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Note

An attempt to derive a new Karplus-type equation of vicinal proton–carbon coupling constants for C–O–C–H segments of bonded atoms

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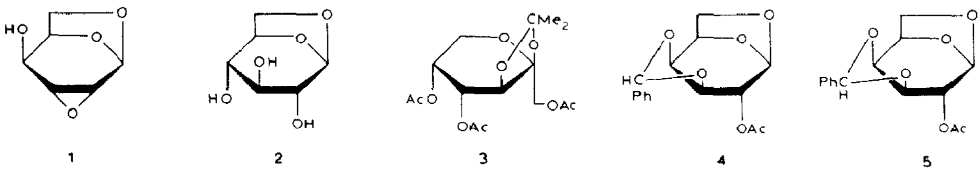
Determination of the stereochemistry of molecules in solution plays a crucial role in understanding their interaction in chemical and biochemical reactions. In n.m.r. spectroscopy, the angular dependence of vicinal coupling constants is often utilized in conformational analysis. The three-bond C–O–C–H proton–carbon long-range coupling constants[1] ($^3J_{C-H}$) provide valuable information about the conformation of compounds possessing this segment. Despite the potential of vicinal $^3J_{C-H}$ coupling constants for the conformational analysis of oligosaccharides, polysaccharides, and glycoconjugates, routine applications have been complicated by experimental difficulties involved in their measurement using classical ^{1}H-coupled ^{13}C n.m.r. spectroscopy and a limited knowledge of the angular dependence of $^3J_{C-H}$. In spite of a fairly large experimental effort expended in establishing the dependence on dihedral angles[2–6], a satisfactory relationship in an analytical form similar to the Karplus equation for proton–proton coupling constants[7] has not been obtained.

Here we propose a new Karplus-type relationship between the magnitude of the vicinal proton–carbon coupling constant $^3J_{C-H}$ and dihedral angle for C–O–C–H arrays of bonded atoms. It is based on the precise measurement of long-range proton–carbon coupling constants in a series of conformationally rigid carbohydrate derivatives having known X-ray structures. Moreover, the all measured carbon atoms were sp^3 hybridized, and the structures meet the condition of a constant sum of the substituent electronegativities, thus avoiding the influence of electronegativity factors on the magnitudes of coupling constants[1,3].

The values of $^3J_{C-H}$ were determined at 298 K in D_2O or $CDCl_3$, using an existing selective two-dimensional *J*-resolved experiment developed by Bax and Freeman[8], and the selective two-dimensional INEPT[9], in the modified version[10] where all ^{1}H pulses were soft ($\gamma B_2/2\pi \approx 20$ Hz). The accuracy of measured proton–carbon coupling-constants $^3J_{C-H}$ based on analysis of the first-order spectra was 0.1



Scheme

Hz. As usual in the case of three-bond coupling constants[1], we assumed that all ${}^3J_{C-H}$ values were positive.

To provide compounds having conformationally rigid structures, we have synthesized five monosaccharide derivatives, namely 1,6:2,3-dianhydro-β-D-gulopyranose[11] (**1**), 1,6-anhydro-β-D-glucopyranose[12] (**2**), 1,4,5-tri-*O*-acetyl-2,3-*O*-isopropylidene-β-D-fructopyranose[13] (**3**), 2-*O*-acetyl-1,6-anhydro-*exo*-3,4-*O*-benzylidene-β-D-galactopyranose[14] (**4**), and 2-*O*-acetyl-1,6-anhydro-*endo*-3,4-*O*-benzylidene-β-D-galactopyranose[14] (**5**); (see Scheme). These compounds were prepared as reported in the literature: **1** (ref. 15, 16), **2** (ref. 17), **3** (ref. 18), **4** (ref. 19), and **5** (ref. 19). We were thus able to obtain 14 values of ${}^3J_{C-H}$ coupling constants, and these are shown in Table I, together with the corresponding dihedral angles from X-ray structures. Values of ${}^3J_{C-H}$ for compounds **4** and **5** were remeasured and are in most cases similar to those already published[14]. Data obtained from compounds **1**–**5** cover the interval 80–280°. We have not yet prepared rigid compounds containing fixed C–O–C–H segments having dihedral angles in the 0–60° range. In order to complete the data we have therefore included values for ${}^3J_{C-H}$ from the following compounds: cyclomaltohexaose[4], 5.2 Hz (10°); phenyl 3-*O*-

TABLE I

MEASURED VICINAL PROTON–CARBON COUPLING CONSTANTS FOR DIFFERENT DIHEDRAL ANGLES OF C–O–C–H ARRAYS OF BONDED ATOMS IN COMPOUNDS **1**–**5**

Compound	*Array*	*Angle (deg.)*	${}^3J_{C-H}$ *(Hz)*
1	H-6endo–C-6–O-1–C-1	109	1.4
1	H-6exo–C-6–O-1–C-1	230	2.2
1	H-5–C-5–O-5–C-1	154	5.6
2	H-1–C-1–O-1–C-6	141	5.1
2	H-1–C-1–O-5–C-5	199	5.1
2	H-5–C-5–O-5–C-1	164	5.9
3	H-3–C-3–O-7–C-7[a]	86	0
4	H-4–C-4–O-7–C-7[a]	119	2.3
4	H-1–C-1–O-1–C-6[a]	136	5.1
5	H-3–C-3–O-3–C-7[a]	279	0
5	H-4–C-4–O-4–C-7[a]	131	3.2
5	H-1–C-1–O-1–C-6	137	5.2
5	H-7–C-7–O-4–C-4[a]	216	4.1
4	H-7–C-7–O-3–C-3[a]	127	5.2

[a] The carbon atom designated C-7 is from isopropylidene or benzylidene rings.

acetyl-β-D-xylopyranoside[5], 2.6 Hz (60°); and 1,2-*O*-ethylidene-β-D-glucopyranoside[5], 2.0 Hz (60°). It must be pointed out that in the foregoing compounds the dihedral angles are only estimated values and therefore the precision of these data is lower.

The obtained 17 points were used to set up 17 expressions of the Karplus-type equation of the form $^3J_{C-H} \approx A\cos^2\Phi - B\cos\Phi + C$. This type of equation was used to describe the dependence of proton–carbon coupling constants on dihedral angle for C–C–C–H arrays of bonded atoms[1]. Solution of these simultaneous equations yielded the values of the A, B, and C constants and gave the following expression

$$^3J_{C-H} = 5.7\cos^2\Phi - 0.6\cos\Phi + 0.5$$

for the conformation dependence of vicinal proton–carbon constants $^3J_{C-H}$ on the dihedral angle Φ between vicinal hydrogen and carbon in the C–O–C–H arrays of bonded atoms and which is shown as the solid line in the Figure.

The proposed new Karplus-type curve can be used in the conformational analysis of compounds containing C–O–C–H arrays of bonded atoms. The measurements of $^3J_{C-H}$ coupling constants using new two-dimensional n.m.r. techniques together with the proposed Karplus-type curve thus provide a promising approach in attempts to achieve a more detailed insight into the conformational properties of such complex biological compounds as oligosaccharides, polysaccharides, and glycoconjugates.

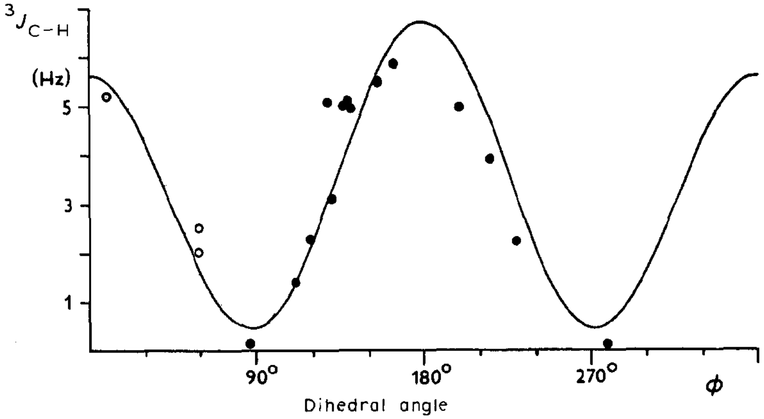


Fig. 1. Relationship between $^3J_{C-H}$ and the C–O–C–H dihedral angle Φ. Data represented by open circles taken from refs. 3, 4; data represented by filled circles, this work.

REFERENCES

1 P. E. Hansen, *Progr. NMR Spectroscopy*, 14 (1981) 175–296.
2 R. U. Lemieux, T. L. Nagabhushan, and B. Paul, *Can. J. Chem.*, 50 (1972) 773–776.
3 J. A. Schwarz and A. S. Perlin, *Can. J. Chem.*, 50 (1972) 3667–3676.
4 G. K. Hamer, F. Balza, N. Cyr, and A. S. Perlin, *Can. J. Chem.*, 56 (1978) 3109–3116.
5 H. Thøgersen, *Ph.D. Thesis, The Technical University of Denmark*, Lyngby, 1977.
6 F. H. Cano, C. Foces-Foces, J. Jimenes-Barbero, A. Alemany, M. Bernabe, and M. Martin-Lomas, *J. Org. Chem.*, 52 (1987) 3367–3372.
7 M. J. Karplus, *J. Chem. Phys.*, 30 (1959) 11–15.
8 A. Bax and R. Freeman, *J. Am. Chem. Soc.*, 104 (1982) 1099–1100.
9 T. Jippo, O. Kamo, and K. Nagayama, *J. Magn. Resonance*, 66 (1986) 344–348.
10 M. Hricovíni, I. Tvaroška, D. Uhrín, and G. Batta, *Carbohydr. Res.*, in press.
11 B. Berking and N. C. Seeman, *Acta Crystallogr., Ser. B*, 27 (1971) 1752–1760.
12 Y. J. Park, H. S. Kim, and G. A. Jeffrey, *Acta Crystallogr., Ser. B*, 27 (1971) 220–227.
13 P. Köll and J. Kopf, *Chem. Ber.*, 109 (1976) 3346–3357.
14 F. H. Cano, C. Foces-Foces, J. Jimenes-Barbero, M. Bernabe, and M. Martin-Lomas, *Carbohydr. Res.*, 155 (1986) 1–10.
15 M. Černý, V. Gut, and J. Pacák, *Collect. Czech. Chem. Commun.*, 26 (1961) 2542–2550.
16 M. Černý, I. Buben, and J. Pacák, *Collect. Czech. Chem. Commun.*, 28 (1963) 1569–1578.
17 M. V. Rao and M. Nagarajan, *Carbohydr. Res.*, 162 (1987) 141–144.
18 K. Heyns, W. D. Soldat, and P. Köll, *Chem. Ber.*, 108 (1975) 3619–3632.
19 C. Subero, L. Fillol, and M. Martin-Lomas, *Carbohydr. Res.*, 86 (1980) 27–32.