tane, 3-MP = 3-methylpentane, 2,3-DMB = 2,3-dimethylbutane, 2,4-DMP = 2,4-dimethylpentane.
(3) S. L. Bennett and F. H. Field, *J. Am. Chem. Soc.*, **94**, 5188 (1972).
(4) D. P. Beggs and F. H. Field, *J. Am. Chem. Soc.*, **93**, 1567 (1971).
(5) E. W. McDaniel, "Collision Phenomena in Ionized Gases", Wiley-Interscience, New York, N.Y., 1964, Chapter 9.
(6) Calculated using $\Delta H_f°$ (tetramethylcyclopropane) = −19.6 kcal/mol obtained by the method of group equivalents: J. L. Franklin, J. G. Dillard, H. M. Rosenstock, J. T. Herron, K. Draxl, and F. H. Field, *Natl. Stand. Ref. Data Ser., Natl. Bur. Stand.*, **No. 26,** 45 (1969).
(7) The heat of formation of *tert*-butyl ion was obtained by an electron impact measurement of the ionization potential of *tert*-butyl radical: F. P. Lossing and G. P. Semeluk, *Can. J. Chem.*, **48**, 955 (1970).
(8) G. A. Olah and C. U. Pittman, *Adv. Phys. Org. Chem.*, **4**, 305 (1966).
(9) D. M. Brouwer, *Recl. Trav. Chim. Pays-Bas*, **87**, 210 (1968); D. M. Brouwer and H. Hogeveen, *Prog. Phys. Org. Chem.*, **9**, 179 (1972).

Calculation of Dihedral Angles from Vicinal Proton Coupling Constants and Substituent Electronegativities

T. P. Forrest

Contribution from the Chemistry Department, Dalhousie University, Halifax, Nova Scotia, Canada. *Received June 1, 1974*

Abstract: A method is presented for the calculation of proton dihedral angles from vicinal coupling constants and electronegativities of substituents. Results for several examples of conformationally mobile systems are compared to results obtained by the *R*-value method of calculating dihedral angles. Other examples of compounds to which the *R*-value method cannot be applied are given and the values of dihedral angles obtained from this method are compared to those obtained by empirical valence-force minimization calculations.

Dihedral angles have frequently been estimated from vicinal proton coupling constants by means of a Karplus[1] relationship, in spite of the problems inherent in this type of calculation.[2] In a Karplus equation, (1) for example, the

$$J = A \cos^2 \phi - B \cos \phi + C \qquad (1)$$

constants *A*, *B*, and *C* may vary considerably from compound to compound and difficulties arise in the selection of appropriate values of these constants.

One of the major factors which can alter the values of these constants is the electronegativity of the substituents on the atoms to which the coupled protons are bonded. Alteration of the constants in order to take into account the effect of the electronegativity of substituents does not appear to be completely satisfactory since the effect of an electronegative substituent is also angle dependent, being greatest when the substituent is antiperiplanar to a coupled proton.[3]

Buys[4] has developed a method of calculating dihedral angles, which attempts to compensate for other factors influencing the coupling constant, by quantification of Lambert's[5] *R*-value method of detecting distortion in cyclic systems. In this method the ratio, *R*, of J_{trans} to J_{cis} is determined and the dihedral angle, ϕ_{ae}, is calculated from eq 2.

$$\cos \phi_{\mathbf{ae}} = [3/(4R + 2)]^{1/2} \qquad (2)$$

The *R* value may be obtained only for compounds having one of the specific structural types listed by Lambert:[6] (i) a CH_2CH_2 or CH_2CHR group in a molecule with two rapidly equilibrating equivalent conformers, (ii) a CH_2CH_2 group in a completely rigid molecule, or (iii) a $CHRCH_2CHR'$ group in a completely rigid molecule with R and R′ trans to each other.

In this paper we wish to report a method of calculating dihedral angles which may be applied to these systems as well as other ring systems which cannot be analyzed by the *R*-value method. In the present study we have used a method[7] for estimating gauche coupling constants in ethane fragments, based on a correlation between coupling constants and electronegativity of substituents as well as their orientation relative to the coupled protons. The expected value of a gauche coupling constant of two protons with a dihedral angle of 60° is calculated from eq 3, where ΔX is

$$J = (4.1 + 0.63\Sigma\Delta X)(1 - 0.462\Delta X_1)(1 - 0.462\Delta X_2) \qquad (3)$$

the electronegativity[8] difference between the substituent and hydrogen, $\Sigma\Delta X$ is the sum of ΔX's of all substituents on the ethane framework, and ΔX_1 and ΔX_2 are the ΔX's of the two substituents antiperiplanar to the coupled protons.

The calculated coupling constant is then compared to the observed coupling constant and the difference taken to indicate a divergence of the dihedral angle from normal. The method of calculation of the dihedral angle is illustrated below for the example 1,4-dioxane. The expected value of J_{ae} is calculated from eq 3 to be 2.06 Hz, whereas the observed[5] value, J_{cis}, is 2.78 Hz. From the calculated value of J_{ae} and eq 4, a value for *A* is determined.

$$J_{\text{calcd}} = A \cos^2 60 - 0.3 \qquad (4)$$

This calculated value of the constant *A* (10.4 in this case) is then used with the observed coupling constant (eq 5) to calculate a value for the dihedral angle ϕ_{ae}.

$$\cos \phi_{\mathbf{ae}} = [(J_{\text{obsd}} + 0.3)/A]^{1/2} \qquad (5)$$

The calculated values of ϕ_{ae} for a series of conformationally mobile compounds are given in Table I and are compared with the values of ϕ_{ae} calculated by the ratio method of Buys.[4] It can readily be seen that the two methods are compatible, the results obtained in each case being remarkably close.

For those compounds in Table I where X and Y (Figure 1) are different, the observed J_{cis} will be the average of two different gauche coupling constants, J_{2a3e} and J_{3a2e}. In order to calculate ϕ_{ae} in these cases the two dihedral angles, ϕ_{2a3e} and ϕ_{3a2e}, are assumed to be the same (as was assumed in the calculations by the ratio method[4]) and the average of J_{2a3e} and J_{3a2e} is used to calculate a value for *A*.

Having obtained good agreement of the results from this method with those of the ratio method, dihedral angles which could not be determined by the ratio method were

Table I. Comparison of Dihedral Angles Calculated from Substituent Electronegativities and from *R* values

Compd	J_{ae} Calcd	J_{ae} Obsd	ϕ_{ae} Calcd	ϕ_{ae} *R* method	Ref
1,4-Dioxane	2.29	2.78	57	58	5
Cyclohexane-*3,3,4,4,5,5,6,6*-d_8	3.75	3.73	60	58	12
1,1,4,4-Tetramethylcyclohexane	3.75	4.03	59	57	5
cis-Naphthodioxane	2.29	2.95	56	58	13
1,4-Dithiane	3.75	2.40	66	65	5
1,4-Diselenane	3.81	2.43	66	64	5
Piperazine	3.14	3.04	60	58	5
Cyclohexane-1,4-dione	3.75	6.23	51	50	5
Cyclohexane-1,4-dioxime	3.75	6.5	50	47	14
Cyclohexene-*1,2,3,3,6,6*-d_6	3.75	2.95	63	63	15
Cyclohexanone-*4,4*-d_2	3.75	5.01	55	54	5
Tetrahydropyran-*4,4*-d_2	3.14[a]	3.87[a]	57	56	17
Piperidine-*4,4*-d_2	3.48[a]	3.77[a]	59	57	17
Thiane-*4,4*-d_2	3.75[a]	3.26[a]	62	61	17
Selenane-*4,4*-d_2	3.78[a]	3.09[a]	63	61	17
Tellurane-*4,4*-d_2	3.91[a]	3.12[a]	63	61	17
1,4-Oxathiane	3.14[a]	2.65[a]	62	62	18
Morpholine	2.75[a]	3.04[a]	58	58	18
1,3-Dioxane	3.14[a]	3.8[a]	57	55	19
4-Thiochromanone	3.75[a]	3.45[a]	61	61	20
4-Thiochromanone 4,4-dioxide	3.75[a]	4.14[a]	58	58	20
Benzocycloheptene-*5,5*-d_2	3.75[a]	1.1[a]	73	73	11

[a] Average value, J_{cis}, of two different J_{ae} values.

Table II. Calculated Dihedral Angles in Conformationally Restricted Compounds

Compd	Coupled protons	J_{calcd}	J_{obsd}	ϕ_{calcd}	Ref
trans-4-*tert*-Butylcyclohexanol (1)	1a2e	4.42	4.3	60	21
cis-4-*tert*-Butylcyclohexanol (2)	1e2a	1.77	3.0	51	21
	1e2e	3.60	2.7	64	
tert-Butylcyclohexane (3)	1a2e	3.96	3.03	64	22
	2e3a	3.75	3.61	61	
	3e4a	3.75	3.77	60	
	3a4e	3.75	3.76	60	
cis-3-Methyl-*trans*-4-methylcarbomethoxycyclohexane-*2,2,3,4,5,5*-d_6 (4)	1a2e	3.96	3.9	60	23
trans-1,2-Cyclohexanediol (5)	2a3e	4.42	4.5	60	24
cis-2-Phenyl-3,4-dimethylmorpholine (6)	2a3e	1.94	2.7	55	25
trans-1-Fluoro-2-iodocyclohexane-*3,3,6,6*-d_4 (7)	1e2e	3.96	3.03[a]	64	26
2-*tert*-Butyl-1,3-dioxane (8)	4e5e	1.68	1.3	63	27
	4e5a	4.22	5.0	57	
	4a5e	2.07	2.6	56	

[a] Spectrum of diaxial conformer obtained at −100°.

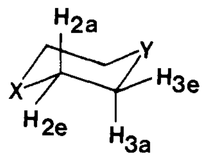


Figure 1.

calculated for several other compounds. The calculated values of a few examples which illustrate some trends that were observed are given in Table II.

It is of interest to note the difference in the effect of axial and equatorial substituents on the dihedral angles of the protons in six-membered rings. In those cases having an equatorial substituent (compounds **1**, **4**, and **5**) the dihedral angles, ϕ_{ae}, of the axial proton on the same carbon as the substituent are normal. Altona[9] has concluded on the basis of geometries determined by X-ray and empirical valence-force minimization methods that an equatorial substituent on a six-membered ring causes very little change in the dihedral angles of the protons of the ring. He noted an exception in the case of the *tert*-butyl group which forces the axial proton on the same carbon toward the center of the ring creating a dihedral angle, ϕ_{ae}, for this proton of 63°, in good agreement with the value of 64° obtained for this proton in *tert*-butylcyclohexane (Table II).

In the case of axial substituents, valence-force minimization calculations[9] showed that an axial substituent generally causes ϕ_{ea}, for the proton on the same carbon as the substituent, to decrease and ϕ_{ee} to increase. For example, an axial methyl group was calculated to cause the equatorial proton to have dihedral angles of $\phi_{ea} = 50°$ and $\phi_{ee} = 64°$. These values are very close to those found in this study for the dihedral angles of the equatorial proton on a carbon bearing an axial hydroxyl group (in *cis*-4-*tert*-butylcyclohexanol (**2**), $\phi_{ea} = 51°$, $\phi_{ee} = 64°$). Other compounds, **6** and **7**, with axial substituents show a similar distortion of dihedral angles.

It is difficult to estimate the reliability of the values of dihedral angles determined by this method since compounds with accurately determined dihedral angles are not available as models. Although modern X-ray diffraction methods can give accurate dihedral angles involving heavier atoms, the location of hydrogen atoms can be obtained with much less precision. However, a comparison can be made between the X-ray data and calculated proton dihedral angles if one assumes that the dihedral angle of the ring atoms is similar in magnitude to the axial–equatorial proton dihedral angle. Such a comparison has been made[6] for several

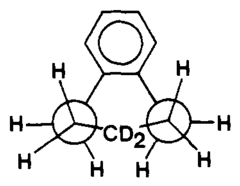
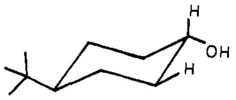
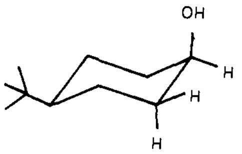


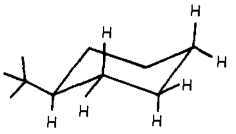
Figure 2.



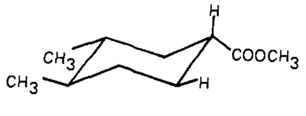
1



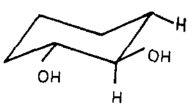
2



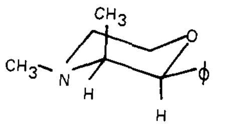
3



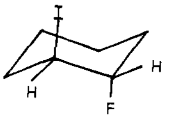
4



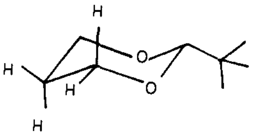
5



6



7



8

examples determined by the R-value method and a good correlation was obtained.

Neither the R-value method or the method presented in this paper can claim to determine precise values of dihedral angles; however, both have a major advantage over other applications of the Karplus equation, such as the DAERM method,[10] in that they compensate for substituent electronegativities. The present method requires the use of an empirical factor (electronegativity), whereas the R-value method does not; it assumes that the electronegativity of the substituents affects the coupling constants multiplicatively and equivalently.[6] The electronegativity values used in this paper are Huggins' values[8] of the atoms directly bonded to the ethane fragment, the same scale as was used in establishing eq 3. For substituent atoms which are themselves bonded to strongly electronegative elements problems may arise in the evaluation of the electronegativity of such substituents and caution is in order in these cases.

In eq 3, one term, $(4.1 + 0.63\Sigma\Delta X)$, is angle independent, whereas the other terms, $(1 - 0.462\Delta X_1)$ and $(1 - 0.462\Delta X_2)$, are angle dependent because they apply only to those substituents which have a dihedral angle of 180° with the coupled protons. The angle-dependent terms should be affected by a change in dihedral angle, and the value of the constant (0.462) should decrease with a deviation of the substituent-proton dihedral angle from 180°. For a small change this decrease is likely to be insignificant compared to the effect of changing the proton–proton dihedral angle which is near 60°, a point of maximum slope in the Karplus curve. An attempt was made to estimate the error caused by a deviation of the substituent-proton dihedral angle from 180° by assuming a $\cos^2$ relation between the factor (0.462) for the substituent effect and dihedral angle. By making such a correction for the compound in Table I with the largest deviation of dihedral angle (cyclohexane-1,4-dioxime), an error of 0.3° was indicated.

It should also be pointed out that eq 3 was derived primarily from acyclic compounds which were assumed to have dihedral angles of 60°, and normal bond angles, so that the formula should not be applied to compounds in which other factors that affect vicinal coupling constants are altered. The method should be useful in compounds containing large rings which exhibit little ring strain; an example of its applicability to seven-membered rings is shown for benzocycloheptene-*5,5-d*$_2$ (Figure 2).

The value calculated for ϕ_{4a3e} is 73°, in perfect agreement with that obtained by the ratio method or by direct application of a Karplus equation.[11]

In conclusion, the present method, which has yielded results for conformationally mobile compounds comparable to those obtained from the R-value method, has the disadvantage of requiring an evaluation of the electronegativities of substituents, but it has the important advantage of requiring only one coupling constant between two gauche protons. Since the R-value method requires four couplings between four protons or two averaged couplings between equilibrating pairs of protons, the present method can be used on molecules or parts of molecules that cannot be analyzed by the R-value method (for examples see Table II). In rigid molecules the method yields individual values of dihedral angles rather than average values as obtained in some cases by the R-value method.

Acknowledgment. The financial assistance of the National Research Council of Canada and the hospitality of the University of Guelph where the work was carried out are acknowledged.

References and Notes

(1) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).
(2) M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963).
(3) D. H. Williams and N. S. Bhacca, *J. Am. Chem. Soc.*, **86**, 2742 (1964); H. Booth, *Tetrahedron Lett.*, 411 (1965).
(4) H. R. Buys, *Recl. Trav. Chim. Pays-Bas*, **88**, 1003 (1969).
(5) J. B. Lambert, *J. Am. Chem. Soc.*, **89**, 1836 (1967).
(6) J. B. Lambert, *Acc. Chem. Res.*, **4**, 87 (1971).
(7) T. P. Forrest, *Org. Magn. Reson.*, **6**, 355 (1974).
(8) M. L. Huggins, *J. Am. Chem. Soc.*, **75**, 4123 (1953).
(9) C. Altona and M. Sundaralingam, *Tetrahedron*, **26**, 925 (1970).
(10) K. N. Slessor and A. S. Tracey, *Can. J. Chem.*, **49**, 2874 (1971).
(11) M. St-Jaques and C. Vaziri, *Org. Magn. Reson.*, **4**, 77 (1972).
(12) E. W. Garbisch and M. G. Griffith, *J. Am. Chem. Soc.*, **90**, 6543 (1968).
(13) C. Altona and E. Harvinga, *Tetrahedron*, **22**, 2275 (1966).
(14) H. Saito and K. Nukada, *J. Mol. Spectrosc.*, **18**, 355 (1965).
(15) E. W. Garbisch, Abstracts, 155th National Meeting of the American Chemical Society, San Francisco, Calif., 1968, No. P65.
(16) J. B. Lambert, R. E. Carhart, P. W. R. Corfield, and J. H. Enemark, *Chem. Commun.*, 999 (1968).
(17) J. B. Lambert, R. G. Keske, and D. K. Weary, *J. Am. Chem. Soc.*, **89**, 5921 (1967).
(18) W. B. Smith and B. A. Shoulders, *J. Phys. Chem.*, **69**, 579 (1965).
(19) C. Barbier, J. Delmau, and J. Ranft, *Tetrahedron Lett.*, 3339 (1964).
(20) J. B. Lambert and F. R. Koeng, *Org. Magn. Reson.*, **3**, 389 (1971).
(21) F. A. L. Anet, *J. Am. Chem. Soc.*, **84**, 1053 (1962).
(22) J. D. Remijnse, H. van Bekkum, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **90**, 779 (1971).
(23) J. P. Aycard, R. Guese, J. Berger, and H. Bodst, *Org. Magn. Reson.*, **5**, 473 (1973).
(24) R. U. Lemieux and J. W. Town, *Tetrahedron Lett.*, 1229 (1963).
(25) D. Dvornik and G. Schilling, *J. Med. Chem.*, **8**, 466 (1965).
(26) L. D. Hall and D. L. Jones, *Can. J. Chem.*, **51**, 2914 (1973).
(27) H. R. Buys and E. L. Eliel, *Tetrahedron Lett.*, 2779 (1970).