

Alkoxylation sites in naturally occurring coumarins using ^1H NMR

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Abstract. A comparison of ^1H NMR spectra of acetoxy coumarin and alkoxy coumarin shows that an aromatic proton para to the site of difference undergoes a larger change in chemical shift. In absence of a para proton, ortho protons undergo this change. These help in locating alkoxylation sites in naturally occurring coumarins.

Keywords. Alkoxylation sites; coumarins; proton NMR.

1. Introduction

The ^1H NMR alkoxylation [$\Delta\text{H}(\text{OAc: O-alkyl})$] shifts have been shown to be useful for locating alkoxylation sites in flavones (Kalidhar 1989a, b) and anthraquinones (Kalidhar 1989c, d). This paper shows that these shifts are useful in coumarins as well.

2. Discussion

The ^1H NMR spectra (table 1) of 5-acetoxy-4-methyl-7-pentyl-coumarin (15) and 5-methoxy-4-methyl-7-pentylcoumarin (16) show different chemical shifts. The change is measured with the alkoxylation [$\Delta\text{H}(\text{OAc: O-alkyl})$] shift defined by the δ value of an aromatic proton in acetoxy coumarin minus that in alkoxy coumarin (both as peracetates). The alkoxylation shifts (table 2) from (15) and (16) are $\Delta\text{H6} = +0.22$ and $\Delta\text{H8} = +0.33$. The proton H8 is para to the site of difference in (15) and (16) and its shift ΔH8 is larger.

The alkoxylation shifts in 6-acetoxy-7-methoxycoumarin (26) and 6-geranyloxy-7-methoxycoumarin (28) are $\Delta\text{H3} = +0.08$; $\Delta\text{H4} = +0.07$, $\Delta\text{H5} = +0.35$ and $\Delta\text{H8} = +0.13$ (tables 1 and 2). There is no proton para to the site of difference in (26) and (28) and the proton H5, which is ortho to the site of difference, has undergone a larger change in chemical shift.

The literature data for a large number of coumarins have been shown in table 1 and the shifts have been assigned in table 2. Expected trends have been observed in all cases.

When there is a methoxy (or an alkoxy) group on the aromatic ring, it increases electron densities at ortho and para positions. Replacement with OAc prevents the release of electrons. The ortho and para protons are, therefore, downfield in acetoxy than in alkoxy coumarin. This explains the trend of the shifts mentioned earlier.

Table 1. ¹H NMR literature data for nuclear protons in coumarins.

Substituents		Chemicals shifts (δ, CDCl ₃)										Reference
OAc	OMe	Other groups	Compd.	H3	H4	H5	H6	H8	H8	H8	Reference	
5,7	—	3-CH ₂ -CO ₂ Et 4-Me	1	—	—	—	6-80	7-00	—	—	Parmar <i>et al</i> (1987)	
—	5,7	3-CH ₂ -CO ₂ Et 4-Me	2	—	—	—	6-35	6-45	—	—	Parmar <i>et al</i> (1987)	
6,7	—	3-CH ₂ -CO ₂ Et 4-Me	3	—	—	7-11	—	7-35	—	—	Parmar <i>et al</i> (1987)	
—	6,7	3-CH ₂ -CO ₂ Et 4-Me	4	—	—	6-70	—	6-88	—	—	Parmar <i>et al</i> (1987)	
7	—	8-I	5	6-42	8-10	7-68	7-14	—	—	—	Ahluwalia <i>et al</i> (1980)	
—	—	7-O-8-I	6	6-24	8-06	7-65	6-91	—	—	—	Ahluwalia <i>et al</i> (1980)	
7,8	—	3-CH ₂ -CO ₂ Et 4-Me	7	—	—	7-45	7-10	—	—	—	Parmar <i>et al</i> (1987)	
—	7,8	3-CH ₂ -CO ₂ Et 4-Me	8	—	—	7-24	6-78	—	—	—	Parmar <i>et al</i> (1987)	
7	—	3,4-Me 8-I	9	—	—	7-40	6-96	—	—	—	Ahluwalia <i>et al</i> (1988)	
—	—	3,4-Me 7-O-8-I	10	—	—	7-65	6-90	—	—	—	Ahluwalia <i>et al</i> (1988)	
7	4	5-Me	11	5-60	—	—	6-75	6-92	—	—	Oliveira <i>et al</i> (1972)	
—	4	5-Me 7-O-glu Ac	12	5-55	—	—	6-62	6-77	—	—	Oliveira <i>et al</i> (1972)	
4	—	5-Me 7-O-glu Ac	13	6-15	—	—	6-70	6-82	—	—	Oliveira <i>et al</i> (1972)	
—	4,7	5-Me	14	5-50	—	—	6-60	6-60	—	—	Oliveira <i>et al</i> (1972)	
5	—	4-Me 7-C ₃ H ₁₁	15	*	—	—	6-80	7-08	—	—	Malik (1977)	
—	5	4-Me 7-C ₃ H ₁₁	16	*	—	—	6-58	6-77	—	—	Malik (1977)	
5	—	4,7-Me	17	*	—	—	6-78	7-03	—	—	Malik (1977)	
7	—	4-Ph 8-I	18	*	—	—	6-58	6-73	—	—	Malik (1977)	
—	—	4-Ph 7-O-8-I	19	6-38	—	7-32	7-05	—	—	—	Ahluwalia <i>et al</i> (1980)	
—	—	4-Ph 7-O-8-I	20	6-40	—	7-54	6-92	—	—	—	Ahluwalia <i>et al</i> (1980)	
7	—	3-Ph 8-CHPh	21	6-24	—	7-42	6-75	—	—	—	Ahluwalia <i>et al</i> (1978a)	
—	7	3-Ph 8-CHPh	22	6-25	—	7-55	6-72	—	—	—	Ahluwalia <i>et al</i> (1978a)	
7	5,6	—	23	6-33	7-93	—	—	6-85	—	—	Wagner and Bladt (1975)	
—	5,6,7	—	24	6-22	7-90	—	—	6-61	—	—	Wagner and Bladt (1975)	
—	—	5,6-OCH ₂ O 7-O	25	6-18	7-96	—	—	6-46	—	—	Ahluwalia <i>et al</i> (1978b)	
6	7	—	26	6-35	7-70	7-22	—	6-95	—	—	Joshi <i>et al</i> (1980)	
—	7	6-O-ger	27	6-64	7-75	7-15	—	6-95	—	—	Joshi <i>et al</i> (1980)	
—	7	6-O-ger	28	6-27	7-63	6-87	—	6-82	—	—	Talapatra <i>et al</i> (1973)	

*The δ values for H3 are not given (probably the quartet for one proton, weak signal, could not be detected). Abbreviations: Glu - glucoside, ger - geranyl.

Table 2. Alkoxylation [$\Delta H(\text{OAc: O-alkyl})$][†] shifts in coumarins.

Comparisons	$\Delta H3$	$\Delta H4$	$\Delta H5$	$\Delta H6$	$\Delta H8$
<i>4-Alkoxylation shifts</i>					
<u>13:12</u>	+0.60	—	—	+0.08	+0.05
<i>5-Alkoxylation shifts</i>					
<u>15:16</u>	*	—	—	+0.22	+0.31
<u>17:18</u>	*	—	—	+0.20	+0.30
<i>6-Alkoxylation shifts</i>					
<u>26:27</u>	-0.29	-0.05	+0.07	—	0.00
<u>26:28</u>	+0.08	+0.07	+0.35	—	+0.13
<i>7-Alkoxylation shifts</i>					
<u>5:6</u>	+0.18	+0.04	+0.03	+0.23	—
<u>9:10</u>	—	—	-0.25	+0.06	—
<u>11:14</u>	+0.10	—	—	+0.15	+0.32
<u>19:20</u>	-0.02	—	-0.22	+0.13	—
<u>21:22</u>	-0.01	—	-0.13	+0.03	—
<u>23:24</u>	+0.11	+0.03	—	—	+0.24
<u>23:25</u>	+0.15	+0.27	—	—	+0.39
<i>5,7-Dialkoxylation shifts</i>					
<u>1:2</u>	—	—	—	+0.45	+0.55
<i>6,7-Dialkoxylation shifts</i>					
<u>3:4</u>	—	—	+0.41	—	+0.47
<i>7,8-Dialkoxylation shifts</i>					
<u>7:8</u>	—	—	+0.21	+0.32	—

[†] $\Delta H(\text{OAc: O-alkyl}) = \delta$ values of a nuclear proton in acetoxy coumarin minus that in alkoxy coumarin (both as peracetates).

*The shift cannot be calculated from table 1 data.

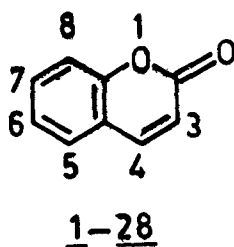


Figure 1. Structures of the naturally occurring coumarins used in this work (1-28 are as given in table 1).

The ¹H NMR spectra (table 1) of 7-acetoxy-4-methoxy-5-methylcoumarin (11) and 7-tetraacetoxyglucosyloxy-4-methoxy-5-methylcoumarin (12) show the following changes in chemical shifts $\Delta H3 = +0.05$; $\Delta H6 = +0.13$ and $\Delta H8 = +0.15$. This change in chemical shift is measured with glycosyloxylation [$\Delta H(\text{OAc: O-gly Ac})$] shifts defined by δ value of an aromatic proton in acetoxy coumarin minus that in

glycosyloxycoumarin (both as peracetates). In absence of a proton para to the site of difference, ortho protons H6 and H8 have undergone larger changes in chemical shifts. The similarity between alkoxylation and glycosyloxylation shifts (Kalidhar 1989) is seen in coumarins as well.

3. Conclusions

Alkoxylation shifts [$\Delta H(\text{OAc: O-alkyl})$] are useful for locating alkoxylation sites in naturally occurring coumarins, as has been shown in this work.

References

- Ahluwalia V K, Khanduri C H and Sharma N D 1988 *Indian J. Chem.* **B27** 748
Ahluwalia V K, Kumar D and Gupta Y K 1978a *Indian J. Chem.* **B16** 579
Ahluwalia V K, Prakash C and Bala S 1980 *Monatsh. Chim.* **111** 877
Ahluwalia V K, Prakash C, Gupta M C and Mehta S 1978b *Indian J. Chim.* **B16** 591
Joshi B S, Viswanthan N, Kaul C L and Grewal R S 1980 *Indian J. Chem.* **B19** 495
Kalidhar S B 1989a *J. Chem. Res. (S)* 311
Kalidhar S B 1989b *J. Chem. Res. (M)* 2416
Kalidhar S B 1989c *Phytochemistry* **28** 2455
Kalidhar S B 1989d *Phytochemistry* **28** 3459
Malik O P 1977 *Indian J. Chem.* **B15** 194
Oliveira A G P, Silva L G F E and Gottlieb O R 1972 *Phytochemistry* **11** 3515
Parmar V S, Singh S and Rathore J S 1987 *J. Indian Chem. Soc.* **64** 254
Talapatra S K, Chaudhuri M K and Talapatra B 1973 *Phytochemistry* **12** 236
Wagner H and Bladt S 1975 *Phytochemistry* **14** 2061