Xanthone Studies

V.* Hydroxyl Proton Chemical Shifts of Hydroxyxanthones with Allylic Substituents

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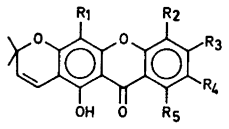
In a previous communication[1] the hydroxyl proton chemical shifts in DMSO-d_6 of hydroxy- and methoxy-substituted xanthones were reported and correlated with the oxygenation patterns. Several naturally occurring xanthones also have allylic side chains, which may be cyclized to pyrano or furano ring systems.[2] An investigation of the influence of these substituents upon the hydroxyl proton chemical shifts measured in DMSO-d_6 has therefore been undertaken. The results reported here (Table 1) are for thirteen xanthones with one or two hydroxyl groups and one or two allylic substituents in the same ring, and for jacareubin (I), isojacareubin (II), maculatoxanthone (III), mangostin (IV), and an oxidatively-cyclized derivative (V) of mangostin.

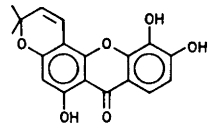
The resonance of the 1-hydroxyl ** proton is shifted 0.25 – 0.35 ppm to lower field when an allylic substituent is introduced into the *ortho* position, *e.g.* 1-hydroxy-2-allyl- and 1,3-dihydroxy-2-allylxanthone, while this is not the case for a 2- or 3-hydroxyl proton (see later); a *para*-substituent produces no shift, *e.g.* 1,3-dihydroxy-4-allylxanthone. This may be interpreted mainly as a steric effect. The *ortho* substituent forces the 1-hydroxyl group closer to the xanthone carbonyl, thereby augmenting the chelation of the hydroxyl proton. The same effect is operative with even greater magnitude when the steric crowding is increased, as for example in 1,3-dihydroxy-2,4-diallylxanthone (shifted by 0.45 ppm) and 1-hydroxy-2-(1,1-dimethyl-2-propenyl)-xanthone (shifted by 0.85 ppm). The presence of the dimethyl-chromen moiety with the pyrano ring linearly fused to the xanthone nucleus, as in



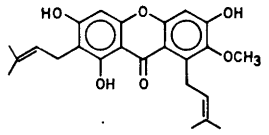
I $R_1=R_4=R_5=H$, $R_2=R_3=OH$

III $R_4=R_5=H$, $R_2=R_3=OH$
R_1=Lavandulyl

V $R_1=R_2=H$ $R_3=OH$, $R_4=OCH_3$
$R_5=CH_2-CH=C(CH_3)_2$



II



IV

jacareubin (I) and maculatoxanthone (III), also causes a large shift (0.6 – 0.7 ppm). This can be interpreted as arising from a combination of a steric and a resonance effect since, for isomers in which the pyrano ring is angularly fused, *e.g.* isojacareubin (II), the resonance of the 1-hydroxyl proton is shifted to lower field to a lesser extent (0.4 ppm), steric effects being absent.

The steric diminution of the hydrogen bonding distance between the chelating groups may also be effected by an allylic substituent in the 8-position; this again leads to a downfield shift of the 1-hydroxyl proton, for example 0.35 ppm for 1,5-dihydroxy-8-(3-methyl-2-butenyl)-xanthone. When resonance effect or/and steric compression operates from both the 2- and the 8-position as in mangostin(IV) and its oxidatively cyclized derivative(V), the chemical shifts of the 1-hydroxyl proton are the lowest measured.

The chemical shifts of the 2- or 3-hydroxyl protons are not influenced by the presence of a single *ortho*-situated allyl group, *e.g.* 2-hydroxy-1-allyl-, 3-hydroxy-4-allyl-, and 1,3-dihydroxy-2-allyl-xanthone. However, when surrounded by two allyl-substituents as in 2-hydroxy-

* Part IV see Ref. 1.

** The numbering system is based on 9-xanthenone as the parent compound.

Table 1. Chemical shifts of xanthone hydroxyl protons in DMSO-d_6.

	δ for OH at position (the value for the corresponding hydroxy xanthone [1] is given in parenthesis)			
	1(8)	2(7)	3(6)	4(5)
1-Hydroxy-2-allyl [4]	12.90(12.55)			
1-Hydroxy-2-(1,1-dimethyl-2-propenyl) [5]	13.40(12.55)			
2-Hydroxy-1-allyl [5]		9.80(9.85)		
2-Hydroxy-1,3-diallyl [5]		8.75(9.85)		
3-Hydroxy-4-allyl [5]			10.95(10.90)	
3-Hydroxy-2,4-diallyl [5]			9.90(10.90)	
4-Hydroxy-3-allyl [6]				10.00(10.35)
1,3-Dihydroxy-2-allyl [7]	13.00(12.70)		11.00(10.95)	
1,3-Dihydroxy-4-allyl [7]	12.75(12.70)		11.00(10.95)	
1,3-Dihydroxy-2,4-diallyl [7]	13.15(12.70)		10.00(10.95)	
1,3-Dihydroxy-2-(3-methyl-2-butenyl) [5]	13.00(12.70)		11.00(10.95)	
1,3-Dihydroxy-2,4-bis(3-methyl-2-butenyl) [5]	13.05(12.70)		9.95(10.95)	
1,5-Dihydroxy-8-(3-methyl-2-butenyl) [8]	12.95(12.60)			10.20(10.40)
Jacareubin (I) [5]	13.65(12.95)			
Isojacareubin (II) [5]	13.35(12.95)			
Maculatoxanthone (III) [9]	13.55(12.95)			
Mangostin (IV) [10]	13.90(13.05)			
V [11]	13.95(13.05)			

1,3-diallyl- and 3-hydroxy-2,4-diallyl-xanthone these hydroxyl protons show *upfield* shifts (1.1 and 1.0 ppm, respectively), which may be attributed to the partial inhibition of intermolecular hydrogen bonding between the phenolic proton and a solvent molecule. An alternative explanation, which has been presented for the observation of an upfield shift (1.2 ppm) of the hydroxyl proton in 2,6-dimethylphenol,[3] is that resonance has been inhibited by the hydrogen bonded hydroxyl group not being coplanar with the ring. This explanation does not seem valid for the xanthones, however, since the 2- and the 3-hydroxyl protons experience nearly the same shifts in the *o,o'*-disubstituted compounds. If the 3-hydroxyl group, situated *para* to the carbonyl group, is sterically hindered from being coplanar with the aromatic nucleus its proton would be expected to show an upfield shift. For the 2-hydroxyl group, being *para* to the ether bridge, the same situation should, if anything, lead to a shift in the opposite direction.

The 4-hydroxyl group can only have a single *ortho*-situated allylic substituent, yet its presence also causes an upfield shift in, for example, 4-hydroxy-3-allyl-xanthone (shifted by 0.35 ppm). In this case the other *ortho*-position is occupied by an ether bridge instead of an allylic substituent so that the steric crowding might be expected to be less.

Experimental. ^{1}H-NMR-spectra were recorded as previously described.[1] All compounds were synthesized or isolated in this laboratory (references in Table 1).

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