Reactions of Keten Acetals. Part 7.[1] Total Syntheses of the Tetramethyl Ethers of the 1-Acyl-2,4,5,7-tetrahydroxyanthraquinones Rhodolamprometrin and Rhodocomatulin

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Acylketen acetals or (better) their trimethylsilyl enol ethers condense regiospecifically with 2-halogeno-1,4-naphthoquinones. Reactions of 1,1-dimethoxy-3-trimethylsilyloxyhexa-1,3-diene and -octa-1,3-diene with 2-chloro-6,8-dimethoxy-1,4-naphthoquinone gave the corresponding 1-alkyl-2,4,5,7-tetramethoxyanthraquinones. The latter underwent spontaneous photochemical oxidation at the benzylic position and yielded the title compounds. The method has been adapted to provide a simple synthesis of questin.

αβ-UNSATURATED aldehydes, ketones, and esters in the presence of strong base are known to give cycloaddition products, presumably through their enolates.[2] It was expected that the readily accessible acylketen acetals would at certain temperatures behave as 1-hydroxyvinylketen acetals, and regiospecifically [1,3] give anthraquinones having substitution patterns not easily obtained by other means (*e.g.* 3-hydroxyl-1-methoxy- and 1-alkyl-2,4-dimethoxyanthraquinones).

The acylketen acetals (4)—(6) were obtained by Friedel–Crafts reactions of acyl chlorides with 1,1-dichloroethylene followed by methoxydehalogenation.[4] This method yielded mainly orthoesters, confirming an earlier observation;[5] however the acylketen acetals could easily be isolated after heating the crude products at 150 °C under normal pressure for several hours (at higher temperatures, esters are also obtained). Moreover the use of slightly less (*ca.* 1.8 equiv.) than the calculated amount of methoxide was important in order to avoid secondary reactions.

In a preliminary experiment a large excess of the acetylketen dimethyl acetal (4) was heated with 2-bromo-5-chloro-8-hydroxy-6-methyl-1,4-naphthoquinone (10) for 30 min at 120 °C; the desired reaction occurred, but with concomitant transetherification, giving the 1-hydroxy-6,8-dimethoxyanthraquinone (12) rather than the expected 1,6-dihydroxy-8-methoxy-derivative (14). The yield (39%) was inferior to that

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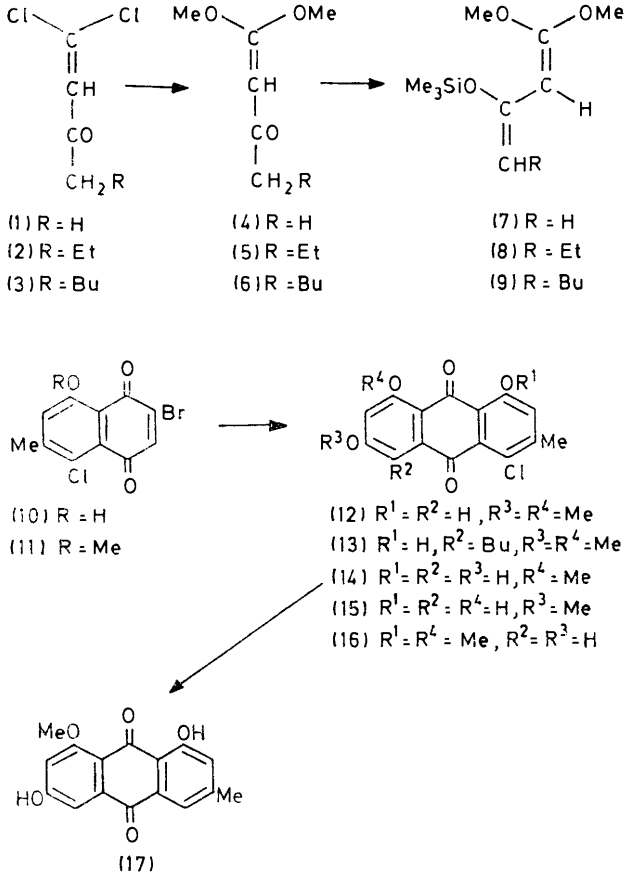
[2] H. Meerwein, *Chem. Ber.*, 1944, **77**, 227; P. G. Sammes and T. W. Wallace, *J.C.S. Chem. Comm.*, 1973, 524.

[3] J. Banville, J.-L. Grandmaison, G. Lang, and P. Brassard, *Canad. J. Chem.*, 1974, **52**, 80.

[4] I. Heilbron, E. R. H. Jones, and M. Julia, *J. Chem. Soc.*, 1949, 1430; A. N. Nesmeyanov, O. A. Reutov, and A. S. Gudkova, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1961, 260.

[5] F. Pochat and E. Levas, *Bull. Soc. chim. France*, 1972, 3151.

obtained previously [3] with keten dimethyl acetal, but provided the prospect of preparing the 1-alkyl-2,4-dimethoxy-analogues. This possibility was examined with 1,1-dimethoxyoct-1-en-3-one (6) and the same substrate (10) as before, and the 1-butylanthraquinone (13) was isolated in 23% yield. When the reaction was



applied to the less reactive (no free *peri*-hydroxy-group [3]) 2-chloro-6,8-dimethoxy-1,4-naphthoquinone (18),[6] only 10% of the expected quinone (22) was obtained (nevertheless the procedure is extremely simple.)

It seemed advisable at this point either to increase the affinity of the quinone by cleaving the 8-methoxy-group or to convert the enone into a more reactive form. The recent preparation of *trans*-1-methoxy-3-trimethylsilyloxybuta-1,3-diene [7] from *trans*-4-methoxybut-3-en-2-one, chlorotrimethylsilane, triethylamine, and zinc chloride seemed to provide the more promising alternative, even though the effect of the presence of a Lewis acid known to catalyse the polymerisation [8] of more reactive keten acetals was problematic.

Under the prescribed conditions 4,4-dimethoxybut-3-en-2-one (4) was converted into the trimethylsilyloxybutadiene (7) in 67% yield; however the use of zinc chloride with this type of compound was found to have a deleterious effect, a yield of 88% being obtained later without it. The higher homologues (8) and (9) could also be obtained with only slightly decreased efficiency. Earlier work [9] on the silyl enol ethers derived from aldehydes and ketones led to the assumption that mixtures of *cis*- and *trans*-isomers of (8) and (9) would be encountered. However the products decomposed during g.l.c. and their n.m.r. spectra did not reveal the expected duplication of signals.

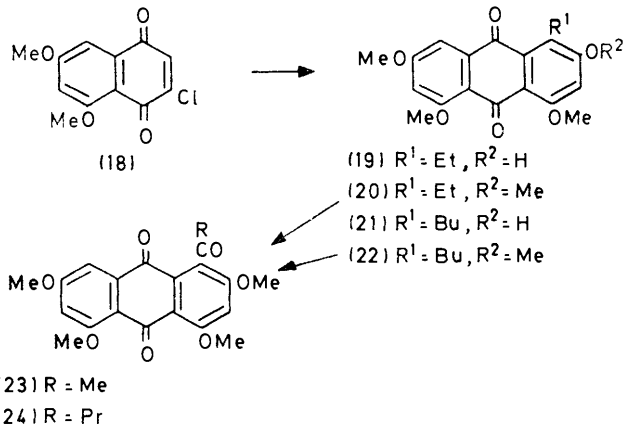
The usefulness of the new compounds was first tested by treating the diene (7) with the usual substrate, the juglone (10). At room temperature, the cycloaddition was complete within a few min, giving a colourless adduct which was then pyrolysed at 150 °C. Hydrolysis [10] of the silylated compound by refluxing briefly in dilute hydrochloric acid gave the desired anthraquinone (14) in 87% yield. When methanolysis of the silyl ether was attempted before the pyrolytic step, three products were isolated in similar amounts: the 1,6-dihydroxy-8-methoxyanthraquinone (14) (the normal product) and the 1,8-dihydroxy-6-methoxy- and 1-hydroxy-6,8-dimethoxy-anthraquinones (15) and (12) resulting from initial addition of methanol to the enol ether with and without acidolysis of the acetal. It was also observed that the presence of *peri*-hydroxy-groups on the naphthoquinones, which generally have a favourable effect in the case of unsubstituted keten acetals, is not important when these conjugated reagents are used: a (90%) yield of the anthraquinone (16) was produced from the juglone ether (11) and the diene (7).

A new and simple preparation of questin (17) illustrates one use of these dienes. In spite of its structural simplicity, this compound was not obtained by synthesis until 1972.[11] A simple reductive dechlorination by sodium dithionite of the anthraquinone (14) obtained earlier gave questin in 70% yield.

Rhodolamprometrin and the mono- and di-methyl ethers of rhodocomatulin are natural products extracted from tropical crinoids,[12] and the synthesis of their completely *O*-methylated derivatives could now be envisaged with the type of diene just described. As expected the formation of bulky adducts from the conjugated keten acetals (8) and (9) and 2-chloro-6,8-dimethoxy-1,4-napthoquinone (18) was more difficult, and required heating at 120 °C for nearly 1 h. Subsequent pyrolysis produced considerable decomposition and it was eventually found that the aromatisation was best carried out by refluxing in methanol for 12 h. The crude products had two constituents: the tetramethoxy-anthraquinone (20) or (22), resulting as before from

[6] A. Castonguay and P. Brassard, *Synth. Comm.*, 1975, **5**, 377 (other methods will be communicated shortly).
[7] S. Danishefsky and T. Kitahara, *J. Amer. Chem. Soc.*, 1974, **96**, 7807.
[8] S. M. McElvain, *Chem. Rev.*, 1949, **45**, 453.
[9] H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, 1969, **34**, 2324.
[10] A. E. Pierce, 'Silylation of Organic Compounds,' Pierce Chemical Co., Rockford, Illinois, 1968, p. 447.
[11] R. F. Curtis, C. H. Hassall, and D. R. Parry, *J.C.S. Perkin I*, 1972, 240.
[12] M. D. Sutherland and J. W. Wells, *Austral. J. Chem.*, 1967, **20**, 515; R. H. Thomson and T. R. Erdman, *J.C.S. Perkin I*, 1972, 1291.

addition of methanol to the enol ether, and the 2-hydroxyanthraquinone (19) or (21). The mixtures were methylated directly and gave the tetra-*O*-methyl ethers (20) and (22) in 81 and 64% yields, respectively.



The last step in the syntheses, the oxidation of the highly hindered benzylic position, was not expected to be easily accomplished. Indeed a variety of the usual reagents either left the substrates unchanged or caused considerable decomposition. It was observed in the meantime that 1-butyl-2,4,5,7-tetramethoxyanthraquinone (22), although not expected to be unstable, seemed to undergo slow deterioration. A sample deliberately left exposed to air and daylight for 2 weeks was partly converted into a new compound. The i.r. spectrum of this substance showed the characteristic absorption of a hindered benzylic ketone, and n.m.r. confirmed the transformation of a butyl into a butyryl group. This process can be accelerated by bubbling oxygen into a boiling ethanolic solution of the 1-alkyl-2,4,5,7-tetramethoxyanthraquinone (20) or (22) while irradiating with a 500 W photoflood lamp. After 2—3 h the substrate had disappeared and the corresponding compound (23) or (24) was isolated in 34 or 47% yield, respectively. This spontaneous oxidation of a hindered benzylic position appears to be without precedent in quinone chemistry.

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 Varian A-60 and Bruker HX-90 spectrometers (tetramethylsilane as internal standard). Woelm silica gel (activity III), was used throughout for dry column chromatography.

1,1-*Dichlorohex*-1-*en*-3-*one* (2).—Anhydrous aluminium chloride (133.4 g, 1.00 mol) was added in small portions with stirring to butanoyl chloride (106.6 g, 1.00 mol) in an ice-bath, followed at room temperature by 1,1-dichloroethylene (dropwise; 2 h). The mixture was stirred for 2 h more, poured on ice (1 kg), and extracted with carbon tetrachloride (5 × 100 ml). The extracts were steam-distilled and the distillate extracted with the same solvent (5 × 100 ml). After washing with 2% sodium hydrogen carbonate and drying at 0 °C over sodium sulphate (in the presence of hydroquinone and magnesium oxide), the organic phase was distilled and gave the *enone* (2) (83.7 g, 50%), b.p. 88—90° at 20 mmHg; n_D^{23} 1.484 0; $\nu_{max.}$ (film) 1 695 (C:O) and 1 575 cm^{-1} (C:C); δ (90 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 7.0 Hz, 6-H_3), 1.64 (2 H, sextet, *J* 7.0 Hz, 5-H_2), 2.53 (2 H, t, *J* 7.0 Hz, 4-H_2), and 6.69 (1 H, s, 2-H) (Found: Cl, 42.85. $C_6H_8Cl_2O$ requires Cl, 42.45%).

1,1-*Dichloro-oct*-1-*en*-3-*one* (3).—A similar reaction with hexanoyl chloride (134.6, 1.00 mol) gave the *enone* (3) (94.3 g, 48%), b.p. 106—110° at 10 mmHg; n_D^{23} 1.480 0; $\nu_{max.}$ (film) 1 696 and 1 575 cm^{-1}; δ (90 MHz; $CDCl_3$) 0.89 (3 H, t, *J* 6.5 Hz, 8-H_3), *ca.* 1.10—1.78 (6 H, m, 5-, 6-, and 7-H_2), 2.55 (2 H, t, *J* 7.5 Hz, 4-H_2), and 5.02 (1 H, s, 2-H) (Found: C, 49.5; H, 6.35; Cl, 36.35. $C_8H_{12}Cl_2O$ requires C, 49.25; H, 6.2; Cl, 36.35%). When the distillation is carried out at 0.5 mmHg two products are obtained: the ketone (3), b.p. 60—64°, and 1,1,1-trichlorooctan-3-one, b.p. 68—72°; n_D^{24} 1.472 2; $\nu_{max.}$ (film) 1 728 cm^{-1}; δ (60 MHz; neat) 0.89 (3 H, t, *J* 5.0 Hz, 8-H_3), *ca.* 1.10—1.90 (6 H, m, 5-, 6-, and 7-H_2), 2.60 (2 H, t, *J* 6.0 Hz, 4-H_2), and 3.92 (2 H, s, 2-H_2) [this product is unstable and decomposes to the unsaturated ketone (3) within a few hours].

4,4-*Dimethoxybut*-3-*en*-2-*one* (4).—To a stirred solution of sodium methoxide [from sodium (20.7 g, 0.900 mol)] in absolute methanol (480 ml), kept at room temperature, was added (2 h) 4,4-dichlorobut-3-en-2-one [4] (64.8 g, 0.466 mol). The mixture was stirred for 2 h more at the same temperature, filtered, and distilled to give 4,4,4-trimethoxybutan-2-one (56.4 g, 74%), b.p. 82—84° at 12 mmHg; n_D^{25} 1.4228; $\nu_{max.}$ (film) 1 718 (C:O) cm^{-1}; δ (90 MHz; CCl_4) 2.12 (3 H, s, 1-H_3), 2.77 (2 H, s, 3-H_2), and 3.24 [9 H, s, 4,4,4-$(MeO)_3$]. Pyrolysis of this orthoester (240.0 g) at 140—145 °C (4 h) gave the acylketen acetal (4) (68.0 g, 35%), b.p. 104—105° at 10 mmHg n_D^{21} 1.492 0 (lit.,[5] b.p. 116—117° at 12 mmHg; n_D 1.491 5); $\nu_{max.}$ (film) 1 680 (C:O), 1 600br (C:C), and 1 280 and 1 235 cm^{-1} (C·OR); δ (60 MHz; neat) 2.11 (3 H, s, 1-H_3), 3.75 and 3.80 [2 × 3 H, 2s, 4,4-$(OMe)_2$], and 4.58 (1 H, s, 3-H), and 4,4,4-trimethoxybutan-2-one (133.0 g, 55%).

1,1-*Dimethoxyhex*-1-*en*-3-*one* (5).—A similar reaction with 1,1-dichlorohex-1-en-3-one (2) (80.0 g, 0.478 mol), sodium (19.8 g, 0.861 mol), and absolute methanol gave a mixture of 1,1,1-*trimethoxyhexan*-3-*one* (70.5 g, 73%), b.p. 53—54° at 0.2 mmHg; n_D^{26} 1.426 5; $\nu_{max.}$ (film) 1 703 (C:O), and 1 125 and 1 095 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$) 0.83 (3 H, t, *J* 7.0 Hz, 6-H_3), 1.56 (2 H, sextet, *J* 7.0 Hz, 5-H_2), 2.53 (2 H, t, *J* 7.0 Hz, 4-H_2), 2.83 (2 H, s, 2-H_2), and 3.29 [9 H, s, 1,1,1-$(OMe)_3$] (Found: C, 56.6; H, 9.4. $C_9H_{18}O_4$ requires C, 56.8; H, 9.5%); and the *acylketen acetal* (5) (7.3 g, 10%), b.p. 74—76° at 0.2 mmHg; n_D^{23} 1.482 1; $\nu_{max.}$ (film) 1 672 (C:O), 1 604 (C:C), and 1 241 and 1 181 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$) 0.90 (3 H, t, *J* 7.0 Hz, 6-H_3), 1.59 (2 H, approx. q, 5-H_2), 2.44 (2 H, t, *J* 7.5 Hz, 4-H_2), 3.73 and 3.82 [2 × 3 H, 2s, 1,1-$(OMe)_2$], and 4.60 (1 H, s, 2-H) (Found: C, 60.9; H, 8.85. $C_8H_{14}O_3$ requires C, 60.75; H, 8.9%). Pyrolysis of 1,1,1-trimethoxyhexan-3-one (36.0, 0.19 mol) at 150 °C (3 h) gave the unchanged orthoester (18.7 g, 52%), b.p. 94—103° at 20 mmHg, and the acylketen acetal (5) (12.9 g, 43%), b.p. 74—80° at 0.2 mmHg.

1,1-*Dimethoxyoct*-1-*en*-3-*one* (6).—An analogous reaction with 1,1-dichloro-oct-1-en-3-one (3) (36.0 g, 0.184 mol),

sodium (7.6 g, 0.330 mol), and absolute methanol (170 ml) gave a mixture of 1,1,1-trimethoxyoctan-3-one (28.2 g, 40%), b.p. 70—71° at 0.05 mmHg; n_D^{20} 1.436 7; $\nu_{max.}$ (film) 1 705 (C:O) and 1 250 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$ 0.89 (3 H, t, *J* 7.0 Hz, 8-H_3), *ca.* 1.17—1.72 (6 H, m, 5-, 6-, and 7-H_2) 2.56 (2 H, t, *J* 7.0 Hz, 4-H_2), 2.56 (2 H, s, 2-H_2), and 3.28 [9 H, s, 1,1,1-$(OMe)_3$]; and the *acylketen acetal* (6) (6.0 g, 18%), b.p. 86—90° at 0.5 mmHg; n_D^{24} 1.460 7; $\nu_{max.}$ (film) 1 680 (C:O), 1 600 (C:C), and 1 230 cm^{-1} (C·OR); δ (90 MHz; neat) 0.87 (3 H, t, *J* 6.0 Hz, 8-H_3), *ca.* 1.10—1.70 (6 H, m, 5-, 6-, and 7-H_2), 2.43 (2 H, t, *J* 7.0 Hz, 4-H_2), 3.71 and 3.77 [2 × 3 H, 2s, 1,1-$(OMe)_2$], and 4.55 (1 H, s, 2-H) (Found: C, 64.2; H, 10.0. $C_{10}H_{18}O_3$ requires C, 64.5; H, 9.75%).

1,1-*Dimethoxy*-3-*trimethylsilyloxybuta*-1,3-*diene* (7).—To a solution of 4,4-dimethoxybut-3-en-2-one (4) (85.0 g, 0.653 mol), triethylamine (147.0 g, 1.452 mol), and dry benzene (180 ml) was added (15 min) chlorotrimethylsilane (133.0 g, 1.224 mol). The mixture was stirred at 38 °C for 3 h, then at room temperature for 16 h, filtered, distilled to give the *diene* (7) (116.3 g, 88%), b.p. 84—87° at 10 mmHg; n_D^{23} 1.464 0; $\nu_{max.}$ (film) 1 657 (diene), 1 272 and 1 251 (C·OR), and 850 cm^{-1} (Si·C str.); δ (60 MHz; neat) 0.14 (9 H, s, 3-$OSiMe_3$), 3.52 and 3.61 [2 × 3 H, 2s, 1,1-$(OMe)_2$], 3.99 (1 H, d, *J* 1.0 Hz, 4-H), 4.07 (1 H, d, *J* 1.0 Hz, 4-H), and 4.39 (1 H, s, 2-H) (Found: C, 53.6; H, 9.1. $C_9H_{18}SiO_3$ requires C, 53.45; H, 8.95%).

1,1-*Dimethoxy*-3-*trimethylsilyloxyhexa*-1,3-*diene* (8).— A similar reaction with 1,1-dimethoxyhex-1-en-3-one (5) (20.0 g, 0.26 mol), triethylamine (40 ml), benzene (40 ml), and chlorotrimethylsilane (25.6 g, 0.236 mol) yielded the diene (8) (23.0 g, 77%), b.p. 60—68° at 0.3 mmHg; n_D^{24} 1.461 4; $\nu_{max.}$ (film) 1 650 and 1 620 (C:C), 1 250 and 1 230 (C·OR), and 835 cm^{-1} (Si·C str.); δ (90 MHz; $CDCl_3$) 0.15 (9 H, s, 3-$OSiMe_3$), 0.93 (3 H, t, *J* 7.0 Hz, 6-H_3), 2.04 (2 H, sextet, 5-H_2), 3.56 and 3.65 [2 × 3 H, 2s, 1,1-$(OMe)_2$], 3.98 (1 H, s, 2-H), and 4.78 (1 H, t, *J* 7.0 Hz, 4-H). The compound appeared to be unstable and an acceptable analysis was not obtained.

1,1-*Dimethoxy*-3-*trimethylsilyloxyocta*-1,3-*diene* (9).— An analogous reaction of 1,1-dimethoxyoct-1-en-3-one (6) (10.0 g, 0.053 7 mol) with chlorotrimethylsilane (11.0 g, 0.101 mol) and triethylamine (16 ml) in benzene (15 ml) gave the diene (9) (11.5 g, 82%), b.p. 70—80° at 0.2 mmHg; n_D^{24} 1.458 2; $\nu_{max.}$ (film) 1 655 (C:C), 1 250 (C·OR), and 841 cm^{-1} (Si·C str.); δ (90 MHz; $CDCl_3$) 0.17 (9 H, s, 3-$OSiMe_3$), 0.90 (3 H, t, *J* 7.0 Hz, 8-H_3), *ca.* 1.17—1.44 (4 H, m, 6-, and 7-H_3), *ca.* 1.83—2.17 (2 H, m, 5-H_2), 3.56 and 3.65 [2 × 3 H, 2s, 1,1-$(OMe)_2$], 3.99 (1 H, s, 2-H), and 4.78 (1 H, t, *J* 7.0 Hz, 4-H). The compound becomes discoloured rapidly and a correct analysis was not obtained.

4-*Chloro*-1-*hydroxy*-6,8-*dimethoxy*-3-*methylanthraquinone* (12).—A mixture of 2-bromo-5-chloro-8-hydroxy-6-methyl-1,4-naphthoquinone (10) (600 mg, 1.99 mmol) and 4,4-dimethoxybut-3-en-2-one (4) (1.301 g, 10.0 mmol) was heated at 120 °C for 30 min, then chromatographed on silica gel (60 g) (dry column; chloroform), and gave the anthraquinone (12) (258 mg, 39%), m.p. 215.0—215.5° (from ethanol–benzene) (lit.,[3] m.p. 213.0—213.5°), identical with a sample obtained previously (mixed m.p., t.l.c., and i.r. and n.m.r. spectra).

1-*Butyl*-8-*chloro*-5-*hydroxy*-2,4-*dimethoxy*-7-*methylanthraquinone* (13).—A similar reaction between the naphthoquinone (10) (400 mg, 1.33 mmol) and 1,1-dimethoxyoct-1-en-3-one (6) (750 mg, 4.03 mmol) (120 °C; 1 h) gave, after chromatography on silica gel (60 g) (dry column; benzene–ethyl acetate, 9 : 1), the *anthraquinone* (13) (120 mg, 23%), m.p. 162.5—163.0° (from methanol); $\lambda_{max.}$ (EtOH) 229, 255, 264, 285, and 425 nm (log ε 4.51, 4.29, 4.32, 4.16, and 4.08); $\nu_{max.}$ (KBr) 1 673 (C:O), 1 632 (chelated C:O), 1 585 (aryl), and 1 232 and 1 202 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$) 0.95 (3 H, t, *J* 7.0 Hz, 4′-H_3), *ca.* 1.37—1.67 (4H, m, 2′- and 3′-H_2), 2.43 (3 H, s, 7-CH_3), 2.91 (2 H, t, *J* 8.0 Hz, 1′-H_2), 3.97 (3 H, s, 2-OCH_3), 4.03 (3 H, s, 4-OCH_3), 6.65 (1 H, s, 3-H), 7.04 (1 H, s, 6-H), and 12.86 (1 H, s, 5-OH); *m/e* 388/390 (M^+) (Found: C, 64.55; H, 5.45. $C_{21}H_{21}ClO_5$ requires C, 64.85; H, 5.45%).

4-*Chloro*-1,6-*dihydroxy*-8-*methoxy*-3-*methylanthraquinone* (14).—To a suspension of 2-bromo-5-chloro-8-hydroxy-6-methyl-1,4-naphthoquinone (10) (600 mg, 1.99 mmol) in dry benzene (10 ml) was added 1,1-dimethoxy-3-trimethylsilyloxybuta-1,3-diene (7) (490 mg, 2.42 mmol). The mixture rapidly became homogeneous; it was refluxed for 1 h, and evaporated, and the residue heated at 145 °C for 1 h.

(*a*) The crude intermediate, when refluxed for 5 min in methanol (5 ml) and dilute hydrochloric acid (5%; 5 ml), gave the *anthraquinone* (14) (547 mg, 86%), m.p. 303—304° (from ethanol); $\lambda_{max.}$ (EtOH) 222, 251, 273, 286, and 434 nm (log ε 4.49, 4.09, 4.20, 4.24, and 3.90); $\nu_{max.}$ (KBr) 3 250 (free OH), 1 668 (C:O), 1 625 (chelated C:O), 1 598 (aryl), and 1 230 and 1 198 cm^{-1} (C·OR); δ [90 MHz; $(CD_3)_2SO$] 2.32 (3 H, s, 3-CH_3), 3.86 (3 H, s, 8-OCH_3), 6.69 (1 H, d, *J* 2.0 Hz, 7-H), 7.00 (1 H, d, *J* 2.0 Hz, 5-H), 7.14 (1 H, s, 2-H), and 13.62 (1 H, s, 1-OH); *m/e* 318/320 (M^+) (Found: C, 60.35; H, 3.35. $C_6H_{11}ClO_5$ requires C, 60.3; H, 3.5%).

(*b*) When methanol (5 ml) was added to the mixture before pyrolysis, three products were obtained by chromatography on silica gel (60 g) (dry column; chloroform) (in order of decreasing R_F value): 4-*chloro*-1,8-*dihydroxy*-6-*methoxy*-3-*methylanthraquinone* (15) (188 mg, 30%), m.p. 209—210° (from ethanol); $\lambda_{max.}$ (EtOH) 226, 252, 269, 288, and 440 nm (log ε 4.47, 4.19, 4.24, 4.12, and 4.04); $\nu_{max.}$ (KBr) 1 674 (C:O), 1 621 (chelated C:O), 1 605 (aryl), and 1 260 and 1 230 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$) 2.48 (3 H, s, 3-CH_3), 3.92 (3 H, s, 6-OCH_3), 6.67 (1 H, d, *J* 2.5 Hz, 7-H), 7.18br (1 H, s, 2-H), 7.33 (1 H, d, *J* 2.5 Hz, 5-H), and 12.04 and 12.69 (2 × 1 H, 2s, 1- and 8-OH); *m/e* 318/320 (M^+) (Found: C, 60.35; H, 3.25; Cl, 10.7. $C_{16}H_{11}ClO_5$ requires C, 60.3; H, 3.5; Cl, 11.15%); 4-chloro-1-hydroxy-6,8-dimethoxy-3-methylanthraquinone (12) (216 mg, 33%), m.p. 214.5°; and 4-chloro-1,6-dihydroxy-8-methoxy-3-methylanthraquinone (14) (160 mg, 25%), m.p. 299—300°. (The two latter compounds were identical to those prepared earlier.)

4-*Chloro*-6-*hydroxy*-1,8-*dimethoxy*-3-*methylanthraquinone* (16).—A similar reaction [method (a)] with 2-bromo-5-chloro-8-methoxy-6-methyl-1,4-naphthoquinone (11) (316 mg, 1.00 mmol), 1,1-dimethoxy-3-trimethylsilyloxybuta-1,3-diene (7) (404 mg, 2.00 mmol) and benzene (5 ml) gave the anthraquinone (16) (300 mg, 90%), m.p. 293° (from 1,2-dichloroethane) (lit.,[13] 294—295°), identical with a sample prepared previously (mixed m.p., t.l.c., and i.r. and n.m.r. spectra).

1,6-*Dihydroxy*-8-*methoxy*-3-*methylanthraquinone* (*Questin*) (17).—A mixture of 4-chloro-1,6-dihydroxy-8-methoxy-3-methylanthraquinone (14) (637 mg, 2.00 mmol), sodium hydroxide (1.80 g), sodium dithionite (9.60 g), ethanol (50 ml), and water (50 ml) was stirred under nitrogen for 12 h at room temperature. Air was then bubbled (3 h) vigorously through the solution, which was then diluted with

water (300 ml), acidified with dilute hydrochloric acid (10%), saturated with sodium chloride, and extracted with ethyl acetate. Evaporation of the extract, crystallisation of the residue from ethanol, and chromatography on silica gel (40 g) of the mother liquor (dry column; chloroform–ethyl acetate–methanol, 69 : 30 : 1) gave questin (17) (401 mg, 70%), m.p. 300—301° (lit., 303,[11] 301—303[13]); $\lambda_{max.}$ (EtOH) 224, 248, 285, and 430 nm (log ε 4.55, 4.14, 4.35, and 3.95); $\nu_{max.}$ (KBr) 3 360 (free OH), 1 673 (C:O), 1 629 (chelated C:O), 1 591 (aryl), and 1 266 and 1 211 cm^{-1} (C·OR); δ [60 MHz; $(CD_3)_2SO$] 2.38 (3 H, s, 3-CH_3), 3.92 (3 H, s, 8-OCH_3), 6.85 (1 H, d, *J* 2.0 Hz, 7-H), 7.10br (1 H, s, 2-H), 7.21 (1 H, d, *J* 2.0 Hz, 5-H), and 7.40br (1 H, s, 4-H); *m/e* 284 (M^+) (Found: C, 67.9; H, 4.4. $C_{16}H_{12}O_5$ requires C, 67.6: H, 4.25%).

1-*Ethyl*-2,4,5,7-*tetramethoxyanthraquinone* (20).—A mixture of 2-chloro-6,8-dimethoxy-1,4-naphthoquinone (18) (1.00 g, 3.98 mmol) and 1,1-dimethoxy-3-trimethylsilyloxyhexa-1,3-diene (8) (1.09 g, 4.75 mmol) was heated at 120 °C for 1 h, diluted with absolute methanol (20 ml), and refluxed overnight. Dilute hydrochloric acid (5%; 10 ml) was added to the hot suspension, which was refluxed briefly, cooled, diluted with water (100 ml), and extracted with ethyl acetate (3 × 100 ml). The extract was evaporated and the residue was methylated in the usual way by refluxing for 18 h in a mixture of dimethyl sulphate (7.6 g), potassium carbonate (7.8 g), and acetone (100 ml). The crude product was chromatographed on silica gel (60 g) (dry column; chloroform–ethyl acetate, 9 : 1), giving the *anthraquinone* (20) (1.14 g, 81%), m.p. 189.5—190.0° (from methanol); $\lambda_{max.}$ (EtOH) 224, 265sh, 286, and 410 nm (log ε 4.64, 4.32, 4.47, and 3.86); $\nu_{max.}$ (KBr) 1 660 (C:O), 1 595 (aryl), and 1 240 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$) 1.21 (3 H, t, *J* 7.5 Hz, 2′-H_3), 3.03 (2 H, q *J* 7.5 Hz, 1′-H_2), 3.92, 3.93, 3.94, and 3.99 (4 × 3 H, 4s, 2-, 4-, 5-, and 7-OCH_3), 6.70 (1 H, d, *J* 2.5 Hz, 6-H), 6.73br (1 H, s, 3-H), and 7.16 (1 H, d, *J* 2.5 Hz, 8-H); *m/e* 356 (M^+) (Found: C, 67.45; H, 5.8. $C_{20}H_{20}O_6$ requires C, 67.4; H, 5.65%).

1-*Butyl*-2,4,5,7-*tetramethoxyanthraquinone* (22).—A similar reaction between 2-chloro-6,8-dimethoxy-1,4-naphthoquinone (2.00 g, 7.94 mmol) and 1,1-dimethoxy-3-trimethylsilyloxyocta-1,3-diene (9) (2.50 g, 9.50 mmol) gave the *anthraquinone* (22) (1.94 g, 64%), m.p. 154.5—155.0° (from carbon tetrachloride); $\lambda_{max.}$ (EtOH) 226, 270, 288, and 420 nm (log ε 4.50, 4.19, 4.33, and 3.76); $\nu_{max.}$ (KBr) 1 661 (C:O), 1 598 (aryl), and 1 249 and 1 214 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$) 0.97 (3 H, approx. t, *J ca.* 6.5 Hz, 4′-H_3), *ca.* 1.33—1.66 (4 H, m, 2′- and 3′-H_2), 3.00 (2 H, approx. t, *J ca.* 7.0 Hz, 1′-H_2), 3.90, 3.94, and 3.98 (6 H, 3 H, and 3 H, 3s, 2-, 4-, 5-, and 7-OCH_3), 6.68 (1 H, d, *J* 2.5 Hz, 6-H), 6.72br (1 H, s, 3-H), and 7.16 (1 H, d, *J* 2.5 Hz, 8-H); *m/e* 384 (M^+) (Found: C, 68.6; H, 6.4. $C_{22}H_{24}O_6$ requires C, 68.75; H, 6.3%).

1-*Acetyl*-2,4,5,7-*tetramethoxyanthraquinone* (*Tetra*-O-*methylrhodolamprometrin*) (23).—Oxygen was bubbled into a solution of 1-ethyl-2,4,5,7-tetramethoxyanthraquinone (20) (200 mg, 0.56 mmol) in ethanol (20 ml), which was simultaneously heated under reflux and irradiated with a 500 W photoflood lamp (2 h). The residue obtained after evaporation of the solvent was chromatographed on silica gel (60 g) (dry column; chloroform–ethyl acetate, 9 : 1) and gave the *acetylanthraquinone* (23) (70 mg, 34%), m.p. 260.5—261.0° (methanol); $\lambda_{max.}$ (EtOH) 224, 284, and 415 nm (log ε 4.54, 4.41, and 3.77); $\nu_{max.}$ (KBr) 1 700 (C:O), 1 655 (quinone C:O), 1 598 (aryl), and 1 260 and 1 235 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$) 2.57 (3 H, s, 1-$COCH_3$), 3.90, 3.91, 3.96, and 4.01 (4 × 3 H, 4s, 2-, 4-, 5-, and 7-OCH_3), 6.77 (1 H, d, *J* 2.5 Hz, 6-H), 6.79 (1 H, s, 3-H), and 7.23 (1 H, d, *J* 2.5 Hz, 8-H); *m/e* 370 (M^+) and 355 ($M - CH_3$) (Found: C, 64.7; H, 5.0. $C_{20}H_{18}O_7$ requires C, 64.85; H, 4.9%).

1-*Butanoyl*-2,4,5,7-*tetramethoxyanthraquinone* (*Tetra*-O-*methylrhodocomatulin*) (24).—A similar reaction (3 h) with 1-butyl-2,4,5,7-tetramethoxyanthraquinone (22) (200 mg, 0.520 mmol) in ethanol (10 ml) gave the butanoylanthraquinone (24) (97 mg, 47%), m.p. 200—201° (from benzene) (analytical sample, m.p. 210.0—210.5°) (lit.,[12] m.p. 203—204 and 211—212°); $\lambda_{max.}$ (EtOH) 224, 284, 342, and 415 nm (log ε 4.62, 4.38, 3.63, and 3.79); $\nu_{max.}$ (KBr) 1 695 (C:O), 1 660 (quinone C:O), 1 595 (aryl), and 1 247 and 1 205 cm^{-1} (C·OR); δ (90 MHz; $CDCl_3$) 1.03 (3 H, t, *J* 7.5 Hz, 4′-H_3), 1.86br (2 H, sextet, 3′-H_2), 2.75 (2 H, t, *J* 7.5 Hz, 2′-H_2), 3.88, 3.93, and 3.99 (6 H, 3 H, and 3 H, 3s, 2 , 4-, 5-, and 7-OCH_3), 6.74 (1 H, d, *J* 2.5 Hz, 6-H), 6.77br (1 H, s, 3-H), and 7.20 (1 H, d, *J* 2.5 Hz, 8-H); *m/e* 398 (M^+) and 355 ($M - C_3H_7$) (Found: C, 66.4; H, 5.45. $C_{22}H_{22}O_7$ requires C, 66.3; H, 5.55%), identical (mixed m.p., t.l.c. in four solvent systems, and i.r. spectra) with an authentic sample.

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