Total Syntheses of the Methyl Ether Ester Derivatives of the Coccid Anthraquinones Laccaic Acid D and Kermesic Acid

By **Guy Roberge** and **Paul Brassard,*** Department of Chemistry, Laval University, Quebec, Canada G1K 7P4

4-Methoxy-2-trimethylsiloxypenta-1,3-diene and its 3-methoxycarbonyl derivative react readily and regiospecifically with halogenoquinones; the reactions have led to simple syntheses of deoxyerythrolaccin, laccaic acid D, and kermesic acid.

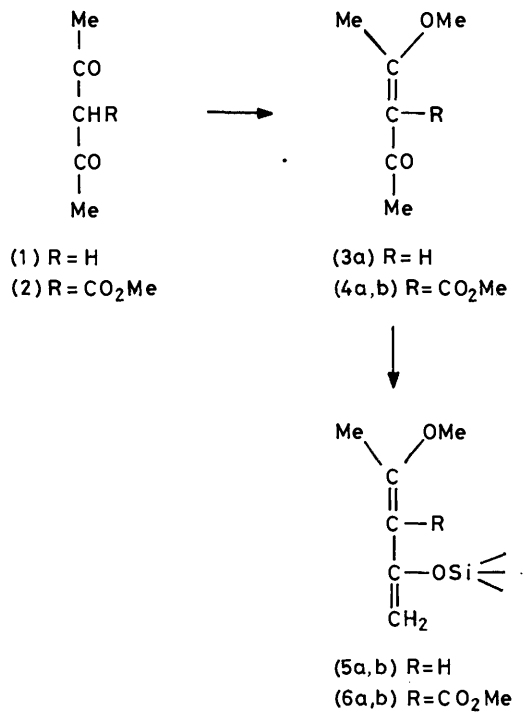
THE most common substitution pattern in naturally occurring anthraquinones is that of the prototype emodin (1,3,8-trihydroxy-6-methylanthraquinone). However, in coccid insect pigments the orientation in one of the rings is often inverted, as in deoxyerythrolaccin (1,3,6-trihydroxy-8-methylanthraquinone). Compounds showing the latter feature have been accessible only with difficulty, and only the simplest examples (erythrolaccin,[1,2] isoerythrolaccin,[3] and deoxyerythrolaccin [3,4]) have previously been obtained by total synthesis.

[1] P. Yates, A. C. Mackay, L. M. Pande, and M. Amin, *Chem. and Ind.*, 1964, 1991.
[2] N. S. Bhide and A. V. Rama Rao, *Indian J. Chem.*, 1969, **7**, 996.
[3] A. R. Mehendale, A. V. Rama Rao, and K. Venkataraman, *Indian J. Chem.*, 1972, **10**, 1041.
[4] A. R. Mehandale, A. V. Rama Rao, I. N. Shaikh, and K. Venkataraman, *Tetrahedron Letters*, 1968, 2231.

The successful use of 1,1-dimethoxy-3-trimethylsiloxyalka-1,3-dienes (conjugated keten acetals) in cycloaddition reactions for the synthesis of rhodolamprometrin and rhodocomatulin derivatives [5] prompted us to examine the application of analogous substances to the preparation of the title compounds. The conversion of β-methoxy-αβ-unsaturated ketones into trimethylsiloxydienes [6] was chosen as the most promising approach.

RESULTS AND DISCUSSION

In the preliminary investigation, the methyl enol ether of pentane-2,4-dione (1), (*E*)-4-methoxypent-3-en-2-one (3a), was converted with partial isomerisation into a mixture of the two stereoisomers of 4-methoxy-2-trimethylsiloxypenta-1,3-diene (5a,b) (the vinylogue of a keten acetal) in 73% yield by treatment with chlorotrimethylsilane, triethylamine, and anhydrous zinc chloride. The usefulness of the reagent was first tested toward a fairly reactive juglone, 2-bromo-5-chloro-8-hydroxy-6-methyl-1,4-naphthoquinone (7). Two products were obtained which, in view of the known orientational effects in the juglone, the subsequently established regiospecificity of the reaction, and the spectral characteristics were identified as 4-chloro-1,6-dihydroxy-3,8-dimethylanthraquinone (8) (25%) and its 6-methyl ether (9) (53%). The latter probably arose through addition of methanol



(1) R = H
(2) R = CO_2Me

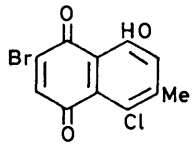
(3a) R = H
(4a,b) R = CO_2Me

(5a,b) R = H
(6a,b) R = CO_2Me

to the intermediate trimethylsilyl enol ether. When the crude material was methylated before purification only one compound was obtained, the 1,6-dimethyl ether (10) (61%) (as in the methylation of all other anthraquinones the dimethyl sulphate–anhydrous potassium carbonate–acetone method was used).

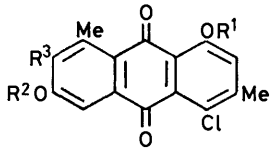
[5] J. Banville and P. Brassard, *J.C.S. Perkin I*, 1976, 1852.

In an analogous condensation with 2-chloro-6,8-dimethoxy-1,4-naphthoquinone (14), a 31% yield of tri-*O*-methyldeoxyerythrolaccin (16) was isolated, identical with the authentic derivative. The fact that no other quinonoid substance was detected in this or other reaction mixtures establishes the complete regiospecificity



(7)

(5a,b) or (6a,b)



(8) $R^1 = R^2 = R^3 = H$
(9) $R^1 = R^3 = H$, $R^2 = Me$
(10) $R^1 = R^2 = Me$, $R^3 = H$
(17) $R^1 = R^2 = Me$, $R^3 = CO_2Me$

of the initial cycloaddition involving this diene. The yield of the reaction could be raised to 61% by an improved procedure. The use of more severe conditions (heating without solvent) decreased the amount of anthraquinone (to 55%) and also produced 2,6,8-trimethoxy-1,4-naphthoquinone (27%) resulting from methanolysis of the reactive 2-chloronaphthoquinone. The reactivity of the substrate was increased by cleavage of the 8-methyl ether. By this means a 75% yield of the same trimethyl ether could be obtained after methylation.

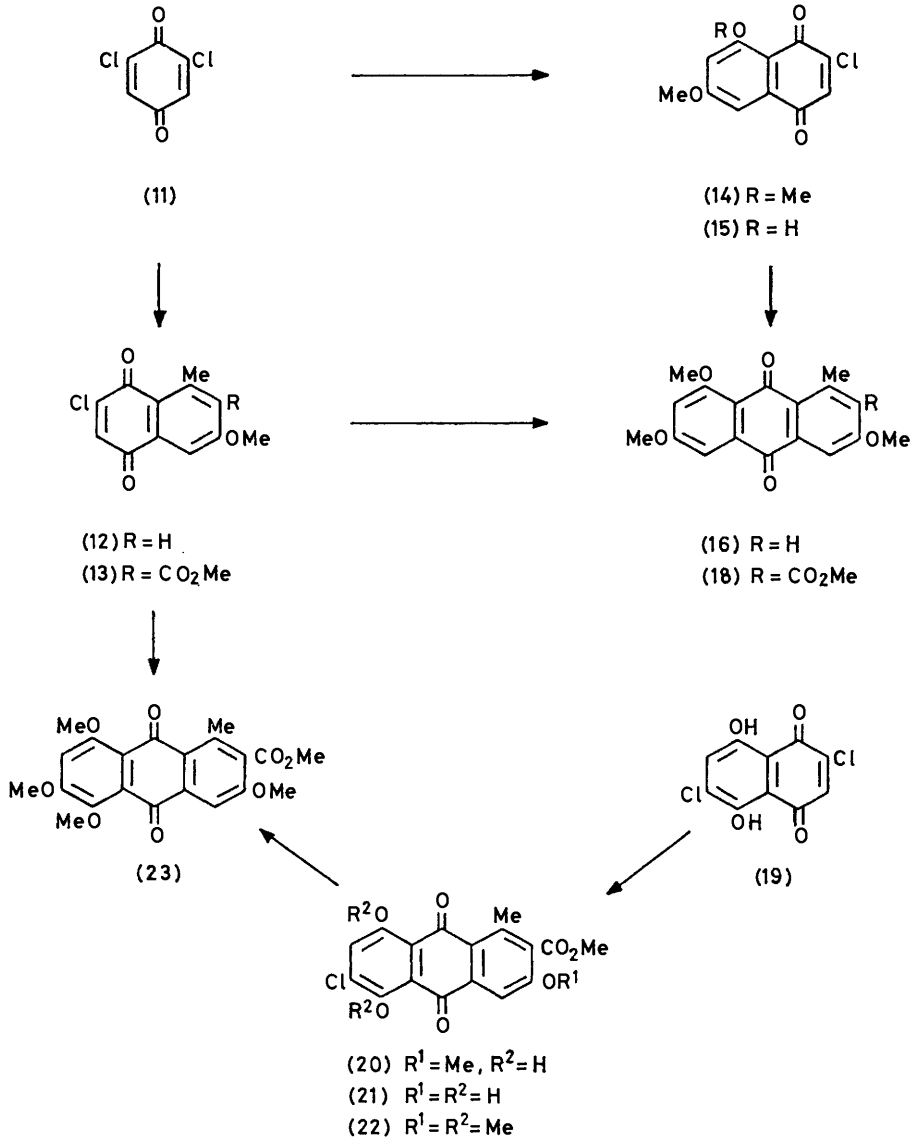
The two consecutive annelations required to prepare deoxyerythrolaccin from 2,6-dichloro-1,4-benzoquinone (11) by this approach were also investigated in inverse sequence. Condensation of the mixture of dienes with this quinone proceeded as usual except that the final methylation of the crude product required methyl iodide–silver(I) oxide–chloroform as did the methylation of all other naphthoquinones in this series. The expected 2-chloro-6-methoxy-8-methyl-1,4-naphthoquinone (12) was formed in 22% yield on the 2-mmol scale (larger quantities produced uncontrollable reactions during refluxing). The reaction progressed more smoothly in tetrahydrofuran when started at −70 °C but the yield did not exceed 28%. This naphthoquinone then reacted with the previously described 1,1-dimethoxy-3-trimethylsiloxybuta-1,3-diene [5] and gave deoxyerythrolaccin trimethyl ether (16) in 90% yield, which can readily be demethylated to the natural product

[6] S. Danishefsky and T. Kitahara, *J. Amer. Chem. Soc.*, 1974, **96**, 7807.

by either anhydrous aluminium chloride or pyridinium hydrochloride.

The syntheses of the carboxylated coccid anthraquinones laccaic acid D and kermesic acid as their methyl ether esters could now be envisaged by using an analogous diene, 4-methoxy-3-methoxycarbonyl-2-trimethylsiloxypenta-1,3-diene (6a,b). Methyl diacetylacetate (2) was methylated according to the procedure of Chong and Clozy [7] and gave the *C*-alkylated product (24—38%) and a mixture of the (*E*)- and (*Z*)-4-methoxy-3-methoxycarbonylpent-3-en-2-one (4a,b) (11—47%), which was converted in the usual manner into a mixture of the corresponding trimethylsiloxy-enol ethers (6a,b) (77%). A condensation of the latter dienes with a standard substrate, 2-bromo-4-chloro-8-hydroxy-6-methyl-1,4-naphthoquinone (7), under the usual conditions gave a 44% yield of 5-chloro-3,8-dimethoxy-2-methoxycarbonyl-1,6-dimethylanthraquinone (17). However, from a reaction with 2-chloro-6,8-dimethoxy-1,4-naphthoquinone (14), even at 120 °C and without solvent, no anthraquinone was produced and only 2,6,8-trimethoxy-1,4-naphthoquinone (32%) was isolated. Use of the more reactive 2-chloro-8-hydroxy-6-methoxy-1,4-naphthoquinone [8] (15) did give a 30—34% yield of methyl laccate D trimethyl ether (18), after methylation. An authentic sample of this compound could not be obtained but all the physical and spectral characteristics of our product are in agreement with published data.[4]

The foregoing anthraquinone was obtained more satisfactorily by using the inverse sequence of steps. 2,6-Dichloro-1,4-benzoquinone (11) was condensed with



[7] R. Chong and P. S. Clozy, *Tetrahedron Letters*, 1966, 741.

[8] J.-L. Grandmaison and P. Brassard, *J. Org. Chem.*, 1978, **43**, 1435.

the 4-methoxy-3-methoxycarbonyl-2-trimethylsiloxypenta-1,3-dienes (6a, b) to give 2-chloro-6-methoxy-7-methoxycarbonyl-8-methyl-1,4-naphthoquinone (13) in 39% yield, which could be increased to 48% by initiating the reaction at −35 °C. Subsequent reaction of this naphthoquinone with 1,1-dimethoxy-3-trimethylsiloxybuta-1,3-diene [5] gave a 92% yield of the methyl ether ester of laccaic acid D (18).

Finally the synthesis of kermesic acid was undertaken by first attempting to condense the mixture of dienes (6a,b) with 2,6-dichloronaphthazarin (19). Use of a large excess (3 equiv.) of the diene and separation of the crude products before methylation gave a 60% yield of 6-chloro-5,8-dihydroxy-3-methoxy-2-methoxycarbonyl-1-methylanthraquinone (20) and a smaller amount of the unmethylated product (21). Substitution of the chlorine by methoxide in (20) using sodium methoxide and copper(I) iodide in dimethylformamide and methanol [9] gave a 52% yield, after methylation, of the permethylated derivative of kermesic acid (23), identical with authentic material [48% of the trimethyl ether (22) was also recovered]. By prolonging the reaction time for this process to 24 h, a 90% yield of the desired product was obtained. Finally condensation of 2-chloro-6-methoxy-7-methoxycarbonyl-8-methyl-1,4-naphthoquinone (13) prepared earlier with a new reagent, 1,1,4-trimethoxy-3-trimethylsiloxybuta-1,3-diene [8] gave a 94% yield of methyl tetra-*O*-methylkermesate (23) (45% from 2,6-dichloro-1,4-benzoquinone).

EXPERIMENTAL

M.p.s were taken for samples in capillary tubes with a Thomas–Hoover apparatus (calibrated thermometer). I.r. and u.v. spectra were determined with Beckman IR-12 and DK-1A spectrophotometers, respectively. N.m.r. spectra were recorded with a Bruker HX-90 spectrometer (tetramethylsilane as internal standard). Mass spectra were obtained with a Varian M-66 spectrometer. Woelm silica gel, activity III, for dry column chromatography was used throughout.

(E)-4-*Methoxypent*-3-*en*-2-*one* (3a).—The *O*-methylation of acetylacetone (1) (110 g, 1.10 mol) with dimethyl sulphate (101.5 ml, 1.10 mol), anhydrous potassium carbonate (151.5 g), and dry acetone (700 ml), according to the method of Chong and Clozy,[7] gave the *E*-isomer [10] (65.8 g, 52.5%), b.p. 78—82 °C (24 mmHg); $\nu_{max.}$ (film) 1 681 (C=O), 1 590 (C=C), and 1 068 cm^{-1} (C–O–C); $\delta(CDCl_3)$ 2.12 (3 H, s, 5-H_3), 2.24 (3 H, s, 1-H_3), 3.65 (3 H, s, 4-OMe), and 5.51 (1 H, s, 3-H).

(E)- *and* (Z)-4-*Methoxy*-3-*methoxycarbonylpent*-3-*en*-2-*one* (4a,b).—An analogous reaction with methyl diacetylacetate [11] (2) (63.2 g, 0.40 mol), dimethyl sulphate (50.4 g, 0.40 mol), and potassium carbonate (55.2 g) in dry acetone (300 ml), upon distillation of the crude product, gave a first fraction (b.p. 65—83 °C at 0.5 mmHg) consisting of the *C*-alkylation product (16.7 g), 3-*methoxycarbonyl*-3-*methylpentane*-2,4-*dione* (24%), b.p. 75—78 °C at 0.5 mmHg; $\nu_{max.}$ (film) 1 710br cm^{-1} (C=O); $\delta(CDCl_3)$ 1.61 (3 H, s, 3-H_3), 2.24 (6 H, s, 1-, 5-H_3), and 3.82 (3 H, s, 3-CO_2Me) (Found: C. 55.6; H, 7.05. $C_8H_{12}O_4$ requires C, 55.8; H, 7.05%).

A higher-boiling fraction (b.p. 83—95 °C at 0.5 mmHg) was a mixture of the corresponding (E)- *and* (Z)-*methyl ethers* (4a,b) (32.2 g, 47%), b.p. 85—90 °C at 0.5 mmHg; $\nu_{max.}$ (film) 1 700br (C=O), 1 609, 1 580 (C=C), and 1 085 cm^{-1} (C–O–C); $\delta(CDCl_3)$ 2.12 and 2.29 (2 s, 5-H_3), 2.36 and 2.42 (2 s, 1-H_3), 3.68 and 3.78 (2 s, 4-OMe), and 3.82 (s, 3-CO_2Me) (Found: C, 55.55; H, 7.05. $C_8H_{12}O_4$ requires C, 55.8; H, 7.05%).

(E)- *and* (Z)-4-*Methoxy*-2-*trimethylsiloxypenta*-1,3-*diene* (5a,b).—To a suspension of anhydrous zinc chloride (800 mg) in triethylamine (46 g, 0.44 mol) was added 4-methoxypent-3-en-2-one (3a) (22.8 g, 0.20 mol) in benzene (60 ml) followed by freshly distilled chlorotrimethylsilane (43.4 g, 0.40 mol) according to the procedure of Danishefsky and Kitahara.[6] Distillation gave the *dienes* (5a,b) (27.1 g, 73%), b.p. 75—78 °C at 15 mmHg; $\nu_{max.}$ (film) 1 658, 1 590 (diene), 1 072 (C–O–C), and 840 cm^{-1} (Si–C str.); $\delta(CDCl_3)$ 0.21 (s, 2-$OSiMe_3$), 1.83 and 2.01 (2 approx. d, $J < 1$ Hz, 5-H_3), 3.48 (s, 4-OMe), *ca.* 3.94—4.17 (2 m, 1-H_2), 4.87 and 4.97 (2 approx. q, $J < 1$ Hz, 3-H) (Found: C, 58.0; H, 9.8. $C_9H_{18}O_2Si$ requires C, 58.0; H, 9.75%).

(E)- *and* (Z)-4-*Methoxy*-3-*methoxycarbonyl*-2-*trimethylsiloxypenta*-1,3-*diene* (6a,b).—A similar reaction using zinc chloride (600 mg), triethylamine (48 ml), 4-methoxy-3-methoxycarbonylpent-3-en-2-one (4a,b) (25.8 g, 0.15 mol) in benzene (45 ml) and chlorotrimethylsilane (38.1 ml) gave a fraction distilling between 78 and 84 °C at 0.2 mmHg consisting of a mixture of the *dienes* (6a,b) (28.3 g, 77%), b.p. 78—80 °C (0.5 mmHg); $\nu_{max.}$ (film) 1 701 (CO_2CH_3), 1 610 (C=C), 1 088 (C–O–C), and 850 cm^{-1} (Si–C str.); $\delta(CDCl_3)$ 0.22 and 0.25 (2, s, 2-$OSiMe_3$), 1.99 and 2.28 (2 s, 5-H_3), 3.55 and 3.57 (2 s, 4-OMe), 3.66 (s, 3-CO_2Me), 4.04 and 4.25 (2 m, 1-H_2) (Found: C, 54.1; H, 8.0. $C_{11}H_{20}O_4Si$ requires C, 54.05; H, 8.25%).

Reaction of (E)- *and* (Z)-4-*Methoxy*-2-*trimethylsiloxypenta*-1,3-*diene* (5a,b) *with* 2-*Bromo*-5-*chloro*-8-*hydroxy*-6-*methyl*-1,4-*naphthoquinone* (7).—(*a*) To a suspension of the juglone (7) (300 mg, 1.00 mmol) in anhydrous benzene (5 ml) was added dropwise a solution of the dienes (5a,b) (230 mg, 1.25 mmol) in the same solvent (5 ml). The mixture, after slight spontaneous warming, was refluxed for 1 h and then evaporated to dryness. The residue was heated at 125 °C for 0.5 h and at 140 °C for 0.5 h, then hydrolysed by refluxing for 5 min in tetrahydrofuran (5 ml) and aqueous 5% hydrochloric acid (5 ml). The cooled mixture was filtered and the dried solid separated by dry column chromatography. Chloroform eluted 4-*chloro*-1-*hydroxy*-6-*methoxy*-3,8-*dimethylanthraquinone* (9) (170 mg, 54%), m.p. 183—184 °C (benzene); $\nu_{max.}$ (KBr) 1 670 (C=O), 1 632 (chelated C=O), and 1 600br cm^{-1} (aryl); $\delta(CDCl_3)$ 2.46 (3 H, s, 3-Me), 2.74 (3 H, s, 8-Me), 3.93 (3 H, s, 6-OMe), 6.95 (1 H, d, J 2.5 Hz, 7-H), 7.12 (1 H, s, 2-H), 7.57 (1 H, d, J 2.5 Hz, 5-H), and 13.52 (1 H, s, 1-OH); *m/e* 318/316 (M^+) (Found: C, 64.1; H, 4.15; Cl, 11.4. $C_{17}H_{13}ClO_4$ requires C, 64.45; H, 4.15; Cl, 11.2%). Chloroform–ethyl acetate (4 : 1) eluted 4-*chloro*-1,6-*dihydroxy*-3,8-*dimethylanthraquinone* (8) (75 mg, 25%), m.p. 267—268 °C (chloroform); $\nu_{max.}$ (KBr) 3 400br (6-OH), 1 651 (C=O), 1 631 (chelated C=O), and 1 607 cm^{-1} (aryl); $\delta[(CD_3)_2SO]$ 2.32 (3 H, s, 3-Me), 2.57 (3 H, s, 8-Me), 6.91 (1 H, d, J 2.5 Hz, 7-H), 7.19 (1 H, s, 2-H), 7.27 (1 H, d, J 2.5 Hz, 5-H), 11.05 (1 H, s, 6-OH), and 13.36 (1 H, br s, 1-OH);

[9] A. McKillop, B. D. Howarth, and R. J. Kobylecki, *Synth. Comm.*, 1974, **4**, 35.

[10] D. V. C. Awang, *Canad. J. Chem.*, 1971, **49**, 2672.

[11] Z. Yoshida, H. Ogoshi, and T. Tokumitsu, *Tetrahedron*, 1970, **26**, 5691.

m/e 304/302 (M^+) (Found: C, 63.0; H, 3.9. $C_{16}H_{11}ClO_4$ requires C, 63.5; H, 3.65%).

(*b*) In another experiment the residue after pyrolysis was hydrolysed with methanol (5 ml) and 5% hydrochloric acid (5 ml). The dried solid (290 mg) was methylated by refluxing with dimethyl sulphate (1.50 g, 12.0 mmol), anhydrous potassium carbonate (1.80 g, 13.2 mmol), and dry acetone (50 ml) for 6 h. Dry column chromatography (benzene) gave 4-*chloro*-1,6-*dimethoxy*-3,8-*dimethylanthraquinone* (10) (200 mg, 61%), m.p. 224—225 °C (benzene); $\nu_{max.}$ (KBr) 1 665 (C=O) and 1 600 cm^{-1} (aryl); δ(CF_3CO_2D) 2.64 (3 H, s, 3-Me), 2.81 (3 H, s, 8-Me), 4.10 (3 H, s, 6-OMe), 4.29 (3 H, s, 1-OMe), 7.18 (1 H, d, *J* 2.5 Hz, 7-H), 7.53 (1 H, s, 2-H), and 7.69 (1 H, d, *J* 2.5 Hz, 5-H); *m/e* 332/330 (M^+) (Found: C, 65.05; H, 4.7; Cl, 11.05. $C_{18}H_{15}ClO_4$ requires C, 65.35; H, 4.55; Cl, 10.7%).

2-*Chloro*-6-*methoxy*-8-*methyl*-1,4-*naphthoquinone* (12).—To a solution of 2,6-dichloro-1,4-benzoquinone (11) (354 mg, 2.00 mmol) in tetrahydrofuran (10 ml) at −35 °C was added slowly (15 min) 4-methoxy-2-trimethylsiloxypenta-1,3-diene (5a,b) (390 mg, 2.10 mmol) cooled to the same temperature. The solution was stirred for 1 h, allowed to warm to 20 °C slowly, stirred at this temperature for 1 h, refluxed for 1 h, and finally evaporated to dryness. The residue was pyrolysed at 140 °C for 1 h, hydrolysed by refluxing for 10 min in methanol (10 ml) and 2% hydrochloric acid (10 ml), and filtered from the cold reaction medium. Methylation was carried out by stirring for 24 h in chloroform (50 ml), methyl iodide (4.0 ml), and silver(I) oxide (2.2 g). Chromatography (benzene) of the crude ether gave the pure *naphthoquinone* (12) (132 mg, 28%), m.p. 161—162 °C (benzene or ether); $\nu_{max.}$ (KBr) 1 670 (C=O) and 1 600br cm^{-1} (aryl); $\lambda_{max.}$ (ethanol) 209, 227(sh), 269, and 400 nm (log ε 4.46, 4.09, 4.27, and 3.38); δ($CDCl_3$) 2.71 (3 H, s, 8-Me), 3.92 (3 H, s, 6-OMe), 6.98 (1 H, d, *J* 3.0 Hz, 7-H), 7.12 (1 H, s, 3-H), and 7.44 (1 H, d, *J* 3.0 Hz, 5-H); *m/e* 238/236 (M^+) (Found: C, 60.75; H, 3.9; Cl, 14.9. $C_{12}H_9ClO_3$ requires C, 60.9; H, 3.85; Cl, 15.0%).

1,3,6-*Trimethoxy*-8-*methylanthraquinone* (*Tri*-O-*methyldeoxyerythrolaccin*) (16).— (*a*) To a suspension of 2-chloro-6,8-dimethoxy-1,4-naphthoquinone [12] (14) (252 mg, 1.00 mmol) in dry benzene (5 ml) was added in two portions 4-methoxy-2-trimethylsiloxypenta-1,3-diene (5a,b) (460 mg, 2.50 mmol) in the same solvent (10 ml). The mixture was refluxed for 3.5 h, (the second portion of diene was added after 90 min), evaporated to dryness, and pyrolysed at 140 °C for 90 min. The residue was hydrolysed by refluxing for 10 min in methanol (5 ml) and 5% hydrochloric acid (5 ml). After cooling, filtering, and drying, the crude material was methylated as before [compound (10)] and the product, purified by dry column chromatography (chloroform), gave *tri*-O-*methyldeoxyerythrolaccin* (16) (95 mg, 31%), m.p. 203—204 °C (methanol) (lit.,[3,4] 205 °C); $\nu_{max.}$ (KBr) 1 654 (C=O) and 1 600 cm^{-1} (aryl); $\lambda_{max.}$ (ethanol) 218, 278, and 400 nm (log ε 4.53, 4.54, and 3.67); δ($CDCl_3$) 2.79 (3 H, s, 8-Me), 3.92, 3.94, and 3.97 (9 H, 3 s, 1,3,6-OMe), 6.74 (1 H, d, *J* 2.5 Hz, 2-H), 6.97 (1 H, d, *J* 2.5 Hz, 7-H), 7.34 (1 H, d, *J* 2.5 Hz, 4-H), and 7.55 (1 H, d, *J* 2.5 Hz, 5-H); *m/e* 312 (M^+) (Found: C, 69.55; H, 5.45. $C_{18}H_{16}O_5$ requires C, 69.2; H, 5.15%).

(*b*) In a similar experiment the diene (5a,b) (230 mg) in dry xylene (5 ml) was added to a suspension of the naphthoquinone (14) (252 mg) in the same solvent (5 ml). After 1 h the temperature of the mixture was raised to 100 °C for 7 d. Two 230-mg portions of the diene were introduced after 20 and 44 h. The crude product was hydrolysed and methylated as before and gave, after chromatography (chloroform–ethyl acetate 20 : 1), the same anthraquinone (16) (190 mg, 61%).

(*c*) Analogously the diene (5a,b) (560 mg, 3.00 mmol) in benzene (5 ml) was added to a suspension of 2-chloro-8-hydroxy-6-methoxy-1,4-naphthoquinone [8] (15) (238 mg, 1.00 mmol) in the same solvent (5 ml). The mixture was stirred for 1 h at room temperature, refluxed for 1 h, and evaporated to dryness. The residue was pyrolysed at 130 °C for 1.5 h, then hydrolysed, methylated, and purified by chromatography as above to give the anthraquinone (16) (225 mg, 72%).

(*d*) When a mixture of the naphthoquinone (15) (1.00 mmol) and the diene (5a,b) (2.00 mmol) in xylene (10 ml) was kept at 100 °C for 24 h and worked up in the usual way a 75% yield of the anthraquinone (16) (234 mg) was obtained.

(*e*) A mixture of 2-chloro-6-methoxy-8-methyl-1,4-naphthoquinone (12) (236 mg, 1.00 mmol) and 1,1-dimethoxy-3-trimethylsiloxybuta-1,3-diene [5] (404 mg, 2.00 mmol) in anhydrous benzene (15 ml) was stirred for 1 h, refluxed for 1 h, and evaporated to dryness. The residue after pyrolysis (1 h at 145 °C) was hydrolysed and methylated in the usual way [as for compound (10)] and gave the anthraquinone (16) (280 mg, 90%).

5-*Chloro*-3,8-*dimethoxy*-2-*methoxycarbonyl*-1,6-*dimethylanthraquinone* (17).—A solution of 4-methoxy-3-methoxycarbonyl-2-trimethylsiloxypenta-1,3-diene (6a,b) (305 mg, 1.25 mmol) in dry benzene (5 ml) was added dropwise to a suspension of the juglone (7) (301 mg, 1.00 mmol) in the same solvent (5 ml). The mixture was stirred at room temperature for 1 h, refluxed for 1 h, and evaporated. The residue after pyrolysis (1 h at 130 °C) was hydrolysed and methylated in the usual way [compound (10)]. Chromatography (benzene) yielded the *anthraquinone* (17) (172 mg, 44%), m.p. 215—216 °C (carbon tetrachloride); $\nu_{max.}$ (KBr) 1 725 (ester), 1 673 (C=O), and 1 582 cm^{-1} (aryl); δ($CDCl_3$) 2.52 (3 H, s, 6-Me), 2.63 (3 H, s, 1-Me), 3.96, 3.98, and 3.99 (9 H, 3 s, 2-CO_2Me and 3,8-OMe), 7.18 (1 H, s, 7-H), and 7.51 (1 H, s, 4-H); *m/e* 390/388 (M^+) (Found: C, 61.45; H, 4.55. $C_{20}H_{17}ClO_6$ requires C, 61.8; H, 4.4%).

3-*Chloro*-7-*methoxy*-6-*methoxycarbonyl*-5-*methyl*-1,4-*naphthoquinone* (13).—A procedure analogous to that described for the preparation of compound (12), and involving 2,6-dichloro-1,4-benzoquinone (11) (354 mg, 2.00 mmol) and the dienes (6a,b) (512 mg, 2.10 mmol), gave, after chromatography (chloroform), the *naphthoquinone* (13) (280 mg, 48%), m.p. 160—161 °C (carbon tetrachloride); $\nu_{max.}$ (KBr) 1 725 (ester), 1 661 (C=O), and 1 580 cm^{-1} (aryl); $\lambda_{max.}$ (chloroform) 272, 284sh, and 390 nm (log ε 4.42, 4.18, and 3.40); δ(CF_3CO_2D) 2.71 (3 H, s, 5-Me), 4.09 and 4.13 (6 H, 2 s, 6-CO_2Me and 7-OMe), 7.33 (1 H, s, 2-H), and 7.73 (1 H, s, 8-H); *m/e* 296/294 (M^+) (Found: C, 56.8; H, 3.9; Cl, 12.05. $C_{14}H_4ClO_5$ requires C, 57.05; H, 3.75; Cl, 12.05%).

3,6,8-*Trimethoxy*-2-*methoxycarbonyl*-1-*methylanthraquinone* (*Methyl Laccate* D *Trimethyl Ether*) (18).—(*a*) The method chosen for the synthesis of anthraquinone (16) [method (*c*)] was applied in this case using 2-chloro-8-hydroxy-6-methoxy-1,4-naphthoquinone [8] (15) (238 mg, 1.00 mmol) and 4-methoxy-3-methoxycarbonyl-2-trimethylsiloxypenta-1,3-diene (6a,b) (730 mg, 3.00 mmol). Chromatography (chloroform–ethyl acetate 20 : 1) gave the *tetramethyl ester ether of laccaic acid* D (18) (126 mg, 34%), m.p.

[12] J.-L. Grandmaison and P. Brassard, *Tetrahedron*, 1977, **33**, 2047.

221—222 °C (methanol) (lit.,[4] 226 °C); $\nu_{max.}$ (KBr) 1 725 (ester), 1 667 (C=O), and 1 595br cm^{-1} (aryl); $\lambda_{max.}$ (ethanol) 220, 279, 325, and 410 nm (log ε 4.50, 4.56, 3.85, and 3.68); δ($CDCl_3$) 2.68 (3 H, s, 1-Me), 3.96 and 3.98 (12 H, 2 s, 2-CO_2Me and 3,6,8-OMe), 6.75 (1 H, d, *J* 3.0 Hz, 7-H), 7.30 (1 H, d, *J* 3.0 Hz, 5-H), and 7.61 (1 H, s, 4-H); *m/e* 370 (M^+) (Found: C, 64.85; H, 4.75. $C_{20}H_{18}O_7$ requires C, 64.85; H, 4.9%).

(*b*) The ester was also prepared as for the anthraquinone (16) [method (*e*)] from 3-chloro-7-methoxy-6-methoxycarbonyl-5-methyl-1,4-naphthoquinone (13) (294 mg, 1.00 mmol) and 1,1-dimethoxy-3-trimethylsiloxybuta-1,3-diene [5] (404 mg, 2.00 mmol). Chromatography as above gave the anthraquinone (18) (340 mg, 92%).

6-*Chloro*-5,8-*dihydroxy*-3-*methoxy*-2-*methoxycarbonyl*-1-*methylanthraquinone* (20).—A solution of 4-methoxy-3-methoxycarbonyl-2-trimethylsiloxypenta-1,3-diene (6a,b) (510 mg, 2.10 mmol) in benzene (5 ml) was added to a suspension of 2,6-dichloronaphthazarin [13,14] (19) (180 mg, 0.70 mmol) in the same solvent (5 ml). The mixture was stirred for 1 h, refluxed for 3 h, and evaporated. The residue was pyrolysed at 140 °C for 1 h and then hydrolysed in the usual manner. Chromatography (chloroform) gave the *anthraquinone* (20) (156 mg, 60%), m.p. 257—258 °C (acetone); $\nu_{max.}$ (KBr) 1 725 (ester), 1 625 (chelated C=O), and 1 573 cm^{-1} (aryl); $\lambda_{max.}$ (chloroform) 269sh, 276, 305, and 470 nm (log ε 4.46, 4.51, 4.00, and 4.01); δ($CDCl_3$) 2.74 (3 H, s, 1-Me), 3.98 and 4.04 (6 H, 2 s, 2-CO_2Me and 3-OMe), 7.43 (1 H, s, 7-H), 7.82 (1 H, s, 4-H), 13.11 and 13.23 (2 H, 2 s, 5,8-OH); *m/e* 378/376 (M^+) (Found: C, 57.4; H, 3.35; Cl, 9.2. $C_{18}H_{13}ClO_7$ requires C, 57.4; H, 3.5; Cl, 9.2%). A second zone consisted of 6-*chloro*-3,5,8-*trihydroxy*-2-*methoxycarbonyl*-1-*methylanthraquinone* (21) (80 mg, 32%), m.p. 248—249 °C (acetone); $\nu_{max.}$ (KBr) 3 240 (OH), 1 690 (ester), 1 623 (chelated C=O), and 1 579 cm^{-1} (aryl); $\lambda_{max.}$ (chloroform) 240, 281, and 470 nm (log ε 4.39 4.44, and 4.01); *m/e* 364/362 (M^+) (Found: C, 56.0; H, 3.15; Cl, 9.85. $C_{17}H_{11}ClO_7$ requires C, 56.3; H, 3.05; Cl, 9.8%).

3,5,6,8-*Tetramethoxy*-2-*methoxycarbonyl*-1-*methylanthraquinone* (*Methyl Tetra*-O-*methylkermesate*) (23).—(*a*) A mixture of 6-chloro-5,8-dihydroxy-3-methoxy-2-methoxycarbonyl-1-methylanthraquinone (20) (152 mg, 0.404 mmol), sodium methoxide (from 1.50 g of sodium), copper(I) iodide (150 mg), absolute methanol (30 ml), and anhydrous dimethylformamide [9] (30 ml) was refluxed for 24 h, then poured into water (300 ml), acidified, and filtered. Methylation as for compound (10) gave the *ester ether* (23) (145 mg, 90%), m.p. 193—194 °C (methanol) (lit.,[15] 196 °C); $\nu_{max.}$ (KBr) 1 717 (ester), 1 669 (C=O), and 1 583 cm^{-1} (aryl); $\lambda_{max.}$ (ethanol) 224, 266, 280, and 415 nm (log ε 4.46, 4.46, 4.41, and 3.88); δ($CDCl_3$) 2.64 (3 H, s, 1-Me), 3.94 and 3.98 (15 H, 2 s, 2-CO_2Me and 3-,5-,6-,8-OMe), 6.80 (1 H, s, 7-H), and 7.54 (1 H, s, 4-H); *m/e* 400 (M^+) (Found: C, 63.25; H, 5.15. $C_{21}H_{20}O_8$ requires C, 63.0; H, 5.05%). This compound was obtained earlier along with the corresponding isokermesate in a partial synthesis.[16]

When the foregoing reaction mixture was heated for only 3.5 h, and the crude product methylated in the usual way and separated by chromatography, two substances were isolated: the *kermesic acid derivative* (23) (52%) and 6-*chloro*-3,5,8-*trimethoxy*-2-*methoxycarbonyl*-1-*methylanthraquinone* (22) (48%), m.p. 227—228 °C (methanol); $\nu_{max.}$ (KBr) 1 725 (ester), 1 678 (C=O), and 1 578 cm^{-1} (aryl); δ($CDCl_3$) 2.62 (3 H, s, 1-Me), 3.97 (12 H, br s, 2-CO_2Me and 3-,5-,8-OMe), 7.36 (1 H, s, 7-H), and 7.54 (1 H, s, 4-H); *m/e* 406/404 (M^+) (Found: C, 59.15; H, 4.4; Cl, 8.5. $C_{20}H_{17}ClO_7$ requires C, 59.35; H, 4.25; Cl, 8.75%).

(*b*) The ester ether (23) was also prepared as for the anthraquinone (16) [method (*e*)] from 3-chloro-7-methoxy-6-methoxycarbonyl-5-methyl-1,4-naphthoquinone (13) (294 mg, 1.00 mmol) and 1,1,4-trimethoxy-3-trimethylsiloxybuta-1,3-diene [8] (464 mg, 2.00 mmol). Chromatography (chloroform) after hydrolysis and methylation gave the anthraquinone (23) (373 mg, 94%).

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