Tetrahedron Letters No. 16, pp 1311 - 1314, 1976. Pergamon Press. Printed in Great Britain.

CARBON-13 NMR SPECTRAL STUDIES OF ALOENIN AND ITS DERIVATIVES. CARBON-13 SIGNAL ASSIGNMENT PROBLEM OF 4-METHOXY-2-PYRONES

Kazuo Tori

Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, 553 Japan

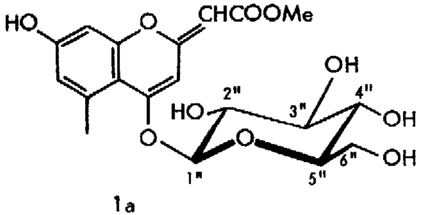
and

Toshifumi Hirata, Osamu Koshitani and Takayuki Suga*

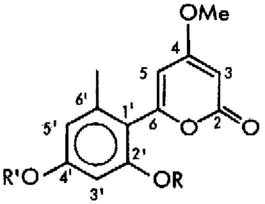
Department of Chemistry, Faculty of Science, Hiroshima University,
Higashisenda-machi, Hiroshima, 730 Japan

(Received in Japan 26 February 1976; received in UK for publication 11 March 1976)

Recently,[1] we reported the structure of aloenin (1b), a bitter glucoside isolated from Aloe arborescens Mill.,[2,3] revising the former structure 1a[2,3] on the bases of chemical and spectroscopic evidence. In order to confirm the structure more rigorously, we investigated natural-abundance ^{1}H noise-decoupled ^{13}C FT NMR spectra of 1 and its derivatives (2-11). Signal assignment of C-2, C-4, and C-6 in 6-substituted 4-methoxy-2-pyrone rings, which have frequently been found in natural products, has been a controversial problem (see compounds 12-16).[4-7] In fact, our preliminary assignments[2] in accord with the reported results[4] were different from those of yangonin (14).[5] However, in the course of the present study we found that our new assignments of these ^{13}C signals in aloenin and its derivatives are also different from those of 14. In view of the importance of the assignment problem in biosynthetic studies[8] of this kind of compounds,[4] we wish to report our results promptly.



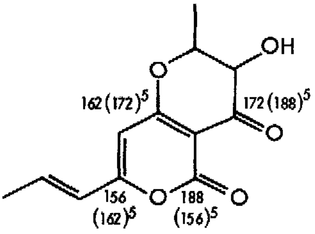
1a



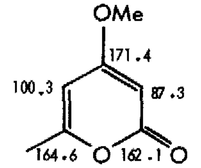
1b: R = G, R' = H
2: R = H, R' = Me
3: R = R' = Me
4: R = GAc$_4$, R' = Me
5: R = Ac, R' = Me
6: R = GAc$_4$, R' = Ac
7: R = R' = Ac

G = β-D-glucosyl
GAc$_4$ = tetra-O-acetyl-β-D-glucosyl

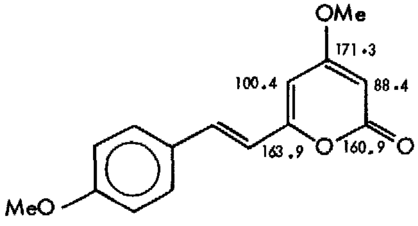
δ_C values



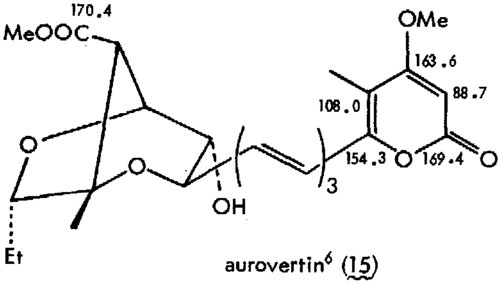
radicinin[4] (**12**)



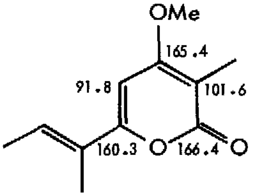
4-methoxy-6-methyl-2-pyrone[5] (**13**)



yangonin[5] (**14**)



aurovertin[6] (**15**)



nectriapyrone[7] (**16**)

The ^{13}C signals for **1**-**11** were generally assigned using known chemical shift rules,[9] ^{1}H single-frequency off-resonance (SFORD) and/or selective decoupling techniques[9] in combination with C_6D_6-induced ^{1}H shifts,[10] and chemical-shift comparisons among compounds. The methylation and acetylation shifts in o-hydroxyacetophenones[11] were useful for assigning the benzene ring carbons of all the compounds examined (see the TABLE); the deuteriation effect[12] (-0.6 ppm) was clearly detected for C-2' of **8**, which has an abnormal chemical shift due to an intramolecular hydrogen-bond.

Signals due to C-2, C-4, and C-6 in the 2-pyrone ring were distinguished as follows. Selective ^{1}H decouplings irradiated at H-3, H-5, and 4-OCH_3 frequencies revealed the C-2, C-4, and C-6 signal assignments because $^{2}J_{C(2)-C(3)-H(3)}$ (4.7 Hz) < $^{2}J_{C(6)-C(5)-H(5)}$ (7.5 Hz) is known for 2-pyrone.[13] Hydrogen-bonding shifts[9] of the C-2 carbonyl peaks were distinguished when a CD_3OH-$CDCl_3$ (1 : 1) mixed solvent was used for **3**, **4**, and **6** (the derivatives are not soluble in pure MeOH) as shown in the TABLE. Finally, the lanthanide-induced shift (LIS) method[14] was applied to **3** employing Yb(fod)$_3$ in $CDCl_3$. The largest LIS value was obtained for the C-2 peak as indicated in the TABLE. The LIS values for C-2, C-3, C-4, C-9, C-10, and 4-OMe peaks in 4-methoxycoumarin[15] were +114.0, +44.0, +21.5, +20.5, +18.0, and +5.0 ppm, respectively, in a similar experiment.

TABLE. ^{13}C Chemical Shift Data,[a] δ_C in CDCl$_3$

Carbon No.	1b^{b}	2^{c}	3^{d,e}	4^{d,f}	5	6^{d,f}	7
2	165.5	166.2	165.2 (+2.6) [+112.6]	164.7 (+2.0)	164.5	164.3 (+2.0)	164.2
3	88.4	88.2	88.2 (+0.4) [+50.6]	88.2 (+0.3)	88.6	88.5 (+0.4)	88.9
4	171.7	171.7	171.2 (+2.0) [+23.6]	171.1 (+0.9)	170.7	170.9 (+1.3)	170.5
5	105.0	104.8	104.6 (+1.4) [+21.4]	105.0 (+0.8)	104.1	105.0 (+1.0)	104.4
6	159.3	156.4	158.7 (+1.2) [+25.2]	157.4 (+0.7)	157.7	156.6^{g}(+0.8)	156.8
1'	114.7	113.0	114.8 (+0.5) [+12.4]	115.6 (0.0)	118.4	120.3 (+0.3)	123.3
2'	157.8	159.2	158.9 (+1.3) [+12.2]	155.5 (+0.6)	150.0	155.1^{g}(+0.7)	149.4
3'	102.0	99.5	96.1 (+0.8) [+7.8]	99.7 (+0.4)	106.1	106.2 (+0.8)	114.2
4'	161.0	161.6	161.8 (+1.4) [+4.2]	161.5 (+0.6)	161.2	152.3 (+0.8)	151.8
5'	112.4	108.1	107.0 (+1.1) [+4.2]	108.9 (+0.6)	114.0	117.7 (+0.7)	121.1
6'	140.0	139.8	139.9 (+0.8) [+10.8]	140.2 (+0.3)	140.0	140.2 (+0.6)	140.1
1"	102.7			98.8 (+0.1)		98.8 (+0.1)	
2"	74.5			70.6 (+0.7)		70.6 (+0.8)	
3"	78.1			72.6 (+0.4)		72.6 (+0.6)	
4"	71.0			68.3 (+0.6)		68.3 (+0.7)	
5"	78.1			72.0 (+0.3)		72.0 (+0.4)	
6"	62.3			62.0 (+0.5)		62.0 (+0.6)	
4-OMe	56.0	56.0	55.8 (+1.0) [+8.0]	55.9 (+0.5)	55.9	55.9 (+0.7)	56.0
4'-OMe		55.2	55.3 (+0.4) [+5.4]	55.3 (+0.3)	55.5		
6'-Me	20.2	20.4	20.2 (0.0) [+8.6]	20.3 (0.0)	20.3	19.7^{h}((0.0)	20.1^{h}
OMe			55.8 (+0.4) [+5.0]				
CO$\underline{\text{Me}}$					20.8	21.1^{h}	{20.7^{h} 21.1^{h}
$\underline{\text{C}}$OMe					169.2	168.5	168.7x2

[a] ^{13}C NMR spectra were determined with a Varian NV-14 FT NMR spectrometer operating at 15.087 MHz at 30° using CDCl$_3$ and/or C$_6$D$_6$ solutions containing TMS as an internal reference (δ_C 0) in 8-mm spinning tubes; precisions of δ_C are about ±0.1. FT measurement conditions were as follows: spectral width, 3923 Hz; acquisition time, 0.6 sec; pulse flipping angle, 13°; number of data points, 4820.

[b] Determined in pyridine-d$_5$ at 60°.

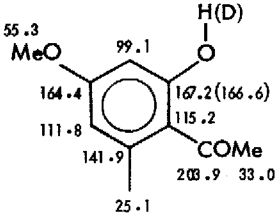
[c] Determined in CDCl$_3$—CD$_3$OD (9 : 1).

[d] Figures in parentheses are shift values observed in CDCl$_3$—CD$_3$OH (1 : 1) in ppm.

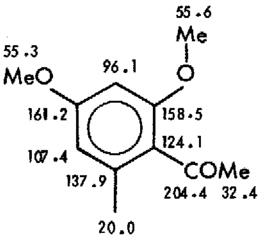
[e] Figures in square brackets are Yb(fod)$_3$-induced shifts in ppm (an LIS value was taken as the slope of the linear initial part of an LIS curve plotted against molar ratio of the shift reagent to substrate; Yb(fod)$_3$ was purchased from Stohler Isotope Chemicals).

[f] δ_C values for the tetraacetyl groups are 20.5 x 4, 170.4, 169.9, 169.3, and 169.0.

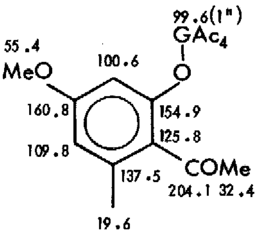
[g] Assignments may be interchanged in each vertical column.



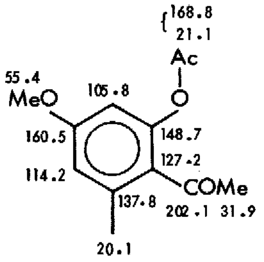
8



9



10



11

δ_C values

The signals due to the sugar moiety of **1** appear at almost the same positions as those of methyl β-D-glucopyranoside[9] in pyridine-d_5 except the anomeric C-1" signal, which was shifted upfield by about -3 ppm from the position of the C-1 signal of methyl glucoside. Similar behavior was also observed for the sugar moieties of **4**, **6**, and **10**, and methyl tetra-O-acetyl-β-D-glucopyranoside in $CDCl_3$.[16] On the other hand, anomeric carbon signals in sugar moieties of some steroid and triterpene glycosides were found to resonate at almost the same position as those in the corresponding methyl glycosides.[16,17] Furthermore, chemical shift changes in aromatic aglycone carbons due to glycosidation (from **2** to **4** as shown in the TABLE) will also be useful for structure elucidation of natural glycosides having aromatic aglycones.

We conclude that (1) the present ^{13}C NMR data on derivatives **2**-**11** are in harmony with the revised structure of aloenin **1b**, (2) caution should be exercised in assigning 2-pyrone-ring carbon signals until a firm substitution rule is found for the chemical shifts of the pyrone ring, and (3) the signal of an anomeric carbon bonded to -O-aglycone in a phenolic glycoside resonates at a field higher (by about -3 ppm) than that of the methyl glycoside.

Incidentally, we note that the confusion in assignment such as described here does not occur in the case of ^{13}C spectra of coumarin derivatives.[5,15,18]

REFERENCES

(1) T. Suga, T. Hirata and K. Tori, Chem. Lett. 715 (1974).
(2) T. Suga, T. Hirata and M. Odan, Ibid. 547 (1972).
(3) K. Makino, A. Yagi and I. Nishioka, Chem. Pharm. Bull. **21**, 149 (1973).
(4) M. Tanabe, H. Seto and L. F. Johnson, J. Amer. Chem. Soc. **92**, 2157 (1970).
(5) W. V. Turner and W. H. Pirkle, J. Org. Chem. **39**, 1935 (1974).
(6) L. J. Mulheirn, R. B. Beechey, D. P. Leworthy and M. D. Osselton, J.C.S. Chem. Comm. 874 (1974).
(7) M. S. R. Nair and S. T. Carey, Tetrahedron Lett. 1655 (1975).
(8) For a review, see U. Séquin and A. I. Scott, Science **186**, 101 (1974).
(9) For a review, see J. B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York (1972).
(10) For a leading reference, see K. Nikki, N. Nakagawa and Y. Takeuchi, Bull. Chem. Soc. Japan **48**, 2902 (1975).
(11) M. Kobayashi, Y. Terui, K. Tori and N. Tsuji, Tetrahedron Lett. 619 (1976); Y. Terui, K. Tori and N. Tsuji, Ibid. 621 (1976).
(12) F. W. Wehrli, J.C.S. Chem. Comm. 663 (1975).
(13) A. A. Chalmers and K. G. R. Pachler, Can. J. Chem. **53**, 1980 (1975).
(14) For a review, see B. C. Mayo, Chem. Soc. Rev. **2**, 49 (1973).
(15) N. J. Cussans and T. N. Huckerby, Tetrahedron **31**, 2719 (1975).
(16) K. Tori, unpublished results.
(17) L. Radics, M. Katar-Peredy, S. Corsano and L. Standoli, Tetrahedron Lett. 4287 (1975).
(18) For examples, see R. D. Lapper, Ibid. 4293 (1974); N. J. Cussans and T. N. Huckerby, Tetrahedron **31**, 2587, 2591 (1975); S. A. Sojka, J. Org. Chem. **40**, 1175 (1975); H. Gunther, J. Prestien and P. Joseph-Nathan, Org. Magn. Resonance **7**, 339 (1975).