Osage Orange Pigments. XIV. The Structure of Macluraxanthone[1a-c]

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Macluraxanthone, a root bark pigment of the osage orange (*Maclura pomifera* Raf.), is shown to be 12-(1,1-dimethylallyl)-5,9,10-trihydroxy-2,2-dimethyl-2*H*,6*H*-pyrano[3,2-*b*]xanthen-6-one (**5**) almost solely by spectroscopic methods. Macluraxanthone is believed to be the first case of a natural phenolic compound substituted with an isoprenoid unit in the form of a 1,1-dimethylallyl group. The biosynthetic implications of this are discussed and a possible biosynthetic route to macluraxanthone is proposed.

In a previous paper[1a] we have described the isolation and partial characterization of three new pigments, macluraxanthone, osajaxanthone, and alvaxanthone, from the root bark of the osage orange (*Maclura pomifera* Raf.). The pigments were tentatively assigned substituted polyhydroxyxanthone structures on the basis of their ultraviolet spectra and various diagnostic tests. We wish to report herein the elucidation of structure of the pigment found in major amount, macluraxanthone, and to propose a possible biosynthetic route to it.

Methylation or acetylation of macluraxanthone under mild conditions gave a yellow dimethyl ether and a yellow diacetate, respectively, while the application of more severe reaction conditions gave a colorless trimethyl ether and a very light yellow triacetate. It was concluded therefore that macluraxanthone possesses three hydroxyl groups, one of which is chelated with the xanthone carbonyl, hindered, or both.

Hydrogenation of macluraxanthone proceeded stepwise to give dihydro and tetrahydro derivatives. Dihydro- and tetrahydromacluraxanthone each gave yellow dimethyl ethers and diacetates under mild reaction conditions, and colorless trimethyl ethers and triacetates under more severe conditions, thus demonstrating the absence of any new hydroxyl groups. Complete hydrogenation of macluraxanthone trimethyl ether gave a product identical with that obtained by vigorous methylation of tetrahydromacluraxanthone. Treatment of macluraxanthone with maleic anhydride yielded no Diels–Alder adduct, showing the olefinic double bonds to be nonconjugated. The ultraviolet spectra of dihydromacluraxanthone, its ethers, and acetates show little change from those of the corresponding macluraxanthone derivatives, but the spectra of tetrahydromacluraxanthone derivatives are significantly different. Thus one of the double bonds of macluraxanthone is isolated, but the second is conjugated with the main chromophore since its reduction is accompanied by a change in ultraviolet spectra.[2] Contrary to our previous report,[1b] this spectral change, though small, is significant.

It has been reported previously[1a] that the similarity of the ultraviolet spectrum of our pigment with those of known xanthones[3-5] indicated that it had a xanthone nucleus. This was confirmed by comparing the infrared spectra of macluraxanthone and its derivatives with the spectra of various natural[3-5] and synthetic[6,7] xanthones.

The key to the structure of macluraxanthone was obtained from the n.m.r. spectra of its derivatives. The spectra of the diacetates and dimethyl ethers of macluraxanthone, dihydro-, and tetrahydromacluraxanthone all included a very low field signal; for example, the diacetate and dimethyl ether of macluraxanthone gave sharp singlets at τ −3.40 and −3.78, respectively. Such a signal can be due only, in this case, to a strongly hydrogen-bonded phenolic proton. Thus macluraxanthone must possess a hydroxyl group *ortho* to the xanthone carbonyl, on C-1 of the xanthone nucleus which requires severe conditions to methylate or acetylate.[8] The spectrum of macluraxanthone trimethyl ether is shown in Fig. 1. The two doublets at τ 1.99 and 3.04 comprise an aromatic AB system. The chemical shift of the low-field doublet indicates that it can be due only to a proton *ortho* to the xanthone carbonyl, on C-8 of the xanthone nucleus. The adjacent C-7 position must bear the other aromatic proton to account for the magnitude of the coupling (J = 9.4 c.p.s.) between the two. The sharp singlet at τ 8.59 and the doublets at τ 3.21 and 4.30 (J = 10.0 c.p.s.) reveal the presence of a 2,2-dimethylchromene ring.[9,10] The methoxyl protons give the three sharp signals at τ 6.01, 6.06, and 6.07. Except for the AB system, no other signals due to aromatic protons are present.

The presence of a xanthone nucleus, a 2,2-dimethylchromene ring, three hydroxyl groups, and two aromatic protons leaves only a C_5H_9 fragment unaccounted for in macluraxanthone. The portion of the spectrum of the trimethylether corresponding to the C_5H_9 residue consists of a sharp singlet at τ 8.28 of such relative area that it was attributed to two equivalent methyl groups and an ABX system (according to a first order analysis τ 3.54, 5.09, and 5.18; $J_{a,x}$ = 17.9, $J_{b,x}$ = 10.0, and $J_{a,b}$ = 1.0 c.p.s.), which can only be

(1) (a) Preceding paper in this series: M. L. Wolfrom, E. E. Dickey, P. McWain, A. Thompson, J. H. Locker, O. M. Windrath, and F. Komitsky, Jr., *J. Org. Chem.* **29**, 689 (1964). Preliminary communications: (b) M. L. Wolfrom, J. H. Looker, E. E. Dickey, P. McWain, and A. Thompson, Abstracts, 119th National Meeting of the American Chemical Society, Boston, Mass., April, 1951, p. 16M; (c) 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, *Tetrahedron Letters*, 749 (1963); (d) Postdoctoral Fellow of the Graduate School, deceased.

(2) *Cf.*, for example, M. L. Wolfrom, W. D. Harris, G. F. Johnson, J. E. Mahan, S. M. Moffett, and B. S. Wildi, *J. Am. Chem. Soc.*, **68**, 406 (1946).

(3) P. Yates and G. H. Stout, *ibid.*, **80**, 1691 (1958).

(4) J. C. Roberts, *Chem. Rev.*, **61**, 591 (1961).

(5) F. E. King, T. J. King, and L. C. Manning, *J. Chem. Soc.*, 3931 (1953); 563 (1957).

(6) P. K. Grover, G. D. Shah, and R. C. Shah, *ibid.*, 3982 (1955).

(7) G. D. Shah and R. C. Shah, *J. Sci. Ind. Res.* (India), **15B**, 630 (1956).

(8) The numbering system (see structure of **5**) used in this discussion is based on xanthen-9-one as the parent compound, not on 2*H*,6*H*-pyrano[3,2-*b*]xanthen-6-one which is later shown to be the parent system.

(9) B. F. Burrows and W. D. Ollis, *Proc. Chem. Soc.*, 177 (1960).

(10) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "Varian High Resolution Nuclear Magnetic Resonance Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962, No. 344.

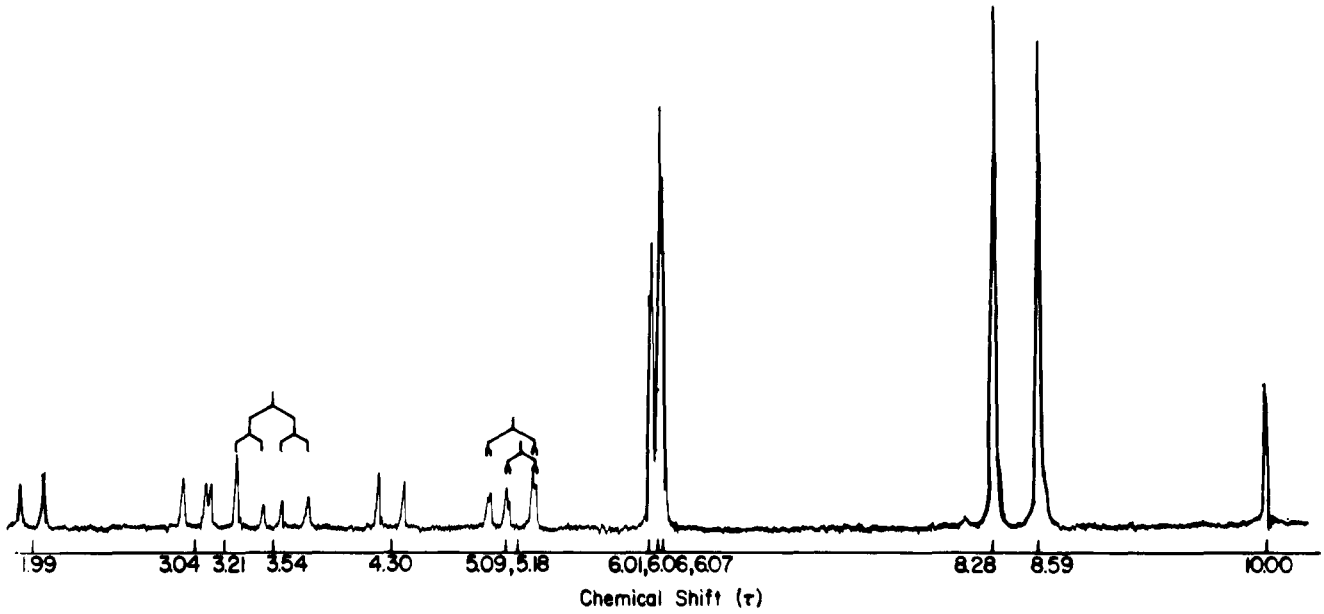
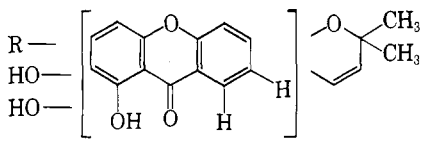


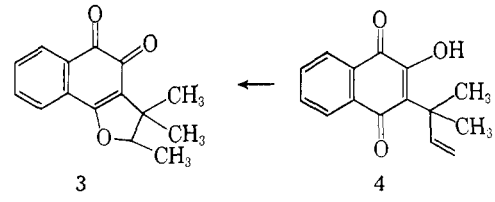
Fig. 1.—N.m.r. spectrum of macluraxanthone trimethyl ether (**5**) in deuteriochloroform on a Varian A-60 spectrometer. One line of the X quartet is hidden under the inner line of the doublet at 3.21. The high-field halves of the A and B quartets seem superposed in this spectrum but all four lines are observed in a slow sweep spectrum on a Varian HR-60 spectrometer. Differences between this spectrum and that of the corresponding dihydro derivative are noted in the introduction.

due to a vinyl group linked to a carbon atom with no hydrogens on it.[11,12] The only structure of the C_5H_9 fragment consistent with the above is a 1,1-dimethylallyl group. Confirmation of this point is obtained by an examination of the spectrum of any dihydromacluraxanthone derivative. For instance, the spectrum of dihydromacluraxanthone trimethyl ether differs significantly from that of macluraxanthone trimethyl ether only in that the signal due to the geminal dimethyls of the 1,1-dimethylallyl group of the latter is moved slightly upfield to τ 8.35, and the ABX system due to the vinyl group has disappeared, being replaced by a triplet at τ 9.25 and a quartet at τ 7.97 (J = 7.6 c.p.s.), which is the familiar spectrum of an isolated ethyl group in which the methylene protons are coupled only with the adjacent methyl group. Thus, in dihydromacluraxanthone the 1,1-dimethylallyl group has been reduced to a 1,1-dimethylpropyl group. A partial structure for macluraxanthone may then be written as **1** and that of dihydromacluraxanthone as **2**.



1, R = CH_2 = CH—$C(CH_3)_2$—
2, R = CH_3—CH_2—$C(CH_3)_2$—

Treatment of macluraxanthone with acid under various conditions yielded only resinous material or the pigment was recovered unchanged. This served to indicate that the 1,1-dimethylallyl group cannot be *ortho* to a free hydroxyl, since otherwise it would be expected to isomerize cleanly to a furan ring in a manner analogous to the reaction used in the synthesis of DL-dunnione (**3**) from the precursor (**4**) in 86% yield.[13] This, coupled with the above evidence, narrows the possible structures for macluraxanthone to **5** and **7**.



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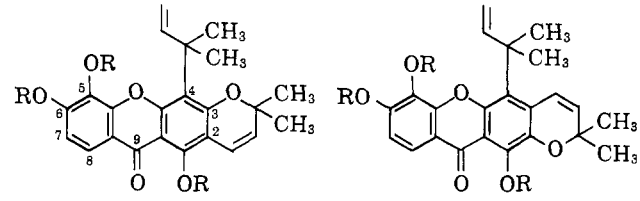
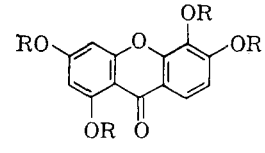


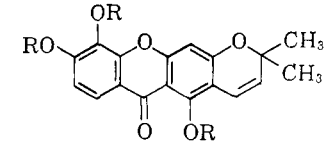
5, R = H
6, R = CH_3

7, R = H
8, R = CH_3

That the correct structure is **5** is evident from a comparison of the ultraviolet spectra of tetrahydromacluraxanthone and 1,3,5,6-tetrahydroxyxanthone[7] (**9**, Fig. 2). The ultraviolet spectra of polyoxygenated xanthones vary significantly with change in the oxygenation pattern.[3,4] The spectra of 1,3,5,6-tetrahydroxyxanthone (**9**) and tetrahydromacluraxanthone differ only in that the maxima of the latter are shifted bathochromically, as would be expected, due to alkyl substitution on the main chromophore. One would



9, R = H
10, R = CH_3CO



11, R = H
12, R = CH_3

(11) Reference 10, No. 155.

(12) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 238.

(13) R. G. Cooke, *Australian J. Sci. Research*, **3**, 481 (1950).

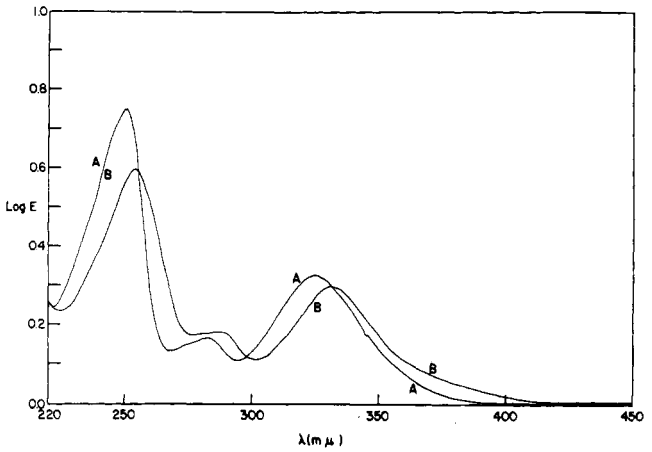


Fig. 2.—Ultraviolet spectra (absolute ethanol) of 1,3,5,6-tetrahydroxyxanthone (**9**, curve A) and tetrahydromacluraxanthone (curve B) on a Cary Model 14 recording spectrophotometer.

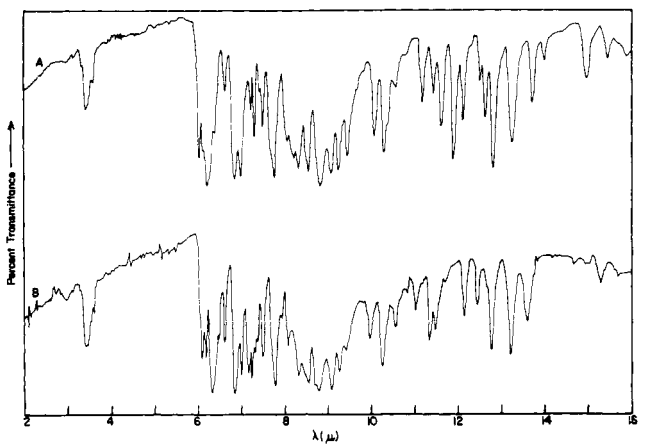
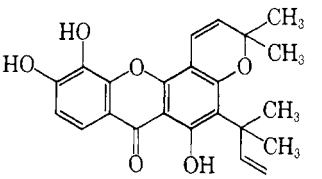


Fig. 3.—Infrared spectra of jacareubin trimethyl ether (**12**, curve A) and macluraxanthone trimethyl ether (**6**, curve B) as potassium bromide pellets.

not expect such close similarity if macluraxanthone had structure **7**, and its tetrahydro derivative had the corresponding structure. The spectrum of macluraxanthone (**5**) itself (Table I) differs significantly from that of 1,3,5,6-tetrahydroxyxanthone (**9**) because of the conjugated double bond of the chromene ring in the former. However, the spectra of macluraxanthone and its dihydro derivative correspond to that of the closely related xanthone, jacareubin[5] (**11**), which is also substituted with a [3,2-*b*]-2,2-dimethylchromene ring (Table I). Furthermore, derivatives of macluraxanthone (**5**) give ultraviolet spectra markedly similar to the corresponding derivatives of jacareubin (**11**) and 1,3,5,6-tetrahydroxyxanthone (**9**, Table I), differing only as expected due to varying degrees of alkylation. The infrared spectra (Fig. 3) of the trimethyl ethers of jacareubin (**12**) and macluraxanthone (**6**) are also strikingly similar. Also, one phloroglucinol ring is a common feature of the great majority of naturally occurring xanthones.[4]

In retrospect, the weakest piece of evidence concerning the structure of macluraxanthone is the nonisomerization of the pigment under acidic conditions. This is because of the negative character of this evidence, and also, one might expect the 1,1-dimethylallyl group to isomerize to a trimethylvinyl group, as below, but no such product could be isolated. Apparently the conditions required for such a rearrangement are sufficient to cause other, deep-seated transformations in macluraxanthone. However, considering the infrared and ultraviolet spectral evidence alone, there can be no doubt that macluraxanthone is a 1,3,5,6-tetraoxygenated xanthone. The presence of the aromatic AB system in the n.m.r. spectra of macluraxanthone derivatives precludes the placement of the 1,1-dimethylallyl group or the chromene ring on the pyrogallol ring of the parent xanthone. Since macluraxanthone possesses a C-1 hydroxyl group, again only two possible structures for it can be written (**5** and **13**).



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Structure **13** can be ruled out on the basis that the 1-hydroxyl would be so sterically hindered by the tertiary alkyl group substituted in the *ortho* position, that it could not be methylated or acetylated under the conditions which fully methylate or acetylate macluraxanthone; special procedures would be required for characterization of this type of severely hindered hydroxyl.[14] The dimethyl ether of **13** would probably be insoluble in Claisen's alkali and give no ferric chloride test,[14] whereas macluraxanthone dimethyl ether is readily soluble and gives a positive ferric chloride test. Finally, the ultraviolet spectrum of **13** probably would not correspond so closely to that of jacareubin (**11**) as does the spectrum of macluraxanthone, since the conjugated olefinic linkages are positioned differently. Thus, again, without recourse to the acid isomerization data, one can only conclude that the structure of macluraxanthone is **5**.

To our knowledge, macluraxanthone is the first example of a plant phenolic bearing an isoprenoid unit as a 1,1-dimethylallyl group. 'Echinulin, a nonphenolic mold metabolite possesses this group, however,[15] and dunnione[13] (**3**) may arise from the precursor (**4**) in nature, also.[16] Another example of a naturally occurring phenol bearing this group in the same cyclized form as dunnione is atrovenetin,[17] from *Penicillium atrovenetum*. An apparently closely related pigment,

(14) G. H. Stillson, D. W. Sawyer, and C. K. Hunt, *J. Am. Chem. Soc.*, **67**, 303 (1945).

(15) A. J. Birch, G. E. Blance, S. David, and H. Smith, *ibid.*, **83**, 3128 (1961).

(16) W. D. Ollis and I. O. Sutherland, "Recent Developments in the Chemistry of Natural Phenolic Compounds," W. D. Ollis, Ed., Pergamon Press, London, 1961, p .74.

(17) D. H. R. Barton, P. de Mayo, G. A. Morrison, and H. Raistrick, *Tetrahedron*, **6**, 48 (1959); G. A. Morrison, I. C. Paul, and G. A. Sim, *Proc. Chem. Soc.*, 352 (1962).

TABLE I

ULTRAVIOLET SPECTRA OF MACLURAXANTHONE DERIVATIVES AND KNOWN XANTHONES[a]

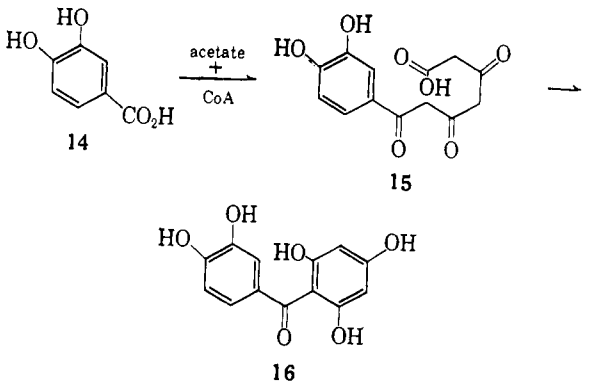
Compound	λ_{max}, mμ (log ε)
Macluraxanthone (**5**)	242 (4.31), 283 (4.64), 338 (4.28)
Dihydromacluraxanthone	243 (4.38), 286 (4.63), 338 (4.32)
Jacareubin (**11**)[b]	240 (4.09), 279 (4.61), 334 (4.26)
Tetrahydromacluraxanthone	254 (4.60), 287 (4.07), 332 (4.31)
Dihydrojacareubin[b, c]	251 (4.55), 284 (4.05), 330 (4.24)
1,3,5,6-Tetrahydroxyxanthone (**9**)[d]	251 (4.42), 283 (3.81), 324 (4.21)
Tetrahydromacluraxanthone dimethyl ether	248 (4.57), 262 (4.28), 289 (3.91), 327 (4.30), 355 (3.79)[e]
Dihydrojacareubin dimethyl ether[b]	246 (4.63), 255 (4.33),[e] 285 (3.85), 322 (4.40), 346 (3.79)[e]
1-Hydroxy-3,5,6-trimethoxyxanthone[d]	245 (4.67), 282 (4.03), 314 (4.37), 338 (3.97)[e]
Tetrahydromacluraxanthone diacetate	243 (4.43), 266 (4.30), 324 (4.17), 366 (3.62)
1-Hydroxy-3,5,6-triacetoxyxanthone	237 (4.32), 254 (4.40), 292 (4.11),[e] 297 (4.16), 351 (3.74)
Tetrahydromacluraxanthone triacetate	243 (4.64), 267 (3.89),[e] 279 (3.89), 313 (4.23)
1,3,5,6-Tetraacetoxyxanthone (**10**)[d]	241 (4.65), 268 (4.18), 285 (4.05),[e] 320 (3.75),[e] 331 (3.84)
Tetrahydromacluraxanthone trimethyl ether	249 (4.73), 282 (3.97), 317 (4.38)
1,3,5,6-Tetramethoxyxanthone	244 (4.69), 287 (4.09),[e] 304 (4.34)

[a] Spectra were taken in absolute ethanol on a Cary Model-14 recording spectrophotometer. [b] See ref. 5. [c] H. B. Bhat and K. Venkataraman, *Tetrahedron*, **19**, 77 (1963). [d] See ref. 7. [e] Inflection.

herqueinone from *Penicillium herquei*,[18] yields isomeric trimethyl ethers, one of which, trimethylherqueinone B, has been shown to contain an oxetan ring[19] possibly derived in nature by cyclization of a 1,1-dimethylallyl unit.

The occurrence of the 1,1-dimethylallyl group is of biogenetic interest in that its presence indicates that probably an aromatic precursor has attacked "γ,γ-dimethylallyl pyrophosphate" in a manner analogous to an S$_N$2′ substitution.[16] Another possibility is an *ortho* Claisen-type rearrangement of an *O*-3,3-dimethylallyl precursor to a *C*-1,1-dimethylallyl compound. Several *O*-3,3-dimethylallyl compounds are known in nature,[16,20] and this type of rearrangement can take place at low temperatures under catalysis.[21]

Roberts[4] has commented on the possible biosynthetic route or routes to xanthones and has pointed out that a scheme involving the condensation of an aromatic acid with three acetate units to a poly(β-keto) acid which cyclizes to a benzophenone precursor is acceptable.[22] Thus it may be possible that the biosynthesis of macluraxanthone proceeds from shikimate-derived 3,4-dihydroxybenzoic acid (**14**) by condensation with acetate to the poly(β-keto) acid (**15**),[22] which cyclizes to form maclurin (**16**). The oxide linkage could be closed by an oxidative mechanism[23] to 1,3,5,6-tetrahydroxyxanthone (**9**) which could be condensed with isoprene units as "γ,γ-dimethylallyl pyrophosphate"[16] to form macluraxanthone (**5**). It is believed that the introduction of isoprene units on plant phenolics takes place at a late stage in their biosynthesis.[16,24] It is perhaps significant that maclurin (**16**) has been isolated from *Maclura tinctoria*, a tree closely related to the osage orange (*Maclura pomifera*).[25] Maclurin has been reported to be present in the wood[26] and the outer tissues of the roots[27] of the osage orange, but no experimental papers are cited, and a recent investigation of the wood[28] failed to demonstrate its presence.



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Macluraxanthone joins the rare class of isoprenoid substituted xanthones which includes jacareubin,[5] mangostin,[3] and celibixanthone.[29] The relationship between jacareubin,[5] macluraxanthone, and morellin[30] is of interest. An *O*-isoprenoid xanthone has been reported,[31] but apparently this structure must be reconsidered.[32]

Further work on the structures of the two pigments accompanying macluraxanthone is in progress in this laboratory.

(18) F. H. Stodola, K. B. Raper, and D. I. Fennell, *Nature*, **169**, 773 (1951).

(19) J. Cason, J. S. Correia, R. B. Hutchison, and R. F. Porter, *Tetrahedron*, **18**, 839 (1962).

(20) M. L. Wolfrom and F. Komitsky, Jr., "Recent Progress in the Chemistry of Natural and Synthetic Colouring Matters and Related Fields," T. S. Gore, B. S. Joshi, S. V. Sunthankar, and B. D. Tilak, Ed., Academic Press, New York, N. Y., 1962, p. 287.

(21) W. Gerrard, M. F. Lappert, and H. B. Silver, *Proc. Chem. Soc.*, 19 (1957).

(22) A. J. Birch, *ibid.*, 3 (1962).

(23) H. Erdtman and C. A. Wachtmeister, "Festschrift Arthur Stoll," Birkhäuser, Basel, 1957, p. 156; J. R. Lewis, *Chem. Ind.* (London), 159 (1961); *Proc. Chem. Soc.*, 373, (1963).

(24) W. B. Whalley, "Recent Developments in the Chemistry of Natural Phenolic Compounds," W. D. Ollis, Ed., Pergamon Press, London, 1961, p. 20.

(25) R. Wagner, *J. prakt. Chem.*, [1]**51**, 82, 91 (1850).

(26) C. D. Mell, *Textile Colorist*, **53**, 749 (1931).

(27) A. Schatz, N. D. Cheronis, V. Shatz, and G. S. Trelawny, *Proc. Penn. Acad. Sci.*, **28**, 44 (1954).

(28) R. A. Barnes and N. N. Gerber, *J. Am. Chem. Soc.*, **77**, 3259 (1955).

(29) G. H. Stout, V. F. Stout, and M. J. Welsh, *Tetrahedron Letters*, 541 (1962); *Tetrahedron*, **19**, 667 (1963).

(30) G. Kartha, G. N. Ramachandran, H. B. Bhat, P. M. Nair, V. K. V. Raghavan, and K. Venkataraman, *Tetrahedron Letters*, 459 (1963).

(31) H. Auterhoff, H. Freudendorf, W. Liesenklas, and C. Schwandt, *Angew. Chem., Intern. Ed. Engl.*, **1**, 455 (1962).

(32) N. H. Dyson and W. Rigby, *J. Chem. Soc.*, 1858 (1963).

Experimental[33]

Dihydromacluraxanthone.—A suspension of 25 mg. of platinic oxide in 2.5 ml. of absolute ethanol contained in a quantitative hydrogenation apparatus was saturated with hydrogen. A solution of 229 mg. of macluraxanthone[1a] in 10 ml. of ethanol was introduced, and hydrogenation was allowed to proceed until 14.4 ml. of hydrogen had been absorbed; the theoretical volume of hydrogen at 24° and 174 mm. is 13.6 cc. The time required was 9 min. Filtration of the reaction mixture, evaporation to dryness, and recrystallization of the residue from carbon tetrachloride gave tiny yellow needles, 209-mg. yield, m.p. 181–182°.

Anal. Calcd. for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10. Found: C, 69.92; H, 6.08.

Tetrahydromacluraxanthone.—An ethanol solution of 302 mg. of macluraxanthone was hydrogenated as described for the preparation of dihydromacluraxanthone, except that 33 mg. of platinic oxide was used, and hydrogenation was allowed to continue until uptake of hydrogen ceased. The total absorbed was 35.3 ml.; the theoretical amount is 35.8 ml. Filtration of the reaction mixture, evaporation to dryness, and recrystallization of the residue from benzene yielded 282 mg. of tiny yellow plates, m.p. 206–207°. Sometimes a dimorphous form was obtained with m.p. 204–205°. X-ray powder diffraction data[34] were for high melting dimorph—8.03 (3), 6.04 (2), 4.85, 4.47 (4), 4.01, 3.30 (1), 3.15, 2.92, 2.66, 2.44, 2.32, 2.22, 2.14 (5), 2.04, 1.91, 1.83, 1.68 Å.; low melting form—8.50, 6.62 (2), 5.48, 4.77, 4.28 (1), 3.88 (3), 3.50, 3.31 (4), 2.98 (4), 2.67 (4), 2.34, 2.22, 2.13, 1.93, 1.67 Å.

Anal. Calcd. for $C_{23}H_{26}O_6$: C, 69.31; H, 6.58. Found: C, 69.28; H, 6.73.

Macluraxanthone Diacetate.—A solution of 100 mg. of macluraxanthone in 20 drops of pyridine was cooled to 0°, and 3 ml. of previously cooled acetic anhydride was added. The reaction mixture was kept at 0° overnight, and the resulting crystalline mass was stirred with 50 ml. of water. Filtration and recrystallization from ethanol–water yielded 67 mg. of fluffy yellow needles, m.p. 194–195°. Ultraviolet absorption[33] spectra showed bands at 244 mμ (log ε 3.94), 272 (4.25) inflection, 294 (4.52) inflection, 300 (4.55), and 337 (4.06).

Anal. Calcd. for $C_{23}H_{20}O_6(COCH_3)_2$: C, 67.77; H, 5.48; CH_3CO, 17.99. Found: C, 67.87; H, 5.41; CH_3CO, 17.66.

Dihydromacluraxanthone Diacetate.—An amount of 47 mg. of dihydromacluraxanthone was acetylated as described for the preparation of macluraxanthone diacetate. Recrystallization from ethanol–water yielded 16 mg. of fluffy yellow needles, m.p. 179–180°. Ultraviolet absorption[33] showed bands at 244 mμ (log ε 4.20), 267 (4.28), 295 (4.41) inflection, 302 (4.46), and 334 (4.08).

Anal. Calcd. for $C_{27}H_{28}O_8$: C, 67.49; H, 5.87. Found: C, 67.32; H, 5.86.

Tetrahydromacluraxanthone Diacetate.—An amount of 200 mg. of tetrahydromacluraxanthone was acetylated as described for the preparation of macluraxanthone diacetate. Recrystallization from ethanol–water yielded 159 mg. of fluffy yellow needles, m.p. 154–155°.

Anal. Calcd. for $C_{23}H_{24}O_6(COCH_3)_2$: C, 67.21; H, 6.27; CH_3CO, 17.84. Found: C, 67.16; H, 6.48; CH_3CO, 17.07.

Macluraxanthone Dimethyl Ether.—A solution of 200 mg. of macluraxanthone in methylene chloride, cooled to 0°, was treated with an excess of ethereal diazomethane. The solution was kept at 0° for several hours, then at room temperature overnight. Filtration to remove polyethylene, evaporation, and recrystallization of the residue yielded 195 mg. of yellow needles, m.p. 162–163°. Ultraviolet absorption[33] showed bands at 247 mμ (log ε 4.22), 289 (4.57), 333 (4.26), and 365 (3.66) inflection. Macluraxanthone dimethyl ether gave a bright green color with alcoholic ferric chloride and dissolved in Claisen's alkali to give a yellow solution.

Anal. Calcd. for $C_{23}H_{20}O_4(OCH_3)_2$: C, 71.08; H, 6.20; OCH_3, 14.69. Found: C, 71.00; H, 6.27; OCH_3, 14.54.

Dihydromacluraxanthone Dimethyl Ether.—An amount of 200 mg. of dihydromacluraxanthone was methylated as described above for the preparation of macluraxanthone dimethyl ether. Recrystallization from ethanol–water yielded 173 mg. of yellow needles, m.p. 205–206°. Ultraviolet absorption[33] showed bands at 248 mμ (log ε 4.32), 289 (4.53), 333 (4.27), and 369 (3.57) inflection.

Anal. Calcd. for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.41; H, 6.63.

Tetrahydromacluraxanthone Dimethyl Ether.—An amount of 300 mg. of tetrahydromacluraxanthone was methylated as described above for the preparation of macluraxanthone dimethyl ether. Recrystallization from ethanol–water yielded 264 mg. of yellow needles, m.p. 160–161°.

Anal. Calcd. for $C_{23}H_{24}O_4(OCH_3)_2$: C, 70.41; H, 7.09; OCH_3, 14.55. Found: C, 70.16; H, 7.09; OCH_3, 16.59.

Macluraxanthone Triacetate.—A mixture of 100 mg. of macluraxanthone, 0.5 g. of sodium acetate, and 5 ml. of acetic anhydride was refluxed for 2 hr. and poured into 50 ml. of water. Filtration of the resulting precipitate and recrystallization from ethanol–water yielded 88 mg. of light yellow needles, m.p. 182–183°. Ultraviolet absorption[33] showed bands at 245 mμ (log ε 3.85) inflection, 269 (4.84), 295 (4.21) inflection, and 312 (3.98).

Anal. Calcd. for $C_{23}H_{19}O_6(COCH_3)_3$: C, 66.92; H, 5.42; CH_3CO, 24.80. Found: C, 66.87; H, 5.50; CH_3CO, 25.15.

Dihydromacluraxanthone Triacetate.—An amount of 100 mg. of dihydromacluraxanthone was acetylated as described for the preparation of macluraxanthone triacetate. Recrystallization from ethanol–water yielded 96 mg. of light yellow needles, m.p. 170–171°. Ultraviolet absorption[33] showed bands at 245 mμ (log ε 4.23) inflection, 267 (4.45), and 318 (4.10).

Anal. Calcd. for $C_{29}H_{30}O_9$: C, 66.66; H, 5.79. Found: C, 66.75; H, 5.72.

Tetrahydromacluraxanthone Triacetate.—An amount of 100 mg. of tetrahydromacluraxanthone was acetylated as described for the preparation of macluraxanthone triacetate. Recrystallization from ethanol–water yielded 70 mg. of fluffy white needles, m.p. 179–180°.

Anal. Calcd. for $C_{23}H_{23}O_6(COCH_3)_3$: C, 66.39; H, 6.15; CH_3CO, 24.61. Found: C, 66.28; H, 5.94; CH_3CO, 24.74.

Macluraxanthone Trimethyl Ether.—A solution of 300 mg. of macluraxanthone in 10 ml. of acetone over 2.5 g. of potassium carbonate was brought to reflux, and 1.5 ml. of dimethyl sulfate was added dropwise over a period of 1 hr. The mixture was refluxed overnight, the inorganic material was filtered, and the filtrate was reduced to dryness under reduced pressure. Recrystallization of the residue from ether–petroleum ether and 95% ethanol yielded 280 mg. of white prisms, m.p. 98°. Ultraviolet absorption[33] showed bands at 254 mμ (log ε 4.60), 272 (4.53), and 314 (4.25).

Anal. Calcd. for $C_{23}H_{19}O_3(OCH_3)_3$: C, 71.55; H, 6.46; OCH_3, 21.33. Found: C, 71.48; H, 6.35; OCH_3, 21.14.

Dihydromacluraxanthone Trimethyl Ether.—An amount of 265 mg. of dihydromacluraxanthone was methylated as described above for the preparation of macluraxanthone trimethyl ether. Recrystallization from ether–petroleum ether yielded 220 mg. of white prisms, m.p. 120–121°.

Anal. Calcd. for $C_{26}H_{30}O_6$: C, 71.22; H, 6.90. Found: C, 71.11; H, 6.97.

Tetrahydromacluraxanthone Trimethyl Ether.—An amount of 200 mg. of tetrahydromacluraxanthone was methylated as described for the preparation of macluraxanthone trimethyl ether. Recrystallization from ether–petroleum ether and methanol–water yielded 180 mg. of white prisms, m.p. 112–113°.

An amount of 300 mg. of macluraxanthone trimethyl ether was hydrogenated as described for the preparation of tetrahydromacluraxanthone. Recrystallization as above gave a product shown to be identical, by mixture melting point and infrared spectrum, with the substance obtained above by methylation of tetrahydromacluraxanthone; the yield was 267 mg.

Anal. Calcd. for $C_{23}H_{23}O_3(OCH_3)_3$: C, 70.90; H, 7.32; OCH_3, 21.13. Found: C, 70.74; H, 6.86; OCH_3, 21.82.

Attempted Acid Isomerization of Macluraxanthone.—An amount of 100 mg. of macluraxanthone was dissolved in 5 ml. of hot acetic acid. The solution was allowed to cool to room temperature and 0.20 ml. of concentrated hydrochloric acid was added. After standing overnight at room temperature, the

(33) Melting points were taken in a Hershberg apparatus using total immersion thermometers. N.m.r. spectra were taken on saturated deuteriochloroform solutions with a tetramethylsilane internal reference standard, using a Varian A-60 n.m.r. spectrometer. Ultraviolet spectra were taken in absolute ethanol on a Cary Model 14 recording spectrophotometer. These are recorded in Table I or below as λ_{max}^{EtOH} in mμ (log ε). Infrared spectra were taken in potassium bromide pellets on a Perkin-Elmer Infracord spectrophotometer.

(34) Interplanar spacing, Å., Cu Kα radiation; relative intensities were estimated visually and the strongest lines were numbered in order of decreasing intensity.

solution was diluted with water and the resinous precipitate was separated by decantation. The precipitate was taken up in warm ethanol and the solution was passed through a column of acid-washed Magnesol-Celite.[1a] The eluate was warmed and diluted to incipient opalescene with hot water. On standing overnight, crystalline macluraxanthone separated; the recovery was 17 mg., identified by its infrared spectrum.

An amount of 300 mg. of macluraxanthone in 25 ml. of ethanol was brought to reflux and about 100 mg. of *p*-toluenesulfonic acid was added. After refluxing 12 hr., the ethanol solution was reduced to a small volume under reduced pressure and diluted with water. Filtration and recrystallization of the crude precipitate gave pure starting material; the recovery was 148 mg., identified by its mixture melting point with an authentic sample and by its infrared spectrum. The above methods had been found suitable for the isomerization of osajin and pomiferin.[2]

The Attempt to Obtain a Diels–Alder Adduct of Macluraxanthone.—A solution of 100 mg. of macluraxanthone in xylene was refluxed for 2 hr. with a large excess of maleic anhydride. On processing, the pigment was recovered as the sole product; the recovery was 78 mg.

1,3,5,6-Tetrahydroxyxanthone.[7]—A mixture of 18.0 g. of anhydrous phloroglucinolcarboxylic acid, 18.0 g. of anhydrous pyrogallol, and 200 ml. of phosphorus oxychloride was warmed to 70° and 80.0 g. of freshly fused zinc chloride was added. The reaction mixture was stirred at 70° for 1.5 hr., cooled, and poured into 2.5 l. of ice and water and stirred for 0.5 hr. The precipitate was filtered, washed with 500 ml. of water, and recrystallized from ethanol–water. After vacuum drying at 78°, the crude xanthone was sublimed at 220–230° and 0.03 mm. The sublimate was recrystallized from ethanol–water, yielding 6.19 g., m.p. 352–354°; lit. m.p. 310°,[5] 320°,[35] 357°.[7]

1-Hydroxy-3,5,6-trimethoxyxanthone.—An amount of 1.00 g. of 1,3,5,6-tetrahydroxyxanthone was treated with ethereal diazomethane as described for the preparation of macluraxanthone dimethyl ether. Recrystallization from acetic acid–water yielded 0.71 g. of long yellow needles, m.p. 183–184°; lit m.p. 182–183°,[5] 185°.[7]

1,3,5,6-Tetraacetoxyxanthone.—A solution of 1.00 g. of 1,3,5,6-tetrahydroxyxanthone in 10 ml. of pyridine was cooled to 0° and 40 ml. of precooled acetic anhydride was added. The solution was kept at 0° overnight and then poured into 500 ml. of water. Filtration and recrystallization from acetic acid–water yielded 0.98 g. of long white needles, m.p. 248°, undepressed upon admixture with an authentic sample prepared by the method of Tanase.[5,35]

1-Hydroxy-3,5,6-triacetoxyxanthone.—An amount of 4.35 g. of triacetyl borate[36] was added to a solution of 1.00 g. of 1,3,5,6-tetrahydroxyxanthone in 40 ml. of acetic anhydride, and the mixture was refluxed for 15 min. The red solution was cooled and diluted to 100 ml. with absolute ether. On standing at 0° for 3 hr., bright yellow needles of the borate complex were deposited, which were filtered, washed well with ether, and decomposed by boiling in water. Filtration and recrystallization from acetic acid–water yielded 0.51 g. of long yellow needles, m.p. 168–169°.

Anal. Calcd. for $C_{13}H_5O_6(COCH_3)_3$: C, 59.07; H, 3.65; CH_3CO, 33.42. Found: C, 58.78; H, 3.68; CH_3CO, 33.33.

1,3,5,6-Tetramethoxyanthone.—A solution of 1.00 g. of 1,3,5,6-tetrahydroxyanthone in 75 ml. of acetone over 25 g. of potassium carbonate was brought to reflux and 15.0 ml. of dimethyl sulfate was added. The mixture was refluxed overnight and filtered, and the filtrate was reduced to dryness under reduced pressure. Recrystallization of the residue from methanol–water and ether–petroleum ether yielded 0.92 g. of white plates, m.p. 146–147°.

Anal. Calcd. for $C_{13}H_4O_2(OCH_3)_4$: C, 64.56; H, 5.10; OCH_3, 39.23. Found: C, 64.63; H, 5.30; OCH_3, 39.65.

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Ozonolysis of Naphthalenes. The Aromatic Products[1]

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Ozonolyses of naphthalene, 2,3-dimethylnaphthalene, 2-hydroxynaphthalene, 2-methoxynaphthalene, and 2-ethoxynaphthalene in participating and nonparticipating solvents are reported. In methanol the first three compounds give the same product, 4-methoxy-2,3-benzodioxan-1-ol. 2-Methoxy- and 2-ethoxynaphthalene react differently to give 1,4-dimethoxy-2,3-benzodioxan. The above named peroxides can be converted to methyl phthalaldehydate, phthalaldehydic acid, and phthalic acid in high yields. In nonparticipating solvents the peroxidic ozonolysis products appear to be diozonides.

Naphthalene (Ia) previously[1] has been ozonized by Harries,[3] Seekles,[4] and Wibaut and Kampschmidt.[5] In addition, the ozonolyses of 1,4- and 2,3-dimethylnaphthalene (Ib),[5,6] 1- and 2-methylnaphthalene,[7] 1- and 2-phenylnaphthalene,[8] 1- and 2-hydroxynaphthalene (Ic),[9a] and 2,3-dihydroxynaphthalene[9b] have been reported. Two moles of ozone per mole of the naphthalene compound readily were absorbed, after which absorption continued more slowly, apparently involving attack on the other ring; the homologs of naphthalene were attacked almost exclusively in the methylated ring by the first 2 mole equiv. of ozone.[5,7]

Until our earlier report,[1] only "nonparticipating" solvents (solvents which do not enter into the formation of the peroxidic ozonolysis product[10]) had been

(1) For a preliminary report on part of this work, see P. S. Bailey and F. J. Garcia-Sharp, *J. Org. Chem.*, **22**, 1008 (1957). More recent aspects were reported at the 18th Southwest Regional Meeting of the American Chemical Society, Dallas, Tex., December, 1962.

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