

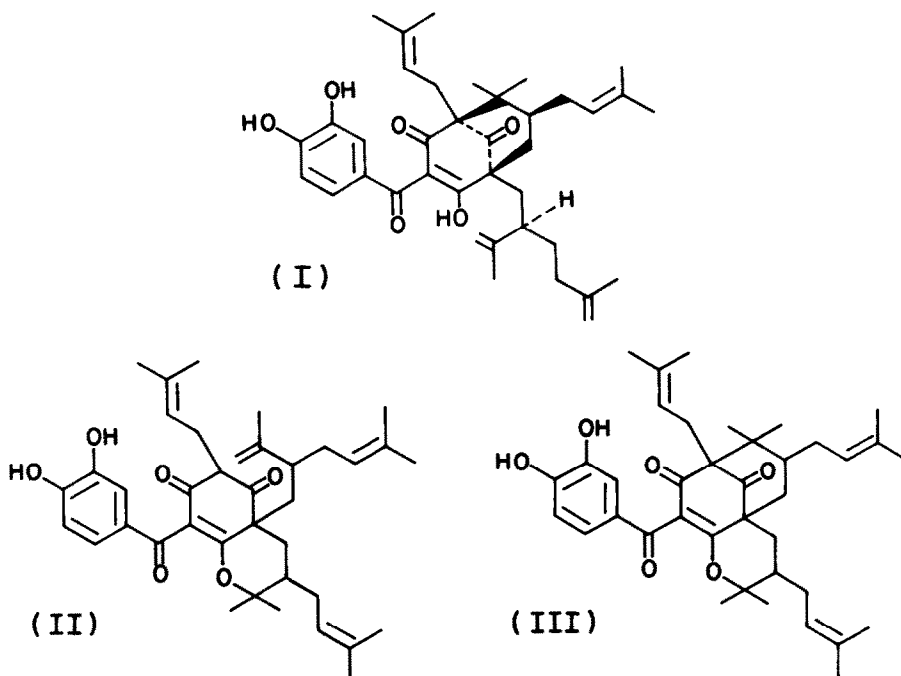
REVISED STRUCTURE OF XANTHOCHYMOL

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We recently examined a natural product isolated from a plant extract by Dr. S. C. Basa¹, Regional Research Laboratory, Orissa, India. On the basis of an X-ray crystal structure analysis we established the structure as I (C₃₈H₅₀O₆, mol wt 602.82) with the absolute configuration depicted in the stereoscopic drawing shown in Figure 1.



We then discovered that two isomers of I, namely xanthochymol (II) and isoxanthochymol (III), both from fruits of *Garcinia xanthochymus*, have been reported in the literature.^{2*} The structure of III had been determined from an X-ray crystallographic analysis of its di-*p*-bromobenzenesulfonate, whereas the structure of II was deduced from that of III by a comparison of

* After we had determined the structure of I we were informed by Dr. Basa that his material also had been isolated from *Garcinia xanthochymus*.

the physical and chemical data for II and III. We had several reasons to doubt the correctness of the structure II for xanthochymol, especially since it seemed likely that this compound was identical with I. Direct comparison of I with authentic xanthochymol³ by nmr, mp, and mmp has now conclusively confirmed their identity.

Our sample dissolved in deuteriochloroform (20 mg in 0.3 ml) gave the following 100 MHz proton nuclear magnetic resonance data: δ TMS 1.02, 1.18 (2s, 3 each, $>\text{CMe}_2$), 1.56 x 2, 1.71 x 2 (2s, 6 each, $-\text{CH}=\text{CMe}_2$ x 2), 1.75, 1.81 [2s, 3 each, $-\text{C}(\text{Me})=\text{CH}_2$ x 2], 1.00-2.30 (CH x 2 + CH_2 x 6), 4.43, 4.65 (2s, 2 each, $-\text{C}(\text{Me})=\text{CH}_2$ x 2), 4.90, 5.00 (2m, 1 each, $-\text{CH}=\text{CMe}_2$ x 2), 6.60, 6.95, 7.00 ABX, 3, J(AB)ortho 9 and J(BX)meta 2 Hz, aromatic), 6.41, 6.78 (broad, 1 each, OH x 2). The slightly broad singlets at 4.43 and 4.65 together with the methyl bands at 1.75 and 1.81 indicate that two isopropenyl groups are present, while the two multiplets at 4.90 and 5.00 together with bands at 1.56 and 1.71 indicate that two isopropylidene groups are present. Thus, significant differences in the NMR spectra of xanthochymol and isoxanthochymol include the presence of bands due to two terminal methylene groups in xanthochymol and two methyl groups on a saturated carbon (δ 0.93 and 1.24) in the isoxanthochymol spectrum.

These findings are confirmed by the ^{13}C NMR spectrum of the same solution which showed two triplets at 109.8 and 113.5 for two terminal methylene carbons [$-\text{C}(\text{Me})=\text{CH}_2$ x 2] and two doublets at 123.9 and 124.2 for methine carbons of two trisubstituted olefin groups ($-\text{CH}=\text{CMe}_2$ x 2). The rest of the assignments are as follows: δ 17.4, 26.6 (ring $>\text{CMe}_2$), 18.2, 18.5, 26.1, 26.3 ($-\text{CH}=\text{CMe}_2$ x 2), 22.8, 23.0 [$-\text{C}(\text{Me})=\text{CH}_2$ x 2], 27.2, 29.2, 32.1, 35.7, 36.8, 42.9 (6 CH_2), 43.6, 46.7 (2 CH), 49.8 (C-5), 58.1 (C-8), 70.0 (C-4), 115.2 (C-2), 114.5, 116.6, 120.2 (C-15,12,16), 127.9, 133.1, 135.4, 143.8, 146.1, 147.5, 149.9 (C-11,19,26,13,36,14,31), 194.0, 194.9, 198.6 (3 enolizable carbonyls $\text{O}=\text{C}$), 209.2 (non-enolizable carbonyl $\text{O}=\text{C}$). The position of the four alkene double bonds in the molecule were determined by crystal structure analysis.

Crystals of I are orthorhombic, space group $\text{P2}_12_12_1$, with $a = 8.955(5)$, $b = 18.732(10)$, $c = 21.288(10)\text{\AA}$, and $d_{\text{calcd}} = 1.121\text{ g cm}^{-3}$ for $Z = 4$. The crystal used for X-ray crystallography measured approximately $0.25 \times 0.35 \times 0.35$ mm. The diffraction data were measured on a Hilger-Watts diffractometer by $\theta - 2\theta$ scans (Ni filtered $\text{Cu K}\alpha$ radiation, pulse height discrimination). A total of 4062 independent reflections with $\theta < 76^\circ$ were measured, of which 2712 were considered observed [$I > 2.5\sigma(I)$]. The initial solution of the structure was obtained by a multiple solution procedure,⁴ as implemented in

the "Multan74" set of computer programs.⁵ The unweighted discrepancy index at the conclusion of the isotropic refinement of the 44 carbon and oxygen atoms was $R = 0.135$.

The anisotropic refinement of the structure was carried out by block-diagonal least squares in which the matrix was partitioned into four blocks. The positions of the hydrogen atoms were calculated from the molecular geometry. In the final refinement the carbon and oxygen atoms had anisotropic thermal parameters and the hydrogen atoms had isotropic temperature factors. The hydrogen atoms were included in the structure factor calculations but their parameters were not varied. The final unweighted and weighted discrepancy indices are $R = 0.059$ and $wR = 0.061$ for the 2712 observed reflections. There are no peaks greater than $\pm 0.3 \text{ e } \text{Å}^{-3}$ on the final difference map.

It was possible to establish the absolute configuration of I from the X-ray data. To do this, two additional refinements were made taking into account the anomalous dispersion correction for oxygen ($\Delta f' = 0.047$, $\Delta f'' = 0.032$ ⁶). In one refinement the correct value of the imaginary part of the anomalous dispersion correction ($\Delta f''$) was used and in the other refinement the sign of $\Delta f''$ was reversed (equivalent to refining the enantiomer). At the end of the two refinements, the configuration corresponding to the lower wR value (0.0611 vs. 0.0614) was taken as the absolute configuration. According to the test described by Hamilton,⁷ the configuration corresponding to the higher wR value may be rejected at the 0.005 significance level.

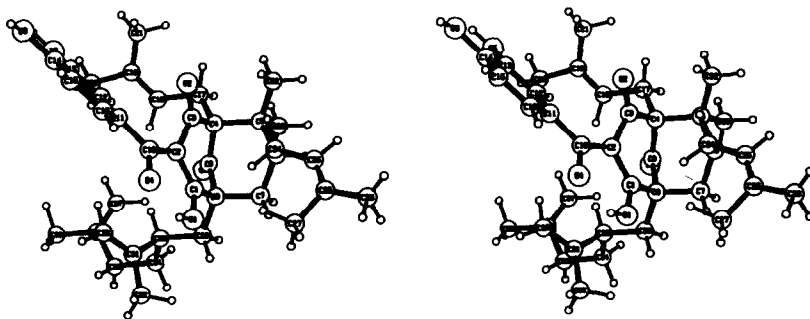


Figure 1. A stereoscopic drawing of I showing its conformation and absolute configuration.

References

1. We thank Dr. S. C. Basa for this sample which he isolated from *Garcinia xanthochymus*.
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Table 1. Bond Lengths (Angstroms) in Xanthochymol (I).

C(1)-O(1)	1.294	C(4)-C(9)	1.496	C(11)-C(16)	1.398	C(26)-C(27)	1.50
C(3)-O(2)	1.218	C(4)-C(17)	1.539	C(12)-C(13)	1.371	C(26)-C(28)	1.44
C(9)-O(3)	1.215	C(5)-C(6)	1.576	C(13)-C(14)	1.371	C(29)-C(30)	1.52
C(10)-O(4)	1.279	C(5)-C(22)	1.509	C(14)-C(15)	1.38	C(30)-C(31)	1.53
C(13)-O(5)	1.366	C(5)-C(23)	1.54	C(15)-C(16)	1.38	C(30)-C(34)	1.53
C(14)-O(6)	1.364	C(6)-C(7)	1.54	C(17)-C(18)	1.49	C(31)-C(32)	1.50
C(1)-C(2)	1.400	C(6)-C(24)	1.56	C(18)-C(19)	1.310	C(31)-C(33)	1.32
C(1)-C(8)	1.508	C(7)-C(8)	1.56	C(19)-C(20)	1.52	C(34)-C(35)	1.55
C(2)-C(3)	1.464	C(8)-C(9)	1.508	C(19)-C(21)	1.43	C(35)-C(36)	1.49
C(2)-C(10)	1.440	C(8)-C(29)	1.541	C(24)-C(25)	1.48	C(36)-C(37)	1.34
C(3)-C(4)	1.546	C(10)-C(11)	1.463	C(25)-C(26)	1.27	C(36)-C(38)	1.46
C(4)-C(5)	1.613	C(11)-C(12)	1.394				

Table 2. Bond Angles (degrees) in Xanthochymol (I).

O(1)-C(1)-C(2)	122.4	C(1)-C(8)-C(7)	109.3	C(4)-C(17)-C(18)	112.1
O(1)-C(1)-C(8)	114.6	C(1)-C(8)-C(9)	110.5		
C(2)-C(1)-C(8)	123.0	C(1)-C(8)-C(29)	109.3	C(17)-C(18)-C(19)	127.6
		C(7)-C(8)-C(9)	103.3		
C(1)-C(2)-C(3)	117.5	C(7)-C(8)-C(29)	111.5	C(18)-C(19)-C(20)	120.1
C(1)-C(2)-C(10)	117.6	C(9)-C(8)-C(29)	112.8	C(18)-C(19)-C(21)	126.1
C(3)-C(2)-C(10)	123.4			C(20)-C(19)-C(21)	113.8
		O(3)-C(9)-C(4)	123.2		
O(2)-C(3)-C(2)	122.0	O(3)-C(9)-C(8)	121.0	C(6)-C(24)-C(25)	111.8
O(2)-C(3)-C(4)	119.1	C(4)-C(9)-C(8)	115.6		
C(2)-C(3)-C(4)	118.9			C(24)-C(25)-C(26)	131.5
		O(4)-C(10)-C(2)	117.8		
C(3)-C(4)-C(5)	111.0	O(4)-C(10)-C(11)	116.0	C(25)-C(26)-C(27)	122.5
C(3)-C(4)-C(9)	111.4	C(2)-C(10)-C(11)	126.0	C(25)-C(26)-C(28)	123.9
C(3)-C(4)-C(17)	107.1			C(27)-C(26)-C(28)	113.5
C(5)-C(4)-C(9)	103.4	C(10)-C(11)-C(12)	122.4		
C(5)-C(4)-C(17)	112.8	C(10)-C(11)-C(16)	118.2	C(8)-C(29)-C(30)	114.8
C(9)-C(4)-C(17)	111.3	C(12)-C(11)-C(16)	119.1		
		C(11)-C(12)-C(13)	119.7	C(29)-C(30)-C(31)	115.1
C(4)-C(5)-C(6)	110.9			C(29)-C(30)-C(34)	110.0
C(4)-C(5)-C(22)	112.3	O(5)-C(13)-C(12)	118.8	C(31)-C(30)-C(34)	108.8
C(4)-C(5)-C(23)	108.8	O(5)-C(13)-C(14)	120.0		
C(6)-C(5)-C(22)	111.0	C(12)-C(13)-C(14)	121.1	C(30)-C(31)-C(32)	117.0
C(6)-C(5)-C(23)	106.8			C(30)-C(31)-C(33)	120.8
C(22)-C(5)-C(23)	106.7	O(6)-C(14)-C(13)	117.5	C(32)-C(31)-C(33)	122.2
		O(6)-C(14)-C(15)	122.7		
C(5)-C(6)-C(7)	113.0	C(13)-C(14)-C(15)	119.8	C(30)-C(34)-C(35)	115.1
C(5)-C(6)-C(24)	117.4			C(34)-C(35)-C(36)	116.3
C(7)-C(6)-C(24)	111.6	C(14)-C(15)-C(16)	120.2		
				C(35)-C(36)-C(37)	123.4
C(6)-C(7)-C(8)	114.1	C(11)-C(16)-C(15)	120.0	C(35)-C(36)-C(38)	113.8
				C(37)-C(36)-C(38)	122.7