The limits have been estimated from results obtained by microwave and electron diffraction techniques.[10]

Two types of six-membered ring, expected to exist in chair-forms, have been considered: compounds with large holding groups which could be assumed to be in one conformation only and compounds which, owing to symmetry properties, existed in two energetically equivalent conformations. The compounds have been taken to be in one or two conformations only, and no vibrational correction has been applied. Different degrees of ring buckle and slight ring distortions due to the presence of heteroatoms or double bonds have been taken into account in the choice of the dihedral angles.[10] These corrections appeared to be of minor importance except in the case of compounds related to cyclohexene or cyclohexanone.

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[9] (*a*) R. E. Glick and A. A. Bothner-By, *J. Chem. Phys.*, 1956, **25**, 362; (*b*) R. J. Abraham and K. G. R. Pachler, *Mol. Phys.*, 1963, **7**, 165; (*c*) A. A. Bothner-By, 'Advances in Magnetic Resonance,' Academic Press, New York and London, 1965, vol. I, p. 195.

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RESULTS

Altogether 231 coupling constants from 137 compounds have been analysed. The calculations with equation (2) have been carried through for a set of ε values ranging from -5 to 15°. The best agreement has been found for $\varepsilon = 5°$. Table 4 contains the results of the least-squares analysis. Figure 4 compares the experimental couplings with values calculated with equation (2) by use of the corresponding parameters in Table 4. Some typical values are in Table 5.

TABLE 5

Some observed and calculated vicinal coupling constants

No.	Compound	Coupling constant (Hz)	Obs.	Calc.
1	$CH_3{\cdot}CH_2Li$	J_{av}	8·4	8·37
2	$CH_3{\cdot}CH_3$	J_{av}	8·0	7·48
3	$(CH_3{\cdot}CH_2)_3P$	J_{av}	7·6	7·52
4	$CH_3{\cdot}CH_2Cl$	J_{av}	7·07	6·67
5	$(CH_3)_2CHCl$	J_{av}	6·31	6·37
6	$(CH_3)_2CHOH$	J_{av}	6·05	6·19
7	$CH_3{\cdot}CHCl_2$	J_{av}	6·1	5·85
8	$(CH_3)_3C{\cdot}CH_2{\cdot}CH_2Li$ (*trans*)	J_{trans}	15·5	15·02
		J_{gauche}	3·5	4·14
9	$ClCH_2{\cdot}CH_2Cl$ (*gauche*)	$\frac{1}{2}(J_{trans} + J_{gauche})$	7·15	6·72
		J'_{gauche}	2·9	2·51
10	Cyclohexane	$\frac{1}{2}(J_{aa} + J_{ee})$	8·07	8·15
		J_{ae}	3·73	3·95
11	Cyclohexene	$\frac{1}{2}(J_{3a4a} + J_{3e4e})$	8·94	8·35
		J_{3a4e}	2·95	3·43
12	Tetrahydropyran	$\frac{1}{2}(J_{2a3a} + J_{2e3e})$	7·41	7·11
		$\frac{1}{2}(J_{2a3e} + J_{2e3a})$	3·87	3·43
13	Selenan	$\frac{1}{2}(J_{2a3a} + J_{2e3e})$	8·46	8·55
		$\frac{1}{2}(J_{2a3e} + J_{2e3a})$	3·09	3·33
14	1,4-Dioxan	$\frac{1}{2}(J_{aa} + J_{ee})$	6·11	6·07
		J_{ae}	2·78	2·90
15	1,4-Diselenan	$\frac{1}{2}(J_{aa} + J_{ee})$	8·49	8·78
		J_{ae}	2·43	3·41
16	2-t-Butyl-1,3-dioxan	J_{4a5a}	12·4	12·23
		J_{4a5e}	2·6	3·27
		J_{4e5a}	5·0	4·47
		J_{4e5e}	1·3	1·77
17	4,4-Dimethyl-1,3-dioxan	$\frac{1}{2}(J_{aa} + J_{ee})$	6·9	7·00
		$\frac{1}{2}(J_{ae} + J_{ea})$	3·9	3·87
18	1,3-Dioxolan	J_{cis}	7·3	7·02
		J_{trans}	6·0	5·70
19	1,3-Oxothiolan	J_{cis}	5·58	6·26
		J_{trans}	6·12	6·41

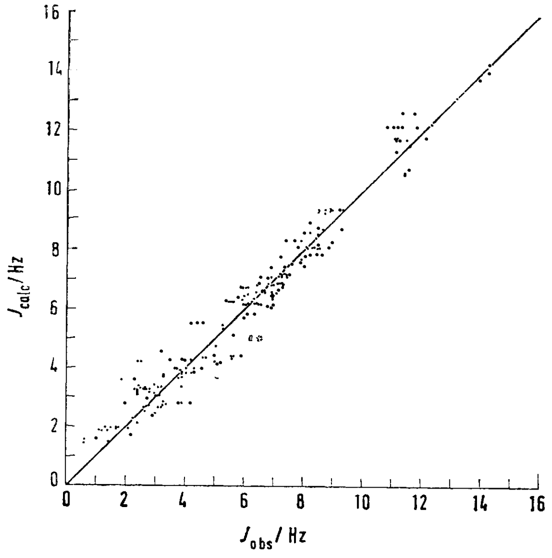

FIGURE 4 Calculated and observed vicinal proton couplings. Most of the experimental values are taken from the following sources: Refs. (3) and (9*b*); H. Booth, 'Progress in NMR Spectroscopy, Pergamon Press, Oxford, 1969; vol. 5, p. 149; J. B. Lambert, *Accounts Chem. Res.*, 1971, **4**, 87 and *J. Amer. Chem. Soc.*, 1967, **89**, 1836; H. R. Buys, *Rec. Trav. chim.*, 1969, **88**, 100; E. L. Eliel and M. C. Knoeber, *J. Amer. Chem. Soc.*, 1968, **90**, 3444; D. J. Pasto, F. M. Klein, and T. W. Doyle, *ibid.*, 1967, **89**, 4368.

DISCUSSION

A comparison of two sets of parameters in Table 4 indicates that equations (1) and (2) are equivalent for all practical purposes. The slightly lower r.m.s. value for equation (1) is probably due to the incorporation of one extra variable. It is noteworthy that the best ε value is identical to the theoretical value obtained from the slope of the plot of ε_X against $\Sigma\Delta N_X$ in Figure 3.

The A values in equations (1) and (2) correspond to the average vicinal coupling constants observed for ethyl derivatives with threefold symmetry. The dependence of this constant on the electronegativity of substituents [$7{\cdot}48 - 0{\cdot}74\Sigma\Delta N_X$ and $7{\cdot}49 - 0{\cdot}76\Sigma\Delta N_X$ for equations (1) and (2), respectively] is in accord with similar formulae derived for monosubstituted ethanes [11] ($7{\cdot}9 - 0{\cdot}7\Sigma\Delta N_X$) and a series of acyclic and cyclic compounds with CH–CH fragments [9b] ($7{\cdot}7 - 0{\cdot}8\Sigma\Delta N_X$). The following parameters for the Karplus equation have been suggested for the s-butyl fragment: [9c] $A = 7$, $B = -1$, and $C = 5$. These values are close to those calculated from the parameters in Table 4: 6·89, $-1{\cdot}89$, and 4·42 for equation (1) and 6·88, $-1{\cdot}66$, and 4·60 for equation (2).

The difference between observed and calculated coupling constants (Figure 4) may be attributed to a number of factors which are known to influence proton–proton couplings. A first uncertainty lies in the geometry assumed for the selected compounds. Slight changes in bond angles and bond lengths would affect the couplings,[12] but also the exact conformations and proton dihedral angles are not known. The neglect of vibrational effects is another source of error, although it has been argued that this would only lead to minor differences.[13] Many deviations can also be traced back to the presence of heteroatoms with free electron pairs or to π-electron systems. Their influence will also have a pronounced steric dependence.[14] Further, the linear relation between the substituent effect and the electronegativity of the substituents is an approximation and there will certainly be mutual interactions between various substituents on a CH–CH fragment which have been completely neglected.

It is, however, encouraging that many of the deviations between observed and calculated couplings appear to be of a systematic nature. It should therefore be possible to isolate some of these secondary effects on the basis of the above calculations. Coupling constants

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[11] C. N. Banwell and N. Sheppard, *Discuss. Faraday Soc.*, 1962, **34**, 115.

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[14] M. Anteunis, *Bull. Soc. chim. belges*, 1966, **75**, 413.

calculated for substituted ethanes, for instance, are generally too small, while those for five-membered rings are too large. Serious discrepancies exist for six-membered ring compounds with heteroatoms in 1- and 3-positions. Here apparently, the second heteroatom in the β-position to the CH_2–CH_2–X fragment influences the couplings significantly.

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