J Indian Inst Sci , Jan.–Feb 1992, **72**, 15–22

Structural aspects in naturally occurring phenolics using ^{1}H nmr acylation and alkoxylation shifts

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Received on December 11, 1990, Revised on March 20, 1991

Abstract

The trends for ^{1}H nmr acylation shifts [ΔH(OAc:OH)] have been shown to be similar to those for alkoxylation [ΔH(OAc:OMe)] and glycosyloxylation [ΔH(OAc:O-gly Ac)] shifts. This observation is helpful for structural determination in naturally occurring phenolics.

Key words: ^{1}H nmr, acylation shifts, alkoxylation shifts, glycosyloxylation shifts, anthraquinones, flavones, pterocarpans, xanthones, coumarins, chalcones, chromones.

1. Introduction

Alkoxylation [ΔH(OAc:OMe)] and glycosyloxylation [ΔH(OAc:O-glyAc)] shifts have been shown to be useful for structural studies in flavones[1], anthraquinones[2,3], isoflavones[4], xanthones[5] and coumarins[6]. In this paper, chalcones and chromones are shown to conform to this pattern. It also shows similarities amongst alkoxylation, glycosyloxylation and acylation [ΔH(OAc:OH)] shifts.

2. Discussion

^{1}H nmr (δ, $CDCl_3$) of physcion (**1**)[7] shows signals at 7·08(H-2), 7·60(H-4), 7·35(H-5) and 6·65(H-7), and its acetate (**2**)[7] at 7·05(H-2), 7·85(H-4), 7·55(H-5) and 6·75(H-7). The acylation shifts [ΔH(OAc:OH)] from **2**:**1** are ΔH-2 = −0·03, ΔH-4 =+ 0·25, ΔH-5 = +0·20 and ΔH-7 = +0·10. Structures **2** and **1** differ at C-1 and C-8 and protons H-4 (*para* to C-1) and H-5 (*para* to C-8) have undergone larger changes in chemical shifts.

The acylation shifts from 9-hydroxyfuro (2′, 3′:3, 2) pterocarpan (**3**)[8] and its acetate (**4**)[8] are ΔH-1 = −0·04, ΔH-4 = −0·02, ΔH-7 = +0·12, ΔH-8 = +0·25, ΔH-10 = +0·22, ΔH-4′= −0·03 and ΔH-5′ = −0·02 (**4**:**3**). Structures 4 and 3 differ at C-9, with no proton *para* to C-9. The two protons, H-8 and H-10, which are *ortho* to C-9, have undergone larger changes in chemical shifts. The acylation shifts from

Table I
^{1}H nmr literature data for nuclear protons in chromones

Substituents						*Chemical shifts (δ, $CDCl_3$)*				
OH	*OMe*	*OAc*	*Me*	*Other groups*		*H-2*	*H-3*	*H-6*	*H-7*	*H-8*
5–Oxygenated chromones										
–	–	5	–	2-$CH=CH_2$ 3-$CH(COOMe)_2$	**11**[13]	–	–	7·01	7·64	7·38
5	–	–	–	2-$CH=CH_2$ 3-$CH(COOMe)_2$	**12**[13]	–	–	6·90	7·52	6·78
5,7-Dioxygenated chromones										
–	–	5	2	7-0-$gluAc_4$	**13**[14]	–	6·12	6·71	–	6·84
5	–	–	2	7-0-$gluAc_4$	**14**[15]	–	6·00	6·64	–	6·42
–	–	5,7	–	8-$CHPh_2$	**15**[16]	7·60	6·09	7·12	–	–
5	7	–	–	8-$CHPh_2$	**16**[16]	7·63	6·14	6·32	–	–
–	5,7	–	–	8-$CHPh_2$	**17**[16]	7·40	6·06	6·42	–	–
–	–	5,7	–	6-$CHPh_2$	**18**[16]	7·58	6·12	–	–	6·82
5,7	–	–	–	6-$CHPh_2$	**19**[16]	7·49	6·01	–	–	6·66
5	7	–	–	6-$CHPh_2$	**20**[16]	7·44	5·96	–	–	6·36
–	5,7	–	–	6-$CHPh_2$	**21**[16]	7·66	6·17	–	–	6·65
–	–	5,7	–	6-CH_2Ph	**22**[17]	7·58	6·01	–	–	6·72
5,7	–	–	–	6-CH_2Ph	**23**[17]	7·73	6·17	–	–	6·34
–	–	5,7	–	8-CH_2Ph	**24**[17]	7·55	6·03	6·90	–	–
5,7	–	–	–	8-CH_2Ph	**25**[17]	7·57	6·06	6·08	–	–
5,6,7-Trioxygenated chromones										
–	7	5,6	2	–	**26**[15]	–	–	–	–	6·77
–	5,6,7	–	2	–	**27**[15]	–	–	–	–	6·30
6′, 6′-Dimethylpyrano [3′,2′ 6,7] chromones										
–	–	5	2	–	**28**[18]	–	5·93	–	–	6·65
5	–	–	2	–	**29**[18]	–	6·00	–	–	6·27
–	–	5	2,3	–	**30**[19]	–	–	–	–	6·44
5	–	–	2,3	–	**31**[19]	–	–	–	–	6·22
–	5	–	–	2-Ph, 3-Ph	**32**[20]	–	–	–	–	6·75
5	–	–	–	2-Ph, 3-Ph	**33**[20]	–	–	–	–	6·38
6′,6′-Dimethyldihydropyrano [3′,2′ · 6,7] chromones										
5′	–	5	2	–	**34**[21]	–	5·93	–	–	6·75
5,5′	–	–	2	–	**35**[21]	–	5·97	–	–	6·28
–	5	–	2	–	**36**[22]	–	6·00	–	–	6·30

8-hydroxy-1,2,6-trimethoxyxanthone (**5**)[9] and its acetate (**6**)[9] are ΔH-3 = −0·06, ΔH-4 = −0.09, ΔH-5 = +0·31 and ΔH-7 = +0.15 (**6**:**5**).

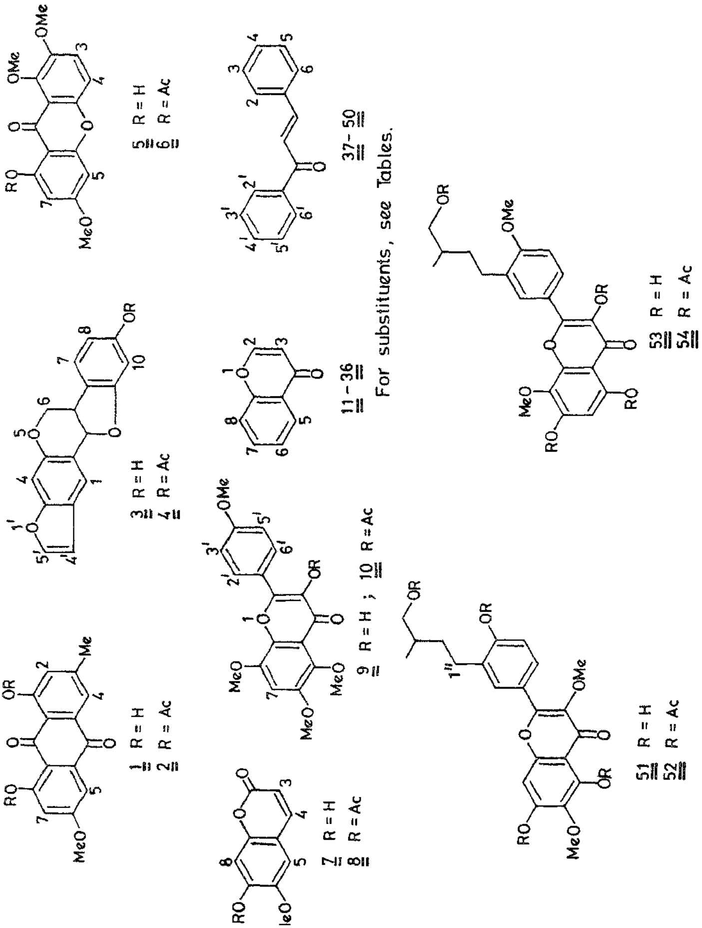
The acylation shifts from 7-hydroxy-6-methoxycoumarin (**7**)[10] and its acetate (**8**)[10] are ΔH-3 = +0·12, ΔH-4 = +0·06, ΔH-5 = +0·04 and ΔH-8 = +0·24 (**8**:**7**).

Table II
Alkoxylation [ΔH(OAc:OMe)] and acylation [ΔH(OAc:OH)] shifts in chromones

Comparison	*ΔH-2*	*ΔH-3*	*ΔH-6*	*ΔH-7*	*ΔH-8*
5-Alkoxylation shifts					
28:36	–	−0·07	–	–	+0·35
5,6-Dialkoxylation shifts					
26:27	–	–	–	–	+0·47
5,7-Dialkoxylation shifts					
15:17	+0·20	+0·03	+0·70	–	–
18:21	−0·08	−0·05	–	–	+0·17
5-Acylation shifts					
11:12	–	–	+0·11	+0·12	+0·60
13:14	–	+0·12	+0·07	–	+0·42
28:29	–	−0·07	–	–	+0·38
30:31	–	–	–	–	+0·22
32:33	–	–	–	–	+0·37
34:35	–	−0·04	–	–	+0·47
5,7-Diacylation shifts					
18:19	+0·09	+0·11	–	–	+0·16
22:23	−0·15	−0·16	–	–	+0·38
24:25	−0·02	−0·03	+0·82	–	–
5-Acylation-7-alkoxylation shifts					
15:16	−0·03	−0·05	+0·80	–	–
18:20	+0·14	+0·16	–	–	+0·46

The acylation shifts from 3-hydroxy-5,6,8,4′-tetramethoxyflavone (**9**)[11] and its acetate (**10**)[11] are ΔH-7 = +0·03, ΔH-2′= −0·34, ΔH-3′= +0·03, ΔH-5′= +0·03 and ΔH-6′= −0·34 (**10**:**9**). This comparison exhibits similarities amongst 3-acylation/alkoxylation/glycosyloxylation shifts in flavones[1]. Numerous other examples of this type may be found in Horie *et al*[12]. The shifts are different and distinct because of negative and numerically larger values of ΔH-2′ and ΔH-6′. When there is 3-OAc in flavones, H-2′ and H-6′ lie in the diamagnetic cone of $> C = O$ ($-O-\overset{O}{\overset{\|}{C}}-CH_3$) resulting in the upfield absorption of these two protons. When there is no 3-OAc, these two protons are downfield and thus the aforesaid trends for ΔH-2′ and ΔH-6′ are observed.

A similar trend for acylation/alkoxylation shifts is observed in the case of chromones and chalcones also. For example, the acylation shifts calculated from 5-hydroxy-2-methylchromone-7-0-glucoside acetate (**14**)[15] and its acetate (**13**)[14] are



For substituents, see Tables.

Fig.1

Table III
^{1}H nmr literature data for aromatic protons in chalcones

Substituents					*Chemical shifts (δ, $CDCl_3$*						
OH	*OMe*	*OAc*	*Other groups*		*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-3′*	*H-5′*
2′,4′,6′-Trioxygenated chalcones											
–	6′	2′,4′	3′-Me	**37**[23]	7·45	7·45	7·45	7·45	7·45	–	6·58
2′	4′,6′	–	3′-Me	**38**[24]	7·43	7·43	7·43	7·43	7·43	–	6·03
–	4′	2′,6′	3′ 	**39**[25]	7·53	7·38	7·38	7·38	7·53	–	6·58
2′,6′	4′	–	3″	**40**[25]	7·63	7·40	7·40	7·40	7·63	–	6·09
–	4′	2′,6′	3′-prenyl	**41**[26]	7·52	7·38	7·38	7·38	7·52	–	6·58
2′,6′	4′	–	3′-prenyl	**42**[26]	7·57	7·35	7·35	7·35	7·57	–	5·99
2′	4′,6′	–	3′-prenyl	**43**[27]	7·55	7·55	7·55	7·55	7·55	–	6·10
6′	2′,4′	–	3′-prenyl	**44**[28]	7·51	7·51	7·51	7·51	7·51	–	6·27
2′,3′,4′,6′-Tetraoxygenated chalcones											
–	2′,3′,4′	6′	–	**45**[29]	7·55	7·39	7·39	7·39	7·55	–	6·49
6′	2′,3′,4′	–	–	**46**[29]	7·65	7·42	7·42	7·42	7·65	–	6·31
3,4,2′,3′,4′,6′-Hexaoxygenated chalcones											
6′	2′,3′,4′	–	3,4-OCH_2O	**47**[30]	7·18	–	–	6·83	7·10	–	6·30
3,4,6,2′,4′,6′-Hexaoxygenated chalcones											
–	3,4,6,4′,6′	2′	–	**48**[31]	7·20	–	–	6·47	–	6·30	6·40
2′	3,4,6,4′,6′	–	–	**49**[31]	7·09	–	–	6·49	–	6·07	5·92
–	3,4,6,2′,4′,6′	–	–	**50**[31]	7·00	–	–	6·43	–	6·12	6·12

ΔH-3 = +0·12, ΔH-6 = +0·07, ΔH-8 = +0·42. Thus, H-8, which is *para* to H-5, undergoes highest shift due to acetylation of 5-OH. Similarly, a comparison of the ^{1}H nmr data for 2′-hydroxy-3,4,6,4′,6′-pentamethoxychalcone (**49**)[31] and its acetate (**48**)[31] reveals highest shift for H-5′, which is at *para* position to the site of acylation. IH nmr data for nuclear protons of chromones from literature are presented in Table I and the shifts determined are given in Table II. The chemical shift values for aromatic protons of chalcones are given in Table III and the acylation/alkoxylation shifts are shown in Table IV. It may be mentioned here that the differences in concentration or temperature may change the numerical values of ΔH, but the overall trend remains unchanged[1-6] and useful.

The only exception to the above trend has been observed in the case of 3′-(3″-methyl-4″-hydroxy)butyl-5,7,4′-trihydroxy-3,5-dimethoxyflavone (**51**), isolated from *Dodonaea viscosa*[32]. The acylation shifts from **51** and its acetate (**52**)[32] are ΔH-8 = +0·44, ΔH-2′ = −0·29, ΔH-5′ = −0·10 and ΔH-6′ = −0·20 (**52**:**51**). These ΔH values suggest that **52** and **51** differ at C-3 and not at C-4′. If **51** and **52** had differed at C-4′, ΔH-5′ would have been positive and large.

It has to be mentioned here that the trioxygenation pattern[33] in the A-ring of **52** has already been shown to be inconstitent with literature data. H-8 and H-6 signals are observed[33] around δ7·20-7·40 and δ6·73-6·80 in 5,7-diacetoxy-6-methoxy- and 5,7-diacetoxy-8-methoxyflavones, respectively. In **52**, the lone aromatic proton of the

Table IV
Alkoxylation [ΔH(OAc:OMe)] and acylation [ΔH(OAc:OH)] shifts in chalcones

Comparisons	*ΔH-2*	*ΔH-3*	*ΔH-4*	*ΔH-5*	*ΔH-6*	*ΔH-3′*	*ΔH-5′*
2′-Alkoxylation shift							
48:50	+0·20	–	–	+0·04	–	+0·18	+0·28
2′-Acylation shift							
48:49	+0·11	–	–	−0·02	–	+0·23	+0·48
6′-Acylation shift							
45:46	−0·10	−0·03	−0·03	−0·03	−0·10	–	+0·18
45:47	–	–	–	–	–	–	+0·19
2′,6′-Diacylation shift							
39:40	−0·10	−0·02	−0·02	−0·02	−0·10	–	+0·49
41:42	−0·05	+0·03	+0·03	+0·03	−0·05	–	+0·59
2′-Alkoxylation-6′-acylation shift							
41:44	+0·01	−0·13	−0·13	−0·13	+0·01	–	+0·31
4′-Alkoxylation-2′-acylation shift							
37:38	+0·02	+0·02	+0·02	+0·02	+0·02	–	+0·55
6′-Alkoxylation-2′-acylation shift							
41:43	−0·03	−0·17	−0·17	−0.17	−0·03	–	+0·48

A-ring absorbs at δ6·86. On the basis of literature data, the structure for the aforesaid compound from *D. viscosa* should be 3′-(3″-methyl-4″-hydroxy)butyl-3,5,7-trihydroxy-8,4′-dimethoxyflavone (**53**) and its acetate (**54**). It is pertinent to mention here that the structure of a flavonol glycoside from *Rudbeckia bicolor* has already been reassessed on similar lines[34].

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