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Experiments Directed Towards the Synthesis of Anthracyclinones. XXIII* A Synthesis of Fridamycin E

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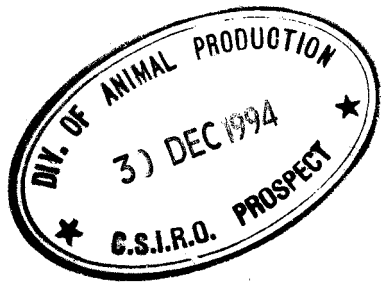

Abstract

Fridamycin E (1) has been synthesized in six steps from the anthrarufin mono(chloroallyl) ether (10). The synthesis was based on a titanium-mediated aldol-like addition of a (−)-menthyl acetate enolate to the ketone (9). Similar additions to the aldehydes (23) and (25) are reported.

Fridamycin E (1) is a member of a group of anthracycline antibiotics isolated from mutants of *Streptomyces parvulus*,[1] which shows high activity against Gram-positive bacteria. Krohn has reported a low yielding synthesis of the enantiomer of fridamycin E based on a Marshalk reductive alkylation of the monomethyl ether (8) by a masked aldehyde derived from (*S*)-lactic acid.[1]

We required the enantiomeric trimethoxyfridamycins (2) and (3) for n.m.r. studies designed to establish the absolute configurations of enantiopure intermediates for vineomycinone syntheses.[2] We report syntheses of both (2) and (3) and the conversion of the former into fridamycin E. The key step in the synthesis was a titanium-mediated aldol-like addition of an enolate of (−)-menthyl acetate[3] to the methyl ketone (9). Similar additions to the aldehydes (23) and (25) are also discussed.

The ketone (9) was prepared from the vinyl chloride (10)[4] in an overall yield of 96% by ether cleavage (BBr_3, CH_2Cl_2, −78°C), methylation (Me_2SO_4, K_2CO_3, acetone), and solvomercuration ($Hg(O_2CCF_3)_2$, CF_3CO_2H, HCO_2H). The intermediate compounds (11) and (12) and the ketone (9) all gave combustion analyses and spectral data appropriate to their structures (see Experimental).

Reaction of the ketone (9) with 3 equiv. of the reagent produced from treatment of lithio-(−)-menthyl acetate with chlorotrisisopropoxytitanium[3] gave

* Part XXII, *Aust. J. Chem.*, 1994, **47**, 1561.

[1] Krohn, K., and Baltus, W., *Tetrahedron*, 1988, **44**, 49.
[2] Pausler, M. G., and Rutledge, P. S., *Aust. J. Chem.*, 1994 **47**, 2149.
[3] Cambie, R. C., Coddington, J. M., Milbank, J. B. J., Pausler, M. G., Rustenhoven, J. J., Rutledge, P. S., Shaw, G. L., and Sinkovich, P. I., *Aust. J. Chem.*, 1993, **46**, 583.
[4] Cambie, R. C., Pausler, M. G., Rutledge, P. S., and Woodgate, P. D., *Aust. J. Chem.*, 1987, **40**, 1063.

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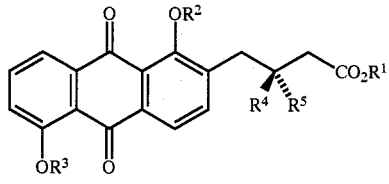
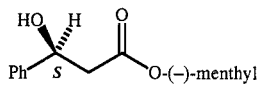
a 1:1 mixture of the diastereomers (4) and (5), which were separated by h.p.l.c. A high-resolution mass spectrum of the (3*S*)-isomer (4), which was eluted first, included a molecular ion at *m/z* 522·2603 consistent with the molecular formula, while infrared absorbances could be assigned to the OH (3500 cm^{-1}), ester carbonyl (1718) and quinone carbonyls (1670). The ^1H n.m.r. spectrum contained an envelope of peaks (δ 0·76–1·97) characteristic of a menthyl group, while the methylene adjacent to the ester carbonyl gave rise to a singlet at 2·49, the diastereotopic benzylic protons to two doublets at 3·00 and 3·09, and the methoxy groups to sharp singlets at 3·92 and 4·04. The ^{13}C n.m.r. spectrum contained the requisite 31 resonances including those of the carbonyl carbons at δ 182·8, 182·4 (quinone) and 172·6 (ester), the carbinol carbon at 71·7, and the two methylene groups of the butanoate side chain at 41·0 (C4) and 44·6 (C2). The optical rotation of (4) was −31·4°.

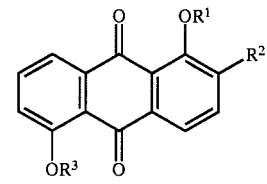
Included in a low-resolution mass spectrum of the diastereomer (5) was a molecular ion of *m/z* 522 consistent with the molecular formula, and in a high-resolution spectrum an $M^{+\bullet} - MeOH$ ion of *m/z* 490·2354, while the i.r. spectrum included an OH absorbance at 3510, and carbonyl absorbances at 1714 (ester) and 1672 cm^{-1} (quinone). The ^1H n.m.r. spectrum included signals characteristic of a menthyl moiety (δ 0·76–2·00), and doublets at 2·47 and 2·51 (methylene adjacent to the ester carbonyl) and at 3·00 and 3·09 (benzylic



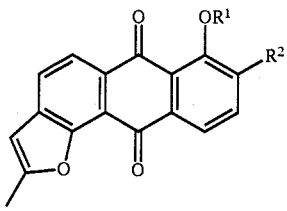
	R^1	R^2	R^3	R^4	R^5
(1)	H	H	H	Me	OH
(2)	Me	Me	Me	Me	OH
(3)	Me	Me	Me	OH	Me
(4)	menthyl	Me	Me	OH	Me
(5)	menthyl	Me	Me	Me	OH
(6)	Me	H	H	Me	OH
(7)	Me	H	Me	Me	OH



(24)



	R^1	R^2	R^3
(8)	H	H	Me
(9)	Me	CH_2Ac	Me
(10)	H	$CH_2C(Cl)CH_2$	$CH_2C(Cl)CH_2$
(11)	H	$CH_2C(Cl)CH_2$	H
(12)	Me	$CH_2C(Cl)CH_2$	Me
(13)	Me	HO, H: CCH_2CO_2menthyl	Me
(14)	Me	H, OH: CCH_2CO_2menthyl	Me
(15)	H	HO, H: CCH_2CO_2menthyl	H
(16)	H	H, OH: CCH_2CO_2menthyl	H
(17)	CH_2CHCH_2	H	CH_2CHCH_2



	R^1	R^2
(25)	H	CHO
(26)	Ac	CHO
(27)	H	HO, H: CCH_2CO_2menthyl
(28)	H	H, OH: CCH_2CO_2menthyl

	R^1	R^2
(29)	Me	HO, H: CCH_2CO_2menthyl
(30)	Me	H, OH: CCH_2CO_2menthyl

methylene). Included among the 31 resonances in the ^{13}C n.m.r. spectrum were those of the carbonyl carbons at δ 182·9 and 182·4 (quinones) and 172·7 (ester), the carbinol carbon at 71·9, and the two methylene groups of the butanoate side chain at 46·8 (C2) and 41·0 (C4). The optical rotation of (5) was −29·9°.

Each of the diastereomers (4) and (5) was transesterified with methanol and potassium carbonate to give the enantiomeric methyl esters (2) and (3). A low-resolution mass spectrum of (3) included a molecular ion at *m/z* 398, and a high-resolution spectrum an $M^{+\bullet} - MeOH$ ion at *m/z* 366·1112. The i.r. spectrum included carbonyl absorbances at 1730 cm^{-1} (ester) and 1669 (quinone). The ^1H n.m.r. spectrum confirmed that transesterification had occurred with the menthyl resonances being replaced by one for an ester methoxyl at δ 3·71. The optical rotation of (3) was +3·9°. The spectral data for the enantiomer (2) was identical, and the optical rotation was −4·1°.

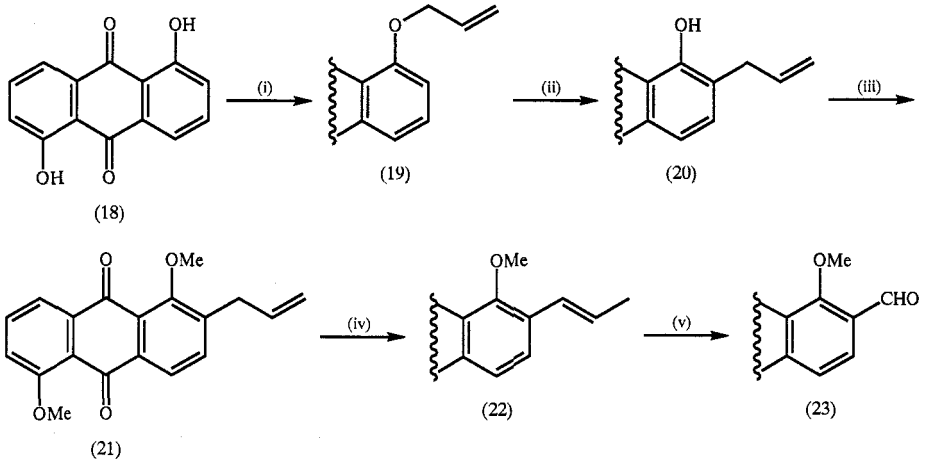
Demethylation of the isomer (2) with an excess of boron tribromide in dichloromethane at −78°C gave the diphenol (6) (74%) and the monophenol (7) (24%) resulting from selective cleavage of the C1′ ether moiety. The latter compound was readily converted into (6) by further treatment with boron tribromide. A high-resolution mass spectrum of the methyl ester (6) included an $M^{+\bullet} - H_2O$ ion at *m/z* 352·0930, with a linked scan showing this fragment to be a daughter of the molecular ion. The i.r. spectrum included carbonyl absorbances due to the ester (1731 cm^{-1}) and the intramolecularly hydrogen-bonded quinone (1633). The ^1H n.m.r. spectrum included two phenolic proton singlets (δ 12·68, 13·19), and the 20 resonances of the ^{13}C n.m.r. spectrum included two attributable to intramolecularly hydrogen-bonded quinone carbonyl groups at δ 187·8 and 188·3.

Hydrolysis of the methyl ester (6) with aqueous potassium hydroxide gave fridamycin E (1) (60%) with an optical rotation of +12°. The rotation compares favourably with that of +9·67° of the natural product,[1] while the melting point and spectral data for (1) compare well with that reported by Krohn for the C3 enantiomer[1] (see Experimental).

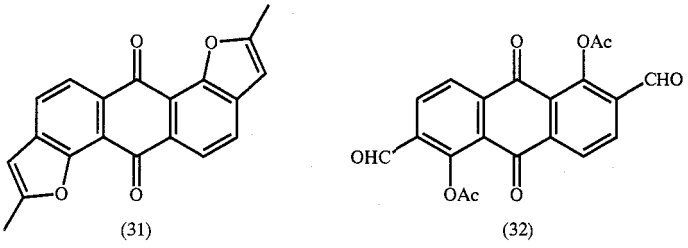
The lack of diastereoselectivity in the formation of (4) and (5) by titanium-mediated aldol addition to the ketone (9) was expected. However, since a similar addition to benzaldehyde had resulted in a modest (28%) diastereomeric excess of the (3*S*)-isomer (24), we were interested in similar additions to anthraquinone aldehydes, and in particular in establishing if a potentially chelating function[5] *ortho* to the aldehyde group would have any significant effect on the diastereofacial selectivity. The *ortho*-substituted aldehydes chosen were (23), prepared from the monoallyl ether of anthrarufin (19) in 84% overall yield as in Scheme 1, and (25) obtained by ozonolysis of the bisfuran (31).[4] Because of the poor solubility of the bisfuran in dichloromethane at −78°C, the optimizing ozonolysis used 2 equiv. of the oxidant for 2 h to give a 1:1 mixture of the substrate (31) and the acetate (26). After hydrolysis of the acetate (26) the phenol (25) and the bisfuran (31) were readily separated by chromatography.

The aldehyde (23) reacted rapidly with the menthyl acetate titanium reagent (2 equiv.) to give the menthyl propanoates (13) and (14) in 92% yield. H.p.l.c. analysis indicated a 1·2:1 ratio of (13) to (14). The absolute configurations for (13) and (14) have been tentatively assigned on the basis of comparison

[5] Reetz, M. T., *Acc. Chem. Res.*, 1993, **26**, 462.



Scheme 1. (i) $K_2CO_3/CH_2{=}CHCH_2Br$/dimethylformamide; (ii) $Na_2S_2O_4$/dimethylformamide/H_2O; (iii) $Me_2SO_4/K_2CO_3/Me_2CO$; (iv) KOH/MeOH; (v) O_3/CH_2Cl_2.



of the h.p.l.c. elution order with that for (24) and its diastereomer.[3] These assignments are also consistent with the (*S*)-selectivity obtained from all related titanium-mediated additions of the (−)-menthyl acetate which we have studied.[2,3] Although each diastereomer gave rise to different ^1H n.m.r. signals, overlapping precluded meaningful integration. This problem was overcome by cleavage of the methyl ether moieties (BBr_3, CH_2Cl_2) to give a mixture of the phenols (15) and (16). The aliphatic (C 3) hydroxy group of each of the phenols gave rise to a different ^1H n.m.r. signal (δ 3·85 and 3·98) which integrated in the ratio of 1·2:1 confirming the diastereoselectivity in the formation of (13) and (14).

The diastereomeric ethers (13) and (14) were separated by h.p.l.c. with (13) being eluted first. Molecular ions of *m/z* 494·2316 and 494·2305 were consistent with the molecular formula of $C_{29}H_{34}O_7$, and each i.r. spectrum included absorbances for an OH group, an ester carbonyl (1728 cm^{-1}) and the quinone carbonyls (1668). Each ^1H n.m.r. spectrum included the envelope of peaks characteristic of a menthyl moiety, and included in the 29 resonances of each ^{13}C n.m.r. spectrum were signals due to the quinone carbonyl carbons at δ 182·8 and 182·2. In the spectra of (13) doublets of doublets due to the diastereotopic C 2 protons appeared at δ 2·67 and 2·90, signals for the C 3 hydroxy and methine protons at 3·90 and 5·48 respectively, the ester carbonyl carbon at 172·4, and the methylene and benzylic carbons of the propanoate side chain at 41·7 and 65·4

respectively. The optical rotation of (13) was −20·8°. In the n.m.r. spectra of (14) doublets of doublets at δ 2·63 and 2·91 and signals at 3·78 and 5·49 were assigned to the diastereotopic C 2 protons, the C 3 hydroxy and H 3 respectively, and signals at 172·3, 41·9 and 65·5 to the ester carbonyl, the C 2 and the C 3 carbons respectively. The optical rotation of (14) was −33·7°.

Because of its poorer solubility than those of benzaldehyde or the anthraquinonyl methyl ethers (9) and (23) more tetrahydrofuran was required to keep the phenolic aldehyde (25) in solution at −78°C. Consequently the reaction of the phenol (25) with 3 equiv. of the (−)-menthyl acetate–titanium reagent was much slower. However, the use of 6 equiv. of the reagent led to the isolation of the menthyl propanoates in 78% yield, and recovery of 10% of the substrate (25). Integration of the n.m.r. signals of the C 3 hydroxy protons at δ 3·87 and 4·01 indicated formation of the esters (27) and (28) in a ratio of 1·3:1. Although the diastereomers (27) and (28) were not separable by h.p.l.c. the spectral data obtained for the mixture were completely consistent with both the retention of the furanoanthraquinone skeleton, and the aldol-like addition to the aldehyde moiety (see Experimental). Further, the mixture of ethers (29) and (30) obtained by methylation of the phenols was separable by h.p.l.c.*

A high-resolution mass spectrum of (29) contained a molecular ion at *m/z* 518·2316 which is consistent with the molecular formula $C_{31}H_{34}O_7$. The i.r. spectrum included an ester carbonyl absorbance (1724) and only one due to the quinone carbonyls (1667 cm^{-1}) indicating that both were free from hydrogen bonding. The ^1H n.m.r. spectrum included the envelope of signals (δ 0·68–2·00) characteristic of a menthyl group, signals due to the diastereotopic C 2 protons at 2·69 and 2·93, and a multiplet attributable to H 3 at 5·50. Resonances for the furan ring protons appeared at δ 2·64 (2′-CH_3) and 6·53 (H 3′), while a three-proton singlet at 3·99 confirmed the presence of the methoxy group. The optical rotation of (29) was −3·9°.

A high-resolution mass spectrum of (30) included a molecular ion at *m/z* 518·2280 which is consistent with the molecular formula $C_{31}H_{34}O_7$, and the i.r. spectrum included ester and quinone carbonyl absorbances (1724 and 1667 cm^{-1}). Again the ^1H n.m.r. spectrum included an envelope of signals attributable to the menthyl group (δ 0·78–1·96), while the diastereotopic C 2 protons gave rise to doublets of doublets at 2·63 and 2·94. A multiplet at δ 5·50 was attributed to H 3, signals at 2·64 (2′-CH_3) and 6·53 (H 3′) to the furan ring, and a three proton singlet at 3·99 to the methoxy group. The optical rotation of (30) was −40·3°.

Although interpretation of these results is limited by the tentative nature of the assignments of absolute configurations to the products, comparison of the addition to the ether (23) with that to benzaldehyde[3] suggests that the *ortho* methoxy group has little effect on the diastereofacial selectivity. There does appear to be a small enhancement of the favouring of the (3*S*)-diastereomer when the *ortho* substituent is a hydroxy group as in (25).

* Again the absolute configurations of (29) and (30) are tentative, having been assigned on the basis of the elution order from h.p.l.c. The configurations of (27) and (28) are based on these assigned to (29) and (30).

Experimental

For general experimental details see ref. 6.

2-(2′-Chloroprop-2′-enyl)-1,5-dimethoxyanthraquinone (12)

The ether (10)[4] (500 mg, 1·28 mmol) in dichloromethane (400 ml) was stirred with boron tribromide (1 ml, 8·8 mmol) at −78°C for 20 min. Quenching with water (10 ml), acidification (20% aqueous hydrochloric acid, 250 ml), workup and crystallization (CH_2Cl_2/hexanes) gave *2-(2′-chloroprop-2′-enyl)-1,5-dihydroxyanthraquinone* (11) (396 mg, 99%), m.p. 170–172° (Found: C, 65·2; H, 3·2. $C_{17}H_{11}ClO_4$ requires C, 64·9; H, 3·5%). λ_{max} 230 ($\log\epsilon$ 4·61), 257 (4·41), 290 (4·07), 425 nm (4·10). ν_{max} (KBr) 3550br (OH, intramolecularly H-bonded), 1635 (CO, H-bonded), 1605, 1435, 1368, 1309, 1240, 893, 785 cm^{-1}. δ_H 3·81, s, 2H, H 1′; 5·30, d, 1H, $J_{3'trans,3'cis}$ 1 Hz, H 3′ (*trans* to Cl); 5·36, d, 1H, $J_{3'cis,3'trans}$ 1 Hz, H 3′ (*cis* to Cl); 7·32, dd, 1H, $J_{6,7}$ 8·0. $J_{6,8}$ 1 Hz, H 6; 7·66, d, 1H, $J_{3,4}$ 8·0 Hz, H 3; 7·68, dd, 1H, $J_{7,8}$ 8·0, $J_{7,6}$ 8·0 Hz, H 7; 7·83, d, 1H, $J_{4,3}$ 8·0 Hz, H 4; 7·84, dd, 1H, $J_{8,7}$ 8·0, $J_{8,6}$ 1 Hz, H 8; 12·64, s, 1H, 5-OH; 13·04, s, 1H, 1-OH. *m/z* 314, 279, 237, 205, 165, 139, 115, 57.

The diphenol (11) (400 mg, 1·27 mmol), anhydrous potassium carbonate (10 g, 72 mmol), dimethyl sulfate (0·5 ml, 5·3 mmol) and acetone (300 ml) were heated under reflux for 6 h. After removing most of the solvent, the suspension was poured onto crushed ice (300 ml), giving a yellow solid, which was removed by filtration, washed with water (500 ml), and dissolved in CH_2Cl_2 (200 ml). Workup, column chromatography on magnesium carbonate (30 g) (CH_2Cl_2/hexanes, 50:50 v/v) and crystallization (CH_2Cl_2/hexanes) gave *2-(2′-chloroprop-2′-enyl)-1,5-dimethoxyanthraquinone* (12) as yellow needles (428 mg, 99%), m.p. 118–119° (Found: C, 66·5; H, 4·2. $C_{19}H_{15}ClO_4$ requires C, 66·6; H, 4·4%). λ_{max} 219 ($\log\epsilon$ 4·89), 257 (4·38), 373 nm (3·81). ν_{max} (KBr) 1675 (CO), 1587, 1572, 1465, 1442, 1388, 1260, 1033, 1000, 963, 792, 688, 628 cm^{-1}. δ_H 3·81, s, 2H, H 1′; 3·94, s, 3H, 1-OCH_3; 4·02, s, 3H, 5-OCH_3; 5·24, s, 1H, H 3′ (*trans* to Cl); 5·34, s, 1H, H 3′ (*cis* to Cl); 7·28, br d, 1H, $J_{6,7}$ 8·4 Hz, H 6; 7·66, d, 1H, $J_{3,4}$ 8·0 Hz, H 3; 7·66, dd unresolved, 1H, H 7; 7·85, br d, 1H, $J_{8,7}$ 7·7 Hz, H 8; 8·03, d, 1H, $J_{4,3}$ 8·0 Hz, H 4. δ_C 39·0, C 1′; 56·3, 5-OCH_3; 62·0, 1-OCH_3; 114·5, C 3′; 116·9, C 6; 119·4, C 8; 120·5, C 10a; 123·0, C 4; 124·7, C 9a; 134·8, C 7; 135·8, C 3; 136·2, 136·8, C 4a,8a; 137·4, C 2′; 139·7, C 2; 158·3, C 1; 159·6, C 5; 181·8, 182·3, C 9,10. *m/z* 342, 327, 307, 289.

1,5-Dimethoxy-2-(2′-oxopropyl)anthraquinone (9)

A solution of the vinyl chloride (12) (100 mg, 0·29 mmol) and mercury(II) trifluoroacetate (180 mg, 0·42 mmol) in formic acid (15 ml, 90% aq) and trifluoroacetic acid (15 ml) was stirred at room temperature for 20 h. Aqueous hydrochloric acid (200 ml, 50% v/v) was added to dissolve a yellow solid, which had precipitated, and the mixture was extracted with CH_2Cl_2 (3×50 ml). Workup and column chromatography on magnesium carbonate (10 g) (CH_2Cl_2/hexanes, 50:50 v/v) gave *1,5-dimethoxy-2-(2′-oxopropyl)anthraquinone* (9) as a pale yellow solid (92 mg, 98%), m.p. 128–129° (Found: C, 70·5; H, 4·9. $C_{19}H_{16}O_5$ requires C, 70·4; H, 5·0%). λ_{max} 227 ($\log\epsilon$ 4·34), 257 (4·45), 374 nm (3·88). ν_{max} (KBr) 1711 (ketone CO), 1672 (quinone CO), 1585, 1572, 1468, 1382, 1318, 1255, 1152, 1036, 952, 796, 723 cm^{-1}. δ_H 2·28, s, 3H, 3′-CH_3; 3·88, s, 5H, 1-OCH_3, H 1′; 4·03, s, 3H, 5-OCH_3; 7·30, br s, 1H, $J_{6,7}$ 7·6 Hz, H 6; 7·56, d, 1H, $J_{3,4}$ 7·9 Hz, H 3; 7·69, dd unresolved, 1H, H 7; 7·87, dd, 1H, $J_{8,7}$ 7·7, $J_{8,6}$ 1 Hz, H 8; 8·04, d, 1H, $J_{4,3}$ 7·9 Hz, H 4. δ_C 29·8, C 3′; 45·1, C 1′; 56·4, 5-OCH_3; 61·8, 1-OCH_3; 117·1, C 6; 119·5, C 8; 120·7, C 10a; 123·2, C 4; 124·6, C 9a; 135·0, C 7; 135·7, 136·4, C 4a,8a; 136·7, C 3; 136·9, C 2; 158·2, C 1; 159·7, C 5; 181·9, 182·6, C 9,10; 204·9, C 2′. *m/z* 324, 292, 282, 267, 43.

Titanium-Mediated Addition of Menthyl Acetate to the Ketone (9)

The dimethoxy ketone (9) in tetrahydrofuran, under nitrogen, was treated with 3 equiv. of the preformed titanium reagent[3] at −78°C until a deep wine red colour developed (*c.* 8 min). After warming towards room temperature until an orange-yellow colour developed (*c.* 5 min),

[6] Cambie, R. C., Holroyd, S. E., Larsen, D. S., Rutledge, P. S., and Woodgate, P. D., *Aust. J. Chem.*, 1992, **45**, 1589.

the reaction was quenched with saturated aqueous ammonium sulfate. Workup followed by p.l.c. (CH_2Cl_2) gave a 1:1 mixture of diastereomers (40 mg, 83%) of the (−)-menthyl anthraquinonylbutanoates (4) and (5), as an orange oil. Further purification by h.p.l.c. (thf/hexanes, 1:9 v/v, flow rate 4 ml/min, detector λ 310 nm) gave (i) *(−)-menthyl (3S)-4-(1′,5′-dimethoxy-9′,10′-anthraquinon-2′-yl)-3-hydroxy-3-methylbutanoate* (4), $[\alpha]_D$ −31·4° (*c*, 1·60 in dioxan) (Found: $M^{+\bullet}$, 522·2603. $C_{31}H_{38}O_7$ requires $M^{+\bullet}$, 522·2617). λ_{max} 227 ($\log\epsilon$ 4·20), 258 (4·33), 374 nm (3·76). ν_{max} (smear) 3500 (OH), 2955, 1718 (ester CO), 1670 (quinone CO), 1590, 1571, 1458, 1255, 1008, 967, 802, 722 cm^{-1}. δ_H 0·76, d, 3H, $J_{9'',8''}$ 7·0 Hz, H 9″; 0·83, m, 1H, H 6″*ax*; 0·88, d, 3H, $J_{10'',8''}$ 7·0 Hz, H 10″; 0·89, d, 3H, $J_{7'',1''}$ 6·5 Hz, H 7″; 1·00, m, 2H, H 5″*ax*,2″*ax*; 1·27, s, 3H, 3-CH_3; 1·37, dddd unresolved, 1H, H 4″; 1·48, m, 1H, H 1″; 1·68, dm, 2H, $J_{5''eq,5''ax}$ 12·1, $J_{6''eq,6''ax}$ 12·1 Hz, H 5″*eq*,6″*eq*; 1·85, m, 1H, H 8″; 1·97, dm, 1H, $J_{2''eq,2''ax}$ 11·9 Hz, H 2″*eq*; 2·49, s, 2H, H 2; 3·00, d, 1H, J_{4a4b} 13·2 Hz, H 4a; 3·09, d, 1H, $J_{4b,4a}$ 13·2 Hz, H 4b; 3·92, s, 3H, 1′-OCH_3; 4·04, s, 3H, 5′-OCH_3; 4·74, ddd, 1H, $J_{3'',4''}$ 10·9, $J_{3'',2''ax}$ 10·9, $J_{3'',2''eq}$ 4·4 Hz, H 3″; 7·30, dd, 1H, $J_{6',7'}$ 8·5, $J_{6',8'}$ 0·8 Hz, H 6′; 7·71, dd unresolved, 1H, H 7′; 7·76, d, 1H, $J_{3',4'}$ 8·0 Hz, H 3′; 7·90, dd, 1H, $J_{8',7'}$ 7·7, $J_{8',6'}$ 0·9 Hz, H 8′; 8·04, d, 1H, $J_{4',3'}$ 8·0 Hz H 4′. δ_C 16·1, C 9″; 20·7, C 10″; 21·9, C 7″; 23·2, C 5″; 26·1, C 8″; 27·2, 3-CH_3; 31·3, C 1″; 34·1, C 6″; 40·8, C 2″; 41·0, C 4; 44·6, C 2; 46·8, C 4″; 56·5, 5′-OCH_3; 61·9, 1′-OCH_3; 71·7, C 3; 74·7, C 3″; 117·0, C 6′; 119·6, C 8′; 120·8, C 10′a; 123·0, C 4′; 124·8, C 9′a; 135·0, C 7′; 136·2, C 4′a; 137·1, C 8′a; 138·3, C 2′; 138·5, C 3′; 158·5, C 1′; 159·7, C 5′; 172·6, C 1; 182·4, 182·8, C 9′,10′. *m/z* (d.e.i.) 522, 504, 490, 366, 293, 282 (100%), 267; and (ii) *(−)-menthyl (3R)-4-(1′,5′-dimethoxy-9′,10′-anthraquinon-2′-yl)-3-hydroxy-3-methylbutanoate* (5), $[\alpha]_D$ −29·9° (*c*, 1·67 in dioxan) (Found: $M^{+\bullet}$ − MeOH, 490·2354. $C_{30}H_{34}O_6$ ($M^{+\bullet}$ − MeOH) requires 490·2355). λ_{max} 226 ($\log\epsilon$ 4·28), 258 (4·40), 375 nm (3·82). ν_{max} (smear) 3500 (OH), 2960, 1714 (ester CO), 1672 (quinone CO), 1590, 1571, 1467, 1312, 1252, 1005, 963, 801, 721 cm^{-1}. δ_H 0·76, d, 3H, $J_{9'',8''}$ 6·9 Hz, H 9″; 0·84, m, 1H, H 6″*ax*; 0·89, d, 3H, $J_{10'',8''}$ 7·3 Hz, H 10″; 0·91, d, 3H, $J_{7'',1''}$ 7·3 Hz, H 7″; 1·02, m, 2H, H 5″*ax*,2″*ax*; 1·26, s, 3H, 3-CH_3; 1·38, dddd unresolved, 1H, H 4″; 1·49, m, 1H, H 1″; 1·68, dm, 2H, $J_{5''eq,5''ax}$ 12·5, $J_{6''eq,6''ax}$ 12·5 Hz, H 5″*eq*,6″*eq*; 1·86, m, 1H, H 8″; 2·00, dm, 1H, $J_{2''eq,2''ax}$ 11·2 Hz, H 2″*eq*; 2·47, d, 1H, $J_{2a,2b}$ 15·7 Hz, H 2a; 2·51, d, 1H, $J_{2b,2a}$ 15·7 Hz, 3·00, d, 1H, $J_{4a,4b}$ 13·2 Hz, H4a; 3·09, d, 1H, $J_{4b,4a}$ 13·2 Hz, H 4b; 3·92, s, 3H, 1′-OCH_3; 4·04, s, 3H, 5′-OCH_3; 4·75, ddd, 1H, $J_{3'',2''ax}$ 10·9, $J_{3'',4''}$ 10·9, $J_{3'',2''eq}$ 4·4 Hz, H 3″; 7·30, br d, 1H, $J_{6',7'}$ 8·2 Hz, H 6′; 7·71, dd unresolved, 1H, H 7′; 7·76, d, 1H, $J_{3',4'}$ 8·0 Hz, H 3′; 7·90, dd, 1H, $J_{8',7'}$ 7·7, $J_{8',6'}$ 0·7 Hz, H 8′; 8·04, d, 1H, $J_{4',3'}$ 8·0 Hz, H 4′. δ_C 16·1, C 9″; 20·8, C 10″; 22·0, C 7″; 23·2, C 5″; 26·1, C 8″; 27·1, 3-CH_3; 31·4, C 1″; 34·1, C 6″; 40·9, C 2″; 41·0, C 4; 44·9, C 2; 46·8, C 4″; 56·6, 5′-OCH_3; 62·0, 1′-OCH_3; 71·9, C 3; 74·8, C 3″; 117·1, C 6′; 119·7, C 8′; 120·9, C 10′a; 123·1, C 4′; 124·9, C 9′a; 135·1, C 7′; 136·3, C 4′a; 137·2, C 8′a; 138·4, C 2′; 138·5, C 3′; 158·6, C 1′; 159·8, C 5′; 172·7, C 1; 182·4, 182·9, C 9′,10′. *m/z* (d.e.i.) 522, 504, 490, 366, 325, 293, 282 (100%), 267.

Transesterification of the Menthyl Butanoates (4) and (5)

A mixture of the menthyl (3*R*)-butanoate (5) (9·3 mg, 0·018 mmol), anhydrous potassium carbonate (100 mg, 0·72 mmol) and methanol (3 ml, 73·8 mmol) was stirred at room temperature for 15 h. Acidification (20% aqueous hydrochloric acid), while cooling on ice, and extraction with CH_2Cl_2 (3×10 ml) gave a yellow solution, which was washed with water (3×20 ml), and dried ($MgSO_4$). Removal of the solvent and p.l.c. (CH_2Cl_2) gave *methyl (3R)-4-(1′,5′-dimethoxy-9′,10′-anthraquinon-2′-yl)-3-hydroxy-3-methylbutanoate* (2) (5·3 mg, 75%), as a yellow oil, $[\alpha]_D$ −4·1° (*c*, 6·53 in dioxan) (Found: $M^{+\bullet}$ − MeOH, 366·1110. $C_{21}H_{18}O_6$ ($M^{+\bullet}$ − MeOH) requires 366·1103). λ_{max} 227 ($\log\epsilon$ 4·20), 2·57 (4·24), 383 nm (3·64). ν_{max} (smear) 3500 (OH), 2950, 1730 (ester CO), 1669 (quinone CO), 1589, 1571, 1463, 1442, 1313, 1250, 1202, 1062, 1003, 963, 864, 800, 720 cm^{-1}. δ_H 1·26, s, 3H, 3-CH_3; 2·52, s, 2H, H 2; 3·02, d, 1H, $J_{4a,4b}$ 13·3 Hz, H 4a; 3·10, d, 1H, $J_{4b,4a}$ 13·3 Hz, H 4b; 3·71, s, 3H, ester OCH_3; 3·92, s, 3H, 1′-OCH_3; 3·97, s, 1H, OH; 4·05, s, 3H, 5′-OCH_3; 7·31, dd, 1H, $J_{6',7'}$ 8·5, $J_{6',8'}$ 1 Hz, H 6′; 7·71, dd, 1H, $J_{7',8'}$ 7·8, $J_{7',6'}$ 8·5 Hz, H 7′; 7·73, d, 1H, $J_{3',4'}$ 8·0 Hz, H 3′; 7·90, dd, 1H, $J_{8',7'}$ 7·8, $J_{8',6'}$ 1 Hz, H 8′; 8·04, d, 1H, $J_{4',3'}$ 8·0 Hz, H 4′. δ_C 27·3, 3-CH_3; 41·1, C 4; 44·4, C 2; 51·7, ester OCH_3; 56·5, 5′-OCH_3; 61·9, 1′-OCH_3; 71·7, C 3; 117·1, C 6′; 119·7, C 8′; 120·9, C 10′a; 123·1, C 4′; 124·9, C 9′a; 135·1,

C7′; 136·3, 137·2, C4′a,8′a; 138·3, C2′; 138·4, C3′; 158·5, C1′; 159·8, C5′; 173·2, C1; 182·4, 182·8, C9′,10′. *m/z* (d.e.i.) 398, 366, 293, 282 (100%), 267.

A similar experiment using the (3*S*)-butanoate (4) (7 mg, 0·013 mmol) gave *methyl (3S)-4-(1′,5′-dimethoxy-9′,10′-anthraquinon-2′-yl)-3-hydroxy-3-methylbutanoate* (3) (3 mg, 58%) as a yellow oil, $[\alpha]_D$ +3·9° (*c*, 3·35 in dioxan) (Found: $M^{+\bullet}$ – MeOH, 366·1112. $C_{21}H_{18}O_6$ ($M^{+\bullet}$ – MeOH) requires 366·1103). (Correct ^{1}H n.m.r., ^{13}C n.m.r. and i.r. spectra.)

Fridamycin E Methyl Ester (6)

The methyl (3*R*)-butanoate dimethyl ether (2) (3·8 mg, 0·0095 mmol) in CH_2Cl_2 (3 ml) was stirred with a solution of boron tribromide (BBr_3) in CH_2Cl_2 (0·2 ml, 4% v/v), at −78°C, for 1 h. Quenching with water (2 ml), warming to room temperature, separation of the orange CH_2Cl_2 layer, addition of CH_2Cl_2 (10 ml), washing with water (3×10 ml), drying ($MgSO_4$), solvent removal and p.l.c. (CH_2Cl_2) gave (i) *methyl (3R)-4-(1′,5′-dihydroxy-9′,10′-anthraquinon-2′-yl)-3-hydroxy-3-methylbutanoate* (fridamycin E methyl ester) (6) (2·6 mg, 74%) as an orange oil, $[\alpha]_D$ +2·1° (*c*, 3·3 in dioxan) (Found: $M^{+\bullet} - H_2O$, 352·0930. $C_{20}H_{16}O_6$ $M^{+\bullet} - H_2O$) requires (352·0947). λ_{max} 230 (log ε 4·53), 257 (4·30), 292 (3·97), 437 nm (3·99). ν_{max} (smear) 3600br (OH), 1731 (ester CO), 1633 (quinone CO, intramolecularly H-bonded), 1596, 1575, 1451, 1426, 1405, 1352, 1291, 1231, 1066, 803, 774, 711 cm^{-1}. δ_H 1·31, s, 3H, 3-CH_3; 2·55, d, 1H, $J_{2a,2b}$ 16·0 Hz, H2$_a$; 2·59, d, 1H, $J_{2b,2a}$ 16·0 Hz, H2$_b$; 3·04, d, 1H, $J_{4a,4b}$ 13·4 Hz, H4$_a$; 3·11, d, 1H, $J_{4b,4a}$ 13·4 Hz, H4$_b$; 3·72, s, 3H, ester OCH_3; 3·91, s, 1H, 3-OH; 7·32, dd, 1H, $J_{6',7'}$ 8·5, $J_{6',8'}$ 1·2 Hz, H6′; 7·68, dd unresolved, 1H, H7′; 7·71, d, 1H, $J_{3',4'}$ 7·8 Hz, H3′; 7·82, d, 1H, $J_{4',3'}$ 7·8 Hz, H4′; 7·85, dd, 1H, $J_{8',7'}$ 7·5, $J_{8',6'}$ 1·2 Hz, H8′; 12·68, s, 1H, 5′-OH; 13·19, s, 1H, 1′-OH. δ_C 27·3, 3-CH_3; 40·5, C4; 44·4, C2; 51·8, ester OCH_3; 71·8, C3; 115·6, C9′a; 116·1, C10′a; 118·9, C4′; 119·4, C8′; 125·0, C6′; 131·8, C4′a; 133·2, C8′a; 134·6, C2′; 136·7, C7′; 139·7, C3′; 161·4, C5′; 162·7, C1′; 173·3, C1; 187·8, 188·3, C9′,10′. *m/z* (d.e.i.) 352, 339, 297, 279, 254 (100%). Linked scan (d.e.i.) 370 → 254; and (ii) *methyl (3R)-4-(1′-hydroxy-5′-methoxy-9′-10′-anthraquinon-2′-yl)-3-hydroxy-3-methylbutanoate* (7) (0·86 mg, 24%) as an orange oil (Found: $M^{+\bullet} - CH_3COCH_2CO_2CH_3$, 268·0741. $C_{16}H_{12}O_4$ ($M^{+\bullet} - CH_3COCH_2CO_2CH_3$) requires 268·0736). λ_{max} 228 (log ε 4·38), 256 (4·21), 284sh (3·87), 412 nm (3·81). ν_{max} (smear) 3493br (OH), 2916, 1728 (ester CO), 1660 (quinone CO), 1629 (quinone CO H-bonded), 1581, 1434, 1361, 1261, 1009, 794 cm^{-1}. δ_H 1·31, s, 3H, 3-CH_3; 2·57, s, 2H, H2; 3·03, d, 1H, $J_{4a,4b}$ 13·4 Hz, H4$_a$; 3·09, d, 1H, $J_{4b,4a}$ 13·4 Hz, H4$_b$; 3·72, s, 3H, ester OCH_3; 3·92, s, 1H, 3-OH; 4·06, s, 3H, 5′-OCH_3; 7·37, dd, 1H, $J_{6',7'}$ 8·5, $J_{6',8'}$ 0·9 Hz, H6′; 7·66, d, 1H, $J_{3',4'}$ 7·8 Hz, H3′; 7·74, dd unresolved, 1H, H7′; 7·76, d, 1H, $J_{4',3'}$ 7·8 Hz, H4′; 7·99, dd, 1H, $J_{8',7'}$ 7·7, $J_{8',6'}$ 0·9 Hz, H8′; 13·00, s, 1H, 1′-OH. *m/z* (d.e.i.) 384, 366, 353, 268 (100%), 253.

Fridamycin E (1)

A solution of fridamycin E methyl ester (6) (2·6 mg, 0·007 mmol) in 15% aqueous potassium hydroxide (5 ml) was stirred at room temperature for 15 h. Excess 20% aqueous hydrochloric acid was added, while cooling on ice, and the product was extracted into CH_2Cl_2 (4×10 ml). Washing with water (3×30 ml), drying ($MgSO_4$) and solvent removal gave fridamycin E (1) as an orange solid (1·6 mg, 64%), m.p. 163–164°, $[\alpha]_D$ +12·0° (*c*, 0·15 in dioxan) [lit.[1] (for *ent*-fridamycin E), m.p. 168°, $[\alpha]_D$ −11° (*c*, 1 in dioxan)]. δ_H 1·36, s, 3H, 3-CH_3; 2·62, s, 2H, H2; 3·08, d, 1H, $J_{4a,4b}$ 13·7 Hz, H4$_a$; 3·14, d, 1H, $J_{4b,4a}$ 13·7 Hz, H4$_b$; 7·34, d, 1H, $J_{6,7}$ 8·4 Hz, H6′; 7·66, d, 1H, $J_{3,4}$ 7·7 Hz, H3′; 7·70, dd, unresolved, 1H, H7′; 7·85, d, 1H, $J_{4,3}$ 7·7 Hz, H4′; 7·86, d, 1H, $J_{8,7}$ 7·4 Hz, H8′; 11·08, s, 1H, COOH; 12·65, s, 1H, 5′-OH; 13·38, s, 1H, 1′-OH.

Ozonolysis of the Bisfuran (31)

The bisfuran (31)[4] (90 mg, 0·28 mmol) in CH_2Cl_2 (1 litre) was stirred with ozone (27 mg, 0·56 mmol) at −78° for 100 min. Dimethyl sulfide (0·4 g, 6·4 mmol) was added, the mixture was stirred at room temperature for 1 h, then washed with water (3×500 ml) and dried ($MgSO_4$), and the solvent was removed. The resulting solid in tetrahydrofuran (100 ml), was stirred vigorously with saturated aqueous sodium hydrogencarbonate (100 ml) at room

temperature for 1 h. After acidification (20% aqueous hydrochloric acid), and removal of the tetrahydrofuran the mixture was extracted with CH_2Cl_2 (3×100 ml). The extract was washed with water (3×200 ml) and dried ($MgSO_4$), and the solvent was removed to give an orange-yellow solid. Filtration through a short column of magnesium carbonate (5 g) (CH_2Cl_2/hexanes, 50:50 v/v) gave starting material (31) (42 mg, 47%). The magnesium carbonate was dissolved in 20% aqueous hydrochloric acid, and the resulting mixture was extracted with CH_2Cl_2 (3×100 ml). Workup and multiple-sweep p.l.c. (CH_2Cl_2/hexanes, 70:30 v/v) gave *7-hydroxy-2-methyl-6,11-dioxo-6,11-dihydroanthra[1,2-b]furan-8-carbaldehyde* (25) (36 mg, 42%) as an orange powder, m.p. 267–270° (Found: C, 70·4; H, 3·2. $C_{18}H_{10}O_5$ requires C, 70·6; H, 3·3%). λ_{max} 241 ($\log\epsilon$ 4·50), 291 (4·36), 411 nm (3·91). ν_{max} (KBr) 3450br (OH, intramolecularly H-bonded), 1688 (CO, aldehyde), 1668 (CO), 1627 (CO, H-bonded), 1590, 1585, 1469, 1252, 1080, 932, 823 cm^{-1}. δ_H 2·66, s, 3H, 2-CH_3; 6·58, d, 1H, $J_{3,4}$ 1 Hz, H3; 7·87, br d, 1H, J 8·0 Hz, 7·88, d, 1H, J 8·1 Hz, H4,9; 8·21, d, 1H, J 8·0 Hz, 8·22, d, 1H, J 8·1 Hz, H5,10; 10·63, s, 1H, CHO; 13·42, s, 1H, OH. *m/z* 306, 278, 250, 222, 165, 97, 43.

A similar reaction using 1 equiv. of ozone for 1 h at −78°, led to the complete recovery of the bisfuran, while the use of three or more equivalents of ozone gave mixtures of the substrate (31), the monofuran (25) and the dialdehyde (32) (^1H n.m.r.).

Monoallylation of 1,5-Dihydroxyanthraquinone (Anthrarufin) (18)

A mixture of anthrarufin (18) (3·3 g, 13·8 mmol), allyl bromide (2·2 g, 18·2 mmol), anhydrous potassium carbonate (8 g, 58 mmol) and dimethylformamide (150 ml) was stirred at 70° under nitrogen for 8 h. The reaction mixture was filtered to remove the potassium carbonate and this was washed with acetone until the washings were colourless. Removal of the solvent from the combined filtrate and washings and column chromatography on silica (200 g) (CH_2Cl_2/hexanes 40:60 v/v) gave (i) anthrarufin (0·98 g, 30%); (ii) *1-hydroxy-5-(prop-2′-enyloxy)anthraquinone* (19) (1·6 g, 41%), m.p. 148–150° (Found: C, 72·7; H, 4·2. $C_{17}H_{12}O_4$ requires C, 72·9; H, 4·3%). λ_{max} 228 ($\log\epsilon$ 4·32), 256 (4·34), 280sh (4·07), 405 nm (3·97). ν_{max} (KBr) 3500br (OH, intramolecularly H-bonded), 1663 (CO), 1632 (CO, H-bonded), 1586, 1473, 1453, 1350, 1249, 1155, 1049, 1000, 790, 700 cm^{-1}. δ_H 4·75, dm, 2H, $J_{1',2'}$ 4·8 Hz, H1′; 5·40, dm, 1H, $J_{3',2'cis}$ 10·6 Hz, H3′ (*cis* to H); 5·68, dm, 1H, $J_{3',2'trans}$ 17·2 Hz, H3′ (*trans* to H); 6·13, ddt, 1H, $J_{2',1'}$ 4·9, $J_{2',3'cis}$ 10·5, $J_{2',3'trans}$ 17·2 Hz, H2′; 7·21, dd, 1H, $J_{2,3}$ 8·4, $J_{2,4}$ 1 Hz, H2; 7·31, dd, 1H, $J_{6,7}$ 8·5, $J_{6,8}$ 1 Hz, H6; 7·64, dd unresolved, 1H, H7; 7·67, dd unresolved, 1H, H3; 7·75, dd, 1H, $J_{8,7}$ 7·6, $J_{8,6}$ 1 Hz, H8; 7·93, dd, 1H, $J_{4,3}$ 7·7, $J_{4,2}$ 1 Hz, H4; 12·45, s, 1H, OH. δ_C 70·0, C1′; 115·6, C10a; 118·2, C9a; 118·3, C3′; 119·3, C2; 119·6, C8; 120·0, C4; 122·9, C6; 132·0, C2′; 134·9, C3; 135·0, C8a; 135·3, C4a; 136·9, C7; 159·4, C1; 161·9, C5; 181·4, C9; 188·5, C10. *m/z* 280 (M), 251, 224, 196, 168, 155, 139, 41; and (iii) the bisether (17) (1·0 g, 22%) (correct ^1H n.m.r. and t.l.c. behaviour).[4]

1,5-Dimethoxy-2-(prop-2′-enyl)anthraquinone (21)

The allyloxyanthraquinone (19) (500 mg, 1·79 mmol) in dimethylformamide (100 ml) was added to a solution of sodium dithionite (500 mg, 2·3 mmol) in dimethylformamide (50 ml) and water (150 ml) at 90°, under nitrogen, and the mixture was heated under reflux for 4 h. Water (100 ml) was added and the product, which crystallized, was collected by filtration, washed with water and dissolved in CH_2Cl_2. Workup gave *1,5-dihydroxy-2-(prop-2′-enyl)anthraquinone* (20) (478 mg, 96%) which crystallized as orange needles, m.p. 150–151° (Found: C, 72·8; H, 4·1. $C_{17}H_{12}O_4$ requires C, 72·9; H, 4·3%). λ_{max} 230 ($\log\epsilon$ 4·51), 257 (4·31), 291 (3·96), 440 nm (3·99). ν_{max} (KBr) 3600br (OH, intramolecularly H-bonded), 1638 (CO, H-bonded), 1595, 1575, 1451, 1424, 1403, 1349, 1297, 1225, 1166, 1074, 901, 781, 715 cm^{-1}. δ_H 3·52, d, 2H, $J_{1',2'}$ 6·7 Hz, H1′; 5·14–5·19, m, 2H, H3′; 6·01, ddt, 1H, $J_{2',1'}$ 6·7, $J_{2',3'cis}$ 9·7, $J_{2',3'trans}$ 17·5 Hz, H2′; 7·29, dd, 1H, $J_{6,7}$ 8·4, $J_{6,8}$ 1 Hz, H6; 7·54, d, 1H, $J_{3,4}$ 7·7 Hz, H3; 7·66, dd, 1H, $J_{7,6}$ 8·4, $J_{7,8}$ 7·6 Hz, H7; 7·76, d, 1H, $J_{4,3}$ 7·7 Hz, H4; 7·81, dd, 1H, $J_{8,7}$ 7·6, $J_{8,6}$ 1 Hz, H8; 12·67, s, 1H, 5-OH; 13·01, s, 1H, 1-OH. δ_C 33·8, C1′; 115·4, C9a; 116·1, C10a; 117·3, C3′; 119·1, 119·3, C4,8; 124·9, C6; 131·3, C4a; 133·2, C8a; 134·7, C2′; 136·4, 136·6, C3,7; 137·4, C2; 160·9, C1; 162·7, C5; 187·8, 188·2, C9,10. *m/z* 280 (M), 265, 262, 251, 237, 149, 57.

A mixture of the dihydroxyanthraquinone (20) (800 mg, 2·9 mmol), anhydrous potassium carbonate (10 g, 72 mmol), dimethyl sulfate (1 ml, 10·6 mmol) and acetone (300 ml) was heated under reflux for 5 h. Most of the solvent was removed, the slurry was poured onto crushed ice, and the yellow solid was collected by filtration, washed with water (500 ml) and then dissolved in CH_2Cl_2. Workup and column chromatography on magnesium carbonate (50 g) (CH_2Cl_2/hexanes, 50:50 v/v) gave *1,5-dimethoxy-2-(prop-2′-enyl)anthraquinone* (21) (812 mg, 91%), m.p. 138–140° (Found: C, 74·2; H, 5·4. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%). λ_{max} 226 (log ϵ 4·29), 257 (4·47), 374 nm (3·91). ν_{max} (KBr) 1668 (CO), 1585, 1571, 1457, 1381, 1251, 1060, 992, 951, 716 cm^{-1}. δ_H 3·55, d, 2H, $J_{1',2'}$ 6·5 Hz, H1′; 3·93, s, 3H, 1-OCH_3; 4·04, s, 3H, 5-OCH_3; 5·09–5·16, m, 2H, H3′; 5·99, ddt, 1H, $J_{2',1'}$ 6·5, $J_{2',3'cis}$ 10·3, $J_{2',3'trans}$ 16·9 Hz, H2′; 7·30, br d, 1H, $J_{6,7}$ 8·4 Hz, H6; 7·60, d, 1H, $J_{3,4}$ 8·0 Hz, H3; 7·70, dd unresolved, 1H, H7; 7·90, dd, 1H, $J_{8,7}$ 7·8, $J_{8,6}$ 1 Hz, H8; 8·03, d, 1H, $J_{4,3}$ 8·0 Hz, H4. δ_C 34·1, C1′; 56·6, 5-OCH_3; 62·0, 1-OCH_3; 117·0, C3′; 117·1, C6; 119·7, C8; 121·0, C10a; 123·4, C4; 125·0, C9a; 135·0, C7; 135·8, C4a; 135·8, 135·9, C2′,3; 137·2, C8a; 141·1, C2; 158·1, C1; 159·8, C5; 182·5, 182·5, 182·9, C9,10. *m/z* 308 (M), 293, 277, 267, 165, 152, 76.

1,5-Dimethoxy-9,10-dioxo-9,10-dihydroanthracene-2-carbaldehyde (23)

A solution of the allylanthraquinone (21) (100 mg, 0·32 mmol) and potassium hydroxide (200 mg, 3·6 mmol) in methanol (60 ml) was heated under reflux for 15 min. Acidification (20% aqueous hydrochloric acid), and pouring onto crushed ice gave a yellow solid which was removed by filtration and dissolved in CH_2Cl_2 (50 ml). Workup and column chromatography on magnesium carbonate (8 g) (CH_2Cl_2/hexanes, 50:50 v/v) gave *1,5-dimethoxy-2-(prop-1′-enyl)anthraquinone* (22) (97 mg, 97%) as a pale yellow solid, m.p. 196–198° (Found: C, 74·2; H, 5·3. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%). λ_{max} 231 (log ϵ 4·23), 274 (4·29), 389 nm (3·85). ν_{max} (KBr) 1670 (CO), 1589, 1557, 1444, 1292, 1255, 1156, 1025, 1000, 957, 801, 721 cm^{-1}. δ_H 1·98, dd, 3H, $J_{3',2'}$ 6·7, $J_{3',1'}$ 1·7 Hz, H3′; 3·92, s, 3H, 1-OCH_3; 4·04, s, 3H, 5-OCH_3; 6·44, dq, 1H, $J_{2',1'}$ 15·9, $J_{2',3'}$ 6·7 Hz, H2′; 6·83, dm, 1H, $J_{1',2'}$ 15·9 Hz, H1′; 7·29, br d, 1H, $J_{6,7}$ 8·4 Hz, H6; 7·70, dd unresolved, 1H, H7; 7·83, d, 1H, $J_{3,4}$ 8·2 Hz, H3; 7·90, dd, 1H, $J_{8,7}$ 7·7, $J_{8,6}$ 1 Hz, H8; 8·03, d, 1H, $J_{4,3}$ 8·2 Hz, H4. δ_C 19·1, C3′; 56·5, 5-OCH_3; 61·9, 1-OCH_3; 117·0, C6; 119·7, C8; 121·0, C10a; 123·5, C4; 124·3, C3; 125·5, C9a; 130·9, 131·9, 131·3, C1′,2′; 134·9, C7; 135·3, C4a; 137·2, C8a; 138·4, C2; 156·5, C1; 159·8, C5; 182·3, 183·0, C9,10. *m/z* 308 (M), 293, 275, 253.

A stream of ozone was bubbled through a solution of the alkene (22) (175 mg, 0·75 mmol) in CH_2Cl_2 (150 ml), at −78°. When the yellow-coloured solution became green, ozone generation was stopped and the solution was stirred at −78° for 1 h. Reduction [$(CH_3)_2S$] and workup gave *1,5-dimethoxy-9,10-dioxo-9,10-dihydroanthracene-2-carbaldehyde* (23) as a pale yellow solid (166 mg, 99%), m.p. 205–206° (Found: C, 68·8; H, 3·9. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%). λ_{max} 247 (log ϵ 4·5), 382 nm (3·82). ν_{max} (KBr) 1692 (aldehyde CO), 1673 (quinone CO), 1586, 1275, 1004, 728 cm^{-1}. δ_H 4·05, s, 3H, 5-OCH_3; 4·10, s, 3H, 1-OCH_3; 7·34, dd unresolved, 1H, H6; 7·75, dd unresolved, 1H, H7; 7·90, dd unresolved, 1H, H8; 8·15, dd unresolved, 1H, H3; 8·20, d, 1H, $J_{4,3}$ 8·1 Hz, H4; 10·55, d, 1H, $J_{CHO,3}$ 0·7 Hz, CHO. δ_C 56·6, 5-OCH_3; 64·6, 1-OCH_3; 117·5, C6; 119·7, C8; 120·7, C10a; 123·4, C4; 126·0, C9a; 133·4, C7; 133·6, C4a; 135·6, C3; 136·8, C8a; 141·1, C2; 160·1, C5; 163·3, C1; 181·4, 182·0, C9,10; 189·0, CHO. *m/z* 296 (M), 268, 237.

Titanium-Mediated Reaction of the o*-Methoxy Aldehyde (23) with Menthyl Acetate*

The *o*-methoxy aldehyde (23) (15 mg, 0·05 mmol), in tetrahydrofuran (10 ml) was stirred with 2 equiv. of the preformed titanium reagent in tetrahydrofuran (0·5 ml) under nitrogen at −78° for 3 min, when the initially red-coloured solution had become orange-yellow. Quenching with saturated aqueous ammonium sulfate, workup and p.l.c. (CH_2Cl_2) gave (i) starting material (23) (0·6 mg, 4%) and (ii) a 1·2:1 mixture of the diastereomeric (−)-menthyl anthraquinonylpropanoates (13) and (14), as a yellow oil (23 mg, 92%), which was further purified by h.p.l.c. (hexanes/tetrahydrofuran, 80:20 v/v, flow rate 4 ml/min, detector λ 280 nm) to give (i) *(−)-menthyl (3S)-3-(1′,5′-dimethoxy-9′,10′-anthraquinon-2′-yl)-3-hydroxypropanoate* (13), $[\alpha]_D$ −20·8° (*c*, 0·62 in dioxan) (Found: $M^{+\bullet}$, 494·2316.

$C_{29}H_{34}O_7$ requires $M^{+\bullet}$, 494·2305). λ_{max} 226 (log ϵ 4·37), 257 (4·45), 378 nm (3·85). ν_{max} 3478 (OH), 1728 (ester CO), 1668 (quinone CO), 1574, 1268, 995, 878, 739 cm^{-1}. δ_H 0·67, d, 3H, $J_{9'',8''}$ 6·9 Hz, H9″; 0·77, d, 3H, $J_{10'',8''}$ 7·0 Hz, H10″; 0·85, m, 1H, H6″*ax*; 0·91, d, 3H, $J_{7'',1''}$ 6·5 Hz, H7″; 0·98, m, 2H, H2″*ax*,5″*ax*; 1·31, dddd unresolved, 1H, H4″; 1·47, m, 1H, H1″; 1·55–1·70, m, 3H, H5″*eq*,6″*eq*,8″; 1·99, dm, 1H, $J_{2''eq,2''ax}$ 1·7 Hz, H2″*eq*; 2·67, dd, 1H, $J_{2a,2b}$ 16·5, $J_{2a,3}$ 8·7 Hz, H2a; 2·90, dd, 1H, $J_{2b,2a}$ 16·5, $J_{2b,3}$ 3·1 Hz, H2b; 3·90, d, 1H, $J_{OH,3}$ 4·4 Hz, OH; 3·95, s, 3H, 1′-OCH_3; 4·04, s, 3H, 5′-OCH_3; 4·72, ddd, 1H, $J_{3'',4''}$ 10·9, $J_{3'',2''ax}$ 10·9, $J_{3'',2''eq}$ 4·4 Hz, H3″; 5·48, m, 1H, H3; 7·31, d, 1H, $J_{6',7'}$ 8·4 Hz, H6′; 7·71, dd unresolved, 1H, H7′; 7·90, d, 1H, $J_{8',7'}$ 7·7 Hz, H8′; 7·96, d, 1H, $J_{3',4'}$ 8·1 Hz, H3′; 8·11, d, 1H, $J_{4',3'}$ 8·1 Hz, H4′. δ_C 16·3, C9″; 20·6, C10″; 22·0, C7″; 23·4, C5″; 26·3, C8″; 31·4, C1″; 34·1, C6″; 40·8, C2″; 41·7, C2; 46·8, C4″; 56·6, 5′-OCH_3; 62·3, 1′-OCH_3; 65·4, C3; 75·1, C3″; 117·2, C6′; 119·7, C8′; 120·9, C10′a; 123·7, C4′; 124·5, C9′a; 132·5, C7′; 135·1, C3′; 136·6, C4′a; 137·1, C8′a; 142·7, C2′; 156·8, C1′; 159·9, C5′; 172·4, C1; 182·2, 182·8, C9′,10′. *m/z* 494 (M), 476, 462, 356, 297; and (ii) (−)-*menthyl (3R)-3-(1′,5′-dimethoxy-9′,10′-anthraquinon-2′-yl)-3-hydroxypropanoate* (14), $[\alpha]_D$ −33·7° (*c*, 0·43 in dioxan) (Found: $M^{+\bullet}$, 494·2305. $C_{29}H_{34}O_7$ requires $M^{+\bullet}$, 494·2305). λ_{max} 226 (log ϵ 4·33), 257 (4·42), 375 nm (3·83). ν_{max} 3470 (OH), 2954, 1728 (ester CO), 1669 (quinone CO), 1574, 1268, 995, 878, 740 cm^{-1}. δ_H 0·77, d, 3H, $J_{10'',8''}$ 6·9 Hz, H10″; 0·89, d, 6H, $J_{9'',8''}$ 6·6, $J_{7'',1}$ 6·6 Hz, H7″,9″; 0·90, m, 2H, H2″*ax*,6″*ax*; 1·06, m, 1H, H5″*ax*; 1·36, dddd unresolved, 1H, H4″; 1·47, m, 1H, H1″; 1·67, dm, 2H, $J_{5''eq,5''ax}$ 10·9, $J_{6''eq,6''ax}$ 10·9 Hz, H5″*eq*,6″*eq*; 1·83, m, 1H, H8″; 1·95, dm, 1H, $J_{2''eq,2''ax}$ 11·7 Hz, H2″*eq*; 2·63, dd, 1H, $J_{2a,2b}$ 16·5, $J_{2a,3}$ 9·2 Hz, H2a; 2·91, dd, 1H, $J_{2b,2a}$ 16·5, $J_{2b,3}$ 3·0 Hz, H2b; 3·78, d, 1H, $J_{OH,3}$ 3·5 Hz, OH; 3·96, s, 3H, 1′-OCH_3; 4·05, s, 3H, 5′-OCH_3; 4·74, ddd, 1H, $J_{3'',4''}$ 10·8, $J_{3'',2''ax}$ 10·8, $J_{3'',2''eq}$ 4·4 Hz H3″; 5·49, m, 1H, H3; 7·31, d, 1H, $J_{6',7'}$ 8·4 Hz, H6′; 7·72, dd unresolved, 1H, H7′; 7·91, d, 1H, $J_{8',7'}$ 7·8 Hz, H8′; 7·97, d, 1H, $J_{3',4'}$ 8·1 Hz, H3′; 8·12, d, 1H, $J_{4',3'}$ 8·1 Hz, H4′. δ_C 16·4, C9″; 20·7, C10″; 22·0, C7″; 23·5, C5″; 26·4, C8″; 31·4, C1″; 34·1, C6″; 40·8, C2″; 41·9, C2; 46·9, C4″; 56·6, 5′-OCH_3; 62·3, 1′-OCH_3; 65·5, C3; 75·2, C3″; 117·3, C6′; 119·7, C8′; 121·0, C10′a; 123·7, C4′; 124·6, C9′a; 132·6, C7′; 135·1, C3′; 136·6, C4′a; 137·1, C8′a; 142·7, C2′; 156·8, C1′; 159·9, C5′; 172·3, C1; 182·2, 182·8, C9′,10′.

Demethylation of (13) and (14)

A mixture of the dimethyl ethers (13) and (14) (14 mg, 0·029 mmol) in CH_2Cl_2 (5 ml) was stirred with a solution of boron tribromide in CH_2Cl_2 (0·8 ml, 4·2% v/v) at −78° for 2 h. After quenching with water the orange CH_2Cl_2 layer was separated and diluted with further CH_2Cl_2 (20 ml). Workup and p.l.c. (CH_2Cl_2) gave a 1·2:1 mixture of the diastereomers of (−)-menthyl 3-(1′,5′-dihydroxy-9′,10′-anthraquinon-2′-yl)-3-hydroxypropanoate (15) and (16) (12·4 mg, 92%) as an orange oil (Found: $M^{+\bullet}$, 466·1990. $C_{27}H_{30}O_7$ requires $M^{+\bullet}$, 466·1991). λ_{max} 228 (log ϵ 4·58), 257 (4·37), 290 (4·04), 438 nm (4·04). ν_{max} (smear) 3498 (OH, H-bonded), 2955, 1728 (ester CO), 1629 (quinone CO, H-bonded), 1430, 1371, 1261, 1086, 789, 692 cm^{-1}. δ_H 0·69, d, *J* 6·9 Hz, 0·78, d, *J* 6·9 Hz, 0·80, d, *J* 7·0 Hz, 0·89, d, *J* 6·7 Hz, 0·92, d, unresolved, 9H, H7″,9″,10″; 0·85–1·12, m, 3H, H2″*ax*,5″*ax*,6″*ax*; 1·18–1·55, m, 2H, H1″,4″; 1·60–1·76, m, 3H, H5″*eq*,6″*eq*,8″; 1·92–2·04, m, 1H, H2″*eq*; 2·68, dd unresolved, 1H, H2a; 3·02, dd unresolved, 1H, H2b; 3·85, d, 1H, $J_{OH,3}$ 4·9 Hz, OH; 3·98, d, 1H, $J_{OH,3}$ 5·0 Hz, OH; 4·75, ddd, 1H, $J_{3'',4''}$ 10·9, $J_{3'',2''ax}$ 10·9, $J_{3'',2''eq}$ 4·3 Hz, H3″; 5·48, m, 1H, H3; 7·32, dd, 1H, $J_{6',7'}$ 8·4, $J_{6',8'}$ 1·2 Hz, H6′; 7·68, dd unresolved, 1H, H7′; 7·84, dd, 1H, $J_{8',7'}$ 7·5, $J_{8',6'}$ 1·2 Hz, H8′; 7·87, d, 1H, $J_{3',4'}$ 7·9 Hz, H3′; 7·95, dd unresolved, 1H, H4′; 12·65, s, 1H, 5′-OH; 13·12, s, 1H, 1′-OH. δ_C 16·4, C9″; 20·6, 20·7, C10″; 22·0, C7″; 23·4, C5″; 26·3, C8″; 31·4, C1″, 34·1, C6″; 40·5, 40·7, 40·8, C2,2″; 46·9, C4″; 65·5, 65·6, C3; 75·1, C3″; 115·4, 116·1, C9′a,10′a; 119·3, 119·4, C4′,8′; 125·1, C6′; 132·0, 133·1, C4′a,8′a; 133·7, C7′; 136·7, C3′; 138·7, C2′; 159·3, C1′; 162·8, C5′; 172·1, 172·2, C1; 187·7, 188·3, C9′,10′. *m/z* 466 (M), 448, 328, 310, 269.

Titanium-Mediated Addition of Menthyl Acetate to the o-Phenolic Aldehyde (25)

The anthrafuranyl aldehyde (25) (20 mg, 0·065 mmol), in tetrahydrofuran (10 ml) was stirred with 3 equiv. of the preformed titanium reagent (0·195 mmol) under nitrogen, at −78°,

for 30 min. The mixture was allowed to warm to room temperature and stirring was continued for 60 min before the reaction was quenched with saturated aqueous ammonium sulfate. Workup and p.l.c. (CH_2Cl_2) gave (i) a 1·3:1 mixture of the diastereomers of (−)-menthyl 3-hydroxy-3-(7′-hydroxy-2′-methyl-6′,11′-dioxo-6′,11′-dihydroanthra[1′,2′-*b*]furan-8′-yl)propanoate (27) and (28) (21 mg, 66%), as an orange solid, m.p. 189–192° (Found: $M^{+\bullet}$, 504·2167. $C_{30}H_{32}O_7$ requires $M^{+\bullet}$, 504·2148). λ_{max} 230 ($\log\epsilon$ 4·45), 284 (4·31), 307sh (3·87), 418 nm (3·96). ν_{max} (KBr) 3530 (OH), 2940, 1724 (ester CO), 1655 (quinone CO), 1627 (quinone CO, H-bonded), 1590, 1428, 1253, 1152, 1071, 973, 930, 817, 732 cm^{-1}. δ_H 0·68, d, *J* 6·9 Hz, 0·77, d, *J* 6·6 Hz, 0·79, d, *J* 6·7 Hz, 0·88, d, *J* 7·4 Hz, 0·89, d, *J* 6·4 Hz, 0·91, d, *J* 6·6 Hz, 9H, H7″,9″,10″; 0·86, m, 1H, H6″*ax*; 1·01, m, 2H, H2″*ax*,5″*ax*; 1·33, dddd unresolved, 1·38, dddd unresolved, 1H, H4″; 1·48, m, 1H, H1″; 1·65, m, 2H, H5″*eq*,6″*eq*; 1·84, m, 1H, H8″; 1·96, dm unresolved, 2·01, dm unresolved, 1H, H2″*eq*; 2·63, s, 3H, 2′-CH_3; 2·69, dd unresolved, 2·73, dd unresolved, 1H, H2$_a$; 3·01, dd, $J_{2_b,2_a}$ 16·3, $J_{2_b,3}$ 3·5 Hz, 3·02, dd, $J_{2_b,2_a}$ 16·3, $J_{2_b,3}$ 3·6 Hz, 1H, H2$_b$; 3·87, d, $J_{OH,3}$ 3·8 Hz, 4·01, d, $J_{OH,3}$ 4·2 Hz, 1H, 3-OH; 4·74, m, 1H, H3″; 5·46, m, 1H, H3; 6·52, s, 1H, H3′; 7·79, d, $J_{4',5'}$ 8·1 Hz, H4′; 7·81, d unresolved, 7·82, d unresolved, 1H, H9′; 7·88, d unresolved, 7·90, d unresolved, 1H, H10′; 8·14, d, 1H, $J_{5',4'}$ 8·1 Hz, H5′; 13·20, s, 13·21, s, 1H, 7′-OH. δ_C 14·7, 2′-CH_3; 16·4, C9″; 20·6, 20·7, C10″; 22·0, C7″; 23·4, C5″; 26·3, C8″; 31·4, C1″; 34·1, C6″; 40·6, 40·9, C2,2″; 46·9, C4″; 65·6, 65·9, C3; 75·0, 75·1, C3″; 103·3, C3′; 115·3, C6′a; 118·1, C11′a; 119·1, C10′; 121·9, C5′; 125·6, C4′; 128·7, C3′a; 132·7, C10′a; 133·4, 133·5, C9′; 137·6, 137·7, C5′a,8′; 151·8, C2′; 158·9, C7′; 162·6, C11′b; 172·1, 172·3, C1; 181·8, C11′; 189·2, C6′. *m/z* 504 (M), 486, 366, 348, 307 (100%), 278; and (ii) starting material (25) (2·8 mg, 14%).

In a similar experiment the phenolic aldehyde (25) (19 mg, 0·071 mmol) in tetrahydrofuran (40 ml) was stirred with 6 equiv. of the titanium reagent at −78° for 4·5 min before the reaction was quenched with saturated aqueous ammonium sulfate. Workup and p.l.c. (CH_2Cl_2EtOAc, 100:2 v/v) gave (i) the phenolic propanoates (27) and (28) (1·3:1) (28 mg, 78%), as an orange oil (correct ^1H n.m.r. and t.l.c. analyses), and (ii) starting material (25) (1·8 mg, 10%).

Methylation of the Anthrafuranylpropanoates (27) and (28)

A mixture of the phenolic menthyl propanoates (27) and (28) (7·7 mg, 0·015 mmol), anhydrous potassium carbonate (250 mg, 1·8 mmol), dimethyl sulfate (75 μl, 0·77 mmol) and acetone (5 ml) was heated under reflux until the purple-brown solution became pale yellow (4 h). After removing most of the solvent the slurry was poured onto crushed ice and the product was extracted into CH_2Cl_2 (4×5 ml). The extract was washed with water (4×20 ml) and dried ($MgSO_4$); removal of the solvent and p.l.c. (CH_2Cl_2) gave the methoxy menthyl propanoates (29) and (30) (5·2 mg, 67%) as a yellow oil. H.p.l.c. (tetrahydrofuran/hexanes, 5:95 v/v (100 min), then tetrahydrofuran/hexanes, 10:90 v/v, flow rate 3·5 ml/min, detector λ 280 nm) gave (i) *(−)-menthyl (3S)-3-hydroxy-3-(7′-methoxy-2′-methyl-6′,11′-dioxo-6′,11′-dihydroanthra[1′,2′-b]furan-8′-yl)propanoate* (29), R_t 170 min, $[\alpha]_D$ −3·9° (*c*, 1·55 in dioxan) (Found: $M^{+\bullet}$, 518·2316. $C_{31}H_{34}O_7$ requires $M^{+\bullet}$, 518·2305). λ_{max} 250 ($\log\epsilon$ 4·19), 283 (4·44), 362 nm (3·98). ν_{max} (smear) 3503 (OH), 2928, 1724 (ester CO), 1667 (quinone CO), 1572, 1317, 1270, 1088, 848, 738 cm^{-1}. δ_H 0·68, d, 3H, $J_{9'',8''}$ 6·9 Hz, H9″; 0·77, d, 3H, $J_{10'',8''}$ 7·0 Hz, H10″; 0·85, m, 1H, H6″*ax*; 0·92, d, 3H, $J_{7'',1''}$ 6·5 Hz, H7″; 1·01, m, 2H, H2″*ax*,5″*ax*; 1·31, dddd unresolved, 1H, H4″; 1·48, m, 1H, H1″; 1·52–1·69, m, 3H, H5″*eq*,6″*eq*, 8″; 2·00, dm, 1H, $J_{2''eq,2''ax}$ 11·3 Hz, H2″*eq*; 2·64, s, 3H, 2′-CH_3; 2·69, dd, 1H, $J_{2_a,2_b}$ 16·6, $J_{2_a,3}$ 8·7 Hz, H2$_a$; 2·93, dd, 1H, $J_{2_b,2_a}$ 16·6, $J_{2_b,3}$ 3·2 Hz, H2$_b$; 3·94, br s, 1H, OH; 3·99, s, 3H, OCH_3; 4·73, ddd, 1H, $J_{3'',4''}$ 10·9, $J_{3'',2''ax}$ 10·9, $J_{3'',2''eq}$ 4·4 Hz, H3″; 5·50, dm unresolved, 1H, H3; 6·53, d, 1H, $J_{3',4'}$ 1·0 Hz, H3′; 7·84, d, 1H, $J_{9',10'}$ 8·1 Hz, H9′; 7·99, dd unresolved, 1H, H4′; 8·17, d, 1H, $J_{10',9'}$ 8·1 Hz, H10′; 8·19, d, 1H, $J_{5',4'}$ 7·7 Hz, H5′. *m/z* (d.e.i.) 518 (M), 500, 380 (100%), 347, 321, 305, 278; and (ii) *(−)-menthyl (3R)-3-hydroxy-3-(7′-methoxy-2′-methyl-6′,11′-dioxo-6′,11′-dihydroanthra[1′,2′-b]furan-8′-yl)propanoate* (30), R_t 185 min, $[\alpha]_D$ −40·3° (*c*, 1·34 in dioxan) (Found: $M^{+\bullet}$, 518·2280. $C_{31}H_{34}O_7$ requires $M^{+\bullet}$, 518·2305). λ_{max} 250 ($\log\epsilon$ 4·25), 282 (4·50), 363 nm (4·05). ν_{max} (smear) 3503 (OH), 2939, 1724 (ester CO), 1667 (quinone CO), 1578, 1317, 1270, 1088, 848, 738 cm^{-1}. δ_H 0·78, d, 3H, $J_{9'',8''}$ 7·0 Hz, H9″; 0·85, m, 1H, H6″*ax*; 0·89, d, 6H, $J_{10'',8''}$ 6·8, $J_{7'',1''}$ 6·8 Hz, H7″,10″; 0·94, m, 1H,

H 2″*ax*; 1·06, m, 1H, H 5″*ax*; 1·37, dddd unresolved, 1H, H 4″; 1·49, m, 1H, H 1″; 1·67, dm, 2H, $J_{5''eq,5''ax}$ 11·1, $J_{6''eq,6''ax}$ 11·1 Hz, H 5″*eq*,6″*eq*; 1·84, m, 1H, H 8″; 1·96, dm, 1H, $J_{2''eq,2''ax}$ 11·6, H 2″*eq*; 2·63, dd, 1H, $J_{2_a,2_b}$ 16·6, $J_{2_a,3}$ 9·3 Hz, H 2_a; 2·64, s, 3H, 2′-CH_3; 2·94, dd, 1H, $J_{2_b,2_a}$ 16·6, $J_{2_b,3}$ 3·0 Hz, H 2_b; 3·81, br d unresolved, 1H, 3-OH; 3·99, s, 3H, OCH_3; 4·75, ddd, 1H, $J_{3'',4''}$ 10·9, $J_{3'',2''ax}$ 10·9, $J_{3'',2''eq}$ 4·4 Hz, H 3″; 5·50, dm, 1H, $J_{3,2_a}$ 9·3 Hz, H 3; 6·53, d, 1H, $J_{3',4'}$ 1·0 Hz, H 3′; 7·84, d, 1H, $J_{9',10'}$ 8·2 Hz, H 9′; 8·00, d, 1H, $J_{4',5'}$ 8·1 Hz, H 4′; 8·17, d unresolved, 1H, H 10′; 8·19, d unresolved, 1H, H 5′. *m/z* (d.e.i.) 518 (M), 500, 380 (100%), 350, 336, 321, 305, 278.