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REVIEW ARTICLE

XANTHONES IN HIGHER PLANTS: BIOGENETIC PROPOSALS AND A CHEMOTAXONOMIC SURVEY

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Abstract—The various proposals concerning xanthone biogenesis in higher plants are assessed. A survey of the distribution of xanthones in angiosperms is given.

It is now 8 years since Roberts[1] reviewed the naturally occurring xanthones. Of the eleven xanthones of angiosperm origin then known, seven occurred in the Gentianaceae, three in the Guttiferae and one (mangiferin) in many families. Since that time, over seventy new xanthones have been found in higher plants. Of these, twenty occur in the Gentianaceae and about fifty in the Guttiferae.

Although biogenetic proposals have already been made[7] concerning the co-occurrence of biphenyls (aucuparins) and xanthones in *Kielmeyera* species, re-assessment of the existing information favours an alternative suggestion that xanthones in higher plants are formed by *direct* oxidative coupling of hydroxybenzophenones.

POSSIBLE BIOGENETIC PATHWAYS

Some xanthones in lower plants have been proved to be totally acetate derived, e.g. griseoxanthone (I), from seven acetate units (Scheme A).[2,3] However, the oxygenation patterns of all xanthones in higher plants suggest that these are formed by a mixed shikimate–acetate pathway. This involves the condensation of shikimate[26] and acetate-derived moieties to form benzophenones or benzophenone-like intermediates which then react intramolecularly to form xanthones. Mechanisms for this intramolecular reaction have been postulated involving either direct phenol oxidative coupling,[4] quinone addition,[5] dehydration between hydroxyl groups on the acetate and shikimate-derived rings[6] or spirodienone formation and subsequent rearrangement to form the xanthone[7] (Schemes B–E).

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[1] J. C. Roberts, *Chem. Rev.* **61**, 591 (1961).

[2] A. J. Birch, R. A. Massy-Westrop, R. W. Rickards and H. Smith, *J. Chem. Soc.* 630 (1958).

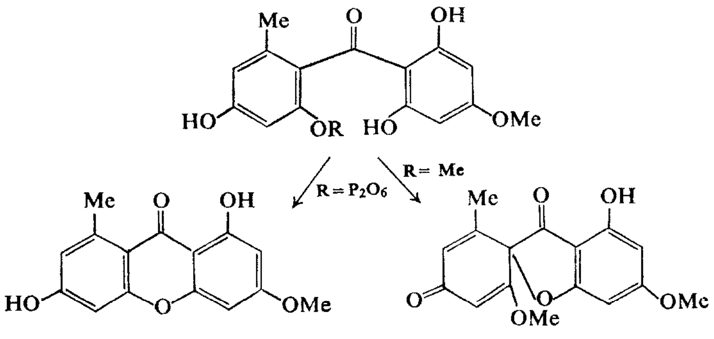
[3] W. J. McMaster, A. I. Scott and S. Tripett, *J. Chem. Soc.* 4628 (1960).

[4] J. R. Lewis, *Proc. Chem. Soc.* 373 (1963).

[5] R. C. Ellis, W. B. Whalley and (in part) K. Ball, *Chem. Comm.* 803 (1967).

[6] K. R. Markham, *Tetrahedron* **21**, 3687 (1965); and previous papers.

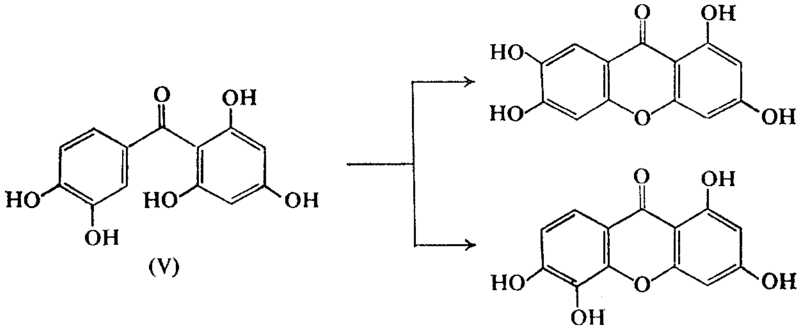
[7] O. R. Gottlieb, *Phytochem.* **7**, 411 (1968).



(I)

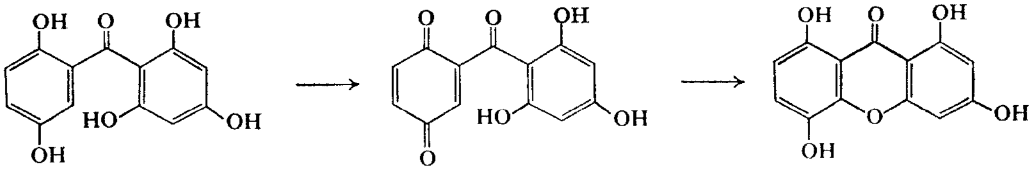
(XVIII)

Scheme A.

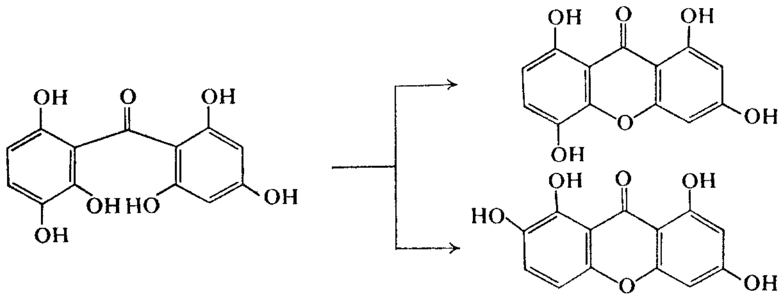


(V)

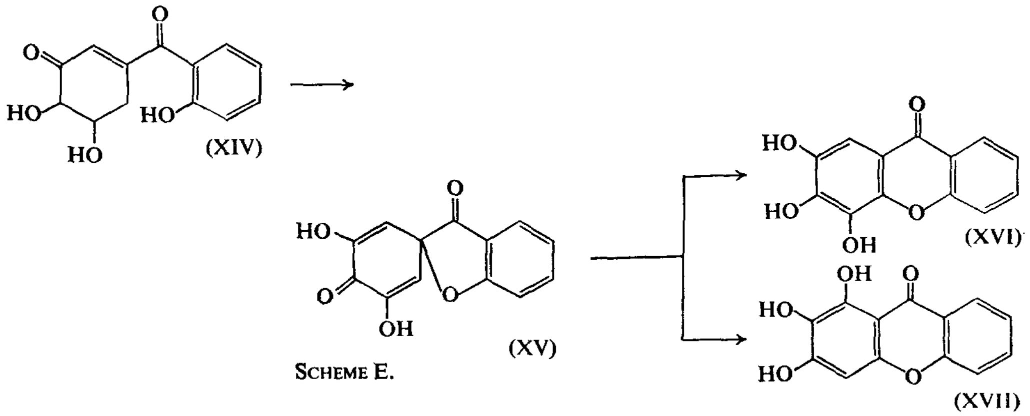
Scheme B.



Scheme C.



Scheme D.



Scheme E.

Gottlieb[7] advocates the spirodienone mechanism (Scheme E) but there is substantial evidence that the phenol oxidative coupling of benzophenones to form xanthones directly (Scheme B) occurs in higher plants.[8,9] Thus a benzophenone is probably formed by condensation of a shikimate-derived moiety, conveniently represented in Fig. 1 by A, B, C or D with an acetate-derived moiety represented by the phenols E, F or G, but it is impossible to say, at this time, at which stage loss or gain of oxygen and cyclization occur. The acetate-derived part as an acyclic β-triketide probably condenses with the shikimate unit as suggested by Wolfrom,[10] and recently supported by the work of Lewis;[9] the above notation is used merely for convenience. In each case linkage is considered to occur at a position *ortho* to an

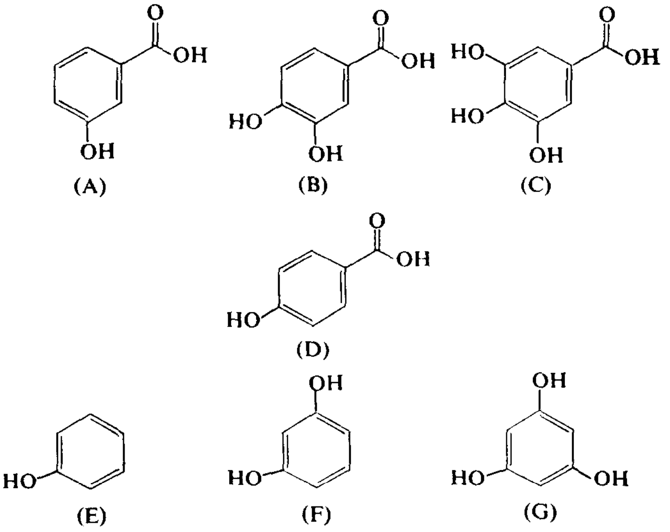


Fig. 1.

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[8] H. D. Locksley, I. Moore and F. Scheinmann, *Tetrahedron* **23**, 2229 (1967).

[9] J. E. Atkinson, P. Gupta and J. R. Lewis, *Chem. Comm.* 1386 (1968); *Tetrahedron* **24**, 1507 (1969).

[10] M. L. Wolfrom, F. Komitsky Jr., G. Fraenkel, J. H. Looker, E. E. Dickey, P. McWain, A. Thompson, P. M. Mundell and O. M. Windrath, *J. Org. Chem.* **29**, 692 (1964).

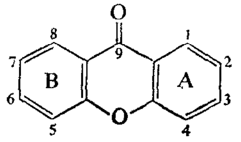
hydroxyl in the acetate-derived ring. For the resorcinol unit F (Fig. 1) the carbonyl group of the derived xanthone is located preferentially between the two resorcinol oxygen functions rather than at a position *ortho* and *para* to each. Thus 1,5- and 1,7-dihydroxyxanthones occur frequently in higher plants, whereas 3,7- and 3,5-dihydroxyxanthones have not been isolated.

Such condensations could give rise to twelve benzophenones (AE, AF etc) (or sixteen if one includes those formed from F by condensation at C-4). Of these twelve benzophenones, nine could undergo phenol oxidative coupling to give a total of fifteen different xanthones† directly (described hereafter as "standard" xanthones). (See Table 1.) Twelve of these "standard" xanthones and a derivative of a thirteenth, formed by additional oxidation, are known. Xanthones having these "standard" oxygenation patterns are indicated (*) in Table 3. No examples of 5,6- or 1,3,5,6,7-oxygenated-xanthones have yet been reported. but on these grounds would be anticipated. Where oxygen functions occur at other than "standard" positions they are always at positions which are either *ortho* or *para* to the "standard" oxygen functions, suggesting that this oxidation might involve quinone formation. If this occurs at the benzophenone stage, xanthone formation may then occur by the quinone addition mechanism suggested by Whalley[5] (Scheme C). The direct oxidative coupling mechanism (Scheme B) affords an explanation for the following observed phenomena:

TABLE 1. BENZOPHENONES AND THE POSITIONS OF OXYGEN IN THE "STANDARD" XANTHONES DERIVED FROM THEM

Benzophenone	Xanthones	
AE	5-	7-
AF	1,5-	1,7-
AG	1,3,5-	1,3,7-
BE	5,6-	6,7-
BF	1,5,6-	1,6,7-
BG	1,3,5,6-	1,3,6,7-
CE	5,6,7-	
CF	1,5,6,7-	
CG	1,3,5,6,7-	

1. Every xanthone so far isolated from higher plants has an oxygen function at C-5 and/or C-7.‡ In order to undergo phenol oxidative coupling to yield a xanthone directly, a benzophenone must have at least one hydroxyl group in each ring, one at C-2 and one at C-3′. In the



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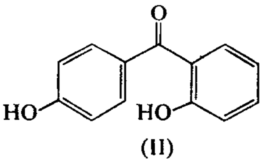
† The numbering system is based on xanthen-9-one as the parent compound. For xanthones in higher plants, we adopt the convention throughout the text that the higher numbered ring is of shikimate derivation.

‡ When there is an oxygen function both at C-5 and C-7 there is always an oxygen at C-6 (Table 3).

simplest case the benzophenone would yield 5- or 7- (≡ 4- to 2-) hydroxyxanthone, depending upon whether coupling occurred *ortho* or *para* to the shikimate hydroxyl group. Any xanthone formed in this way would inevitably have hydroxyl groups at one or both of these positions.

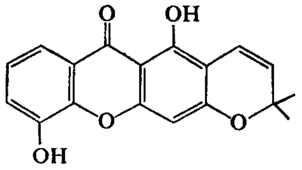
2. No xanthone has yet been isolated from higher plants having a single oxygen function in the shikimate ring at C-6. This follows from 1 above since the "precursor" (II) of such a xanthone would be unable to undergo phenol oxidative coupling to yield the xanthone in one step.



(II)

3. The alternative xanthones having oxygen functions at C-5 and C-7 sometimes co-occur within a species and frequently co-occur within a genus or family. A striking example of this occurs among the xanthones isolated so far from the Gentianaceae. Seventeen of these are based on 1,3,7-trihydroxyxanthones while the other twelve are based on 1,3,5-trihydroxyxanthones. There are many other examples, e.g. 5- and 7-hydroxyxanthones (*Mammea americana*)[11, 12] 1,5- and 1,7-dihydroxyxanthones, 1,5,6- and 1,6,7-trihydroxyxanthones and 1,3,5,6- and 1,3,6,7-tetrahydroxyxanthones (all in *M. africana*)[13] and 6-desoxyjacareubin (III) and osajaxanthone (IV) (in *Calophyllum scriblitifolium*).[14]

4. In rare cases, the benzophenone has been found to co-occur with its daughter xanthone(s): the only examples are maclurin (V) with 1,3,5,6- and 1,3,6,7-tetrahydroxyxanthones (in *Symphonia globulifera*)[8] and 2,3′,4,6-tetrahydroxybenzophenone (VI) with 1,3,7-trihydroxyxanthone (in *Gentiana lutea*).[9] 1,3,6,7-Tetrahydroxyxanthone co-occurs



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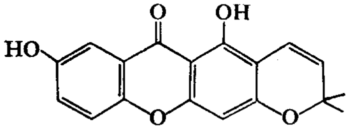

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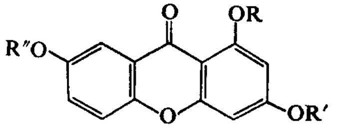
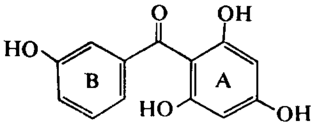


(VII) a. R = R′ = R″ = H
b. R = R″ = H; R′ = Me
c. R = R′ = H; R″ = Me
d. R = H; R′ = R″ = Me
e. R = R′ = R″ = Me



(VI)

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[11] R. A. Finnegan and P. L. Bachmann, *J. Pharm. Sci.* **54**, 633 (1965).

[12] R. A. Finnegan, J. K. Patel and P. L. Bachmann, *Tetrahedron Letters* 6087 (1966).

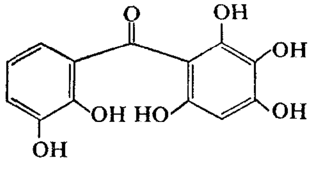
[13] I. Carpenter, unpublished work.

[14] B. Jackson, H. D. Locksley and F. Scheinmann, *J. Chem. Soc.* (c) 2500 (1967).

with maclurin in *Chlorophora tinctoria* (L.) Gaud. (=*Morus tinctoria* L.) (Moraceae) although[40a] the xanthone may be an artefact formed during extraction.

Lewis and co-workers have recently reported[9] the co-occurrence of the benzophenone (VI) with 1,3,7-trioxygenated xanthones (VIIa–e) in *Gentiana lutea*. Tracer experiments show[9] that *l*-phenylalanine is incorporated *in vivo* into benzophenone (VI) as the carbonyl group and ring B, and that acetate is incorporated predominantly into ring A. The benzophenone (VI) is subsequently converted into the xanthones (VIIa–e). These observations provide the most recent *in vivo* evidence concerning the biogenesis of xanthones in higher plants and suggest very strongly that the xanthones are formed directly from the benzophenone by phenol oxidative coupling.

Although the dehydration mechanism (as pyrophosphate elimination) (Scheme D) can also account for xanthone formation, direct oxidative coupling of the benzophenone leads to a simpler explanation of the wide variety of oxidation patterns in xanthones. The four principal oxidation patterns observed in the xanthones from *Frasera albicaulis* (Gentianaceae),[16] viz. 1,2,3,5-, 1,3,4,5-, 1,2,3,7- and 1,3,4,7, require for dehydration, two benzophenone precursors (VIII and IX) whereas for cyclization by coupling only one benzophenone (X) would be needed. The 1,3,5,8- and 1,3,7,8-tetrahydroxyxanthones from the *Gentiana* and *Swertia* genera all appear to have the benzophenone (VI) as their precursor. Oxidation of the benzophenone (VI) at both positions C-2′ and C-6′ yields the benzophenone (XI) which can cyclize by dehydration in two ways to yield either 1,3,5,8- or 1,3,7,8-tetraoxyxanthones. However, oxidation of the benzophenone (VI) at only one of the positions C-2′ and C-6′ yields two benzophenones (XII and XIII), each of which can cyclize by phenol oxidative coupling in a unique way to yield the 1,3,5,8- and 1,3,7,8-tetraoxyxanthones respectively. The quinone addition mechanism[5] would involve prior formation of an *ortho* or *para* quinone by introduction of oxygen at either C-2′ or C-6′ followed by cyclization, and this pathway cannot be excluded.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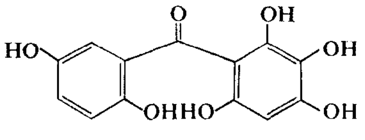
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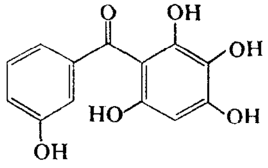
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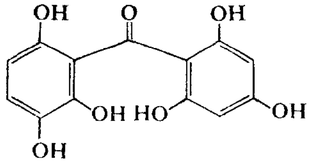
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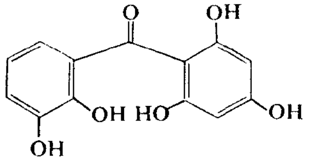
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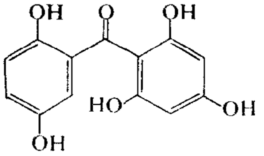
(XIII)

Gottlieb has recently suggested[7] that xanthones in higher plants might be formed from benzoylcyclohexenone precursor (XIV) which could give rise to a spirodienone (XV) (Scheme E). Transformation of this by dienone-phenol rearrangements would yield the isomeric xanthones (XVI and XVII). For this mechanism to occur, the presence of a hydroxyl

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[15] H. D. LOCKSLEY, I. MOORE and F. SCHEINMANN, *J. Chem. Soc.* (C) 430 (1966).

[16] E. N. CHRISTENSEN, Ph.D. Thesis, Univ. Washington (1967), via *Diss. Abs.* (B) **28**, 1851 (1968). G. H. STOUT, E. N. CHRISTENSEN, W. J. BALKENHOL and K. L. STEVENS, *Tetrahedron* **25**, 1961 (1969).

group *para* to the carbonyl substituent is essential and contrasts with the necessity for such a group of the *meta* position if phenol oxidative coupling is to yield a xanthone directly. Significantly, the benzophenone (VI) which is metabolized by *Gentiana lutea* to genitsein does not have a hydroxyl group at the position necessary for spirodienone formation.

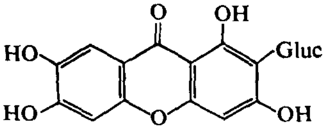
In support of the spirodienone mechanism for xanthone formation the co-occurrence of spirans and xanthones in micro-organism has been cited.[7] However, in this case the spirans are end products and the xanthones are formed by an alternative mechanism[3, 17] (Scheme A). Furthermore, spiranic intermediates have never been isolated from higher plants which contain xanthones.

For pyranoxanthones and isoprenylxanthones we have used the concept that isoprenylation occurs *after* xanthone formation, *ortho* or *para* to a hydroxyl group. Oxidative cyclization of the side-chain onto the adjacent hydroxyl group leads to the pyranoxanthone. Thus for jacareubin the sequence is probably an extension of Scheme B, viz. maclurin → 1,3,5,6-tetrahydroxyanthone → the isoprenyl xanthone (XXVIII) → jacareubin (XXVII).[8, 40b] In support of this suggestion it has been found that xanthones in sequences of this type co-occur in several species, and that this pathway provides a useful synthetic route to pyranoxanthones.[40b] The observed fact that certain naturally occurring xanthones have methoxyl or methylenedioxyl groups involving C-5 and/or C-7 positions suggests that methylation occurs after xanthone formation in these cases.

It is noteworthy that 4-phenylcoumarins[67] and biflavanones[32] occur in the nuts and/or heartwood of certain species which contain xanthones, but any biogenetic relationships between xanthones and flavonoids remains obscure.

TAXONOMIC ASPECTS

Xanthones, other than mangiferin (XIX) which will be considered separately, have been isolated from only four or five families, viz. Gentianaceae, Guttiferae, Hypericoideae (included by Engler and Prantl[19] in Guttiferae), Moraceae and Polygalaceae. These families are not generally regarded[19–22, 30] as being closely related.



(XIX)

[17] A. Rhodes, B. Boothroyd, M. P. McGonagle and G. Somerfield, *Biochem. J.* **81**, 28 (1961); J. F. Grove, *Fortsch. Chem. Org. Naturstoffe* **22**, 203 (1968).

[18] See Ref. 7, Table 1.

[19] A. Engler's *Syllabus der Pflantzenfamilien*, Vol. II, revised by P. Melchior, Bortraeger, Berlin (1964).

[20] Appendix to J. C. Willis, *A Dictionary of the Flowering Plants and Ferns*, 7th Ed. Cambridge University Press (1966).

[21] J. Hutchinson, *The Families of Flowering Plants*, 2nd Ed., Oxford University Press, London (1959).

[22] G. H. M. Lawrence, *Taxonomy of Flowering Plants*, p. 114. Macmillan, New York (1951).

[23] A. Ueno, *Yakugaku Zasshi* **82**, 1482, 1486 (1962), seen in *Chem. Abs.* **59**, 736 (1963).

[24] Mazakazu Maritomi and Toshio Kawasaki, *Chem. Pharm. Bull. Japan* **16**, 760 (1968).

[25] A. H. Williams, *Nature* **202**, 824 (1964).

[26] P. M. Derwick and E. Haslam, *Chem. Comm.* 673 (1968).

[27] T. Swain, *Mem. Soc. Bot. Fr.* 184 (1965).

[28] V. Plouvier, J. Massicot and P. Rivaille, *C. R. Acad. Sci. Paris* (*D*) **264**, 1219 (1967).

[29] M. Guyot, J. Massicot and P. Rivaille, *C. R. Acad. Sci. Paris* (*C*) **267**, 423 (1968).

[30] A. Cronquist, *The Evolution and Classification of Flowering Plants*, p. 129, Nelson, London (1968).

Mangiferin (XIX), the 2-*C*-β-glucoside of 1,3,6,7-tetrahydroxyxanthone occurs widely among angiosperms and has also been reported in a fern with its aglycone[23] and with mangiferin 3-methyl ether in *Mangifera indica* L. (Anacardiaceae)[24] but has never been reported to co-occur with any other xanthone. Instead, it commonly occurs with flavonoid glycosides.[27] Although of no taxonomic significance in the broad sense, its presence or absence at species level may be significant.[25, 42] The distribution of mangiferin (XIX) is summarized in Table 2. Xanthone glycosides are not common. Apart from mangiferin, a *C*-glycoside, the only reported examples of *O*-glycosides are gentianacauloside[28] (*Gentiana acaulis*, Gentianaceae), gentioside[28] (*G. lutea*) and swertianolin[1] (*Swertia japonica*, Gentianaceae). Euxanthic acid, 1-hydroxy-7-*O*-glucuronyl xanthone occurs[1] in the urine of cows fed on mango leaves, which contain mangiferin.

TABLE 2. THE DISTRIBUTION[19] OF MANGIFERIN

Class	Sub. class	Order	Family	Species	Ref.
Filices	Leptosporangiatae	Filicales	Polypodiaceae	*Athyrium mesosorum*	23
Dicotyledoneae	Archichlamydeae	Guttiferales	Guttiferae	*Hypericum acutum*	53
				H. chinense	53
				H. humifusum	53
				H. montanum	53
				H. nummularium	53
				H. pulchrum	53
		Rosales	Leguminosae	*Hedysarum obscurum*	46
		Rutales	Malphighiaceae	*Hiptage madablota*	47
		Sapindales	Anacardiaceae	*Mangifera indica*	48
		Celastrales	Hippocrateaceae	*Salacea prunoides*	49
		Violales	Flacourtiaceae	*Flacourtia indica*	50
				Aphloia theaeformis	51
				A. madagascariensis	52
	Sympetalae	Ebenales	Sapotaceae	*Madhuca utilis*	44
		Tubiflorae	Convolvulacea	*Cuscuta reflexa*	45
Monocotyledoneae		Liliiflorae	Liliaceae	*Anemarrhena rhizoma*	43
				Smilax glycyphylla	25
			Iridaceae	All spp. of *pogoniris* section	42
				Iris pseudacorus	42
				Iris dichotoma	42
				Belamcanda chinensis	42
				Crocus aureus	41
		Graminales	Gramineae	*Cymbopogon afronardus*	41

CORRELATION OF XANTHONE OXYGENATION PATTERN WITH SYSTEMATIC DISTRIBUTION

Over eighty other naturally occurring xanthones have now been isolated from about forty species distributed between four families (Table 3). The extent to which "standard" xanthones undergo additional oxidation seems to vary between families. The phenomenon is, as yet, unknown in the Moraceae, rare in the sub-families (of Guttiferae), Calophylloideae, Clusioideae and Moronoboideae and relatively common in the sub-family Kielmeyeroideae, although in no case is more than one additional oxygen function involved. Xanthones with additional oxygens are also found in the Gentianaceae and Polygalaceae. The twenty-nine xanthones of the Gentianaceae all appear to be based on "standard" 1,3,5- and 1,3,7-trihydroxyxanthones which are usually modified by further oxygenation at one or two of the positions 2-, 4- and 8-. Only three of the xanthones isolated from Gentianaceae have been found elsewhere.[31,32] The Guttiferae and Moraceae (the xanthones from which resemble one another) seem to produce a much wider range of "standard" xanthones (Table 3).

[31] J. Moron, J. Polonsky and H. Pourrat, *Bull. Soc. Chim. Fr.* 130 (1967).

[32] B. Jackson, H. D. Locksley and F. Scheinmann, *J. Chem. Soc.* (c) 1969, in press.

[33] M. M. Krahn, Ph.D. Thesis, Univ., Washington (1968), via *Diss. Abs.* (B) **29** (3), 941 (1968).

[34] M. L. Wolfrom, F. Komitsky, Jr., and P. M. Mundell, *J. Org. Chem.* **30**, 1088 (1965).

[35] P. Yates and G. H. Stout, *J. Am. Chem. Soc.* **80**, 1691 (1958).

[36] O. R. Gottlieb, personal communication.

[37] H. D. Locksley, I. Moore and F. Scheinmann, *J. Chem. Soc.* (c), 2186 (1966).

[38] H. D. Locksley and I. G. Murray, *J. Chem. Soc.* (c), in press.

[39] G. H. Stout, V. F. Stout and M. J. Welsh, *Tetrahedron* **19**, 667 (1963).

[40] A. Jefferson and F. Scheinmann, (a) *Nature* **207**, 1193 (1965); (b) *J. Chem. Soc.* (c) 175 (1966).

[41] E. C. Bate-Smith, *Bull. Soc. Bot. Fr.* 16 (1965).

[42] E. C. Bate-Smith and J. B. Harborne, *Nature* **198**, 1307 (1963).

[43] N. Morita, *Yakugaku Zasshi* **85**, 374 (1965).

[44] B. J. Hawthorne, N. F. James, F. E. King and J. W. W. Morgan, in *Chemistry of Natural and Synthetic Colouring Matters*, p. 331 (edited by T. S. Gore), Academic Press, New York (1962).

[45] S. S. Subramanian and A. G. Nair, *Indian J. Chem.* **4**, 335 (1966).

[46] L. Horhammer and H. Wagner, in *Recent Developments in the Chemistry of Natural Phenolic Compounds* (edited by W. D. Ollis), p. 192, Pergamon Press, Oxford (1961).

[47] R. A. Finnegan, R. A. Stephani, G. Ganguli, S. N. Ganguli and A. K. Bhattacharya, *J. Pharm. Sci.* **57**, 1039 (1968).

[48] S. Iseda, *Bull. Chem. Soc. Japan* **30**, 625 (1957).

[49] J. D. Ramanathan and T. S. Seshadri, *Current Sci.* **29**, 131 (1960).

[50] E. C. Bate-Smith, *J. Linn. Soc.* (*Botany*) **88**, 144 (1963)—(Mangiferin was detected but erroneously reported as euxanthone).

[51] R. R. Paris and E. Etchepare, *Compt. Rend.* **258**, 5277 (1964).

[52] D. Billet, J. Massicot, C. Mercier, D. Anker, A. Mastchenco and C. Mentzer, *Bull. Soc. Chim. Fr.* 3006 (1965).

[53] P. Lebreton and M. P. Bouchez, *Plant. Med. Phytother.* **1** (4), 188 (1967); *Biological Abstracts* **49**, 47248 (1968).

[54] E. Ritchie and W. C. Taylor, *Tetrahedron Letters*, No. 23, 1431 (1964).

[55] M. L. Wolfrom and H. B. Bhat, *Phytochem.* **4**, 765 (1965).

[56] O. R. Gottlieb, M. Taveira Magalhães, M. Camey, A. A. Lins Mesquita and D. de Barros Correa, *Tetrahedron* **22**, 1777 (1966).

[57] D. de Barros Correa, O. R. Gottlieb and M. Taveira Magalhães, *Ann. Acad. Brasil Cienc.* **38**, 296 (1966).

[58] G. M. Stephani, O. R. Gottlieb and M. Taveira Magalhães, unpublished work.

[59] L. D. Antonaccio, L. G. Fonseca e Silva, D. de Barros Correa, O. R. Gottlieb and M. Taveira Magalhães, *Ann. Acad. Brasil Cienc.* **37**, 229 (1965).

[60] L. D. Antonaccio, G. M. Stephani, O. R. Gottlieb and M. Taveira Magalhães, *Ann. Acad. Brasil. Cienc.* **37**, 231 (1965).

[61] O. R. Gottlieb, A. A. Lins Mesquita, E. M. da Silva and M. T. de Melo, *Phytochem*, **8**, 665 (1969).

[62] O. R. Gottlieb, M. Taveira Magalhães and G. M. Stephani, *Tetreahedron* **22**, 1785 (1966).

[63] G. G. de Oliveira, A. A. Lins Mesquita, O. R. Gottlieb and M. Taveira Magalhães, *Ann. Acad. Brasil. Cienc.* **39**, in press.

[64] G. G. de Oliveira, A. A. Lins Mesquita, O. R. Gottlieb and M. Taveira Magalhães, *Ann. Acad. Brasil. Cienc.* **38**, 421 (1966).

[65] Y. L. Chow and H. H. Quon, *Phytochem.* **7**, 1871 (1968).

[66] T. R. Govindachari, B. R. Pai, P. S. Subramaniam, U. R. Rao and N. Muthukumaraswamy, *Tetrahedron* **23**, 243 (1967).

[67] L. Crombie and D. E. Games, *Tetrahedron Letters* **49**, 145 (1966); *J. Chem. Soc.* 2545, 2553 (1967).

[68] M. Ottoni da Silva Pereira, O. R. Gottlieb and M. Taveira Magalhães, *Ann. Acad. Brasil. Cienc.* **39**, 225 (1967).

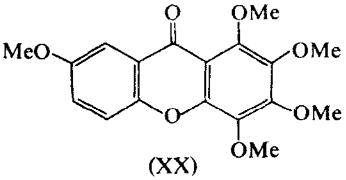
[69] F. E. King, J. T. King and L. C. Manning, *J. Chem. Soc.* 3932 (1953); 563 (1957).

[70] I. Carpenter, H. D. Locksley and F. Scheinmann, *J. Chem. Soc.* (c) 486 (1969).

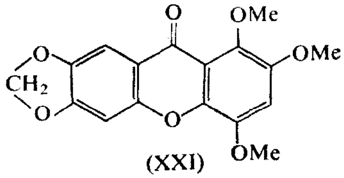
[71] T. R. Govindachari, B. R. Pai, P. S. Subramaniam, U. R. Rao and N. Muthukumaraswamy, *Indian J. Chem.* **6**, 57 (1968).

A number of xanthones has been isolated from species of the genus *Kielmeyera* (Guttiferae) having oxidation patterns which may be considered to be derived from "standard" xanthones by additional oxidation at C-8, i.e. 7,8-, 1,7,8- and 6,7,8-oxygenated xanthones. A 1,7,8-trioxygenated xanthone has also been found in *Calophyllum fragrans*[38] (Guttiferae) but otherwise these systems occur only in the genus *Kielmeyera*. The 5,6,7-trioxygenated xanthones which are quite common in this genus are unknown elsewhere. All species of the genus *Kielmeyera* so far examined have at least two of these unusual oxygenation patterns and this phenomenon appears to be peculiar to this genus.

Only one species in the Polygalaceae has so far yielded xanthones, namely *Polygala paenea*,[31] and the oxidation patterns of the two compounds present are taxonomically curious. Polygalaxanthone B (XX) shares with the xanthones from *Frasera albicaulis* (Gentianaceae) a "standard" 1,3,7-trihydroxyxanthone structure with additional oxygenation at C-2 and C-4. Polygalaxanthone A (XXI) which also has this additional oxygenation at C-2 and C-4 is, however, based on a "standard" 1,6,7-trihydroxyxanthone structure, other examples of which have been found only in the Guttiferae.[13, 32]



(XX)



(XXI)

ISOPRENOID SUBSTITUENTS

Substituents other than oxygen may have chemotaxonomic significance. Methyl- and chloro- groups, often present in xanthones from lower plants,[18] have not been reported but isopentenyl and geranyl substituents are found in many xanthones from the Guttiferae. Geranyl substituents have so far been reported to occur only in xanthones from some species of the genus *Garcinia*. In the case of gambogic acid[76] (XXII), this substituent is cyclized, but in the cases of rubraxanthone[16] (XXIII) (*G. rubra*) and the three xanthones cowaxanthone (XXXIX), cowanin (XL) and cowanol (XLI), recently isolated from *G. cowa* by Krahn,[33] the geranyl side-chain is unmodified. Isopentenyl substituents are common in the Guttiferae and Moraceae but are occasionally modified by terminal oxidation or by cyclization onto *ortho*-hydroxyl groups.[73, 78] Three examples are known of xanthones with two isopentenyl substituents, viz. macluraxanthone[10] (XXIV) and alvaxanthone[34] (XXV) from *Maclura pomifera* Raf. (Moraceae) and mangostin[35] (XXVI) from *Garcinia mangostana* (Guttiferae).

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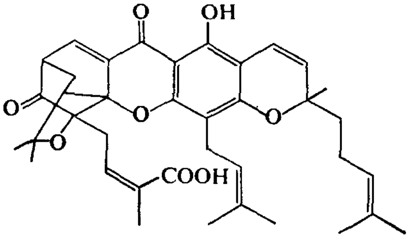
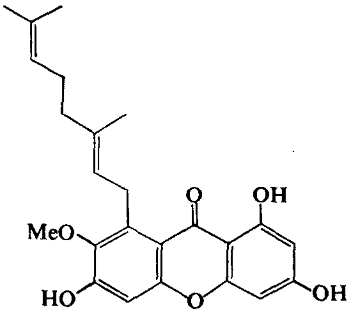
[72] B. Jackson, H. D. Locksley and F. Scheinmann, *J. Chem. Soc.* (c), 178 (1966).
[73] B. Jackson, H. D. Locksley and F. Scheinmann, *Tetrahedron* **24**, 3059 (1968).
[74] B. Jackson, H. D. Locksley and F. Scheinmann, *J. Chem. Soc.* (c), 785 (1967).
[75] B. Jackson, H. D. Locksley, (the late) I. Moore and F. Scheinmann, *J. Chem. Soc.* (c) 2579 (1968).
[76] W. D. Ollis, M. V. J. Ramsay, I. O. Sutherland and S. Mongolsuk, *Tetrahedron* **21**, 1453 (1965).
[77] P. Yates, S. S. Karmarkar, G. H. Stout and V. F. Stout, *Tetrahedron Letters* **24**, 1623 (1963).
[78] C. G. Karanjgaonkar, P. M. Nair and K. Venkataraman, *Tetrahedron Letters* 7, 687 (1966).
[79] D. B. Spoelestra and M. J. van Royen, *Rec. Trav. Chim.* **48**, 370 (1929).
[80] H. D. Locksley, I. Moore and F. Scheinmann, *J. Chem. Soc.* (c) 2186 (1966).
[81] H. D. Locksley, I. Moore and F. Scheinmann, *J. Chem. Soc.* (c) 2265 (1966).
[82] K. R. Markham, *Tetrahedron* **20**, 991 (1964).
[83] K. R. Markham, *Tetrahedron* **21**, 1449, 3687 (1965).
[84] W. J. Balkenhol, Ph.D. Thesis, Univ. Washington (1968), via *Diss. Abs.* (B) **29** (3) 929 (1968).
G. H. Stout and W. T. Balkenhol, *Tetrahedron* **25**, 1947 (1969).

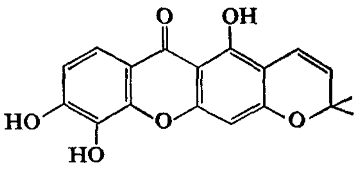


(XXII)



(XXIII)

Although the occurrence of the pyranoxanthone, jacareubin (XXVII) in *Kielmeyera ferruginea*[36] has recently been reported, its presence in each of the six species of *Calophyllum* so far examined suggests that it may have taxonomic value at the generic level in *Calophyllum*. The putative isoprenyl precursor (XXVIII) of jacareubin has been, so far, isolated exclusively from species of *Calophyllum*.



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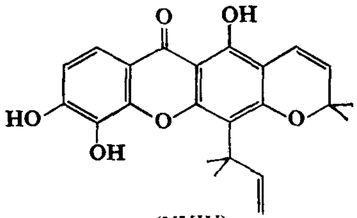

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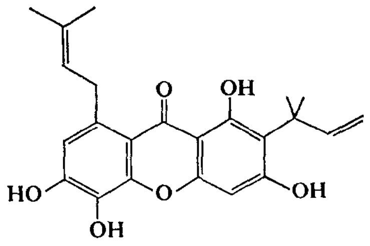

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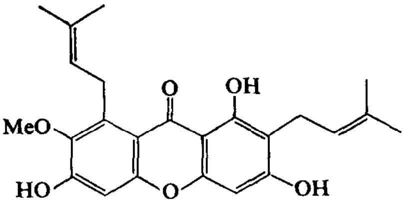

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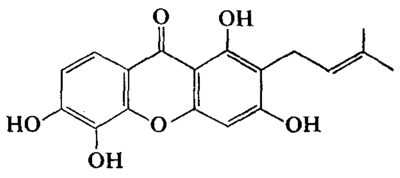

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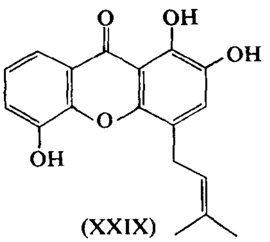

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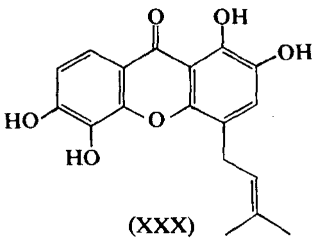

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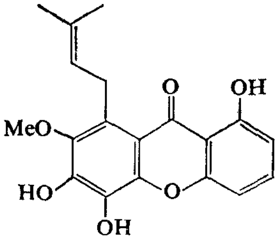
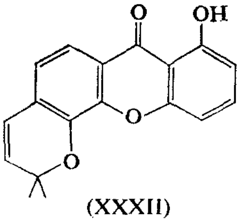


(XXXI)



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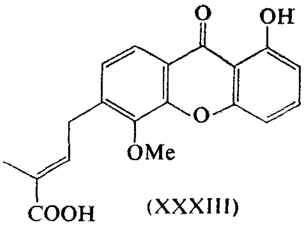

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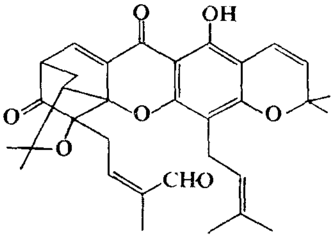

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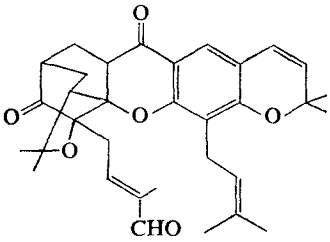

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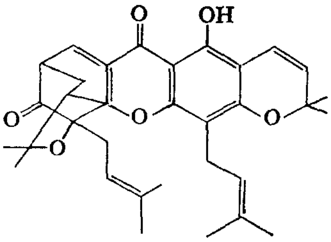

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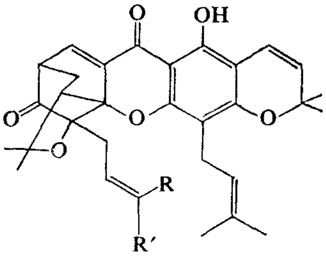
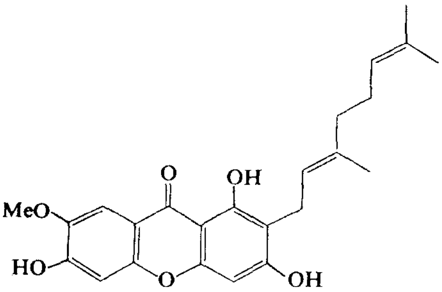
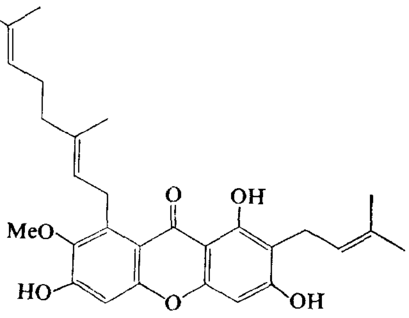


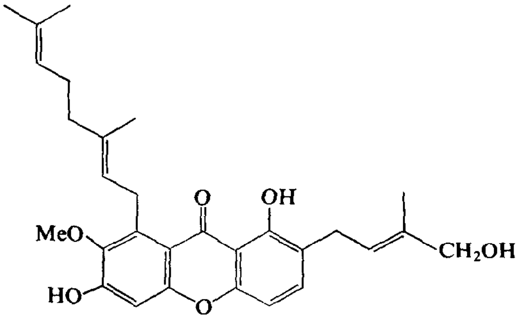
(XXXVII) R = COOH, R′ = CH_3
(XXXVIII) R = CH_3, R′ = COOH



(XXXIX)



(XL)



(XLI)

Celebixanthone (XXXI)[39] from *Cratoxylon celebicum* (Guttiferae) and 1,7-dihydroxyxanthone from *Harungana madagascariensis*[54] are the only xanthones isolated from any member of the sub-family Hypericoideae, apart from mangiferin (XIX) which occurs in a number of *Hypericum* species.[53] It would be of taxonomic interest to know whether any other member of this mainly herbaceous sub-family contains xanthones. Although Engler and Prantl[19] consider the Hypericoideae to be part of the family Guttiferae, Bentham and Hooker,[20] and Hutchinson[21] consider the taxon to be a separate, though closely related, family.

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Note added in proof

Direct comparison[85] has recently shown that "swertianol" is identical with bellidifolin (1,5,6-trihydroxy-3-methoxyxanthone). We suggest that this xanthone should now only be called bellidifolin as past references to "swertianol" refer to incorrect structures. The revised structures for descussatin and swertinin given in Table 3 have now been confirmed.[87]

The following xanthones have recently been isolated from the species indicated:

Swertia Japonica Makino contains:[85]

Norswertianin (1,3,7,8-tetrahydroxyxanthone)
Swertianin (1,7,8-trihydroxy-3-methoxyxanthone)
Methylswertianin (1,8-dihydroxy-3,7-dimethoxyxanthone)
Desmethylbellidifolin } Structures in Table 3
Bellidifolin }

Gentiana Kochiana Perr and Song contains:[86]

Gentiakochianin (=Swertianin[85])
Isogentiacaulin (3,8-dihydroxy-1,7-dimethoxyxanthone)
Decussatin (1-hydroxy-3,7,8-trimethoxyxanthone)

Swertia perennis L. contains:[87]

Swertiaperennin (=Methylswertianin[85])

Swertia decussata Nimino contains:[87]

Swertianin[85] (=gentiakochianin[87])

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[85] M. Komatsu, T. Tomimori and N. Mikuriya, *Chem. Pharm. Bull. Japan* **17**, (1), 155 (1969).
[86] M. Guyot, J. Massicot and P. Rivaille, *C. R. Acad. Sci. Paris* (C) **267**, 423 (1968).
[87] P. Rivaille, J. Massicot, M. Guyot and V. Plouvier, *Phytochemistry*, **8**, 1533 (1969).