Tetrahedron Letters,Vol.23,No.21,pp 2233-2236,1982 0040-4039/82/212233-04$03.00/0
Printed in Great Britain

CRYSTAL AND MOLECULAR STRUCTURE OF ISOGARCINOL

N. Krishnamurthy and B. Ravindranath*
Central Food Technological Research Institute, Mysore 570013, India
and
T. N. Guru Row and K Venkatesan
Department of Organic Chemistry, Indian Institute of Science, Bangalore 560012, India

Abstract. The controversy with regard to the structures of the closely related polyisoprenylated phenolic compounds, garcinol, isogarcinol, camboginol, cambogin, xanthochymol and isoxanthochymol is cleared by X-ray crystallographic analysis of the naturally occurring isogarcinol The unusual UV spectral characteristics of the chromophore of isogarcinol are discussed.

We have recently reported the isolation and suggested the structures of two compounds, viz , garcinol (I) and isogarcinol (II) from Garcinia indica fruit rind[1] Rao and coworkers have isolated four closely related compounds, xanthochymol (III) and isoxanthochymol (IV) from G. xanthochymus[2] and camboginol (I) and cambogin (V) from G. cambogia latex[3]. Xanthochymol could be converted into isoxanthochymol and camboginol to cambogin and, so also, garcinol to isogarcinol[4]

Isoxanthochymol and cambogin are considered to be optical antipodes However, xanthochymol and isoxanthochymol were reported to have similar UV spectra (λ_{max}^{EtOH} 264 and 364 nm)[2], very different from those of cambogin and camboginol (λ_{max}^{EtOH} 230 and 281 nm)[3] The yellow pigment garcinol (λ_{max}^{EtOH} 255 and 365 nm) and the colourless isogarcinol (λ_{max}^{EtOH} 232 and 278 nm), isolated by us, had distinctly different electronic spectra This led us to propose, on the basis of supplementary evidence from IR, NMR and mass spectral data, structures I and II for garcinol and isogarcinol respectively. We also proposed an alternative structure (VI) for camboginol to explain the spectral data[1]. The relationship between isoxanthochymol and cambogin, however, was not clear.

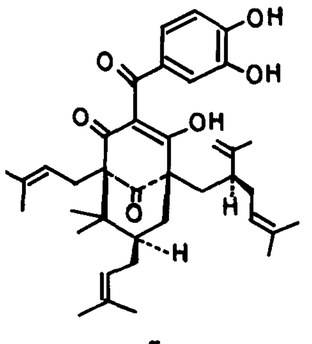
After communicating our paper, a publication appeared[5] from Rao's group, which recorded that the UV spectral maxima for isoxanthochymol were 232 and 275 nm and those for xanthochymol were 264 and 364 nm in cyclohexanone (cyclohexane?) and 230 and 276 nm in ethanol. While such drastic changes in the UV spectrum of xanthochymol with solvent could only be explained as due to the possible isomerisation to isoxanthochymol by a trace of acid that may be present in ethanol[6], the new information opened up the possibility that cambogin and isogarcinol (as also camboginol and garcinol) could be identical. That isoxanthochymol and cambogin (or isogarcinol) are optical antipodes could also be supported. Still, we believed that the structures IV and V for these compounds were incompatible with the UV spectra which indicated that the 1,3-diketone and the aroyl moieties are not conjugated. Though the structures of both isoxanthochymol and cambogin are said to have been determined by X-ray crystallography of their brosylates[2,3], the details have not been published. Also, it was possible that isomerisation to structures IV and V could have occurred during the preparation of the brosylates

In view of the uncertainty, we undertook the X-ray crystallographic analysis of isogarcinol crystals and found, as the following data indicated, that the structure of the compound was, in fact, V The crystals used were orthorhombic and belonged to the space group $\underline{P}2_12_12_1$. The unit cell parameters are: $\underline{a}$ = 11 188(1), $\underline{b}$ = 14.709(1) and $\underline{c}$ = 20.576(2) Å, z = 4 A total of 3004 reflections [2208 with $\underline{I} \geqslant 2\sigma(\underline{I})$] were collected on a Nonius CAD diffractometer (λ= 1.542 Å, $\omega/2\theta$ scan). The direct method programme MULTAN-80 was used for structure determination. The $\underline{E}$ map calculated with a set of phases having the highest figure of merit revealed a stereochemically meaningful fragment of thirty-five atoms. The structure was developed from this by Karle recycling procedure[7] followed by a weighted difference synthesis. The structure was refined by block diagonal least squares procedure to an $\underline{R}$ value of 0.065. The bond lengths and angles are given in Tables 1 and 2.

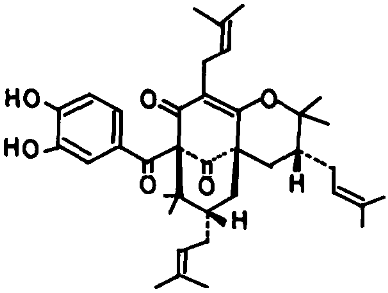
It appears that the fused tricyclic structure in V effectively prevents resonance between the two chromophores though they are adjacent to each other. This is confirmed by the bond length of 1 520 A between C2 - C10 which indicates its complete single bond character in isogarcinol, while that in xanthochymol was shown to be 1.440 Å, suggesting extensive resonance.[8] While steric inhibition of resonance is understandable, the above observation is remarkable for the total suppression of resonance as evidenced by the UV spectrum and the observed bond distances It is also interesting to note that though the resonance is suppressed, the tricyclic structures IV and V are considerably more stable to acid, base or heat treatment, compared to the bicyclic compounds I and III. These apparently contradicting features may be explained as due to the dipolar repulsions between the carbonyl group at C10 and the C1 - O1 and the C3 - O2 bonds, forcing the aroyl group out of the plane of the 1,3-diketone systems. [The ORTEP view (VII) of isogarcinol clearly shows that the orientation of the aroyl group is perpendicular to the plane of the diketone system.] Though such repulsions could also operate in the structures I and III, coplanarity (and thus conjugation) is achieved in these cases by hydrogen bonding of the enolic hydrogen to the C10 carbonyl group. In fact, the torsion angle C1 - C2 - C10 - O4 is 13.2° in xanthochymol is compared to -94.1° in isogarcinol, also, the values for C3 - C2 - C10 - C11 were 32.4° and -98.9° respectively.

It now seems that cambogin and isogarcinol represent the same structure, V, camboginol and garcinol (I) (which have identical physical and chemical properties, including the ^{13}C NMR spectrum) may also be identical, the reported difference in the UV spectra notwithstanding (see note 6). Direct comparison has not been possible. We wish to retain the names garcinol and isogarcinol for I and V in view of the fact they have been isolated from more than one <u>Garcinia</u> species, also, they bring out the interrelationships among the compounds more clearly.

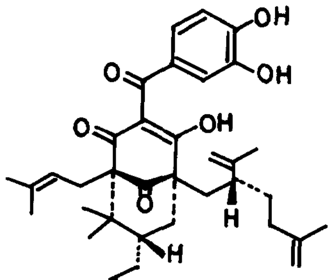
Acknowledgement. The authors wish to thank Dr.J.F.Blount, who kindly provided the coordinates for xanthochymol.



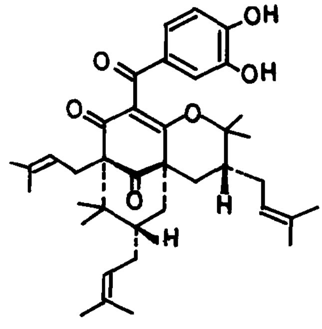
I



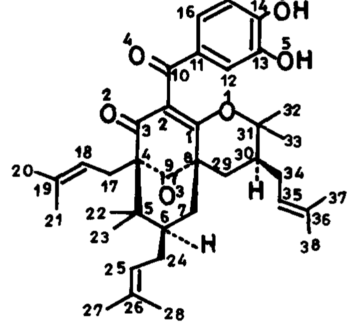
II



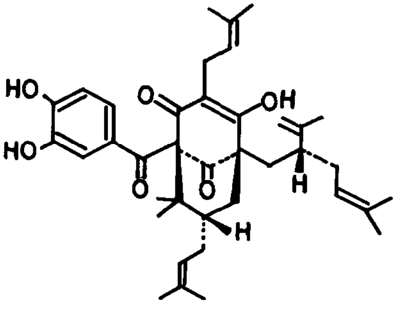
III



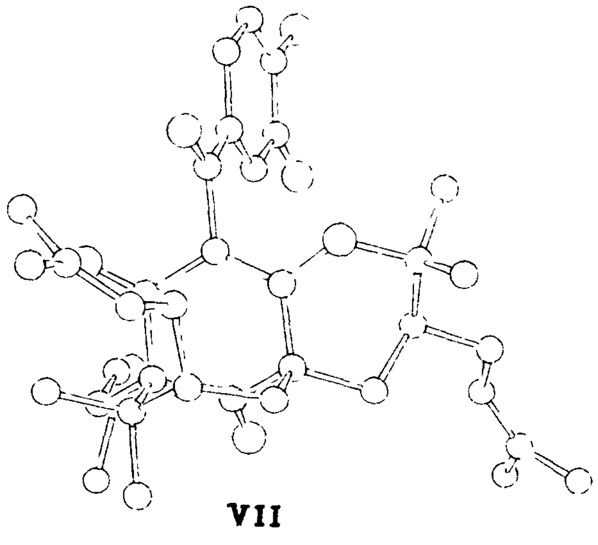
IV



V



VI



VII

Table 1. Bond lengths (Å) (Average standard deviation bond length is 0.008 Å)

C1 - O1	1.333	C3 - C4	1.530	C7 - C8	1.574	C15 - C16	1.396	C29 - C30	1.536
C3 - O2	1.209	C4 - C5	1.620	C8 - C9	1.525	C17 - C18	1.564	C30 - C31	1.511
C9 - O3	1.224	C4 - C9	1.494	C8 - C29	1.550	C18 - C19	1.326	C30 - C34	1.539
C10 - O4	1.234	C4 - C17	1.533	C10 - C11	1.464	C19 - C20	1.540	C31 - C32	1.557
C13 - O5	1.382	C5 - C6	1.548	C11 - C12	1.376	C19 - C21	1.494	C31 - C33	1.552
C14 - O6	1.361	C5 - C22	1.535	C11 - C16	1.409	C24 - C25	1.538	C34 - C35	1.533
C1 - C2	1.330	C5 - C23	1.548	C12 - C13	1.364	C25 - C26	1.302	C35 - C36	1.359
C1 - C8	1.513	C6 - C7	1.570	C13 - C14	1.373	C26 - C27	1.517	C36 - C37	1.566
C2 - C10	1.520	C6 - C24	1.565	C14 - C15	1.391	C26 - C28	1.551	C36 - C38	1.510

Table 2. Bond angles (degrees) (Average standard deviation in bond angle is 0.6°)

O1 - C1 - C2	118.6	C1 - C8 - C7	110.8	C4 - C17 - C18	112.4
O1 - C1 - C8	118.4	C1 - C8 - C9	106.7	C17 - C18 - C19	125.5
C2 - C1 - C8	122.8	C1 - C8 - C29	111.8	C18 - C19 - C20	118.9
C1 - C2 - C3	123.0	C7 - C8 - C9	105.5	C18 - C19 - C21	126.8
C1 - C2 - C10	120.6	C7 - C8 - C29	110.0	C20 - C19 - C21	114.3
C3 - C2 - C10	116.4	C9 - C8 - C29	111.9	C6 - C24 - C25	111.7
O2 - C3 - C2	121.1	O3 - C9 - C4	122.2	C24 - C25 - C26	124.2
O2 - C3 - C4	121.5	O3 - C9 - C8	122.1	C25 - C26 - C27	118.3
C3 - C4 - C5	109.7	C4 - C9 - C8	115.6	C25 - C26 - C28	126.1
C3 - C4 - C9	109.4	O4 - C10 - C2	119.2	C27 - C26 - C28	115.6
C3 - C4 - C17	108.2	O4 - C10 - C11	122.4	C8 - C29 - C30	110.7
C5 - C4 - C9	106.4	C2 - C10 - C11	118.4	C29 - C30 - C31	109.9
C5 - C4 - C17	110.5	C10 - C11 - C12	122.5	C29 - C30 - C34	110.1
C9 - C4 - C17	112.6	C10 - C11 - C16	118.2	C31 - C30 - C34	110.7
C4 - C5 - C6	111.8	C12 - C11 - C16	119.3	C30 - C31 - O1	108.1
C4 - C5 - C22	109.3	C11 - C12 - C13	121.9	C30 - C31 - C32	116.7
C4 - C5 - C23	108.6	O5 - C13 - C12	117.7	O1 - C31 - C32	104.3
C6 - C5 - C22	110.4	O5 - C13 - C14	121.8	C30 - C31 - C33	112.8
C6 - C5 - C23	108.4	C12 - C13 - C14	120.4	O1 - C31 - C33	102.2
C22 - C5 - C23	108.3	O6 - C14 - C13	119.3	C32 - C31 - C33	111.2
C5 - C6 - C7	110.3	O6 - C14 - C15	121.7	C30 - C34 - C35	109.5
C5 - C6 - C24	116.6	C13 - C14 - C15	119.0	C34 - C35 - C36	128.3
C7 - C6 - C24	112.3	C14 - C15 - C16	121.6	C35 - C36 - C37	120.2
C6 - C7 - C8	115.3	C11 - C16 - C15	117.9	C35 - C36 - C38	120.2
				C37 - C36 - C38	119.5

References and notes:

1. N. Krishnamurthy, Y. S. Lewis and B. Ravindranath, Tetrahedron Lett., 22, 793 (1981).
2. C. G. Karanjgaokar, A. V. Rama Rao, K. Venkataraman, S. S. Yemul and K. J. Palmer, Tetrahedron Lett., 4977 (1973).
3. A. V. Rama Rao, G. Venkataswamy and A. D. Pendse, Tetrahedron Lett., 21, 1975 (1980).
4. The isomerisation is conveniently carried out by heating the compound (garcinol) on an oil bath to about 200° for about 10 min. HPLC analysis of the product (Column: Bondapak CN; mobile phase: chloroform containing 1% acetic acid; flow rate: 2.0ml/min.; detector 280nm) showed it to be a mixture of at least six compounds, isogarcinol being predominant. Garcinol and isogarcinol had k' values of 2.4. and 5.4 respectively.
5. A. V. Rama Rao, G. Venkataswamy and S. S. Yemul, Indian J. Chem., 19B, 627 (1980).
6. The UV spectrum of garcinol in ethanol is quite stable and the solution is yellow in colour. However, presence of a trace of alkali or acid caused decolourisation of the solution and the absorption maxima shifted to 232 and 278 nm.
7. J. Karle, Acta Cryst., B24, 182 (1968).
8. J. F. Blount and T. H. Williams, Tetrahedron Lett., 2921 (1976).

(Received in UK 11 March 1982)