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Location of alkoxylation sites in naturally occurring xanthones

SURAJ B. KALIDHAR
Department of Chemistry and Biochemistry, Haryana Agricultural University, Hisar 125 004, Haryana.

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Abstract

The ^1H nmr spectra of acetoxyxanthone and alkoxyxanthone show that there is a large change in chemical shift of aromatic proton which is *para* to the site of difference In the absence of a *para* proton, *ortho* protons undergo large change in chemical shifts. This change is helpful in locating alkoxylation site in naturally occurring xanthones.

Key words: Acetoxyxanthone, alkoxyxanthone, alkoxylation site, flavones, anthraquinones.

1. Introduction

^1H nmr Alkoxylation shifts have been used for structural elucidation in flavones[1] and anthraquinones[2,3]. The present paper deals with the shifts in xanthones.

2. Discussion

The ^1H nmr spectra of 1-acetoxy-2,6-8 trimethoxyxanthone (**11**) and 1,2,6,8-tetramethoxyxanthone (**8**) show that there is a change in the chemical shift of H-4 (proton at C-4). This change is measured with alkoxylation [ΔH(OAc: OMe)] shift defined by δ value of an aromatic proton in acetoxyxanthone minus the δ value in alkoxyxanthone. The alkoxylation shifts from **11**:**8** are ΔH-3 = 0.00; ΔH-4 = + 0.16; ΔH-5 = + 0.01 and ΔH-7 = + 0.01 (Tables I and II). There is a large shift in the case of H-4 which is *para* to the site of difference C-1 in **11** and **8**.

The alkoxylation shifts from 5,6-diacetoxy-1,3-dimethoxyxanthone (**16**) and 1,3,5,6-tetramethoxyxanthone (**17**) are ΔH-2 = + 0.03; ΔH-4 = − 0.16; ΔH-7 = + 0.15 and ΔH-8 = + 0.16 (Tables I and II). The sites of difference here are C-5 and C-6. There is a large shift in the case of H-8 which is *para* to C-5. There is no proton *para* to C-6 and the *ortho* proton H-7 undergoes a large change.

An expected trend has been observed from the comparison of ^1H nmr literature data

Table I
^{1}H nmr literature data for aromatic protons in xanthones

OAc	OMe		Chemical shifts (δ, $CDCl_3$)							
			H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8
1,2,3,5-Tetraoxygenated xanthones										
1,3,5	2	**1**[4]	—	—	—	7.18	—	7.36	7.36	8.08
—	1,2,3,5	**2**[4]	—	—	—	6.84	—	7.25	7.25	7.88
1,2,3,6,8-Pentaoxygenated xanthones										
1,3,8	2,6	**3**[5]	—	—	—	7.25	6.69	—	6.48	—
1,8	2,3,6	**4**[5]	—	—	—	6.72	6.63	—	6.47	—
1,2,3,8-Tetraoxygenated xanthones										
3,8	1,2	**5**[4]	—	—	—	6.92	7.23	7.58	6.89	—
—	1,2,3,8	**6**[4]	—	—	—	6.61	6.88	7.48	6.72	—
1,2,6,8-Tetraxoygenated xanthones										
1,2,6,8	—	**7**[6]	—	—	7.50	7.31	7.21	—	6.80	—
—	1,2,6,8	**8**[6]	—	—	7.27	7.11	6.32	—	6.41	—
8	1,2,6	**9**[6]	—	—	7.29	7.12	6.71	—	6.56	—
2,8	1,6	**10**[6]	—	—	7.40	7.12	6.77	—	6.60	—
1	2,6,8	**11**[6]	—	—	7.27	7.27	6.33	—	6.42	—
1,2,8	6	**12**[6]	—	—	7.43	7.20	6.74	—	6.52	—
1,6,8	2	**13**[7]	—	—	7.21	7.21	7.12	—	6.71	—
1,3,5-Trioxygenated xanthones										
1,5	3	**14**[8]	—	6.55	—	6.73	—	*	*	8.08
5	1,3	**15**[9]	—	6.42	—	6.32	—	*	*	8.17
1,3,5,6-Tetraoxygenated xanthones										
5,6	1,3	**16**[10]	—	6.44	—	6.51	—	—	7.20	8.26
—	1,3,5,6	**17**[10]	—	6.41	—	6.67	—	—	7.05	8.10
1,3,5,8-Tetraoxygenated xanthones										
1	3,5,8	**18**[11]	—	6.50	—	6.90	—	7.20	6.74	—
1,5,8	3	**19**[12]	—	6.53	—	6.65	—	7.33	6.88	—
1,4,7-Trioxygenated xanthones										
1,7	4	**20**[8]	—	6.85	7.15	—	●	*	—	7.90
—	1,4,7	**21**[8]	—	6.68	7.13	—	7.23	7.48	—	7.69
1,4,8-Trioxygenated xanthones										
4,8	1	**22**[8]	—	6.73	7.35	—	7.28	7.65	6.95	—
—	1,4,8	**23**[8]	—	6.63	7.08	—	7.05	7.53	6.77	—
2,3-Dioxygenated xanthones										
3	2	**24**[8]	7.76	—	*	7.23	*	*	*	8.28
—	2,3	**25**[8]	7.63	—	—	6.87	●	*	●	8.30

*Protons in multiplet.

Table II
^{1}H nmr alkoxylation [ΔH(OAc:OMe)]† shifts in xanthones

Comparisons	Alkoxylation shifts							
	ΔH-1	ΔH-2	ΔH-3	ΔH-4	ΔH-5	ΔH-6	ΔH-7	ΔH-8
1-Alkoxylation								
11:8	—	—	0.00	+0.16	+0.01	—	+0.01	—
14:15	—	—	+0.13	+0.41	—	*	*	−0.09
1,2-Dialkoxylation								
12:9	—	—	+0.14	+0.08	+0.03	—	−0.04	—
1,2,6-Trialkoxylation								
7:9	—	—	+0.21	+0.19	+0.50	—	+0.24	—
1,2,6,8-Tetraalkoxylation								
7:8	—	—	+0.23	+0.20	+0.89	—	+0.39	—
1,2,8-Trialkoxylation								
12:8	—	—	+0.16	+0.09	+0.42	—	+0.11	—
1,3,5-Trialkoxylation								
1:2	—	—	—	+0.34	—	+0.11	+0.11	+0.20
1,6-Dialkoxylation								
7:10	—	—	+0.10	+0.19	+0.44	—	+0.20	—
13:9	—	—	−0.08	+0.09	+0.41	—	+0.15	—
1,6,8-Trialkoxylation								
13:8	—	—	−0.06	+0.10	+0.80	—	+0.30	—
1,7-Dialkoxylation								
20:21	—	+0.17	+0.02	—	*	*	—	+0.21
2-Alkoxylation								
7:13	—	—	+0.29	+0.10	+0.09	+0.09	+0.09	—
10:9	—	—	+0.11	0.00	+0.06	—	+0.04	—
2,6,8-Trialkoxylation								
7:11	—	—	+0.23	+0.04	+0.88	—	+0.38	—
2,8-Dialkoxylation								
10:8	—	—	+0.13	+0.01	+0.45	—	+0.19	—
12:11	—	—	+0.16	−0.07	+0.41	—	+0.10	—
3-Alkoxylation								
3:4	—	—	—	+0.53	+0.06	—	+0.01	—
24:25	+0.13	—	—	+0.36	*	*	*	−0.02
3,8-Dialkoxylation								
5:6	—	—	—	+0.31	+0.35	+0.10	+0.17	—
4,8-Dialkoxylation								
22:23	—	+0.10	+0.27	—	+0.23	+0.12	+0.18	—

(Continued)

Table II (*Continued*)

Comparisons	Alkoxylation shifts							
	ΔH-1	ΔH-2	ΔH-3	ΔH-4	ΔH-5	ΔH-6	ΔH-7	ΔH-8
5,6-Dialkoxylation								
16:**17**	—	+0.03	—	−0.16	—	—	+0.15	+0.16
5,8-Dialkoxylation								
19:**18**	—	+0.03	—	−0.25	—	+0.13	+0.14	—
6-Alkoxylation								
7:**12**	—	—	+0.07	+0.11	+0.47	—	+0.28	—
8-Alkoxylation								
9:**8**	—	—	+0.02	+0.01	+0.39	—	+0.15	—

[†] ΔH(OAc:OMe) = δ value of an aromatic proton in acetoxyxanthone minus that in methoxyxanthone.

[*] Shifts which cannot be determined from Table I data.

of 25 xanthones[4-12] (Table I) and the alkoxylation shifts (Table II). The latter are useful in locating alkoxylation sites in naturally occurring xanthones.

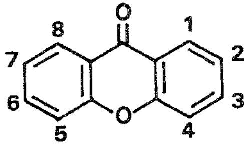
The presence of OMe on the aromatic ring increases electron densities at *ortho* and *para* protons and its replacement with OAc destroys this process. This explains the aforesaid trend of positive shifts.

The partial methylation of 1,2-8-trihydroxy-6-methoxyxanthone (**26**) with CH_2N_2 affords 8-hydroxy-1,2-6-trimethoxyxanthone (**27**). In **26**, there are two chelated hydroxyls, OH-1 and OH-8 at C-1 and C-8, respectively. Of these, OH-1 (and not OH-8) has undergone methylation with diazomethane. We surmise that CH_2N_2 cannot differentiate between OH-1 (chelated) and OH-2 (non-chelated) in 1,2-dihydroxyxanthones.

In 1-acetoxy-2-methoxyxanthones, H-3 and H-4 absorb at the same or close δ value(s) (^{1}H nmr spectra for **11** and **13**, Table I). The 1-alkoxylation shifts from **11**:**8** are ΔH-3 = 0.00 and ΔH-4 = +0.16 (Table II). In 2-acetoxy-1-methoxy-xanthone, H-3 and H-4 resonate at different and distinct values (^{1}H nmr for **10**, Table I). The 2-alkoxylation shifts from **10**:**9** are ΔH-3 = +0.11 and ΔH-4 = 0.00. Thus chemical shifts (δ) and alkoxylation shifts (ΔH) provide a clear cut distinction between naturally occurring 1-hydroxy-2-methoxy- and 2-hydroxy-1-methoxyxanthones. As is evident from the preceding paragraph, CH_2N_2 cannot differentiate between 1-hydroxy-2-methoxy- and 2-hydroxy-1-methoxyxanthones.

The numerical values for ΔH-5 are +0.50 (6-alkoxylation shift, 7:**9**); +0.42 (8-alkoxylation shift, **12**:**8**); +0.89 (6,8-dialkoxylation shift, **7**:**8** as evident from Tables I and II. A significantly larger shift in **7**:**8** is due to the combination of 6- and 8-alkoxylation shifts.

The 6-alkoxylation shifts from **7**:**12** are ΔH-5 = +0.47 and ΔH-7 = +0.28 in the resorcinol ring (Table II). The 8-alkoxylation shifts from **9**:**8** are ΔH-5 = +0.39 and ΔH-7 = +0.15 (Table II). Though these shifts are in order, yet for avoiding confusion due to larger ΔH-5



For substituents, see Table I (1–25) and the text (26–29).

in both cases, it is useful to observe the behaviour of the resorcinol ring with diazomethane. If there is any chelated hydroxyl group in the resorcinol ring, it cannot be methylated with diazomethane.

The ^{1}H nmr spectra of 1,4,8-triacetoxy-3,7-dimethoxy-xanthone (**28**) and 1,8-diacetoxy-4-(tetracetoxy) glucosyloxy-3,7-dimethoxyxanthone (**29**) show that the changes in chemical shifts[13] are ΔH-2 = +0.01; ΔH-5 = +0.07 and ΔH-6 = +0.07. This change in chemical shift is termed as glycosyloxylation [ΔH(OAc:O-gly Ac)] shift defined by δ value of an aromatic proton in acetoxyxanthone minus the corresponding value in glycosyloxyxanthone peracetate. As there is no proton *ortho* or *para* to the site of difference C-4 (in **28** and **29**), there is no large ^{1}H nmr glycosyloxylation shift. This comparison hints similarities between ^{1}H nmr alkoxylation [ΔH(OAc:OMe)] and glycosyloxylation [ΔH(OAc:O-gly Ac)] shifts which have already been shown in anthraquinones[2,3] and flavones[1].

The solvent remaining the same for ^{1}H nmr data, variations in the conditions of temperature, concentration, etc., are likely to change the numerical values of alkoxylation shifts (ΔH) as evident from Table II and published literature[1-4] but the trends remain useful for structural studies. It has to be mentioned here that alkoxylation shifts from the ^{1}H nmr data in different solvents may sometimes mislead if no attention is paid to solvent-induced shifts.

The 5,8-dialkoxylation shifts from 1,5,8-triacetoxy-3-methoxyxanthone (**19**) and 1-acetoxy-3,5,8-trimethoxyxanthone (**18**) are ΔH-2 = +0.03; ΔH-4 = −0.25; ΔH-6 = +0.13 and ΔH-7 = +0.14 (Tables I and II). The negative ΔH-4 invites attention and needs explanation. As ΔH-2 is very close to zero, it is a hint that the ^{1}H nmr data for **18** and **19** have been recorded under almost similar conditions and ΔH-4 cannot be attributed to the differences in concentration, temperature, etc. In **19**, H-4 is in the diamagnetic cone of the carbonyl group present in the acetoxyl at C-5 and hence this proton is upfield. In **18**, there is no acetoxyl group at C-5 and hence H-4 undergoes downfield shift. These situations provide a reasonable explanation for negative ΔH-4. The negative ΔH-4 in the alkoxylation shifts from **16**:**17** lend support to these arguments (Tables I and II). It is observed that 6- or 8-alkoxylation shifts have H-5 ranging from +0.35 to +0.50 as evident from the comparisons **5**:**6**; **7**:**9**; **7**:**10**; **7**:**12**; **9**:**8**; **10**:**8**; **12**:**8**; **12**:**11** and **13**:**9** (Tables I and II). The 8-alkoxylation shifts from 4,8-diacetoxy-1-methoxyxanthone (**22**) and 1,4,8-trimethoxyxanthone (**23**) show ΔH-5 = +0.23 (Tables I and II) and it is a deviation from the range +0.35 to +0.05. The replacement of OAc-8 with OMe-8 increases ΔH-5 and that of OAc-4 with OMe-4 decreases ΔH-5 and as a result ΔH-5 is lower than the aforesaid range. It looks like that replacement of OAc-5 with OMe-5 decreases ΔH-4 and that of OAc-4 with

OMe-4 decreases ΔH-5. It may be noted here that negative shifts have been encountered earlier and 3-alkoxylation shifts in flavones[1] exhibit negative and numerically larger ΔH-2′ and ΔH-6′.

3. Conclusion

The ^{1}H nmr alkoxylation shifts are useful for the location of alkoxylation sites in naturally occurring xanthones.

References

1. Kalidhar, S. B. — Structural elucidations of flavones using ^{1}H nmr spectral shifts of the peracetates, *J. Chem. Res.* (*Synopsis*), 1989, 311; *J. Chem. Res.* (*Miniprint*), 1989, 2416–2433.
2. Kalidhar, S. B. — Location of glycosylation and alkylation sites in anthraquinones by ^{1}H nmr, *Phytochemistry*, 1989, **28**, 2455–2458.
3. Kalidhar, S. B. — Structural elucidations in anthraquinones using ^{1}H nmr glycosylation and alkylation shifts, *Phytochemistry*, 1989, **28**, 3459–3463.
4. Govindachari, T. R., Subramaniam, P. S., Pai, B. R., Kalyanaraman, P. S. and Rao, U. R. — Heartwood constituents of *Calophyllum trapezifolium* Thw: Isolation and structure of two new xanthones, *Indian J. Chem.*, 1971, **9**, 772–775.
5. Ortega, E. P., Garcia, R. E. L., Rabanal, R. M., Darias, V. and Valverde, S. — Two xanthones from *Ixanthus viscosus*, *Phytochemistry*, 1988, **27**, 1912–1913.
6. Rivaille, P., Massicot, J., Guyot, M. and Plouvier, V. — Les xanthones de *Gentiana kochiana*, *Swertia decussata* et *S. perennis* (Gentianacées), *Phytochemistry*, 1969, **8**, 1533–1541.
7. Gottlieb, O. R., Mesquita, A. A. L., Oliveira, G. G. D. and Melo, M. T. D. — Xanthones from *Kielmeyera speciosa*, *Phytochemistry*, 1970, **9**, 2537–2544.
8. Monache, F. D., Mac-Quhae, M. M., Monache, G. D., Bettolo, G. B. M. and Lima, R. A. D. — Xanthones, xantholignoids and other constituents of the roots of *Vismia* guaramirangae, *Phytochemistry*, 1983, **22**, 227–232.
9. Bandarnayake, W. M., Selliah, S. S., Sultanbawa, M. U. S. and Games, D. E. — Xanthones and 4-phenylcoumarins of *Mesua thwaitesii*, *Phytochemistry*, 1975, **14**, 265–269.
10. Walia, S. and Mukerjee, S. K. — Ferrxanthone, a 1,3,5,6-tetraoxygenated xanthone from *Mesua ferrea*, *Phytochemistry*, 1984, **23**, 1816–1817.
11. Agrawal, A. and Singh, J. — Glycosides of two xanthones and a chromone from roots of *Chrozophora prostrata*, *Phytochemistry*, 1988, **27**, 3692–3694.
12. Ahmad, S., Ikram, M., Khan, I. and Galbraith, M. N. — Xanthones of *Swertia purpurescens*, *Phytochemistry*, 1973, **12**, 2542–2543.
13. Lin, C. N., Chang, C. H., Arisawa, M., Shimizu, M. and Morita, N. — Two new xanthone glycosides from *Tripterospermum lanceolatum*, *Phytochemistry*, 1982, **21**, 205–208.