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Camboginol and Cambogin

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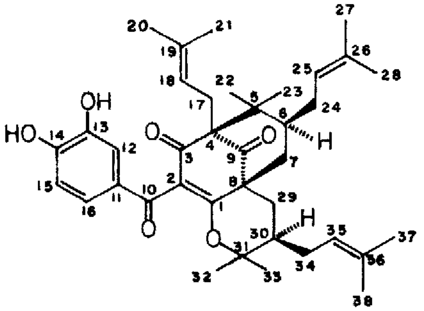
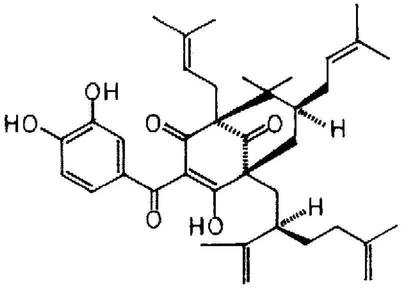
Two isoprenylated benzophenone derivatives, camboginol and cambogin, have been isolated from the latex of Garcinia cambogia. The structure of camboginol and its conversion to cambogin, an enantiomer of isoxanthochymol, has been deduced.

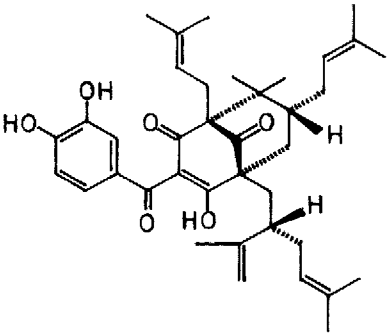
Earlier we have reported the isolation of two isoprenylated benzophenone derivatives, xanthochymol and isoxanthochymol, from the fruits of *Garcinia xanthochymus*, and the structure of isoxanthochymol (I) as determined from the X-ray crystallographic analysis of its di-*p*-bromobenzensulfonate.[1,2] Subsequently, Blount and Williams[3] have determined the X-ray structure for xanthochymol as (II). We now wish to report the structure of camboginol (III) and its conversion to cambogin (IV), both isolated (surprisingly in large quantities) from the latex of *G. cambogia*.



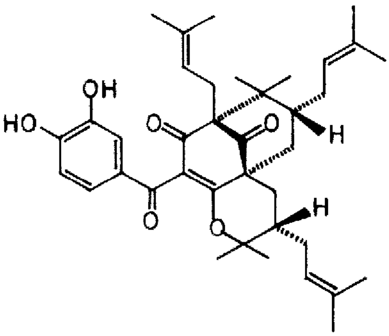
I



II



III



IV

Camboginol, m.p. 132° , $[\alpha]_D^{30}$ - 132.9° (1% $CHCl_3$), was obtained in 37% yield from the latex by a simple crystallisation from pet.ether (60-80°). Chromatography of the remaining residue over a column of silica gel and eluting with hexane gave cambogin (5.5%), m.p. 242° $[\alpha]_D^{30}$ - 209.9° (1% MeOH) in addition to some camboginol.

Camboginol, $C_{38}H_{50}O_6$, $M^{+\cdot}$ 602 [λ_{max} 230 and 281 nm (ϵ 14,960 and 13880): ν max. broad band at 3200-3400 (phenolic OH groups), 1715 and 1660 cm^{-1} (a sixmembered cyclic C=O and a conjugated C=O respectively], resembles closely xanthochymol in several chemical and spectral properties. It shows colour reactions characteristic of catechol group and forms an octahydro derivative (H_2, Pd/c) indicating the presence of four ethylenic double bonds in which the chromophore remains intact. On methylation (DMS, K_2CO_3 in acetone), it gave a mixture of two isomeric trimethyl ethers with nearly identical spectral properties, which on alkaline hydrolysis (5% ethanolic NaOH) gave a dimethyl ether ($M^{+\cdot}$ 630) suggesting the presence of vinylogous ester grouping derived from a β-diketonic function capable of enolising in the alternate directions.

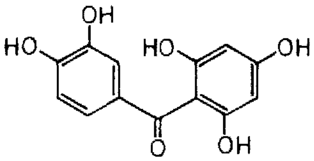
The ^1H NMR spectrum of camboginol in $CDCl_3$ shows the presence of three aromatic protons characteristic of 3,4-dihydroxybenzoyl group [7.05(q); 6.95(d; J=2 Hz), 6.58 (d; J=9 Hz)], three isopropylidine groups (a broad triplet of 3H at 4.9 and 6 Me groups at 1.56 and 1.7), one isopropenyl group (a broad singlet of 2H at 4.36 together with a Me signal around 1.7) and two methyl groups on a saturated carbon (two singlets of 3H each at 1.0 and 1.16), in addition to methylene and methine protons (a complex multiplet of 12H in the regions 1.4 to 2.9). Thus the significant difference in the ^1H NMR spectrum of camboginol compared to xanthochymol is the presence of one terminal methylene in the former while there are two such groups in the latter product.

The above findings are in agreement with the ^{13}C NMR spectrum of camboginol. It shows the presence of three methine carbons of trisubstituted olefinic groups ($CH=CMe_2$ x 3) as doublets at 124.0, 124.2 and 122.7 and a triplet at 112.7 for a terminal methylene carbon ($C(Me)=\underline{C}H_2$). The other assignments are: 209.1 (C-9, non-enolisable $\underline{C}=O$), 194.1, 195.1, 198.9 (C-1, 3, 10; enolisable $\underline{C}=O$); 132.0, 132.9 and 135.3 (C-19, 26, 36; = $\underline{C}Me_2$), 148.1 (C-31; C(Me)=CH_2); 116.6, 114.4, 120.2 (C-12, 15,16; Ar-C-H); 143.8, 150(C-13, 14. Ar-C-OH); 127.8 (C-11; Ar-C-C=O); 116.0 (C-2), 69.8, 58.0 (C-4,8); 49.6 (C-5), 47.0, 43.7 (C-6, 30), 27.0, 29.0, 32.7, 36.3, 42.8 (5CH_2); 17.7, 17.9, 18.2, 25.8, 26.0 (6 Me, C=CMe); 22.7 (C(Me)=CH_2); 17.3 and 26.5 (ring CMe_2).

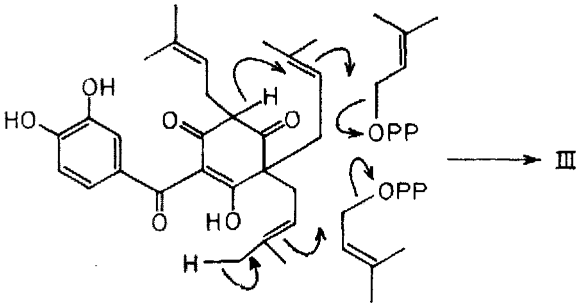
Cambogin, $C_{38}H_{50}O_6$ ($M^{+\cdot}$ 602) shows similar colour reactions, UV and IR as that of isoxanthochymol. On methylation it gave only one dimethyl ether, stable to alkaline hydrolysis and forms a crystalline hexahydro derivative, (H_2, Pd/c) showing the presence of three ethylenic bonds. Ozonolysis of cambogin dimethyl ether followed by oxidation with the Jones reagent and esterification (DMS, K_2CO_3 in acetone) gave a product containing three CH_2COOMe groups. The ^1H NMR spectrum of cambogin is superimposable with that of isoxanthochymol. The ^{13}C spectrum of cambogin (solvent DMSO-d_6) shows the absence of the terminal methylene group and identical with the spectrum of isoxanthochymol. From the fact it has identical chemical and spectral properties as isoxanthochymol but having exactly opposite specific rotation clearly shows that it is an enantiomer of isoxanthochymol. Thus cambogin has the structure with the absolute configuration as depicted in (IV).[4]

Camboginol has been converted to cambogin smoothly by refluxing with benzene solution containing traces of HCl or CF_3COOH. The conversion can also be achieved thermally in a much better way by heating camboginol at 200° for 5 min. The conversion of camboginol to cambogin clearly demonstrated the structure of the former having the absolute configuration as shown in (III).

Biogenetically all these "isoprenylated benzophenone" derivatives might have been derived from maclurin (V) which was regarded as a precursor for many xanthones in higher plants.[5] Reaction of three dimethylallyl pyrophosphate (DMAPP) units on the phloroglucinol ring of maclurin can give rise to an intermediate (VI), which can further react with two additional DMAPP to give camboginol (III). Alternatively, reaction of (VI) with one DMAPP and a isopentenylpyrophosphate may lead to xanthochymol (II). It is significant to note that two different species of *Garcinia* yield enantiomers of a compound with four asymmetric centres. The enzyme which triggers this stereospecific mechanism must be specific.



V



VI

References

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2. G. Venkatswamy, S.S. Yemul, A.V. Rama Rao and K.J. Palmer, Ind. J.Chem. 13, 1355 (1975).

3. J.F. Blount and T.H. Williams, Tetrahedron Letters 2921 (1976).

4. Cambogin was first isolated by Prof. B.R. Pai and his colleagues at Presidency College, Madras, from *G. cambogia* roots and its structure was determined by X-ray crystallographic analysis. See also A.V. Rama Rao, G. Venkatswamy and S.S. Yemul, Chem. and Ind. 92 (1979).

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