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THE USE OF TWO-DIMENSIONAL LONG-RANGE δ_C/δ_H CORRELATION IN CONJUNCTION WITH THE ONE-DIMENSIONAL PROTON-COUPLED ^{13}C NMR SPECTRUM IN THE STRUCTURAL ELUCIDATION OF EKEBERGININE, A NEW CARBAZOLE ALKALOID FROM Ekebergia senegalensis (Meliaceae)

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Summary: A new strategy involving the use of 2D long-range δ_C/δ_H correlation in conjunction with the 1D proton-coupled ^{13}C NMR spectrum has been applied to the structural elucidation of ekeberginine, a new carbazole alkaloid from the stem bark of Ekebergia senegalensis (Meliaceae).

While it has long been recognised[1,2] that long-range carbon-proton coupling constants are useful in assigning ^{13}C NMR spectra and establishing structural connectivity across heteroatoms and quaternary carbons there are few reports, other than in the peptide field,[3,4] of their use to define an extended sequence of bond connectivities and hence for complete structural elucidation. Applications have generally been limited to defining a partial structure and have used time-consuming selective proton decouplings, SPI[4] or 2D selective J-resolved spectra[5] to obtain correlations and measure individual long-range couplings. In this communication we wish to demonstrate that the combination of 2D long-range δ_C/δ_H correlation and consideration of the 1D proton-coupled ^{13}C NMR spectrum can be sufficient to form a powerful method of structural elucidation. In principle 2D non-selective heteronuclear long-range shift correlation methods[6] which also give the values of the coupling constants would render measurement of the proton-coupled ^{13}C NMR spectrum superfluous. In practice, however, we find that limited digital resolution is more of a problem in 2D than 1D spectra and in addition it is common to find that a set of correlations is incomplete. The strategy outlined above is particularly suitable for aromatic compounds and we have applied it to the structural elucidation of ekeberginine (1), a new carbazole alkaloid isolated from the stem bark of Ekebergia senegalensis (Meliaceae).

Ekeberginine (1), $C_{19}H_{19}NO_2$, m.p. 230-231°, readily formed an N-methyl derivative (2), m.p. 155-157°, m/z 307.1589, which has resonances in its 200.13 MHz ^1H NMR spectrum for a dimethylallyl group [δ_H 1.70 and 1.89 (both q, J 1.3 Hz, 3H-4' and 3H-5'), 4.19 (bd septet, J 6.2, 1.3 Hz, 2H-1'), 5.28 (t septet, J 6.2, 1.3 Hz, H-3')], a methoxyl group [δ_H 3.99], an N-methyl group [δ_H 4.13], an aldehyde [δ_H 10.37(s)], an isolated aromatic proton [δ_H 7.43 (s, H-2)] and an ortho-disubstituted benzene ring [δ_H 8.10 (ddd, J 8.0, 1.2, 0.7 Hz, H-5], 7.30 (ddd, J 8.0, 6.9, 1.4 Hz, H-6), 7.51 (ddd, J 8.3, 6.9, 1.2 Hz, H-7) and 7.41 (ddd, J 8.3, 1.4, 0.7 Hz, H-8)]. These data are consistent with the presence of a carbazole moiety with dimethylallyl, methoxyl and aldehyde substituents on one of the rings and suggest that ekeberginine is related to indizoline (3), m.p. 170-171°, from Clausenia indica[7] and heptaphylline (4), m.p. 190-191°, from C. heptaphylla and C. pentaphylla[8]. Ekeberginine (1) differs from (3) and the O-methyl derivative of (4) in physical properties and in the absence of a strongly deshielded H-4 resonance in its ^{1}H NMR spectrum. The ^{13}C NMR spectrum of N-methyl ekeberginine is consistent with the carbazole ring system and the above substituents. 2D one-bond δ_C/δ_H correlation permitted the direct assignment of all the protonated carbons (see Table 1). The structure (2) of N-methyl ekeberginine was then established unambiguously by comparing the pattern and size of the couplings with the observed qualitative correlations and considering the carbon resonances in an appropriate sequence. Although for ease of presentation the results are discussed in terms of the carbazole structure (2), it is important to realise that the bond connectivities obtained lead independently to this structure.

Table 1 lists the ^{13}C chemical shifts, their assignments, the values of the direct and long-range carbon-proton couplings and the observed correlations. The unsubstituted nature of ring B, already defined by the ^{1}H NMR spectrum, was readily confirmed by the observation of correlations of C-5 with H-7, C-6 with H-8, C-7 with H-5, and C-8 with H-6. As each of these signals has only one large coupling and shows only one long-range correlation in the experiments performed (see Table 1) it is reasonable to assume that the observed correlations arise through ^{3}J interactions.[1,2] The olefinic carbon C-3' of the dimethylallyl group was identified by its long-range correlations with the C-1' methylene protons and the methyl groups. Correlation with the N-methyl group identified C-1a and C-8a which were distinguished by the fact that C-8a has ^{3}J interactions with H-5 and H-7 while C-1a has a ^{3}J interaction with the aromatic proton on ring A. This indicates that the aromatic proton is attached either to C-4 or C-2. The assignment of the remaining ring junction carbons C-4a and C-5a followed readily from their correlations with protons in ring B. Thus C-5a has ^{3}J correlations with H-6 and H-8 while C-4a has ^{3}J correlations with H-5 and the C-1' methylene protons. It is clear from the last observation that the dimethylallyl group is attached to C-4 and therefore the isolated aromatic proton must be at C-2. The carbon bearing the aldehyde group, distinctive[2] because of its large ^{2}J interaction (22.6 Hz) with the aldehyde proton, must be C-3, as expected on biogenetic grounds, since it correlates with the C-1' methylene protons. The resonance at δ_C 136.3 is C-4 since it couples with the C-1' methylene protons. Finally the methoxyl group, which couples with the only remaining resonance, must be placed at C-1 which also shows correlations with H-2 and the aldehyde proton. Thus the structure of N-methyl ekeberginine is defined as (2) and hence ekeberginine has structure (1).

The isolation of ekeberginine from E. senegalensis is of considerable taxonomic interest. The Meliaceae family, unlike the Rutaceae family, is a poor source of nitrogen-containing metabolites.[9] The compounds previously isolated from E. senegalensis include the coumarin ekersenin[10] and some complex tetranortriterpenoid derivatives.[11] In the present work the coumarin xanthoxyletin was also obtained.

Table 1.

50.325 MHz ^{13}C NMR data of N-Methyl Ekeberginine (2).

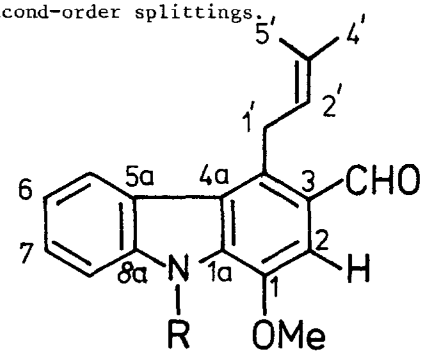
Carbon	δ_C [a]	$^1J_{CH}$	Long-range Couplings and Correlations[b]	
CHO	190.1	172.3	d (4.2)	H-2[c]
1	145.4	-	qdd (4.3, 2.9, 1.4)	OMe, H-2, CHO
8a	141.8	-	ddqd (9, 8, 3, 1)	H-5, H-7, NMe
4	136.3	-	bqd (6.5, 3.5)	2H-1', H-2
1a	134.3	-	dq (8.0, 2.5)	H-2, NMe
3'	132.7	-	septet t (6.2, 1.4)	3H-4', 3H-5', 2H-1'
3	125.7	-	dtd (22.6, 3.8, 1.2)	CHO, 2H-1'[c]
7	125.6	160.5	dt (7.9, 1.2)	H-5
5a	123.0	-	dddd (8.7, 4.9, 1.8, 1.0)	H-6, H-8
5	122.9	159.8	ddd (7.8, 2[d], 0.5[d])	H-7
4a	122.7	-	btdd (6, 2, 0.5)	2H-1', H-5[c]
2'	122.2	155.3	qqt (6, 5, 1)	3H-4', 3H-5', 2H-1'
6	120.2	160.5	dd (7.1, 1.2)	H-8
8	109.2	160.6	dt (8.2, 1.2)	H-6
2	105.5	159.0	d (3.1)	CHO
OMe	55.6	144.5	-	-
NMe	32.2	139.7	-	-
1'	26.5	127.0	d (4.0)	-
4'	25.6	125.7	dqt (7.0, 4.3, 1.3)	H-2'[c], 3H-5'[c]
5'	18.3	125.4	dqt (8.3, 4.2, 0.8)	H-2'[c], 3H-4'[c]

a Relative to $CDCl_3$ at δ 77.0.

b The pulse sequence used was[12] $90°[^1H]-\frac{1}{2}t_1-180°[^{13}C]-\frac{1}{2}t_1-\tau_1-90°[^1H]90°[^{13}C]-\tau_2-$ $BB[^1H]FID[^{13}C]t_2$ with phase cycling to achieve quadrature detection in both dimensions.[13] Two experiments were performed, with τ_1 = 40 ms, τ_2 = 20 ms and τ_1 = 80 ms, τ_2 = 40 ms.

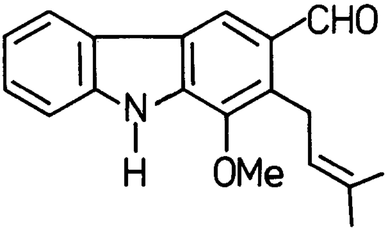
c Only observed in the experiment with τ_1 = 80 ms, τ_2 = 40 ms.

d Approximate value of second-order splittings.

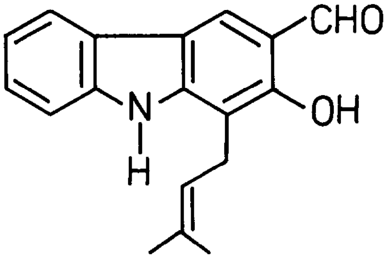


(1) R = H

(2) R = Me



(3)



(4)

References

1. H.E. Gottlieb, Israeli J. Chem., 16, 57 (1977).
2. J.L. Marshall, "Carbon-Carbon and Carbon-Proton NMR Couplings. Applications to Organic Stereochemistry and Conformational Analysis". Verlag Chemie International, Deerfield Beach, Florida (1983).
3. H. Kessler, C. Griesinger, J. Zarbock, and H.R. Loosli, J. Magn. Reson., 57, 331 (1984).
4. C.C.J. Culvenor, P.A. Cockrum, J.A. Edgar, J.L. Frahn, C.P. Gorst-Allman, A.J. Jones, W.F.O. Marasas, K.E. Murray, L.W. Smith, P.S. Steyn, R. Vleggar, and P.L. Wessels, J. Chem. Soc., Chem. Commun., 1259 (1983).
5. H. Seto, H.K. Furihata, and N. Otake, Tetrahedron Letters, 25, 337 (1984); M.J. Gidley and S.M. Bociek, J. Chem. Soc., Chem. Commun., 220 (1985).
6. C. Bauer, R. Freeman, and S. Wimperis, J. Magn. Reson., 58, 526 (1984).
7. B.S. Joshi and D.H. Gawad, Indian J. Chem., 12, 437 (1974).
8. B.S. Joshi, V.N. Kamat, D.H. Gawad, and T.R. Govindachari, Phytochemistry, 11, 2065 (1972).
9. I. Mester in "Chemistry and Chemical Taxonomy of the Rutales", ed. P.G. Waterman and M.F. Grundon, Academic Press, London, 31 (1983).
10. J.I. Okogun, V.U. Enyenihi, and D.E.U. Ekong, Tetrahedron, 34, 1221 (1978).
11. C.W.L. Bevan, D.E.U. Ekong, and D.A.H. Taylor, Nature, 206, 1323 (1965).
12. R. Freeman and G.A. Morris, J. Chem. Soc., Chem. Commun., 684 (1978).
13. A. Bax and G.A. Morris, J. Magn. Reson., 42, 501 (1981).

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