Tetrahedron Vol. 36, pp. 2317 to 2326
Pergamon Press Ltd., 1980 Printed in Great Britain

^{13}C NMR SPECTROSCOPY OF NATURALLY OCCURRING IRIDOID GLUCOSIDES AND THEIR ACYLATED DERIVATIVES[a,b]

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(*Received in Germany* 6 *November* 1979)

Abstract—The ^{13}C NMR spectra of twenty one iridoid glucosides and fourteen acyl iridoid glucosides of various cyclopentane oxidation states have been analysed and their carbon shifts assigned. Evidence is presented which demonstrates that ^{13}C NMR spectroscopy is a valuable and reliable technique for distinguishing the sites of acylation in iridoid glucosides and confirming the predictions of the configuration at C-6 and C-8. A *cis* configuration of vicinal substituents is generally associated with a substantial increase in shielding, as compared with the *trans* analog. The ring size and C-1 configuration in the glucose moiety are also evident from the spectra.

Iridoid glucosides occupy an important position in the field of natural products chemistry and biology since they provide a structural link[1] between terpenes and alkaloids and display an interesting spectrum of biological activity.[2] To date, the structural information of these compounds has been obtained largely by the use of PMR spectroscopy[3] and to some extent by MS.[4,5] There are few ^{13}C NMR data on iridoid glucosides in the literature, despite the abundance of this moiety in plant natural products. Published work includes studies of iridoid glucosides (mainly as their acetate derivatives),[6,7] secoiridoids as such and their acetates,[7–10] valepotriates and related compounds,[11] together with occasional iridoids (only as acetates),[12–14] secoiridoids,[15,16]† and plumieride-type compounds.[17,18] However, some of the assignments reported[7,13,17,18] have to be revised (discussed later) in the light of the data for closely related compounds presented in this study. Recently, we have elucidated the structure of some new iridoid glucosides[19–24] with the aid of ^{13}C NMR spectra.

Compared with other spectroscopic techniques, the ^{13}C NMR spectroscopy is a more reliable tool for the elucidation of structure and configuration of natural and synthetic compounds. To assist the structural and stereochemical assignment of naturally occurring iridoids, we have carried out a systematic ^{13}C NMR study of these compounds where special attention is given to chemical shift data and structural features.

RESULTS AND DISCUSSION

In order to get comparable data, the compounds were measured in CD_3OD, a solvent sufficiently polar to dissolve both iridoids and their esters. The iridoid glucosides are grouped[25] according to the structure of the cyclopentane ring and their chemical shift values are given in Tables 1–4. The signals were assigned[26] by the single-frequency off-resonance decoupling technique, by application of substituent chemical shift rules for OH substitution and acetylation shifts, steric effects and comparison among related compounds.

The assignments of the glucoside portion of iridoids followed from the spectrum of methyl β-D-glucopyranoside.[27] Small deviations from the reported chemical shift values are observed. Tests have shown that solvent shifts of 0.8 ± 0.3 ppm‡ can normally be expected on going from D_2O to CD_3OD, although some C atoms experience slightly larger shifts. In contrast to the C-1 carbons which appear between 93.3–98.5 ppm, the C-1′ carbons are confined to an extremely narrow range (99.9 ± 0.3 ppm) for all the compounds studied showing an apparent lack of sensitivity towards the nature of the aglucone. It has recently been shown[9] that the carbons C-1 and C-1′ can easily be distinguished by their ^{13}C–^{1}H coupling constant. In some of the highly oxygenated iridoids, accurate assignments could not be made for a few signals with similar chemical shifts. This limitation, however, has not affected the conclusions reached in this paper.

The 4-substituted and -unsubstituted iridoid glucosides can easily be distinguished by their single-frequency off-resonance spectra and characteristic chemical shift values (Table 5).

The effects of hydroxylation on the aglucone spectrum. The change from a *trans* 1,2-diol arrangement to the *cis*-, in comparing members of the same set such as **18** and **19** or **33** and **35**, involves an increase in shielding[29] of the carbinol carbons (Tables 3 and 4). The effects of α- and/or β-oxygenation on the chemical shift of the Me signal at C-8 are summarized in the Table 6. In **22** and **28**, the OH group at C-7 is located at a *cis*-γ-position in

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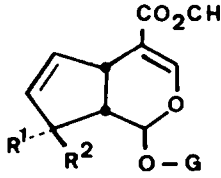
[a] Part of this work was reported by R. K. Chaudhuri and O. Sticher, at the 20th Annual Meeting of the American Society of Pharmacognosy, Purdue University, West Lafayette, Indiana, U.S.A., 29 July–3 August 1979.

[b] A preliminary report of part of this study has appeared; R. K. Chaudhuri, F. Ü. Afifi-Yazar and O. Sticher, *Helv. Chim. Acta* **62**, 1603 (1979).

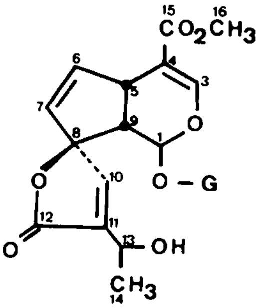
†The structure of xylomolin has recently been revised: M. Nakane, C. R. Hutchinson, D. Van Engen and J. Clardy, *J. Am. Chem. Soc.* **100**, 7079 (1978).

‡4-CO_2H iridoids, on going from CD_3OD to D_2O, show a larger change in the chemical shifts of C-3 and C-4, inducing shielding (~4 ppm) and deshielding (~4 ppm), respectively, as a result of different solvation in the two solvents.

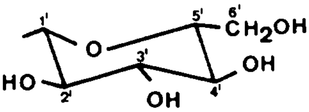


1: Monotropein methyl ester:
R' = OH; R² = CH₂OH

2: Gardenoside:
R' = CH₂OH; R² = OH



3: Plumieride



G = *β*-D-glucose

Fig. 1. Iridoids having a double bond between C-6 and C-7.

relation to the Me group at C-8 and the expected upfield shift (~8 ppm)[28,29] of the Me carbon (C-10) is observed.

The C-5 in **28** is rather shielded and it seems that the axial OH at C-7 exerts this shielding. This shielding effect, however, is absent in the case of **32** and **33**, as compared with **34** and **35** although **32** and **33** have an axial OH function at C-7. This might be a result of conformational differences of the two sets of compounds. This has also been observed in simple cyclopentanols.[29]

Table 1. ^{13}C NMR chemical shifts of iridoids having a double bond between C-6 and C-7

C-Atom	1	2	3
1	95.15	94.41	94.21
3	152.48	152.02	152.50
4	110.53	111.60	110.90
5	38.80	38.92	40.34
6	137.54	135.80[b]	141.46
7	133.65	135.90[b]	150.22
8	85.89	86.34	97.83
9	45.42	52.40	50.73
10	68.26	67.17	129.90
11	-	-	138.53
12	-	-	172.72
13	-	-	63.41
14	-	-	22.45
15	168.97	169.69	168.40
16	51.58	51.62	52.02
1'	99.75	99.98	100.02
2'	74.23	74.72	74.57
3'	77.75[a]	78.41[a]	78.26[a]
4'	71.03	71.65	71.17
5'	77.51[a]	78.02[a]	77.71[a]
6'	62.30	62.86	62.45

Values with same superscript in the vertical column are interchangeable

A long-range effect is observed on going from an equatorial to an axial OH group at C-6. It is evident from the shift values that on going from **5** to **6** or **18** to **19** a shielding (~3 ppm) is caused to the carbon C-4 whereas the C-8 experiences an approximately equivalent deshielding (Table 7). A shift difference of ~1.5 ppm for C-3 in the C-6 epimers is also observed. These effects can be explained on the basis of electric field effects.[30] It is of interest to point out the different chemical shift values for C-6 associated with the equatorial (**5**) and axial (**6**) OH function at that carbon (Table 2). This difference has also been observed in substituted cyclohexanes.[31]

Comparison of the chemical shift values of the C-8 epimers shows that an axial OH function exerts a shielding of 5–7 ppm to C-9 in respect to its equatorial partner (Table 8). In addition a downfield shift of 1–3 ppm is brought about by the C-8(OH) group into C-1 on going from axial to equatorial position. However, the shift of the *β*-carbon (C-9) is a more reliable guide for the configuration at C-8 than the shift of the *γ*-carbon (C-1). A comparison of **1** with **2** shows that a change in configuration at C-8 affects not only C-9 and C-1 but also C-7 and C-6, inducing shielding and deshielding, respectively. It is noteworthy that an OH group at C-5 causes a large downfield shift (~10 ppm) to the carbon C-9 as compared with the corresponding desoxy-compound.

Although the configurational analysis with the help of NMR carried out so far in this series used the proton,[3] this nucleus suffers from two deficiencies. First, proton spectra are complicated by spin–spin coupling which produces frequent overlap and renders spectrum interpretation difficult. Second, the chemical shift differences of protons in only slightly different environments are small and in the order of long range shielding effects. Moreover, owing to the sensitivity of ^{13}C shieldings to minor structural changes, the chemical shift differences exhibited by carbons in different environments are generally larger than for corresponding protons. Thus, ^{13}C NMR data provided here may conveniently be applied for the elucidation of the configuration in iridoid glucosides.[20]

Table 2. ^{13}C NMR chemical shifts of iridoids having a double bond between C-7 and C-8

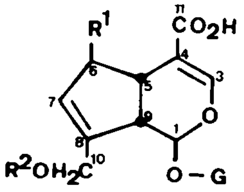
C-Atom	4	5	6	7*	8	9"	10	11
1	98.06	98.80	101.53	101.36	96.85	97.72	98.19	97.83
3	153.18	153.98	155.62	155.39	153.92	141.49	141.59	141.64
4	112.53	111.02	108.27	108.51	114.14	105.72	105.81	105.51
5	36.25	46.97	42.57	42.53	76.23	46.07§	46.45	46.04
6	39.40	82.38	75.33	75.44	46.79	82.74	82.91	82.66
7	128.26	129.92	129.89	132.02	126.66	130.27	130.66	132.59
8	144.22	147.31	151.32	145.98	141.63	147.95	147.79	142.41
9	46.59	45.94	45.73	46.32	56.36	47.89§	47.86	48.39
10	61.13	61.06	61.61	63.84	60.78	61.32	61.47	63.98
11	171.11	172.07	170.92	172.62	168.09	-	-	-
12	-	-	-	-	51.78	-	-	-
1'	99.91	100.16	100.38	100.66	99.78	99.90	100.04	100.08
2'	74.40	74.61	74.83	74.97	74.22	74.81	74.80	74.72
3'	77.72^{a}	78.06^{a}	78.24	78.59^{a}	77.97^{a}	78.07^{a}	77.66	77.99^{a}
4'	71.04	71.28	71.46	71.64	71.20	71.44	71.67	71.27
5'	77.30^{a}	77.57^{a}	77.64	77.95^{a}	77.18^{a}	77.77^{a}	75.62	77.72^{a}
6'	62.25	62.48	62.67	63.05	62.47	62.60	64.58	62.61
1"	-	-	-	-	-	-	135.62	131.02
2"	-	-	-	-	-	-	130.06^{b}	130.54^{b}
3"	-	-	-	-	-	-	129.29^{b}	129.59^{b}
4"	-	-	-	-	-	-	131.58	134.39
5"	-	-	-	-	-	-	129.29^{b}	129.59^{b}
6"	-	-	-	-	-	-	130.06^{b}	130.54^{b}
α	-	-	-	-	-	-	146.54	-
β	-	-	-	-	-	-	118.66	-
CO	-	-	-	172.63	-	-	168.41	167.71

Values with same superscript in the vertical column are interchangeable.

* $COC\underline{H}_3$ = 20.81

" Data taken from Ref 21.

§ Confirmed by selective {^{1}H} -^{13}C decoupling

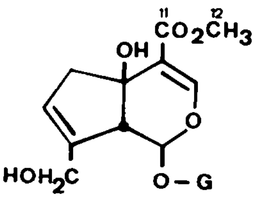


4: Geniposidic acid:
R^1 = R^2 = H

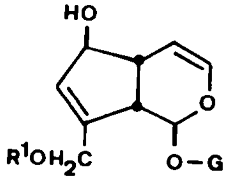
5: Scandoside:
R^1 = β-OH; R^2 = H

6: Desacetyl asperulosidic acid:
R^1 = α-OH; R^2 = H

7: Asperulosidic acid:
R^1 = α-OH; R^2 = COCH$_3$



8: Theviridoside



9: Aucubin: R^1 = H

10: Scrophularioside: R^1 = H
Trans-cinnamoyl at C-6'

11: Melampyroside:
R^1 = Benzoyl

Fig. 2. Iridoids having a double bond between C-7 and C-8.

Table 3. ^{13}C NMR chemical shifts of iridoids having an epoxide ring between C-7 and C-8

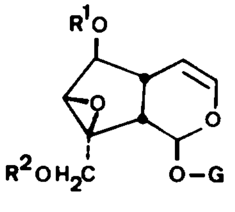
C-Atom	12"	13	14	15"	16"	17	18	19
1	95.33	95.41	95.34	95.06	95.14	95.30	94.87[§]	95.56
3	141.78	141.52	141.69	142.09	142.45	141.72	142.90	144.12
4	104.03	103.59	104.10	102.91	102.99	109.57	107.45	104.26
5	39.10	38.63	39.01	36.51	36.82	76.57	74.52	80.01
6	79.58	79.06	79.57	80.98	81.42	44.42	77.29[a]	77.69[a]
7	62.55	62.51	62.42	60.21	60.30	64.20	66.01	65.75
8	66.23	63.40	66.13	66.72	66.90	67.28	64.18	66.83
9	43.60	43.28	43.32	42.90	43.27	54.45	52.72	52.88
10	61.60	64.03	61.81	61.17	61.35	17.60	17.53	17.59
1'	99.74	100.01	99.72	99.55	99.79	99.63	99.40	99.52
2'	74.82	74.48	74.68	74.55	74.90	74.78	74.31	74.70
3'	78.54[a]	77.86[a]	77.40	78.08[a]	78.71[a]	78.46[a]	77.93[a]	78.22[a]
4'	71.74	71.00	71.48	71.36	71.85	71.82	71.38	71.61
5'	77.70[a]	77.35[a]	75.77	77.34[a]	77.77[a]	77.85[a]	77.93[a]	78.22[a]
6'	62.90	62.51	64.15	62.67	63.00	63.00	62.74	62.86
1"	-	135.19	135.49	127.40	128.86	-	-	-
2"	-	129.77[b]	130.03[b]	115.29	114.90	-	-	-
3"	-	129.12[b]	129.27[b]	146.37	148.14	-	-	-
4"	-	131.41	131.61	149.33	151.72	-	-	-
5"	-	129.12[b]	129.27[b]	116.49*	112.62	-	-	-
6"	-	129.77[b]	130.03[b]	123.19*	123.01*	-	-	-
α	-	146.48	146.65	147.50	147.25	-	-	-
β	-	118.23	118.55	114.40*	114.90*	-	-	-
CO	-	168.13	168.37	168.80	168.79	-	-	-
OCH$_3$	-	-	-	-	56.46	-	-	-

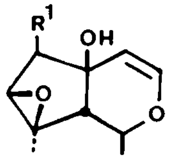
Values with same superscript in the vertical column are interchangeable

* Considering the acetate shift data these assignments were revised (Ref. 21)

" Data taken from Ref. 21

[§] Shift value has been corrected [Helv. chim. Acta, 62, 1603 (1979)]





12: Catalpol:
$R^1 = R^2 = H$

13: Globularin:
$R^1 = R$; $R^2 =$ *Trans*-cinn.

14: Picroside I:
$R^1 = R^2 = H$; *Trans*-cinn. at C-6'

15: Verminoside:
R^1 = Caffeoyl; $R^2 = H$

16: Minecoside:
R^1 = Isoferuloyl; $R^2 = H$

17: Galiridoside:
$R^1 = H$

18: Antirrinoside:
$R^1 = \beta$-OH

19: Procumbide:
$R^1 = \alpha$-OH

Fig. 3. Iridoids having an epoxide ring between C-7 and C-8.

Table 4. ^{13}C NMR chemical shifts of iridoids having a saturated cyclopentane ring

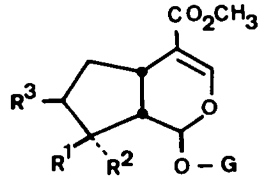
	(a)								(b)							
C-Atom	20	21	22	23	24	25	26	27*	28	29	30^{+}	31	32	33	34§	35
1	97.89	95.57	97.84	95.51	93.75	94.59	93.36	93.97	92.31	93.28	94.40	94.40	93.34	93.48	95.16	96.29
3	152.65	152.01	152.15	140.86	139.54	141.47	140.89	142.61	139.30	142.71	143.83	143.81	140.39	140.45	141.61	141.61
4	112.94	112.67	114.14	107.57	105.84	104.05	110.58	109.31	111.46	108.03	106.64	106.36	106.54	105.84	105.27	106.40
5	35.23	32.88	32.20	30.01	39.68	41.61	71.87	72.55	65.64	72.74	73.24	73.18	37.32	38.38	37.16	38.86
6	34.13^{b}	30.62	42.78	40.90	77.04^{a}	76.76	38.77	38.76	46.55	78.07^{a}	77.87^{a}	77.22^{a}	83.14	83.76	78.34^{a}	78.63^{a}
7	33.31^{b}	39.63	75.08	74.24^{b}	49.10	48.81	40.19	37.93	78.21^{a}	47.31	45.91	45.90	86.42	85.38	79.34^{a}	78.63^{a}
8	36.52	81.03	42.18	153.60	79.28	90.09	79.62	89.97	80.45	78.29	88.43	88.33	80.33	80.23	81.03	81.36
9	49.29	51.58	46.61	45.22	50.50	49.42	60.93	58.25	58.79	59.12	55.20	55.10	48.08	48.89	43.70	44.59
10	20.81	24.97	13.46	111.16	25.06	23.00	24.71	22.21	15.91	25.20	22.51	22.64	64.29	66.41	66.37	69.01
11	169.70	169.26	169.60	-	-	-	-	-	-	-	-	-	-	-	-	-
12	51.58	51.76	51.63	-	-	-	-	-	-	-	-	-	-	-	-	-
1'	100.22	99.43	100.17	99.47	98.79	99.98	99.16	99.48	99.02	99.23	99.75	99.69	99.55	99.68	99.20	100.87
2'	74.78	74.47	74.79	74.83^{b}	73.56	74.63	74.50	74.45	74.58	74.30	74.28	74.11	74.61	74.44	74.61	74.35
3'	78.36^{a}	77.44	78.41^{a}	78.16^{a}	76.74^{a}	77.84^{a}	78.18^{a}	78.07^{a}	78.06^{a}	77.37^{a}	77.42^{a}	77.22^{a}	77.94^{a}	77.59^{a}	77.99^{a}	77.78^{a}
4'	71.61	71.41	71.68	71.65	70.49	71.54	71.72	71.56	71.80	71.56	71.43	71.40	71.54	71.07	70.39	70.83
5'	78.06^{a}	75.27	78.11^{a}	77.97^{a}	76.52^{a}	77.84^{a}	77.58^{a}	77.59^{a}	77.61^{a}	78.16^{a}	77.66^{a}	77.22^{a}	77.71^{a}	77.59^{a}	78.34^{a}	77.43^{a}
6'	62.80	64.03	62.85	62.78	61.63	62.95	62.80	62.72	62.86	62.62	62.68	62.75	62.70	62.45	62.42	62.23
1"	-	127.34	-	-	-	135.59	-	-	-	-	-	135.24	-	135.44	-	135.37
2"	-	115.11	-	-	-	129.82^{b}	-	-	-	-	-	129.73^{b}	-	129.77^{b}	-	129.86^{b}
3"	-	146.32	-	-	-	129.04^{b}	-	-	-	-	-	128.96^{b}	-	129.02^{b}	-	129.16^{b}
4"	-	149.19	-	-	-	131.27	-	-	-	-	-	131.26	-	131.32	-	131.45
5"	-	116.41	-	-	-	129.04^{b}	-	-	-	-	-	128.96^{b}	-	129.02^{b}	-	129.16^{b}
6"	-	123.01	-	-	-	129.82^{b}	-	-	-	-	-	129.73^{b}	-	129.77^{b}	-	129.86^{b}
α	-	147.12	-	-	-	145.72	-	-	-	-	-	145.77	-	146.15	-	146.52
β	-	114.62	-	-	-	120.13	-	-	-	-	-	119.79	-	118.73	-	118.60
CO	-	168.87	-	-	-	168.51	-	173.27	-	-	173.24	168.28	-	168.69	-	169.03

Values with same superscript in the vertical column are interchangeable

* CO-$\underline{C}H_3$ 21.72

$^{+}$ CO-$\underline{C}H_3$ 22.26

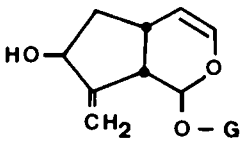
§ A few drops of DMSO-d_6 were added to increase the solubility



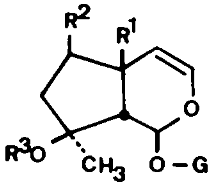
20: Desoxy loganin:
$R^1 = CH_3$; $R^2 = R^3 = H$

21: Ladroside:
$R^1 = OH$; $R^2 = CH_3$; $R^3 = H$
Trans-caffeeoyl at C-6′

22: Loganin:
$R^1 = CH_3$; $R^2 = H$; $R^3 = OH$



23: Antirride

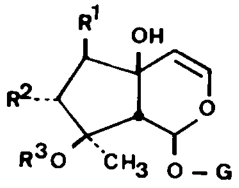


24: Ajugol:
$R^1 = R^3 = H$; $R^2 = \alpha$-OH

25: Laterioside:
$R^1 = H$; $R^2 = \alpha$-OH;
$R^3 =$ *Trans*-cinn.

26: 6-Desoxyharpagide:
$R^1 = OH$; $R^2 = R^3 = H$

27: Reptoside:
$R^1 = OH$; $R^2 = H$; $R^3 = COCH_3$

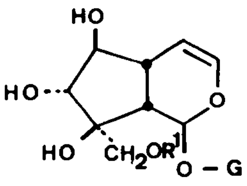


28: Daunoside:
$R^1 = R^3 = H$; $R^2 = OH$

29: Harpagide:
$R^1 = OH$; $R^2 = H$; $R^3 = H$

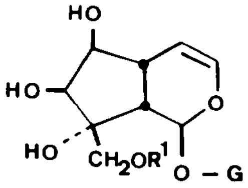
30: Acetyl harpagide:
$R^1 = OH$; $R^2 = H$; $R^3 = COCH_3$

31: Harpagoside:
$R^1 = OH$; $R^2 = H$;
$R^3 =$ *Trans*-cinn.



32: $R^1 = H$

33: Globularimin:
$R^1 =$ *Trans*-cinn.



34: $R^1 = H$

35: Globularinin:
$R^1 =$ *Trans*-cinn.

Fig. 4. Iridoids having a saturated cyclopentane ring.

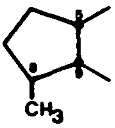
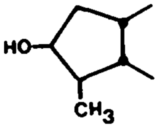
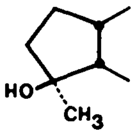
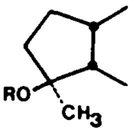
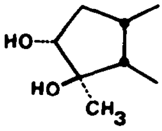
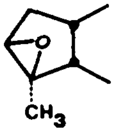
Table 5. Characteristic chemical shift values of 4-substituted and -unsubstituted iridoids

C-Atom	4-Substituted*		4-Unsubstituted	
	Substituent at		Substituent at	
	C-5(H)	C-5(OH)	C-5(H)	C-5(OH)
C-3	153±1	153±1	142±1	142±1
C-4	112±1	114.1§	105±1	109±1

* CO_2H or CO_2CH_3

§ Only one compound studied

Table 6. The effect of oxygenation on the chemical shift of the methyl signal at C-8

Compds.	Substituent(s) on the cyclopentane ring	Chemical Shift (in ppm) of the methyl signal
20		20.8
22		13.5
21,24, 26,29		25.0*
25,27, 30,31		22.6*
28		15.9
17,18, 19		17.6*

R = Acyl, * Averaged Chemical shift values

Table 7. The effects of C-6-hydroxyl group on the chemical shifts of C-4, C-8 and C-3

Compds.	Configuration at C-6 (OH)	γ-Effects on C(4)	γ-Effects on C(8)	δ-Effect on C(3)
5	equatorial	-2.8	+4.0	+1.6
6	axial			
18	equatorial	-3.2	+2.7	+1.2
19	axial			

Shift increments (in ppm) quoted are obtained by substracting the chemical shift value of the equatorial substiuted compound from the axial one.

Table 8. The effects of C-8-hydroxyl group on the chemical shifts of C-9 and C-1

Compds.	Configuration at C-8 (OH)	Chemical shift (in ppm) of C(9)	C(1)
2,21,24, 32,33	equatorial	50 ± 2	93.7 ± 0.5*
1,34,35	axial	44.5 ± 1	95.7 ± 0.5

* The data obtained from 21 is not included.

Table 9. The effects of acylation on the ^{13}C NMR spectra of iridoids

Site of acylation	Observed shifts in carbon signals* 5	6	7	8	9	10	5''	6''
6-O	-2.5	+1.6	-2.3					
8-O**			-1.7	+10.5	-3.9	-2.6		
10-O				- 4.6§		+2.8		
6'-O							-2.1	+2.3

* Shift increments (in ppm) quoted represent averaged values. (+) and (-) indicate low field and high field shift.

** To avoid solvent effect complication, the data obtained from 24 and 25 have not been used.

§ A sizeable shift was not observed in the case of 33 and 35 and these date have been excluded from calculation.

Site of acylation. The effects of acylation on ^{13}C NMR spectra of iridoid glucosides are summarized in Table 9. The shift increments quoted are relative to the equivalent compound lacking acylation at the site. The usefulness of ^{13}C NMR spectroscopy for the determination of the site of acylation, a determination which is often difficult to carry out by other methods, has recently been reported in the flavonoid series.[32] During the course of the structure determination of some acetyl iridoids (valepotriate-type) Bock *et al.*[11] utilized the information obtained from the ^{13}C NMR data in locating the site of acetylation.

The series of compounds under study in the present work includes iridoid glucosides acylated with acetyl, benzoyl, cinnamoyl, caffeeoyl and isoferuloyl groups. Examination of the ^{13}C NMR spectra of these compounds clearly reveals the sites of acylation. Thus, whereas acylation produces a downfield shift (2–3 ppm) in the signal of the α-carbon, it produces an upfield shift (2–5 ppm) to the β-carbon(s). The only exception is observed in the case of **33** and **35**, where no sizeable upfield shift is brought about by acylation of C-10 (OH) into the β-carbon C-8. This might be a case of dual effects on the chemical shift of C-8. Examination of the Dreiding models of **33** and **35** reveals that the acyl CO and the C-8 (OH) are situated close to one another and can be envisioned to be H-bonded. Thus, acylation at C-10 causes an upfield shift to the β-carbon C-8 whereas the chelation[33] between the acyl CO and the C-8 (OH) might cause an approximately equivalent downfield shift to that carbon, thereby keeping the chemical shift values of C-8 in **33** and **35** unchanged.

The acylation of tertiary OH groups (e.g. C-8-OH) clearly represents a special case. As a result of acylation, the α-carbon is shifted *ca* 10 ppm downfield. This is accompanied by significant upfield shifts of the signals of the β-carbons, C-7, C-9 and C-10, the effect being more noticeable at C-9.

A linear relationship has recently been shown[34] to exist between ^{13}C chemical shift of the carbinyl carbon (C_α) of the esters and the *pka* values of the acids from which they are derived. Since free rotation is possible around the carbinyl carbon–ether oxygen bond the acylation effect at C_β can be explained[34] on the basis of steric compression by the CO group or the alkyl/aryl group.

Ring size and C-1 *configuration in glucose.* Methyl glycofuranosides and methyl glycopyranosides of the same sugar have been found to be readily distinguishable by their ^{13}C NMR spectra.[27] By using the established criteria for this distinction it is evident that all the glucose moieties in the glucosides studied are in the pyranose form. With regard to the configuration of the glucosidic bond in the glucosides studied, it is clear from both the constancy of the signals for glucose and from the good agreement with published results for methyl glucosides,[27] that all glucosides have β-D-configuration at C-1′. To obtain this information by chemical means, the treatment of the glycosides with a variety of enzymes is necessary. The glucose linkage at C-1′ can also be determined by the value of $J_{1'2'}$ in ^1H NMR. In the case of spectra recorded in D_2O or CD_3OD, however, the signal of H–C(1′) may be merged into the solvent signal or overlap with other signals. This problem can be solved by higher frequency spectrometers, but the cost of these is often beyond the means of many spectroscopy departments. ^{13}C NMR thus offers a simple unequivocal method to get this information.

In the light of the data obtained from this work the shift for C-8 in penstemide,[17] which resembles very much plumieride (**3**) and dihydroplumieride, is expected to appear at ~96 ppm considering the solvent shift. The configuration at C-8 is not unequivocal as can be seen from the chemical shift value of C-9, if the proposed structure is correct. In the absence of any confirmatory information the shift assignment proposed for some of the carbon signals of oruwacin[18] (structurally similar to **3**) harbors discrepancies with the results of the present work. The spectral assignment of **9** (in D_2O) reported[7,13] earlier has also discrepancies with our results. The remarkable constancy of the chemical shift values of the glucose carbons as well as their distinctive ^{13}C–^1H coupling observed in this and earlier[9] studies suggest the reversal of previous assignments[7,13] of carbons C-1 and C-1′ at **9** as well as in asperuloside[7] and verbenalin[7].

CONCLUSION

According to the results presented in this paper, ^{13}C NMR spectroscopy seems to be more sensitive than other routine analyses, to the position and nature of a given substituent in the iridoid skeleton, providing valuable information for the rapid identification of a known iridoid or proposing the structure of a new one. The ^{13}C NMR data provided here can also be applied for the assignment of E-ring carbons of many indole alkaloids.[35] In conclusion the following points emerge:

(1) The assignment of specific carbons can be achieved with the help of the data provided in this work.

(2) A decision can be made between *cis*-and *trans*-diol in comparing members of the same set, from the chemical shift values of the carbinol carbons.

(3) The Me shift is a suitable probe for the relative configuration at C-8 as well as C-7.

(4) The shifts brought about by the C-6 OH group into the carbons C-4, C-8 and C-3 can be exploited to determine the configuration at C-6.

(5) The shielding caused by a C-8(OH) group to the β-carbon C-9 is a reliable guide for the configuration at C-8.

(6) The α- and β-shift increments brought about by acylation of a hydroxy group to iridoid glucoside carbons can unambiguously be used to locate the position of the acyl group.

(7) The ring size and C-1 configuration in the glucose moiety are also evident from the spectra.

EXPERIMENTAL

Compounds. All compounds but **28**, which was obtained[36] by reduction of **17**, were of natural origin.

Spectra. ^{13}C NMR spectra were obtained at 25.2 MHz in Fourier transform model on a Varian XL-100-12 spectrometer in CD_3OD solution (saturated) at ambient temp using TMS as internal standard. The deuterium signal of the $C\underline{D}_3OD$-solvent was used as lock signal. The chemical shifts are given in ppm downfield from TMS ($\delta_{TMS} = 0$). Compound **24** was recorded in D_2O soln (saturated) using dioxane as external standard.

Addendum. After the preparation of the manuscript of this work two papers dealing with the ^{13}C NMR spectra of iridoid-[K. Weinges and H. von der Eltz, *Ann. Chem.* 1968 (1978)] and secoiridoid-glucosides [S. R. Jensen, S. E. Lyse-Petersen and B. J. Nielsen, *Phytochemistry* **18**, 273 (1979)] came to our notice. Taking the solvent shift (see text) into account, the carbon shift assignments reported for **10**, **12** and **22** are in accord with ours.

Note added in proof—Since the submission of this paper several further investigations involving ^{13}C NMR or iridoid- [Y. Ozaki, S. Johne and M. Hesse, *Helv. Chim. Acta* **62**, 2708, (1979); F. Bailleul,

A. Rabaron, M. Koch and P. Delaveau, *Planta medica* **37**, 316 (1979); R. K. Chaudhuri and O. Sticher, *Helv. Chim. Acta* **63**, 117 (1980)], secoiridoid- [S. Uesato, T. Hasimoto and H. Inouye, *Phytochemistry* **18**, 1981 (1979)], and iridoid enol glucosides [F. Murai and M. Tagawa, *Planta medica* **37**, 234 (1979)], valepotriates [S. R. Jensen, B. J. Nielsen, C. B. Mikkelsen, J. J. Hoffmann, S. D. Jolad, J. R. Cole, *Tetrahedron Letters* 3261 (1979)] and it's decomposition products [R. Denee, R. Bos and B. Hazelhoff, *Planta medica* **37**, 45 (1979)] and an alkaloidal secoiridoid glucoside [R. K. Chaudhuri, O. Sticher and T. Winkler, *Helv. Chim. Acta* **63**, 1045 (1980)] have appeared.

The apparent inconsistency of the ^{13}C NMR spectral data (see text) with the proposed structure of penstemide[17] has been resolved with the revised structure [S. R. Jensen *et al.*, *Tetrahedron Letters* 3261 (1979)].

Acknowledgements—This work was supported by research grants of the Wilhelm Doerenkamp Foundation, the Swiss National Science Foundation and the Swiss Federal Institute of Technology. The authors wish to thank Mr. K. Hiltbrunner, ETH Zürich for kindly recording some of the spectra, Professor H. Inouye, Faculty of Pharmaceutical Sciences, Kyoto University, Japan, for kindly providing the compounds **2** and **20**, Mr. D. Lehmann of this laboratory for isolating some of the compounds, and Miss J. Kyzintas for secretarial help.

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