Phytochemistry, Vol. 28, No. 9, pp. 2455–2458, 1989.
Printed in Great Britain.

0031-9422/89 $3.00+0.00

LOCATION OF GLYCOSYLATION AND ALKYLATION SITES IN ANTHRAQUINONES BY ^{1}H NMR

SURAJ B. KALIDHAR

Department of Chemistry and Biochemistry, Haryana Agricultural University, Hisar 125004, India

(*Received in revised form* 13 *January* 1989)

Key Word Index—Emodin; physcion; morindone; obtusin; dermocybin; anthraquinone; glucosde; gentiobioside; primveroside.

Abstract—A comparison of the ^{1}H NMR data of the peracetate of emodin with those of emodin-*O*-glycosides helps in the location of the sugar residues. The site of *O*-alkylation in emodin can be similarly determined and the method is useful for other anthraquinones.

INTRODUCTION

In 1984, we determined the position of the sugar in physcion-8-*O*-gentiobioside [1] with the help of acylation shift data [2]. In this paper, I describe an alternative procedure for locating the position of alkylation or glycosylation in emodin and related compounds, as well as in other anthraquinones.

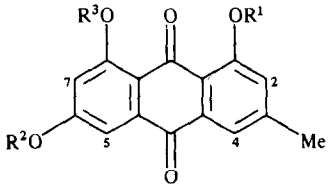
DISCUSSION

A comparison of the ^{1}H NMR data of the peracetates of emodin (**1**) and emodin-8-*O*-glucoside (**2**) shows that H-5, the proton which is *para* to the site of glycosylation, undergoes the most significant change in chemical shift (Tables 1 and 2). This change has been measured by the glycosylation shift of the aromatic proton (ΔH), i.e. the difference between the chemical shifts of the proton in an anthraquinone aglycone peracetate and its glycoside. As is evident from Table 2, H-5 is greatest when the glycoside is at position 8. Similar behaviour has been observed for 8-*O*-alkylation and the shift has been denoted by Δ′H-5.

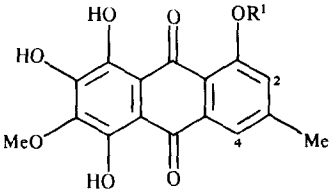
In emodin-1-*O*-glucoside (**6**), the largest shift is that of H-4, which is *para* to the position of glycosylation (Table 2). In the absence of ^{1}H NMR data for physcion-1-*O*-glucoside,* ΔH-4 for dermocybin-1-*O*-glucoside (**14**), which has a cresol ring, has been included in Table 2 and ΔH-4 has been found to be in good agreement with that for emodin-1-*O*-glucoside (**6**). As expected, ΔH-4 is the largest ΔH value when the 1-hydroxyl is alkylated (Tables 1 and 2).

If there is a glycoside at position 6 in emodin (**1**), it can easily be located in view of the fact that emodin-6-*O*-glycoside does not react with diazomethane. It is also possible to ascertain this position with the help of the proposed method. There is no aromatic proton *para* to the site of glycosylation but it has been observed that the two protons *ortho* to the position of the glycoside, i.e. H-5 and H-7, undergo shifts by more than 0.2 and a similar trend has been observed for 6-*O*-alkylation (Tables 1 and 2).

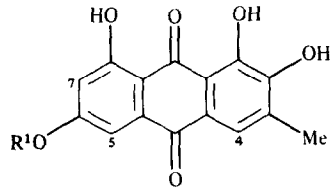
*There is no mention of ^{1}H NMR in the reports [13–15] of physcion-1-*O*-glucoside.



1 R^1,R^2,R^3 = H
2 R^1,R^2 = H, R^3 = glc
3 R^1,R^2 = H, R^3 = gent
4 R^1,R^2 = H, R^3 = prim
5 R^1,R^2 = H, R^3 = glc
6 R^1 = glc, R^2,R^3 = H
7 R^1,R^3 = H, R^2 = Me
8 R^1 = H, R^2 = Me, R^3 = glc
9 R^1 = H, R^2 = Me, R^3 = gent
10 R^1 = H, R^2 = Me, R^3 = prim
11 R^1 = H, R^2,R^3 = Me
12 R^1,R^2,R^3 = Me
13 R^1,R^2 = Me, R^3 = H



14 R^1 = H
15 R^1 = glc

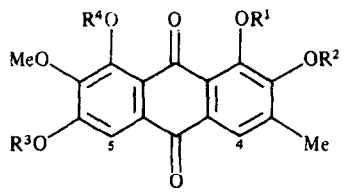


16 R^1 = H
17 R^1 = Me

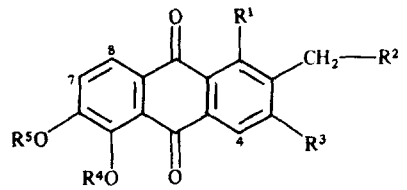
Table 1. Chemical shift (in $CDCl_3$) of aromatic protons in the ^1H NMR spectra of the peracetates of emodin and related compounds

Peracetate of (*br s*)	Chemical shift H-2 (*br s*)	H-4 (*br s*)	H-5 (*d*, $J = 2.5$ Hz)	H-7 (*d*, $J = 2.5$ Hz)
Emodin (**1**) [2]*	7.24	8.03	7.98	7.26
Emodin-8-*O*-glucoside (**2**) [2]	7.23	7.97	7.76	7.31
Emodin-8-*O*-gentiobioside (**3**) [3]	7.19	7.97	7.78	7.29
Emodin-8-*O*-primveroside (**4**) [4]	7.17	7.96	7.78	7.21
Emodin-6-*O*-glucoside (**5**) [2]	7.19	7.91	7.54	6.98
Emodin-1-*O*-glucoside (**6**) [2]	7.35	7.88	7.97	7.29
6-O-Methylemodin (physcion) and derivatives				
Physcion (**7**) [2]	7.24	8.03	7.69	6.92
Physcion-8-*O*-glucoside (**8**) [2]	7.15	7.90	7.42	6.94
Physcion-8-*O*-gentiobioside (**9**) [1]	7.18	7.92	7.50	6.88
Physcion-8-*O*-primveroside (**10**) [5]	7.13	7.88	7.45	6.97
8-*O*-Methylphyscion (**11**) [2]	7.18	7.96	7.36	6.77
1,8-Di-*O*-methylphyscion (**12**) [6]†	7.10	7.64	7.33	6.77
1-*O*-Methylphyscion (**13**) [7]	7.05	7.70	7.60	6.95
Anthraquinones having cresol or resorcinol ring				
Dermocybin (**14**) [2]	7.17	7.86	—	—
Dermocybin-1-*O*-glucoside (**15**) [2]	7.24	7.70	—	—
Alaternin (**16**) [8]	—	8.11	7.95	7.24
6-*O*-Methylalaternin (**17**) [9]	—	7.95	7.50	6.80

*Data from ref. [2] has been reproduced for most of the anthraquinones in this Table.
† No hydroxyl for acetylation in this compound.



18 R^1, R^3 = Me, R^2, R^4 = H
19 R^1 = Me, R^2, R^3, R^4 = H
20 R^1, R^2 = H, R^3, R^4 = Me
21 R^1, R^2, R^4 = H, R^3 = Me
22 R^1, R^2, R^3, R^4 = H



23 R^1 = OH, R^2, R^3, R^4, R^5 = H
24 R^1 = OH, R^2, R^3, R^4 = H, R^5 = prim
25 R^1 = OH, R^2, R^3, R^4 = H, R^5 = rut
26 R^1, R^2, R^4, R^5 = H, R^3 = OH
27 R^1, R^2, R^4 = H, R^3 = OH, R^5 = prim
28 R^1, R^3 = OH, R^2, R^4, R^5 = H
29 R^1, R^3 = OH, R^2, R^4 = H, R^5 = prim
30 R^1, R^2, R^3 = OH, R^4, R^5 = H
31 R^1, R^2 = OH, R^3 = -*O*-prim, R^4, R^5 = H

Table 2. Glycosylation (ΔH)* or alkylation (Δ'H)† shifts in emodin and related compounds

Peracetates of	ΔH-2 (Δ'H-2)	ΔH-4 (Δ'H-4)	ΔH-5 (Δ'H-5)	ΔH-7 (Δ'H-7)
8-*O*-Glycosylation (alkylation)				
1, 2	+0.01	+0.06	+0.22	−0.05
1, 3	+0.05	+0.06	+0.20	−0.03
1, 4	+0.07	+0.07	+0.20	+0.05
7, 8	+0.09	+0.13	+0.27	−0.02
7, 9	+0.06	+0.11	+0.19	+0.04
7, 10	+0.11	+0.15	+0.24	−0.05
13, 12	(−0.05)	(+0.06)	(+0.27)	(+0.18)
6-*O*-Glycosylation (alkylation)				
1, 5	+0.05	+0.12	+0.44	+0.28
1, 7	(0.0)	(0.0)	(+0.29)	(+0.34)
2, 8	(+0.08)	(+0.07)	(+0.34)	(+0.37)
3, 9	(+0.01)	(+0.05)	(+0.28)	(+0.41)
4, 10	(+0.04)	(+0.08)	(+0.33)	(+0.24)
16, 17	—	(+0.16)	(+0.45)	(+0.44)
1-*O*-Glycosylation (alkylation)				
1, 6	−0.11	+0.15	+0.01	−0.03
14, 15	−0.07	+0.16	—	—
7, 13	(+0.19)	(+0.33)	(+0.09)	(−0.03)
11, 12	(+0.08)	(+0.32)	(+0.03)	(0.0)

*$\Delta H = \delta$ value of the aromatic proton in aglycone peracetate minus that in *O*-glycosyl peracetate.
†$\Delta' H = \delta$ value of the aromatic proton in anthraquinone peracetate minus that in *O*-alkyl peracetate.

Table 3. Chemical shift (in $CDCl_3$) of aromatic protons in the ^1H NMR spectra of the peracetates of some 2,7-dioxygenated emodins

Peracetate of	Chemical shift H-4 (*br s*)	H-5 (*s*)
Obtusin (**18**) [10]	7.95	7.70
Aurantio-obtusin (**19**) [10]	7.95	7.92
1-Desmethylchryso-obtusin (**20**) [10]	8.06	7.61
1-Desmethylobtusin (**21**) [10]	8.03	7.72
1-Desmethylaurantio-obtusin (**22**) [10]	8.09	7.94

Table 4. Alkylation shifts of aromatic protons in 2,7-dioxygenated emodins

Peracetates of	Δ′ H-4	Δ′ H-5
19, **18**	0.0	+0.22
21, **20**	−0.03	+0.11
22, **21**	+0.06	+0.22

Table 5. Chemical shift (in $CDCl_3$) of aromatic protons in the ^1H NMR spectra of the peracetates of some 2-methyl (or hydroxymethyl)-anthraquinones

Peracetate of	Chemical shift H-1	H-3	H-4	H-7	H-8
Morindone (**23**) [11]	—	7.60 *d*	8.03 *d*	7.53 *d*	8.17 *d**
Morindone-6-*O*-primveroside (**24**) [11]	—	7.62 *d*	8.03 *d*	7.38 *d*	8.19 *d*
Morindone-6-*O*-rutinoside (**25**) [12]	—	7.61 *d*	8.04 *d*	7.31†	8.20 *d*
3,5,6-trihydroxy-2-methyl anthraquinone (**26**) [11]	8.10 *s*	—	7.82 *s*	7.57 *d*	8.25 *d*
3,5-dihydroxy-2-methylanthraquinone-6-*O*-primveroside (**27**) [11]	8.13 *s*	—	7.83 *s*	7.43 *d*	8.33 *d*
3-hydroxy morindone (**28**) [11]	—	—	7.88 *s*	7.58 *d*	8.20 *d*
3-hydroxy morindone-6-*O*-primveroside (**29**) [11]	—	—	7.87 *s*	7.40 *d*	8.18 *d*
5,6-dihydroxylucidin (**30**) [11]	—	—	7.88 *s*	7.57 *d*	8.20 *d*
5,6-dihydroxylucidin-3-*O*-primveroside (**31**) [11]	—	—	7.73 *s*	7.48 *d*	8.17 *d*

*J = 8–9 Hz.
†Overlapped by $CHCl_3$.

Consequently, for a glycoside, if ΔH-4 gives the highest value then 1-*O*-glycosylation is indicated and when ΔH-5 and ΔH-7 are both more than 0.2, 6-*O*-glycosylation is indicated. When 6-*O*-glycosylation is absent, a large value for ΔH-5 suggests 8-O-glycosylation. The position of *O*-alkylation can be similarily determined in emodin and physcion.

A comparison of the peracetates of aurantio-obtusin (**19**) and obtusin (**18**) shows a higher value for ΔH-5 than for ΔH-4 (Tables 3 and 4). In the absence of a proton *para* to position 6 and in the presence of only one *ortho* proton (H-5), a higher value of ΔH-5 is in accordance with the expected trend. The other alkylation shifts shown in Tables 3 and 4 are consistent with the proposed method.

A comparison of the peracetates of morindone (**23**) and morindone-6-*O*-primveroside (**24**) (Table 5) shows the greatest shift for H-7, in accordance with the expected trend. The other glycosylation shifts shown in Table 6 are also consistent with the proposed method.

Table 6. Glycosylation shifts of aromatic protons in 2-methyl (or hydroxymethyl)-anthraquinones

Peracetates of	ΔH-1	ΔH-3	ΔH-4	ΔH-7	ΔH-8
23, **24**	—	−0.02	0.0	+0.15	−0.02
23, **25**	—	−0.01	−0.01	+0.22	−0.03
26, **27**	−0.03	—	−0.01	+0.14	−0.08
28, **29**	—	—	+0.01	+0.18	+0.02
30, **31**	—	—	+0.15	+0.09	+0.03

REFERENCES

1. Kalidhar, S. B. and Sharma, P. (1984) *Phytochemistry* **23**, 1196.
2. Steglich, W. and Lösel, W. (1969) *Tetrahedron* **25**, 4391.
3. Demuth, G., Hinzo, H., Selligmann, O. and Wagner, H. (1978) *Planta Med.* **33**, 53.
4. Rauwald, H. W. (1983) *Z. Naturforsch.* **38C**, 170.
5. Coskun, M., Sakushima, A., Kitagawa, S. and Nishibe, S. (1984) *Phytochemistry* **23**, 1485.
6. Thomson, R. H. (1971) *Naturally Occurring Quinones* 2nd Edn., p. 74. Academic Press, London.
7. Murakami, T., Ikede, K. and Takido, M. (1968) *Chem. Pharm. Bull.* **16**, 2299.
8. Kitanaka, S., Kimura, F. and Takido, M. (1985) *Chem. Pharm. Bull.* **33**, 1274.

9. Kalidhar, S. B. and Sharma, P. (1985) *J. Indian Chem. Soc.* **LXII**, 411.
10. Kitanaka, S. and Takido, M. (1984) *Chem. Pharm. Bull.* **32**, 860.
11. Inoue, K., Nayeshiro, H., Inouye, H. and Zenk, M. (1981) *Phytochemistry* **20**, 1693.
12. Vermes, B., Farkas, L. and Wagner, M. (1980) *Phytochemistry* **19**, 119.
13. Lal, J. and Gupta, P. C. (1973) *Experientia* **29**, 141.
14. Niranjan, G. S. and Gupta, P. C. (1973) *Planta Med.* **23**, 298.
15. Smith, R. M. and Ali, S. (1979) *N. Z. J. Sci.* **22**, 123.