Application of Benzene-induced Solvents Shifts in Proton Magnetic Resonance Spectra: the Structure of Dimethylmangostin and Mangostin

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MANGOSTIN and its dimethyl ether were assigned the xanthone structures (Ia and Ib) more than a century after mangostin was first isolated from the bark and fruit of the mangosteen tree (*Garcinia mangostana*, Guttiferae).[1] The unambiguous synthesis of a lower homologue (IIa) of dimethylmangostin (Ib) now provides suitable reference compounds to comment on the structures of mangostin and dimethylmangostin.

1,7-Diallyloxy-3,6-dimethoxyxanthone (IIb), m.p. 135°, was prepared by etherification of 1,7-dihydroxy-3,6-dimethoxyxanthone (IIc)[2] with allyl bromide. A Claisen rearrangement of the diallyl ether (IIb) gave 2,8-diallyl-1,6-dihydroxy-3,6-dimethoxyxanthone (IId), m.p. 194°, which on methylation of the hydroxyl group at C-7 gave a lower homologue (IIe), m.p. 123°, of dimethylmangostin (Ib). Attempts to introduce the 3,3-dimethylallyl group by direct substitution into the 2- and 8- positions of 1,3,6,7-tetra-oxygenated xanthones led to subsitution only at ring B in either the 2- or 4- or at both positions to give the xanthones (IIf, IIg, and IIh).

The mechanism of benzene-induced solvent shifts (Δ) in ^{1}H n.m.r. spectra [where Δ p.p.m. = $\tau(C_6D_6) - \tau(CDCl_3) = \delta(CDCl_3) - \delta(C_6D_6)$] recently enunciated,[3] shows that collision complexes between benzene and solute may be localised at any electron-deficient site of a local dipole. Thus the Δ values for aromatic protons and the substituents in

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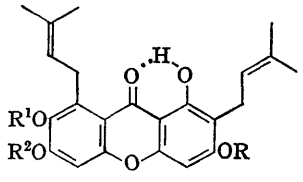
TABLE

^1H n.m.r. chemical shifts (τ) and solvent shifts Δ (p.p.m.) for 1,3,6,7-tetra-oxygenated xanthones with allyl side-chains, using tetramethylsilane as internal reference.

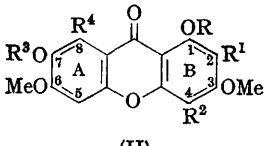
		C-1 OH	H-2	H-4	H-5	H-8	C-3	C-6 OMe	C-7	CH_2		CH=		$=CMe_2$		
(IIg)	C_6D_6*	−3·77	3·76		3·54	2·44	6·75	6·75	6·64	6·4		4·56		8·16		8·32
	$CDCl_3$*	−3·05	3·69		3·21	2·50	6·06	6·08	6·15	6·58		4·83		8·18		8·34
	Δ	−0·72	0·07		0·33	−0·06	0·69	0·67	0·49	−0·18		−0·27		−0·02		−0·02
(IIf)	C_6D_6	−3·78		3·86	3·58	2·43	6·74	6·70	6·66	6·44		4·46		8·13		8·32
	$CDCl_3$	−3·02		3·66	3·21	2·46	6·06	6·08	6·14	6·68		4·82		8·22		8·34
	Δ	−0·76		0·20	0·37	−0·03	0·68	0·62	0·49	−0·24		−0·32		−0·09		−0·02
(IIh)	C_6D_6	−3·8			3·54	2·44	6·44	6·66	6·80	~6·42	~6·42	~4·5		8·20	8·20	8·33
	$CDCl_3$	−3·1			3·19	2·46	6·04	6·07	6·24	6·52	6·62	4·76		8·13	8·22	8·32
	Δ	−0·70			0·35	−0·02	0·40	0·59	0·56	~0·10	~0·20	~0·26		+0·05	−0·02	0·01
(IIa)	C_6D_6	−3·94		3·96	3·67		6·78	6·72	6·42	5·70	6·42	~3·8				
	$CDCl_3$	−3·42		3·75	3·32		6·11	6·18	6·25	5·87	6·65	~4·02				
	Δ	−0·52		0·21	0·35		0·67	0·54	0·17	−0·17	−0·23	~0·22				
(Ib)	C_6D_6	−4·01		3·94	3·67		6·76	6·70	6·42	5·70	6·42	4·48		8·15	8·15	8·33
	$CDCl_3$	−3·46		3·76	3·34		6·12	6·18	6·26	5·92	6·70	4·82		8·19	8·23	8·35
	Δ	−0·55		0·18	0·33		0·64	0·52	0·16	−0·22	−0·28	−0·34		−0·04	−0·08	−0·02
Mangostin	C_6D_6*	−4·12		4·00	3·39			6·80		5·90	6·57	~4·6	−4·8	8·24	8·38	8·46
	$CDCl_3$	−3·74		3·79	3·26			6·25		5·96	6·60	4·78		8·19	8·26	8·34
	Δ	−0·38		0·21	0·13			0·55		−0·06	−0·03	?		0·05	0·12	0·12

τ $CDCl_3$ refers to chemical shifts in deuterochloroform.
τ C_6D_6 refers to chemical shifts in deuterobenzene containing 10% deuterochloroform.
All measurements were carried out on the Varian 100 Mc/sec. n.m.r. spectrometer. Concentrations for the measurements were 20 mg of solute in 0·6 c.c. of solvent except where marked * which refer to measurements as saturated solutions.



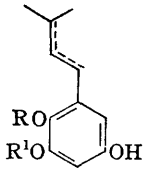
(I)

	R	R^1	R^2
a:	H	Me	H
b:	Me	Me	Me
c:	H	H	OMe



(II)

	R	R^1	R^2	R^3	R^4
a:	H	X	H	Me	X
b:	X	H	H	X	H
c:	H	H	H	H	H
d:	H	X	H	H	X
e:	H	X	H	Me	X
f:	H	Y	H	Me	H
g:	H	H	Y	Me	H
h:	H	Y	Y	Me	H



(III)

a: R=Me, R^1=H
b: R=H, R^1=Me

[X=CH_2·CH:CH_2; Y=CH_2·CH:CMe_2]

xanthones are dependent on the substituents and the substitution pattern, and by comparison with suitable reference compounds the location of substituents in natural xanthones has been established.[4] For 1,3,6,7-tetramethoxyxanthones containing allyl side-chains, the Table shows that $\Delta_{H\text{-}2} \sim 0{\cdot}07$ p.p.m., $\Delta_{H\text{-}4} \sim 0{\cdot}20$ p.p.m. $\Delta_{H\text{-}5} \sim 0{\cdot}35$ p.p.m. and $\Delta_{H\text{-}8} \sim -0{\cdot}03$ p.p.m. The Δ values for the aromatic protons both in dimethylmangostin (0·18 and 0·33 p.p.m.) and its lower homologue (0·21 and 0·35 p.p.m.) confirm the presence of protons at C-4 and C-5 and thus provides independent confirmation for the orientation of the substituents in dimethylmangostin.

As anticipated, the Δ values for the methoxyl groups at C-7 in dimethylmangostin (Ib) and its lower homologue (IIa) are abnormally low (Δ ~ 0·17 p.p.m.) with respect to the other methoxyl groups (Δ ~ 0·6 p.p.m.). Formation of a collision complex at this site is hindered by the steric and polar effects of the two adjacent groups,[5] and in the xanthone series it has been shown that a methoxyl group has a low Δ value when it is flanked by two ether groups,[4] or by a hydroxyl and an ether group,[6] or by an alkyl and an ether group,[6] or by a carbonyl and an alkyl group,[6] or by two alkyl groups. If mangostin has structure (Ia) the hindered methoxyl group at C-7 would be expected to have a relatively low Δ value (< 0·4 p.p.m.). Contrary to these expectations, the methoxyl group in magnostin has a Δ value of 0·55 p.p.m. This surprising result is best explained by locating the methoxyl group elsewhere, and a re-assessment of the evidence[1,7] suggests that mangostin may have structure (Ic).

In the elegant structural studies on mangostin by Yates and Stout,[1] the position of the methoxyl group at C-7 was based on earlier work by Murakami.[7] Alkaline degradation of mangostin

gave a methoxyphenol to which structure (IIIa) was assigned.[7] The only evidence for orientating the methoxyl group next to the side-chain was based on the failure of mild oxidation to give a quinone.[7] If mangostin has structure (Ic), Murakami's phenol will have structure (IIIb) and although such a product (IIIb) should form a quinone, its failure to do so need only mean that incorrect experimental conditions were used, or that cyclisation of the side chain prior to, or after, oxidation[8] was the preferred mode of reaction.

Further experimental work on mangostin is thus required to remove the doubts concerning the orientation of the methoxyl group.

I am indebted to Professors Yates and Stout for gifts of mangostin and dimethylmangostin.

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[1] P. Yates and G. H. Stout, *J. Amer. Chem. Soc.*, 1958, **80**, 1691.
[2] A. Jefferson, Ph.D. Thesis, University of London 1965; A. Jefferson and F. Scheinmann, unpublished work.
[3] J. Ronayne and D. H. Williams, *J. Chem. Soc.* (*B*), 1967, 540.
[4] B. Jackson, H. D. Locksley, and F. Scheinmann, *J. Chem. Soc.* (*C*), 1967, in the press.
[5] J. H. Bowie, J. Ronayne, and D. H. Williams, *J. Chem. Soc.* (*B*), 1967, 535.
[6] F. Scheinmann, unpublished work.
[7] M. Murakami, *Proc. Imp. Acad.* (*Tokyo*), 1931, **7**, 254; *J. Chem. Soc. Japan*, 1932, **53**, 150.
[8] D. McHale and J. Green, *J. Chem. Soc.*, 1965, 506.