

Table I are supposed to be well within $\pm 5\%$, except the rate constant for the chloride ion which is probably not better than $\pm 10\%$ due to the small absorption difference between reactants and products in UV in this reaction. No method was found useful to determine the rate constant for the reaction between methyl tosylate and the cyanide ion.

The UV measurements were performed with a Beckmann DB Spectrophotometer, using 0.1 cm quartz cells. The IR measurements were performed on a Unicam SP 200 Infrared Spectrophotometer using 0.1 cm liquid cells. The temperature during the experiments was $25 \pm 0.2^\circ\text{C}$.

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Xanthone Studies

IV.* Hydroxyl Proton Chemical Shifts in the Structural Investigation of Xanthenes

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^1H NMR-spectroscopy is extensively used in structural investigations of xanthenes. Substitution patterns are usually determined on the basis of chemical shift and spin coupling data for the aromatic protons.¹ This paper presents a supplementary method based upon measurement of the chemical shifts in $\text{DMSO-}d_6$ of the hydroxyl protons of oxygenated xanthenes.

Contrary to experiences reported for similar studies of flavanoids^{2,3} signal detection was not impaired by the small amounts of water invariably present in the solvent and giving rise to a signal at approx. δ 3.5 ppm, nor was excessive signal broadening observed upon keeping the solutions for several hours. In every case investigated the positions and appearances of the hydroxyl signals were not appreciably influenced by the addition of up to 1% (v/v) of water. There was no evidence for the decomposition of any of the xanthenes in DMSO solution.

Xanthenes bearing a 1-hydroxyl** group and one or more methoxyl groups are sparingly soluble in DMSO and their NMR-spectra have, as a result, been recorded in CDCl_3 solution. It was expected, however, that the chemical shift of the 1-hydroxyl proton would be determined mainly by its strong intramolecular hydrogen bonding to the carbonyl group and thus that it would be largely solvent-independent. This has been confirmed in some cases for which spectra have been recorded using both solvents.

The hydroxyl protons of the xanthenes investigated resonate in the region δ 9.25–13.35 ppm (Table I) and thus, because of the influence of the carbonyl group, they are more or less deshielded relative to the hydroxyl proton of phenol (δ 9.30). As

* Part II. *Dansk Tidsskr. Farm.* **46** (1972) 133.

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

Table 1. Chemical shifts of xanthone hydroxyl protons.

Substituents on nucleus	δ for OH at position			
	1(8)	2(7)	3(6)	4(5)
1-hydroxy ⁴	12.55			
» » ^a	12.65			
2-hydroxy ⁵		9.85		
3-hydroxy ⁶			10.90	
4-hydroxy ⁶				10.35
1,2-dihydroxy ⁵	12.40	9.35		
1-hydroxy-2-methoxy ⁵	12.70			
» » » ^a	12.80			
1-methoxy-2-hydroxy ⁵		9.45		
1,3-dihydroxy ⁶	12.70		10.95	
1-hydroxy-3-methoxy ⁷	12.80			
» » » ^a	12.80			
1-methoxy-3-hydroxy ⁸			10.80	
1,4-dihydroxy ⁹	11.70			9.60
1-hydroxy-4-methoxy ^{a 7}	11.90			
1-methoxy-4-hydroxy ⁷				9.60
1,5-dihydroxy ⁷	12.60			10.45
1-hydroxy-5-methoxy ^{a 7}	12.55			
1-methoxy-5-hydroxy ⁷				10.35
1,6-dihydroxy ¹⁰	12.70		11.10	
1-hydroxy-6-methoxy ^{a 6}	12.70			
1-methoxy-6-hydroxy ¹¹			10.80	
1,7-dihydroxy ⁴	12.60	10.05		
1-hydroxy-7-methoxy ⁷	12.60			
» » » ^a	12.60			
1-methoxy-7-hydroxy ⁹		9.90		
1,8-dihydroxy ⁶	11.45; 11.45			
1-hydroxy-8-methoxy ^{a 7}	12.95			
2,3-dihydroxy ¹²		9.75	10.65	
2,6-dihydroxy ⁷		9.90	10.90	
3,4-dihydroxy ⁶			10.45	9.40
3,6-dihydroxy ¹⁰			10.75; 10.75	
1,2,4-trihydroxy ⁷	11.75	9.25		9.60
1,3,6-trihydroxy ¹³	12.90		10.80; 10.90	
1,3,7-trihydroxy ⁷	12.85	9.90	10.90	
1,3-dihydroxy-7-methoxy ¹⁴	12.75		10.95	
1,7-dihydroxy-3-methoxy ¹⁴	12.65	9.85		
1-hydroxy-3,7-dimethoxy ¹⁵	12.85			
» » » ^a	12.75			
1,3-dimethoxy-7-hydroxy ⁷		9.75		
1,7-dimethoxy-3-hydroxy ⁷			10.80	
1,3,8-trihydroxy ¹⁶	11.65; 11.60		11.10	
1,3-dihydroxy-8-methoxy ⁷	13.30		10.85	
1-methoxy-3,8-dihydroxy ⁷	13.25		10.95	
1,5,6-trihydroxy ¹⁶	12.75		10.55	9.40
1,6,7-trihydroxy ⁸	12.90	9.90	10.80	
1,3,5,6-tetrahydroxy ¹⁰	12.95		10.80; 10.40	9.35
1,3,6,7-tetrahydroxy ⁷	13.05	9.70	10.55; 10.65	
1,3,6,8-tetrahydroxy ¹⁰	11.80; 11.80		10.95; 10.95	
1,8-dihydroxy-3,6-dimethoxy ^{a 7}	12.00; 12.00			
1-hydroxy-3,6,8-trimethoxy ^{a 7}	13.35			

^a Measured from 5 % (w/v) solutions in CDCl₃.

Table 2. Xanthone oxygation patterns relative to hydroxyl proton chemical shifts.

δ 9.25–9.45	2- or 7-OH with OR ^a in 1- or 8-position, resp.
δ 9.35–9.60	4- or 5-OH with OR ^a in <i>ortho</i> or <i>para</i> position
δ 9.70–10.05	2- or 7-OH
δ 10.35–10.55	4- or 5-OH
	3- or 6-OH with OR ^a in 4- or 5-position, resp.
δ 10.80–11.10	3- or 6-OH
δ 11.45–12.00	1- and 8-OH when both are present
	1- or 8-OH with OR ^a in 4- or 5-position, resp.
δ 12.50–12.90	1- or 8-OH
δ 12.90–13.35	1- or 8-OH with OR ^a in 3- and 6-position
	1- or 8-OH with OCH ₃ in 8- or 1-position, resp.

^a R=H or CH₃.

shown in Table 2 this influence varies according to the position of substitution and is least at either of the 2(7)- and 4(5)-positions. In the 3(6)-position it is increased through resonance with the carbonyl group. Finally the most strongly deshielded hydroxyl protons are in the chelated 1(8)-position.

Additional shielding effects are in most cases exerted by oxygen functions situated *ortho* or *para* to a hydroxyl group, but the chemical shift of a 2- or 7-hydroxyl proton is only slightly influenced by the presence of an oxygen function in the 3- resp. 6-position, and *vice versa*. As anticipated, the resonance of a 1-hydroxyl proton is shifted upfield if a 2-hydroxyl group is also present. In the case of a 2-methoxyl co-substituent, however, the shift is downfield.

The presence of oxygen functions in the positions *ortho* and *para* to the carbonyl group increases the partial negative charge on the carbonyl oxygen through resonance. The hydrogen bond to the proton of a 1-hydroxyl group is thereby strengthened causing a downfield shift, e.g. 1-hydroxy-3-methoxy- and 1-hydroxy-8-methoxy-xanthone. When both a 1- and an 8-hydroxyl group are present, however, the sharing of the hydrogen bonding site between their respective protons will lead to an upfield shift for each, e.g. 1,8-dihydroxy- and 1,8-dihydroxy-3,6-dimethoxyxanthone.

Experimental. ¹H NMR-spectra were recorded on a JEOL JNM-C-60 HL instrument operating under field sweep conditions at room temperature (18–25°C) and utilizing TMS as an internal standard. Sample concentrations were 5% (w/v). DMSO-*d*₆ was a commercial product containing ≤ 0.1% of D₂O + H₂O.

All compounds were synthesized in this laboratory by methods previously described (references in Table 1).

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