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# Total synthesis of (±)-phomactin G, a platelet activating factor antagonist from the marine fungus *Phoma* sp.

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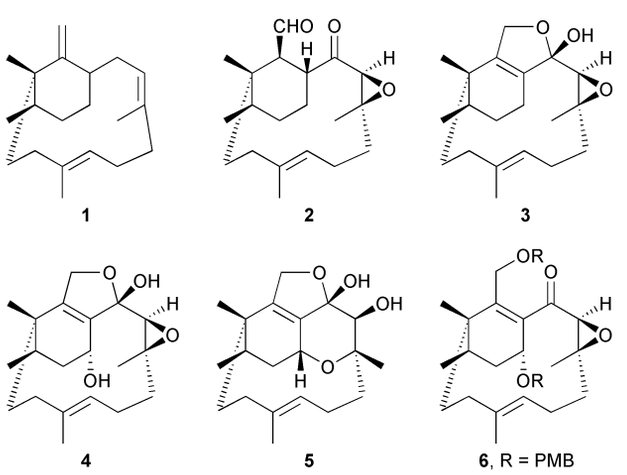
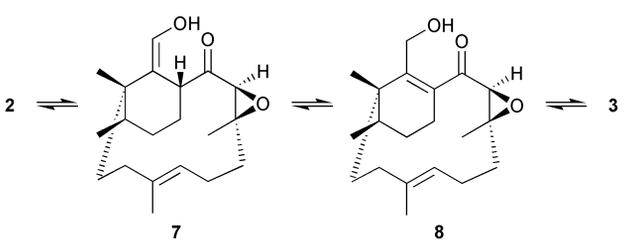
A total synthesis of phomactin G (**3**), which is a central intermediate in the biosynthesis of phomactin A (**5**) in *Phoma* sp. is described. The synthesis is based on a Cr(II)/Ni(II) macrocyclisation from the aldehyde vinyl iodide **9**, leading to **16**, followed by sequential conversion of **16** into the β-epoxide **21** and the ketone **25** which, on deprotection, led to (±)-phomactin G. Phomactin G (**3**) shares an interesting structural homology with phomactin D (**2**), the most potent PAF-antagonist metabolite in *Phoma* sp. It is most likely converted into phomactin A (**5**), by initial allylic oxidation to the transient α-alcohol 'phomactin' structure **4**, known as Sch 49028, followed by spontaneous pyran ring formation.

## Introduction

Phomactin G (**3**) is a co-metabolite, and probable biosynthetic precursor, of the novel platelet activating factor (PAF) antagonist phomactin A (**5**) isolated from the marine fungus *Phoma* sp.[1,2] It is also likely that phomactin G originates from the phomactatriene **1** *via* a sequence of enzymatic oxidations, and that it is converted into phomactin A following allylic oxidation, to **4**,[3] and spontaneous pyran ring formation. In recent work[4] we have developed a concise total synthesis of phomactin A (**5**) whereby the pyran-hemiacetal ring system in the natural product was produced in a single, and final, step on deprotection of the precursor **6**. Interestingly, we found no evidence for the formation of the epoxy cyclic hemiacetal structure **4** during studies of the conversion **6** → **5**, thereby suggesting that involvement of this intermediate is fleeting.[5]




Phomactin G (**3**), the presumed precursor to **4**, shares an interesting structural homology with phomactin D (**2**), which is the most active PAF antagonist metabolite isolated from *Phoma* sp.[6] For example, tautomerisation of phomactin D (**2**) to its enol **7**, followed by isomerisation of **7** to **8**, and spontaneous cyclic hemiacetal formation leads to phomactin G (**3**). In view of the interesting biogenetic interrelationships between the oxygenated phomactins **2-5**, and the central role that phomactin G plays in the biosynthetic sequence between **1** and **5**, we have developed a total synthesis of this metabolite, which is now presented in this paper.




## Results and discussion

Our synthetic strategy towards phomactin G was based on a Cr(II)/Ni(II) mediated macrocyclisation[7] of the aldehyde vinyl iodide **9**, leading to the bicyclo[9.3.1]pentadecane ring system **10**, as a key step. We next planned to convert the allylic alcohol unit in **10** into the epoxy ketone **12** *via* the corresponding β-epoxide intermediate **11**. Finally, we expected that deprotection of the PMB ether group in **12** would lead to the keto alcohol intermediate **8** which would cyclise spontaneously to the cyclic hemiacetal structure, and phomactin G (**3**).

In our total synthesis of phomactin A (**5**) we described a concise route to the substituted cyclohexenol **14a** using five steps starting from the diiodo-diene **13** and commercially available 5-methylcyclohexan-1,3-dione.[4,7] The cyclohexenol **14a** therefore became an ideal precursor for the aldehyde vinyl iodide **9**. Thus, mesylation of **14a**, followed by treatment of the resulting mesylate **14b** with three equivalents of $LiBH_4$ resulted in simultaneous reduction of the PNB ester and mesylate groups in **14b**, producing the cyclohexene methanol **15** in 85% overall yield (Scheme 1). Oxidation of **15** using buffered Dess–Martin periodinane[8] next gave the corresponding aldehyde **9** in essentially quantitative yield. When the aldehyde vinyl iodide **9** was treated with $CrCl_2$ and $NiCl_2$ in a mixture of DMSO and THF, it underwent smooth macrocyclisation to a single diastereoisomer of the doubly allylic alcohol **16** in 47% yield. Smaller amounts (~20%) of the product **17** resulting from reductive cleavage of the carbon-to-iodine bond in **9** were produced concurrently. Inspection and comparison of NMR spectroscopic data measured for the alcohol **16** and similar systems prepared in our earlier studies,[4,5] suggested that the alcohol had the β-stereochemistry shown. This assignment was corroborated following NOE enhancement studies with the alcohol **16**,[9] which correlated with its lowest energy conformation as determined by molecular mechanics calculations.[10]

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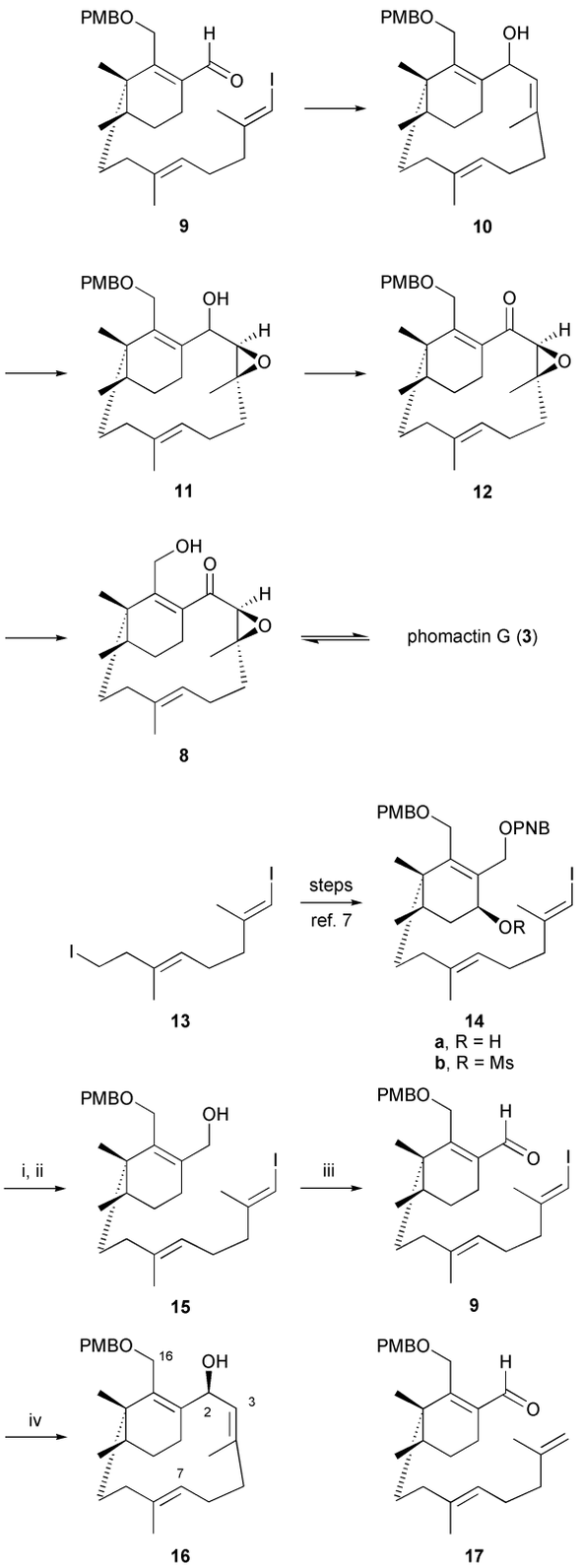
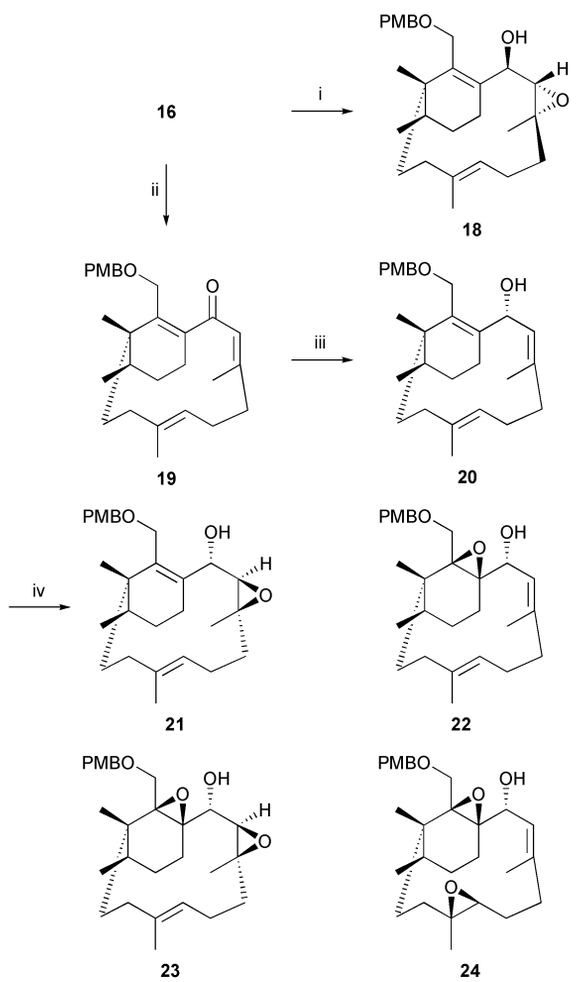



**Scheme 1** *Reagents and conditions*: i, MsCl, DIPEA, $CH_2Cl_2$, 0 °C to rt, 99%; ii, $LiBH_4$, THF, 86%; iii, Dess–Martin periodinane, $NaHCO_3$, $CH_2Cl_2$, 0 °C to rt, 99%; iv, $CrCl_2$ (6 eq.), $NiCl_2$ (1 eq.), DMSO, THF, rt, 47% (**16**) and 20% (**17**).

Not too surprisingly, when the β-orientated allylic alcohol **16** was treated with $VO(acac)_2$ and *t*-BuOOH,[11] the isomeric α-epoxide **18**, instead of the required β-epoxide **11**, was produced, and in excellent yield (Scheme 2). Earlier detailed studies in our laboratory had established that, in order to achieve selective β-epoxidation of the trisubstituted double bond associated with the allylic alcohol in **10**/**16**, we required the corresponding α-orientated hydroxyl group, *i.e.* **20**.[4] Thus,

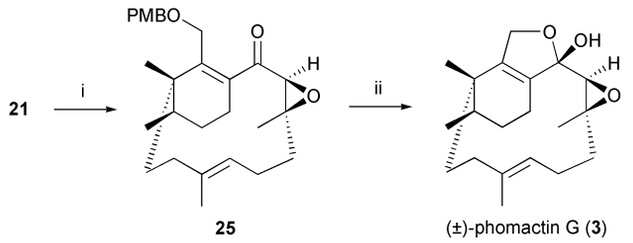



**Scheme 2** *Reagents and conditions*: i, $VO(acac)_2$, *t*-BuOOH, PhH, rt, 90%; ii, Dess–Martin periodinane, $NaHCO_3$, $CH_2Cl_2$, 0 °C to rt, 99%; iii, $CeCl_3 \cdot 7H_2O$, $NaBH_4$, MeOH, $CH_2Cl_2$, −78 °C to 0 °C, 81%; iv, dimethyldioxirane (0.5 eq.), acetone–$H_2O$ (1 : 1), 0 °C, 31% (**21**) (quantitative based on recovered **20**).

the β-alcohol centre in **16** was next inverted to the corresponding α-alcohol **20** by oxidation using Dess–Martin periodinane, followed by selective reduction of the resulting ketone **19** under Luche conditions ($NaBH_4$–$CeCl_3$).

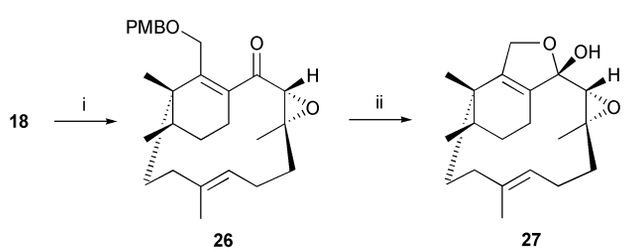
To our surprise and consternation, the selective epoxidation of the α-orientated alcohol **20** to the corresponding β-epoxide **21**, which had been straightforward in some of our related studies with the phomactins,[4] proved to be problematic, yet interesting. Thus, treatment of **20** with $VO(acac)_2$ and *t*-BuOOH led only to the isomeric mono-epoxide **22** and its *bis*-epoxide **23**, in a 1 : 1 ratio and in essentially quantitative yield (Scheme 2). The use of *m*-CPBA also gave the mono-epoxide **22** largely, but also **23** and the interesting isomeric *bis*-epoxide **24**. Treatment of the allylic alcohol **20** with 1 equivalent of dimethyldioxirane[12] gave only the *bis*-epoxides **23** and **24**, along with recovered starting material. To our satisfaction, however when **20** was treated with only 0.5 equivalents of dimethyldioxirane the correct β-epoxide **21** was produced exclusively in 31% yield (quantitative based on recovered **20**).

When the β-epoxy alcohol **21** was oxidised with Dess–Martin periodinane, the corresponding epoxy ketone **25** was secured in 99% yield (Scheme 3). Furthermore, when the PMB ether group in the epoxy ketone **25** was deprotected, using DDQ in $CH_2Cl_2$–$H_2O$, the resulting alcohol underwent spontaneous cyclic hemiacetal ring formation producing (±)-phomactin G (**3**) in 73% overall yield. The synthetic phomactin G displayed proton and carbon NMR spectroscopic data which were closely similar with those reported for the natural product isolated from *Phoma* sp.[1]

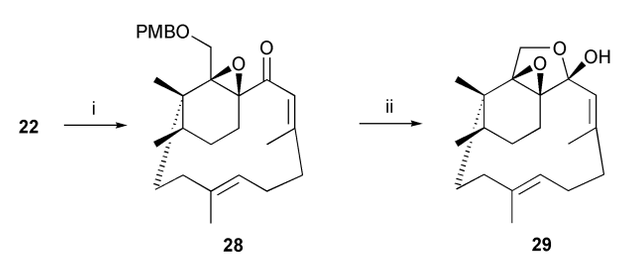



**Scheme 3** *Reagents and conditions*: i, Dess–Martin periodinane, $NaHCO_3$, $CH_2Cl_2$, 0 °C to rt, 99%; ii, DDQ, $CH_2Cl_2$–$H_2O$ (18 : 1), 0 °C to rt, 73%.

As a corollary to synthesising the isomeric structures **18** and **22**, relating to the key intermediate **21** in our total synthesis of phomactin G (**3**), we also converted these structures into other phomactoids for future SAR studies. Thus, oxidation of the epoxide **18** to **26**, followed by deprotection produced the epoxide **27** which is isomeric with phomactin G (Scheme 4). Furthermore, oxidation of the epoxy alcohol **22**, followed by deprotection of the PMB ether group in the resulting epoxy ketone **28** provided a synthesis of the interesting positional isomer **29** of phomactin G (Scheme 5). The biological properties of these phomactin G isomers, and related phomactins prepared in our studies, will be reported elsewhere at a later date.




**Scheme 4** *Reagents and conditions*: i, Dess–Martin periodinane, $NaHCO_3$, $CH_2Cl_2$, 0 °C to rt, 74%; ii, DDQ, $CH_2Cl_2$–$H_2O$ (18 : 1), 0 °C to rt, 95%.




**Scheme 5** *Reagents and conditions*: i, Dess–Martin periodinane, $NaHCO_3$, $CH_2Cl_2$, 0 °C to rt, 99%; ii, DDQ, $CH_2Cl_2$–$H_2O$ (18 : 1), 0 °C to rt, 79%.

## Experimental

### General details

For general experimental details see reference 4*b*. All of the compounds prepared in this paper are racemic.

**[(3*S*,4*R*)-3-((3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dienyl)-2-(4-methoxybenzyloxymethyl)-3,4-dimethylcyclohex-1-enyl]-methanol 15.** Methanesulfonyl chloride (24 μL, 0.30 mmol) was added dropwise over 1 minute to a stirred solution of the alcohol **14a**[7] (0.22 g, 0.30 mmol) in dichloromethane (5.0 mL) containing diisopropylethylamine (0.12 mL, 0.66 mmol) at 0 °C. The mixture was allowed to warm to room temperature over 5 hours, then quenched with 1 M $K_2CO_3$ (4 mL) and stirred for 10 minutes. The separated aqueous phase was extracted with ethyl acetate (3 × 20 mL), and the combined organic extracts were then dried over $Na_2SO_4$ and concentrated *in vacuo* to leave the crude *methanesulfonate* **14b** (0.24 g, 99%) as a viscous oil. A solution of lithium borohydride (2.0 M) in THF (0.52 mL, 1.04 mmol) was added dropwise over 1 minute to a stirred solution of **14b** (0.24 g, 0.30 mmol) in methanol (42 μL, 1.04 mmol) and THF (6.0 mL) at 0 °C. The mixture was allowed to warm to room temperature over 4 hours, then cooled to 0 °C and quenched with 1 M NaOH (4 mL). The mixture was stirred for 10 minutes, and then the separated aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were dried over $Na_2SO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 20–30% diethyl ether in pentane as eluent to give the *alcohol* (0.14 g, 86%) as a colourless oil; $\nu_{max}$ (film)/$cm^{-1}$ 3439, 2926, 1613 and 1249; $\delta_H$ (360 MHz, $CDCl_3$) 7.27 (2H, d, *J* 8.6, 2 × Ar*H*), 6.88 (2H, d, *J* 8.6, 2 × Ar*H*), 5.86–5.85 (1H, m, C=C*H*I), 4.99 (1H, t, *J* 6.8, C=C*H*$CH_2$), 4.50 (1H, d, *J* 11.3, ArC*H*H), 4.46 (1H, d, *J* 11.3, ArCH*H*), 4.08 (1H, d, *J* 10.3, OC*H*HC=C), 4.07 (1H, d, *J* 11.6, C*H*HOH), 3.89 (1H, d, *J* 10.3, OCH*H*C=C), 3.81 (1H, obs., CH*H*OH), 3.81 (3H, s, $OCH_3$), 2.69 (1H, br s, *OH*), 2.23–2.15 (4H, m, $CH_2(CH_3)$C=CHI and C=CC$H_2$), 2.10 (2H, dt, *J* 14.5 and 6.8, C=CHC$H_2$), 1.85–1.78 (1H, m, C*H*H$(CH_3)$C=CH), 1.84 (3H, s, $CH_3$C=CHI), 1.74–1.65 (1H, m, $CH_3CH$), 1.60 (1H, dd, *J* 16.9 and 4.5, CH*H*$(CH_3)$C=CH), 1.55 (3H, s, $CH_3$C=CH), 1.55–1.47 (2H, m, CHC*H*H and C(4°)–C*H*H), 1.45–1.35 (2H, m, CHCH*H* and C(4°)–CH*H*), 0.87 (3H, d, *J* 7.1, $CH_3$CH), 0.86 (3H, s, $CH_3$–C(4°)); $\delta_C$ (90 MHz, $CDCl_3$) 159.3 (Ar–*C*(4°)$OCH_3$), 147.7 (*C*=CHI), 140.5 (C=*C*$CH_2OH$), 138.2 (Ar–*C*(4°)), 136.8 (*C*=C$CH_2OH$), 129.7 (*C*=CH), 129.7 (Ar–*C*H), 122.4 (C=*C*H), 113. 8 (Ar–*C*H), 74.7 (C=*C*HI), 72.8 (Ar*C*$H_2O$), 66.3 (O*C*$H_2$-C=C), 64.1 (*C*$H_2OH$), 55.2 (O*C*$H_3$), 40.8 (*C*(4°)–C=C), 39.4 (*C*$H_2$C=CHI), 35.8 (C(4°)–*C*$H_2$), 34.4 (*C*$H_2$C=CH), 33.1 ($CH_3$*C*H), 29.3 (C=C*C*$H_2$), 26.8 (CH*C*$H_2$), 26.2 (C=CH*C*$H_2$), 23.9 (*C*$H_3$C=CHI), 21.3 (*C*$H_3$–C(4°)), 16.2 (*C*$H_3$C=CH), 16.1 (*C*$H_3$CH); *m*/*z* (ES) 575.1998 ($M^+$ + Na, 100%, $C_{28}H_{41}IO_3Na$ requires 575.1946).

**(3*S*,4*R*)-3-((3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dienyl)-2-(4-methoxybenzyloxymethyl)-3,4-dimethylcyclohex-1-enecarbaldehyde 9.** Dess–Martin periodinane[8] (164 mg, 0.39 mmol) was added to a mixture of the alcohol **15** (57 mg, 0.10 mmol) and $NaHCO_3$ (220 mg, 2.6 mmol) in dichloromethane (5.0 mL) at 0 °C. The mixture was stirred at 0 °C for 30 minutes and then allowed to warm to room temperature over 2.5 hours. The mixture was quenched with saturated aqueous solutions of $NaHCO_3$ (5 mL) and $Na_2S_2O_3$ (5 mL), and then diluted with diethyl ether (12 mL). The separated aqueous phase was extracted with diethyl ether (3 × 12 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 30% diethyl ether in pentane as eluent to give the *aldehyde* (57 mg, 99%) as a colourless oil; $\nu_{max}$ (film)/$cm^{-1}$ 2936, 2861, 1670, 1613 and 1249; $\delta_H$ (360 MHz, $CDCl_3$) 10.4 (1H, s, C*H*O), 7.26 (2H, d, *J* 8.7, 2 × Ar*H*), 6.88 (2H, d, *J* 8.7, 2 × Ar*H*), 5.85 (1H, br s, C=C*H*I), 5.01 (1H, app. t, *J* 6.8, C=C*H*$CH_2$), 4.50 (2H, s, Ar$CH_2$), 4.32 (1H, d, *J* 10.8, OC*H*HC=C), 4.14 (1H, d, *J* 10.8, OCH*H*C=C), 3.81 (3H, s, $OCH_3$), 2.42 (1H, ddd, *J* 18.0, 5.4 and 2.9, C=CC*H*H), 2.22–2.18 (2H, m, $CH_2(CH_3)$C=CHI), 2.11 (2H, app. t, *J* 7.1, C=CHC$H_2$), 2.01 (1H, ddd, *J* 18.0, 10.5 and 6.3, C=CCH*H*), 1.91–1.86 (1H, m, C*H*H$(CH_3)$C=CH), 1.84 (3H, s, $CH_3$C=CHI), 1.79–1.72 (1H, m, $CH_3CH$), 1.71–1.47 (4H, m, CH*H*$(CH_3)$C=CH, CHC*H*H and C(4°)–C$H_2$), 1.56 (3H, s, $CH_3$C=CH), 1.36 (1H, app. dq, *J* 13.2 and 5.4, CHCH*H*), 0.96 (3H, s, $CH_3$–C(4°)), 0.91 (3H, d, *J* 7.0, $CH_3$CH); $\delta_C$ (90 MHz, $CDCl_3$) 193.3 (*C*HO), 159.3 (*C*=CCHO), 158.2 (Ar–*C*(4°)$OCH_3$), 147.6 (*C*=CHI), 138.2 (Ar–*C*(4°)), 136.2 (*C*=CH), 129.6 (Ar–*C*H), 129.4 (C=*C*CHO), 122.8 (C=*C*H), 113.9 (Ar–*C*H), 74.7 (C=*C*HI), 72.9 (Ar*C*$H_2O$), 63.6 (O*C*$H_2$C=C), 55.2 (O*C*$H_3$), 42.5 (*C*(4°)–C=C), 39.3 (*C*$H_2$-

C=CHI), 35.5 (C(4°)–$CH_2$), 34.4 ($CH_2$C=CH), 33.1 ($CH_3$CH), 26.1 (C=CH$CH_2$), 25.6 (CH$CH_2$), 23.8 ($CH_3$C=CHI), 22.4 (C=C$CH_2$), 20.7 ($CH_3$–C(4°)), 16.1 ($CH_3$C=CH), 15.9 ($CH_3$CH); *m/z* (ES) 573.1879 ($M^+$ + Na, 100%, $C_{28}H_{39}IO_3Na$ requires 573.1842).

**(3*E*,7*E*)-(2*S*,11*S*,12*R*)-15-(4-Methoxybenzyloxymethyl)-4,8,11,12-tetramethylbicyclo[9.3.1]pentadeca-1(15),3,7-trien-2-ol 16.** Nickel chloride (38 mg, 0.29 mmol) and chromium chloride (179 mg, 1.46 mmol) were added sequentially to a stirred solution of the aldehyde vinyl iodide **9** (94 mg, 0.17 mmol) in DMSO (37.0 mL) at room temperature in a glove bag under an atmosphere of argon. The mixture was diluted with THF (12.0 mL), then removed from the glove bag, and stirred under a positive pressure of argon for 46 hours. The mixture was cooled to 0 °C and then quenched cautiously with serine (1.0 M in a saturated aqueous solution of $NaHCO_3$, 130 mL). The mixture was stirred vigorously and allowed to warm to room temperature over 1 hour and then diluted with pentane (130 mL). The separated aqueous phase was extracted with diethyl ether (4 × 150 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 10–20–40% diethyl ether in pentane as eluent to give: (i) the *bicyclic alcohol* (34.0 mg, 47%) (eluted second) as a colourless oil, $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3605, 2936, 2858, 2839, 1612, 1248 and 1036; $\delta_H$ (360 MHz, $CDCl_3$) 7.29 (2H, d, *J* 8.3, 2 × Ar*H*), 6.89 (2H, d, *J* 8.3, 2 × Ar*H*), 5.45 (1H, d, *J* 10.7, $CH_2(CH_3)$C=CHC*H*OH), 5.18 (1H, d, *J* 10.7, $CH_2(CH_3)$C=C*H*CHOH), 4.79 (1H, d, *J* 11.0, C=C*H*$CH_2$), 4.46 (1H, d, *J* 11.6, ArC*H*H), 4.41 (1H, d, *J* 11.6, ArCH*H*), 3.82 (3H, s, O$CH_3$), 3.58 (1H, d, *J* 10.8, OC*H*HC=C), 3.42 (1H, d, *J* 10.8, OCH*H*C=C), 2.48 (1H, dd, *J* 18.2 and 3.9, C=CC*H*H), 2.43–2.32 (1H, m, C=CHC*H*H), 2.15 (1H, dd, *J* 14.5 and 12.1, C*H*H(CH$_3$)C=CHCH$_2$), 2.09–1.97 (4H, m, C$H_2$(CH$_3$)C=CH-CHOH, C=CCH*H*, and C=CHCH*H*), 1.84–1.73 (2H, m, CH$_3$-C*H* and CH*H*(CH$_3$)C=CHCH$_2$), 1.60 (3H, s, C$H_3$C=CHCH-OH), 1.56–1.48 (2H, m, C(4°)–C*H*H and CHC*H*H), 1.46 (3H, s, C$H_3$C=CHCH$_2$), 1.44–1.34 (2H, m, C(4°)–CH*H* and CH-CH*H*), 0.84 (3H, d, *J* 6.9, C$H_3$CH), 0.79 (3H, s, C$H_3$–C(4°)); $\delta_C$ (90 MHz, $CDCl_3$) 159.3 (Ar–*C*(4°)OCH$_3$), 141.8 (*C*=CCH-OH), 135.6 (Ar–*C*(4°)), 134.1 (*C*=CH), 132.7 (*C*=CHCHOH), 130.4 (C=*C*CHOH), 129.9 (Ar–*C*H), 127.2 (C=*C*H), 127.2 (C=*C*HCHOH), 113.8 (Ar–*C*H), 72.8 (Ar*C*H$_2$O), 67.9 (*C*HOH), 65.5 (O*C*H$_2$C=C), 55.3 (O*C*H$_3$), 40.6 (*C*(4°)–C=C), 38.3 (*C*H$_2$C= CHCHOH), 34.8 (*C*H$_2$C=CH), 33.2 (CH$_3$*C*H), 31.5 (C(4°)–*C*H$_2$), 26.9 (C=CH*C*H$_2$), 26.8 (CH*C*H$_2$), 23.2 (C=C*C*H$_2$), 21.4 (*C*H$_3$–C(4°)), 16.3 (*C*H$_3$C=CHCHOH), 16.2 (*C*H$_3$CH), 14.9 (*C*H$_3$C=CH); *m/z* (ES) 447.2885 ($M^+$ + Na, 100%, $C_{28}H_{40}O_3Na$ requires 447.2875); and (ii) (3*S*,4*R*)-3-((*E*)-3,7-dimethylocta-3,7-dienyl)-2-(4-methoxybenzyloxymethyl)-3,4-dimethylcyclohex-1-enecarbaldehyde **17** (20.2 mg, 20%) (eluted first) as a colourless oil, $\nu_{max}$ (film)/$cm^{-1}$ 2936, 2878, 1668, 1613 and 1249; $\delta_H$ (360 MHz, $CDCl_3$) 10.0 (1H, s, C*H*O), 7.26 (2H, d, *J* 8.7, 2 × Ar*H*), 6.89 (2H, d, *J* 8.7, 2 × Ar*H*), 5.08 (1H, app. t, *J* 6.8, C=C*H*CH$_2$), 4.70 (2H, br d, *J* 12.9, C=C$H_2$), 4.50 (2H, s, ArC$H_2$), 4.32 (1H, d, *J* 10.8, OC*H*HC=C), 4.14 (1H, d, *J* 10.8, OCH*H*C=C), 3.82 (3H, s, O$CH_3$), 2.42 (1H, ddd, *J* 18.1, 5.4 and 3.0, C=CC*H*H), 2.14–2.09 (2H, m, C=CHC$H_2$), 2.05–2.00 (3H, m, C$H_2$(CH$_3$)C=CH$_2$ and C=CCH*H*), 1.98–1.83 (1H, m, C*H*H(CH$_3$)C=CH), 1.82–1.76 (1H, m, CH$_3$C*H*), 1.73 (3H, s, C$H_3$C=CH$_2$), 1.68–1.60 (3H, m, CH*H*(CH$_3$)C=CH, C(4°)–C*H*H and CHC*H*H), 1.58 (3H, s, C$H_3$C=CH), 1.55–1.49 (1H, m, C(4°)–CH*H*), 1.36 (1H, app. dq, *J* 13.2 and 5.4, CHCH*H*), 0.96 (3H, s, C$H_3$–C(4°)), 0.91 (3H, d, *J* 6.8, C$H_3$CH); $\delta_C$ (90 MHz, $CDCl_3$) 193.4 (*C*HO), 159.4 (*C*=CCHO), 158.4 (Ar–*C*(4°)OCH$_3$), 145.7 (*C*=CH$_2$), 138.2 (Ar–*C*(4°)), 135.3 (*C*=CH), 129.6 (Ar–*C*H), 129.5 (C=*C*CHO), 123.9 (C=*C*H), 113.8 (Ar–*C*H), 109.8 (C=*C*H$_2$), 73.0 (Ar*C*H$_2$O), 63.7 (O*C*H$_2$C=C), 55.2 (O*C*H$_3$), 42.6 (*C*(4°)–C=C), 37.7 (*C*H$_2$C=CH$_2$), 35.5 (C(4°)–*C*H$_2$), 34.4 (*C*H$_2$C=CH), 33.2 (CH$_3$*C*H), 26.2 (C=CH*C*H$_2$), 25.6 (CH*C*H$_2$), 22.5 (*C*H$_3$C=CHI), 22.5 (C=C*C*H$_2$), 20.7 (*C*H$_3$–C(4°)), 16.2 (*C*H$_3$C=CH), 16.0 (*C*H$_3$CH); *m/z* (ES) 447.2892 ($M^+$ + Na, 100%, $C_{28}H_{40}O_3Na$ requires 447.2875).

**(*E*)-(2*R*,3*S*,5*S*,12*S*,13*R*)-16-(4-Methoxybenzyloxymethyl)-5,9,12,13-tetramethyl-4-oxatricyclo[10.3.1.0$^{3,5}$]hexadeca-1(16),8-dien-2-ol 18.** A solution of *tert*-butyl hydroperoxide (0.18 M) in benzene (148 μL, 0.03 mmol) was added dropwise over 1 minute to a stirred solution of vanadyl acetylacetonate (a few crystals) and the allylic alcohol **16** (11.2 mg, 0.03 mmol) in benzene (2.6 mL) at room temperature. The clear orange mixture was stirred at room temperature for 70 minutes. The mixture was quenched with 3–4 drops of dimethyl sulfide, then stirred for 30 minutes and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 45% diethyl ether in pentane as eluent to give the *α-epoxy alcohol* (10.3 mg, 90%) as a colourless oil; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3596, 2939, 2883, 1611 and 1249; $\delta_H$ (360 MHz, $CDCl_3$) 7.25 (2H, d, *J* 8.4, 2 × Ar*H*), 6.87 (2H, d, *J* 8.4, 2 × Ar*H*), 4.80 (1H, d, *J* 10.7, C=C*H*CH$_2$), 4.53 (1H, d, *J* 9.8, CH$_2$(CH$_3$)C–CHC*H*OH), 4.45 (1H, d, *J* 11.8, ArC*H*H), 4.34 (1H, d, *J* 11.8, ArCH*H*), 3.81 (3H, s, O$CH_3$), 3.58 (1H, d, *J* 10.8, OC*H*HC=C), 3.47 (1H, d, *J* 10.8, OCH*H*C=C), 2.65 (1H, d, *J* 9.8, CH$_2$(CH$_3$)C–C*H*CHOH), 2.62 (1H, dd, *J* 17.3 and 3.7, C=CC*H*H), 2.26–2.15 (1H, m, C=CHC*H*H), 2.24 (1H, app. t, *J* 13.1, C*H*H(CH$_3$)C=CHCH$_2$), 2.07–1.96 (3H, m, C*H*H(CH$_3$)C–CHCHOH, C=CHCH*H* and C=CCH*H*), 1.93–1.82 (2H, m, CH$_3$C*H* and CH*H*(CH$_3$)C=CHCH$_2$), 1.65 (1H, dd, *J* 15.4 and 13.1, C(4°)–C*H*H), 1.57–1.53 (1H, m, CHC*H*H), 1.54 (3H, s, C$H_3$C=CH), 1.51–1.49 (1H, m, C(4°)–CH*H*), 1.47–1.37 (1H, m, CHCH*H*), 1.13 (1H, td, *J* 12.9 and 4.2, CH*H*-(CH$_3$)C–CHCHOH), 1.06 (3H, s, C$H_3$C–CHCHOH), 0.88 (3H, d, *J* 6.8, C$H_3$CH), 0.86 (3H, s, C$H_3$–C(4°)); $\delta_C$ (90 MHz, $CDCl_3$) 159.3 (Ar–*C*(4°)OCH$_3$), 137.0 (*C*=CCHOH), 136.9 (Ar–*C*(4°)), 134.4 (*C*=CH), 130.1 (C=*C*CHOH), 129.9 (Ar–*C*H), 125.4 (C=*C*H), 113.8 (Ar–*C*H), 72.4 (Ar*C*H$_2$O), 68.1 (*C*HOH), 65.8 (C–*C*HCHOH), 65.1 (O*C*H$_2$C=C), 62.9 (*C*–CHCHOH), 55.3 (O*C*H$_3$), 40.9 (*C*(4°)–C=C), 37.8 (*C*H$_2$C–CHCHOH), 35.0 (*C*H$_2$C=CH), 33.5 (CH$_3$*C*H), 32.4 (C(4°)–*C*H$_2$), 26.8 (CH*C*H$_2$), 24.7 (C=CH*C*H$_2$), 23.1 (C=C*C*H$_2$), 21.2 (*C*H$_3$–C(4°)), 16.9 (*C*H$_3$C–CHCHOH), 16.3 (*C*H$_3$CH), 15.3 (*C*H$_3$C=CH); *m/z* (ES) 463.2843 ($M^+$ + Na, 100%, $C_{28}H_{40}O_4Na$ requires 463.2824).

**(3*E*,7*E*)-(2*R*,11*S*,12*R*)-15-(4-Methoxybenzyloxymethyl)-4,8,11,12-tetramethylbicyclo[9.3.1]pentadeca-1(15),3,7-trien-2-ol 20.** Dess–Martin periodinane[8] (9.8 mg, 0.023 mmol) was added to a mixture of the β-alcohol **16** (6.4 mg, 0.015 mmol) and $NaHCO_3$ (12.6 mg, 0.15 mmol) in dichloromethane (1.0 mL) at 0 °C. The mixture was stirred at 0 °C for 30 minutes and then allowed to warm to room temperature over 90 minutes. The mixture was quenched with saturated aqueous solutions of $NaHCO_3$ (1.0 mL) and $Na_2S_2O_3$ (1.0 mL), and then diluted with diethyl ether (4 mL). The separated aqueous phase was extracted with diethyl ether (3 × 10 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo* to leave the *dienone* **19** (6.3 mg, 99%) as a colourless oil. Cerium trichloride heptahydrate (8.6 mg, 0.023 mmol) was added to a stirred solution of the dienone **19** (6.2 mg, 0.015 mmol) in dichloromethane (0.5 mL) and methanol (0.5 mL) at −78 °C. The mixture was stirred at −78 °C for 15 minutes, then sodium borohydride (5.4 mg, 0.14 mmol) was added and the resulting mixture was allowed to warm to 0 °C over 5 hours. The mixture was quenched with a saturated aqueous solution of $NH_4Cl$ (0.5 mL), then allowed to warm to room temperature and diluted with water (1.0 mL). The separated aqueous phase was extracted with dichloromethane (3 × 2.0 mL) and the combined organic extracts were

then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 20% diethyl ether in pentane as eluent to give the *α-alcohol* (5.2 mg, 81%) as a colourless oil; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3402, 2930 and 1612; $\delta_H$ (360 MHz, $CDCl_3$) 7.29 (2H, d, *J* 8.6, 2 × Ar*H*), 6.89 (2H, d, *J* 8.6, 2 × Ar*H*), 5.17 (1H, d, *J* 8.5, $CH_2(CH_3)C{=}CHCHOH$), 5.00 (1H, d, *J* 5.8, O*H*), 4.72 (1H, br d, *J* 7.7, $C{=}CHCH_2$), 4.56 (1H, dd, *J* 8.5 and 5.8, $CH_2(CH_3)C{=}CHCHOH$), 4.54 (1H, d, *J* 11.2, ArC*H*H), 4.40 (1H, d, *J* 11.2, ArCH*H*), 4.20 (1H, d, *J* 10.5, OC*H*HC=C), 3.81 (3H, s, $OCH_3$), 3.74 (1H, d, *J* 10.5, OCH*H*C=C), 2.41–2.29 (1H, m, C=CHC*H*H), 2.23–2.20 (1H, m, C*H*H($CH_3$)C=CHCHOH), 2.18–2.16 (1H, m, C*H*H($CH_3$)C=$CHCH_2$), 2.10–2.00 (3H, m, C=C$H_2$ and C=CHCH*H*), 1.97–1.88 (1H, m, CH*H*($CH_3$)C=CHCHOH), 1.85–1.76 (1H, m, CH*H*($CH_3$)C=$CHCH_2$), 1.74–1.68 (1H, m, $CH_3CH$), 1.71 (3H, s, $CH_3C{=}CHCHOH$), 1.65–1.57 (1H, m, C(4°)–C*H*H), 1.51 (3H, s, $CH_3C{=}CH$), 1.49–1.40 (3H, m, C(4°)–CH*H* and $CHCH_2$), 0.83 (3H, d, *J* 6.8, $CH_3CH$), 0.81 (3H, s, $CH_3$–C(4°)); $\delta_C$ (90 MHz, $CDCl_3$) 159.4 (Ar–*C*(4°)$OCH_3$), 142.4 (*C*=CCHOH), 135.5 (Ar–*C*(4°)), 133.1 (*C*=CH), 132.4 (*C*=CHCHOH), 130.3 (Ar–*C*H), 129.2 (C=*C*CHOH), 127.8 (C=*C*HCHOH), 127.2 (C=*C*H), 113.8 (Ar–*C*H), 75.0 (*C*HOH), 72.7 (Ar*C*$H_2O$), 67.4 (O*C*$H_2C{=}C$), 55.3 ($OCH_3$), 41.2 (*C*(4°)–C=C), 36.2 ($CH_2C{=}CHCHOH$), 34.8 ($CH_2C{=}CH$), 33.4 (C(4°)–$CH_2$), 33.1 ($CH_3CH$), 32.4 (C=C$CH_2$), 27.0 ($CHCH_2$), 25.8 ($C{=}CHCH_2$), 21.7 ($CH_3$–C(4°)), 18.3 ($CH_3C{=}CHCHOH$), 16.0 ($CH_3CH$), 15.4 ($CH_3C{=}CH$); *m*/*z* (ES) 447.2832 ($M^+$ + Na, 100%, $C_{28}H_{40}O_3Na$ requires 447.2875).

**(*E*)-(2*S*,3*R*,5*R*,12*S*,13*R*)-16-(4-Methoxybenzyloxymethyl)-5,9,12,13-tetramethyl-4-oxatricyclo[10.3.1.0$^{3,5}$]hexadeca-1(16),8-dien-2-ol 21.** A solution of dimethyldioxirane[12] (0.1 M) in acetone (56 μL, 5.6 μmol) was added dropwise over 2 minutes to a stirred solution of the α-allylic alcohol **20** (4.7 mg, 11 μmol) in acetone (0.5 mL) and water (0.5 mL) at 0 °C. The mixture was stirred at 0 °C for 20 minutes and then concentrated *in vacuo*. A saturated aqueous solution of $NaHCO_3$ (1.0 mL) was added to the residue and the aqueous phase was extracted with ethyl acetate (3 × 5.0 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 20–30% diethyl ether in pentane as eluent to give the *β-epoxy alcohol* (1.5 mg, 31%) as a colourless film, $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3692, 2929, 1602, 1250 and 1038; $\delta_H$ (360 MHz, $CDCl_3$) 7.29 (2H, d, *J* 9.2, 2 × Ar*H*), 6.89 (2H, d, *J* 9.2, 2 × Ar*H*), 4.99 (1H, br t, *J* 6.9, C=C*H*$CH_2$), 4.92 (1H, d, *J* 6.8, O*H*), 4.55 (1H, d, *J* 11.5, ArC*H*H), 4.44 (1H, d, *J* 11.5, ArCH*H*), 4.24 (1H, d, *J* 10.8, OC*H*HC=C), 3.87 (1H, d, *J* 10.8, OCH*H*C=C), 3.81 (3H, s, $OCH_3$), 3.57 (1H, dd, *J* 9.2 and 6.8, $CH_2(CH_3)C$–CHC*H*OH), 3.02 (1H, d, *J* 9.2, $CH_2(CH_3)C$–C*H*CHOH), 2.27 (1H, ddd, *J* 15.2, 11.4 and 1.5, C*H*H($CH_3$)C=$CHCH_2$), 2.11–2.03 (3H, m, C=CHC*H*H and C=C$CH_2$), 1.95–1.90 (1H, m, C=CHCH*H*), 1.89–1.78 (3H, m, CH*H*($CH_3$)C=$CHCH_2$, C*H*H($CH_3$)C–CHCHOH and $CH_3CH$), 1.66–1.51 (4H, m, C(4°)–$CH_2$, CH*H*($CH_3$)C–CHCHOH and CHC*H*H), 1.51 (3H, s, $CH_3C{=}CH$), 1.48–1.41 (1H, m, CHCH*H*), 1.32 (3H, s, $CH_3C$–CHCHOH), 0.87 (3H, d, *J* 7.0, $CH_3CH$), 0.86 (3H, s, $CH_3$–C(4°)); $\delta_C$ (90 MHz, $CDCl_3$) 159.6 (Ar–*C*(4°)$OCH_3$), 138.8 (*C*=CCHOH), 137.8 (Ar–*C*(4°)), 135.4 (*C*=CH), 130.2 (Ar–*C*H), 128.8 (C=*C*CHOH), 125.2 (C=*C*H), 113.9 (Ar–*C*H), 76.3 (*C*HOH), 72.8 (Ar*C*$H_2O$), 67.4 (O*C*$H_2C{=}C$), 65.6 (C–*C*HCHOH), 60.1 (*C*–CHCHOH), 55.3 ($OCH_3$), 41.4 (*C*(4°)–C=C), 36.1 ($CH_2C$–CHCHOH), 35.0 ($CH_2C{=}CH$), 33.5 ($CH_3CH$), 33.1 (C(4°)–$CH_2$), 32.6 (C=C$CH_2$), 26.8 ($CHCH_2$), 23.5 ($C{=}CHCH_2$), 21.8 ($CH_3$–C(4°)), 20.1 ($CH_3C$–CHCHOH), 15.9 ($CH_3C{=}CH$), 15.8 ($CH_3CH$); *m*/*z* (ES) 423.2894 ($M^+$ − OH, 100%, $C_{28}H_{39}O_3$ requires 423.2899); and recovered alcohol (3.3 mg).

**(3*E*,7*E*)-(1*R*,2*R*,11*S*,12*R*,16*S*)-16-(4-Methoxybenzyloxymethyl)-4,8,11,12-tetramethyl-15-oxatricyclo[9.3.2.0$^{1,16}$]hexadeca-3,7-dien-2-ol 22 and 23.** A solution of *tert*-butyl hydroperoxide (0.18 M) in benzene (36 μL, 0.007 mmol) was added dropwise over 1 minute to a stirred solution of vanadyl acetylacetonate (a few crystals) and the α-allylic alcohol **20** (2.7 mg, 0.006 mmol) in benzene (1 mL) at room temperature. The clear orange mixture was stirred at room temperature for 90 minutes. The mixture was quenched with 3–4 drops of dimethyl sulfide, then stirred for 30 minutes and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 20–50% diethyl ether in pentane as eluent to give: (i) the *epoxy alcohol* (1.5 mg, 53%) (eluted first) as a colourless film, $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3690, 2935, 1612, 1247 and 1035; $\delta_H$ (360 MHz, $CDCl_3$) 7.32 (2H, d, *J* 8.7, 2 × Ar*H*), 6.89 (2H, d, *J* 8.7, 2 × Ar*H*), 4.83 (1H, br d, *J* 5.6, C=C*H*$CH_2$), 4.65 (1H, d, *J* 10.3, $CH_2(CH_3)C{=}CHCHOH$), 4.60 (1H, d, *J* 11.6, ArC*H*H), 4.50 (1H, d, *J* 9.7, $CH_2(CH_3)C{=}CHCHOH$), 4.43 (1H, d, *J* 11.6, ArC*H*H), 3.99 (1H, d, *J* 11.3, OC*H*HC–C), 3.81 (3H, s, $OCH_3$), 3.74 (1H, d, *J* 11.3, OCH*H*C–C), 3.37 (1H, br s, O*H*), 2.39–2.31 (1H, m, C*H*H($CH_3$)C=CHCHOH), 2.28 (1H, app. t, *J* 15.7, C*H*H($CH_3$)C=$CHCH_2$), 2.14–2.04 (1H, m, C=CHC*H*H), 1.96 (1H, ddd, *J* 17.0, 11.8 and 4.0, CH*H*-($CH_3$)C=CHCHOH), 1.86–1.77 (2H, m, CH*H*($CH_3$)C=$CHCH_2$ and C–CC*H*H), 1.72 (3H, s, $CH_3C{=}CHCHOH$), 1.69–1.58 (3H, m, $CH_3CH$, C(4°)–C*H*H and C–CCH*H*), 1.51 (3H, s, $CH_3C{=}CH$), 1.51–1.33 (3H, m, C(4°)–CH*H*, C=CHCH*H* and CHC*H*H), 1.14–1.09 (1H, m, CHCH*H*), 1.08 (3H, s, $CH_3$–C(4°)), 0.73 (3H, d, *J* 6.8, $CH_3CH$); $\delta_C$ (90 MHz, $CDCl_3$) 159.1 (Ar–*C*(4°)$OCH_3$), 136.1 (Ar–*C*(4°)), 134.1 (*C*=CHCHOH), 130.7 (*C*=CH), 129.3 (Ar–*C*H), 127.8 (C=*C*HCHOH), 124.5 (C=*C*H), 113.7 (Ar–*C*H), 73.1 (Ar*C*$H_2O$), 70.5 (O*C*$H_2C$–C), 70.1 (*C*HOH), 69.5 (C–*C*), 69.2 (*C*–C), 55.3 ($OCH_3$), 39.8 (*C*(4°)–C–C), 35.7 ($CH_2C{=}CHCHOH$), 34.6 ($CH_2C{=}CH$), 33.5 ($CH_3CH$), 33.0 (C(4°)–$CH_2$), 30.9 (C–C$CH_2$), 24.5 ($CHCH_2$), 24.3 ($C{=}CHCH_2$), 19.4 ($CH_3$–C(4°)), 18.9 ($CH_3C{=}CHCHOH$), 17.2 ($CH_3C{=}CH$), 15.2 ($CH_3CH$); *m*/*z* (ES) 463.2793 ($M^+$ + Na, 100%, $C_{28}H_{40}O_4Na$ requires 463.2824); and (ii) the *bis-epoxide* **23** (1.3 mg, 45%) as a colourless film, $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3534, 2930, 2856, 1612 and 1248; $\delta_H$ (500 MHz, $CDCl_3$) 7.31 (2H, d, *J* 8.5, 2 × Ar*H*), 6.89 (2H, d, *J* 8.5, 2 × Ar*H*), 5.10 (1H, br s, C=C*H*$CH_2$), 4.61 (1H, d, *J* 11.4, ArC*H*H), 4.42 (1H, d, *J* 11.4, ArCH*H*), 3.99 (1H, d, *J* 11.1, OC*H*HC–C), 3.81 (3H, s, $OCH_3$), 3.75 (1H, d, *J* 11.1, OCH*H*C–C), 3.64 (1H, d, *J* 9.5, $CH_2(CH_3)C$–CHC*H*OH), 3.40 (1H, br s, O*H*), 2.55 (1H, d, *J* 9.5, $CH_2(CH_3)C$–C*H*CHOH), 2.46–2.36 (2H, m, *H*H($CH_3$)C–CHCHOH and C*H*H($CH_3$)C=$CHCH_2$), 2.21 (1H, dd, *J* 14.5 and 11.5, C–CC*H*H), 1.92–1.68 (7H, m, C=CHC$H_2$, C(4°)–C$H_2$, H*H*($CH_3$)C–CHCHOH, CH*H*($CH_3$)C=$CHCH_2$ and $CH_3CH$), 1.54–1.48 (2H, m, C–CCH*H* and CHC*H*H), 1.42 (3H, s, $CH_3C$–CHCHOH), 1.41 (3H, s, $CH_3C{=}CH$), 1.20–1.15 (1H, m, CHCH*H*), 1.11 (3H, s, $CH_3$–C(4°)), 0.76 (3H, d, *J* 6.8, $CH_3CH$); $\delta_C$ (125 MHz, $CDCl_3$) 159.3 (Ar–*C*(4°)$OCH_3$), 136.5 (Ar–*C*(4°)), 130.2 (*C*=CH), 129.5 (Ar–*C*H), 127.4 (C=*C*H), 113.8 (Ar–*C*H), 73.2 (Ar*C*$H_2O$), 72.0 (*C*HOH), 69.7 (O*C*$H_2C$–C), 68.9 (C–*C*), 66.0 (*C*–C), 63.1 (C–*C*H), 60.1 (*C*–CH), 55.3 ($OCH_3$), 39.8 (*C*(4°)–C–C), 34.7 ($CH_2C$–CHCHOH), 34.6 ($CH_2C{=}CH$), 33.4 ($CH_3CH$), 32.9 (C–C$CH_2$), 31.6 (C(4°)–$CH_2$), 24.4 ($CHCH_2$), 22.6 ($C{=}CHCH_2$), 21.0 ($CH_3C{=}CH$), 19.4 ($CH_3$–C(4°)), 17.5 ($CH_3C$–CHCHOH), 15.2 ($CH_3CH$); *m*/*z* (ES) 479.2776 ($M^+$ + Na, 100%, $C_{28}H_{40}O_5Na$ requires 479.2773).

**Bis-epoxide 24.** *meta*-Chloroperoxybenzoic acid (9.4 mg, 0.038 mmol, 70–75% in water) was added in portions to a solution of the α-allylic alcohol **20** (14.0 mg, 0.033 mmol) in dichloromethane (0.8 mL) and aqueous phosphate buffer (0.8 mL, pH 7) at 0 °C and stirred for 30 minutes. The mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (1.0 mL) and the separated aqueous phase was extracted with

dichloromethane (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 20–50% diethyl ether in pentane as eluent to give: (i) the *bis-epoxide* (4.0 mg, 26%) (eluted second) as a colourless film, $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3543, 2931, 1612, 1248 and 1036; $\delta_H$ (360 MHz, $CDCl_3$) 7.32 (2H, d, *J* 8.8, 2 × Ar*H*), 6.89 (2H, d, *J* 8.8, 2 × Ar*H*), 4.88 (1H, br d, *J* 9.2, $CH_2(CH_3)C$=C*H*CHOH), 4.66 (1H, d, *J* 11.8, ArC*H*H), 4.53 (1H, d, *J* 9.2, $CH_2(CH_3)C$=CHC*H*OH), 4.48 (1H, d, *J* 11.8, ArCH*H*), 4.03 (1H, d, *J* 11.3, OC*H*HC–C), 3.83 (1H, obs. d, OCH*H*C–C), 3.81 (3H, s, $OCH_3$), 2.56 (1H, br s, O*H*), 2.52 (1H, app. t, *J* 2.9, C–C*H*$CH_2$), 2.46–2.43 (1H, m, C–CHC*H*H), 2.42–2.38 (1H, m, C*H*H$(CH_3)$C–$CHCH_2$), 2.22 (1H, dd, *J* 16.8 and 12.4, C*H*H$(CH_3)$C=CHCHOH), 2.17–1.96 (3H, m, C–CHCH*H*, CH*H*$(CH_3)$C–$CHCH_2$ and C(4°)–C*H*H), 1.91–1.85 (1H, m, C–CC*H*H), 1.79 (3H, s, $CH_3$C=CHCHOH), 1.72–1.51 (3H, m, CH*H*$(CH_3)$C=CHCHOH, C–CCH*H* and C(4°)–CH*H*), 1.47–1.32 (2H, m, CHC*H*H and $CH_3CH$), 1.17–1.14 (1H, m, CHCH*H*), 1.14 (3H, s, $CH_3$C–CH), 1.10 (3H, s, $CH_3$–C(4°)), 0.66 (3H, d, *J* 6.3, $CH_3$CH); $\delta_C$ (90 MHz, $CDCl_3$) 159.3 (Ar–*C*(4°)$OCH_3$), 136.9 (Ar–*C*(4°)), 130.2 (*C*=CHCHOH), 129.4 (Ar–*C*H), 123.8 (C=*C*HCHOH), 113.8 (Ar–*C*H), 73.3 (Ar*C*$H_2O$), 70.8 (O*C*$H_2$C–C), 69.7 (*C*HOH), 69.6 (C–*C*), 68.8 (*C*–C), 64.2 (C–*C*$HCH_2$), 60.2 (*C*–$CHCH_2$), 55.3 (O*C*$H_3$), 39.6 (*C*(4°)–C–C), 34.7 (C–CH*C*$H_2$), 34.4 (*C*$H_2$C–CH), 34.2 ($CH_3$*C*H), 31.4 (*C*$H_2$C=CHCHOH), 31.0 (C–C*C*$H_2$), 26.2 (C(4°)–*C*$H_2$), 24.3 (CH*C*$H_2$), 19.8 (*C*$H_3$–C(4°)), 19.4 (*C*$H_3$C=CHCHOH), 17.1 (*C*$H_3$C–CH), 15.1 (*C*$H_3$CH); *m*/*z* (ES) 479.2796 ($M^+$ + Na, 100%, $C_{28}H_{40}O_5Na$ requires 479.2773); (ii) the *epoxy alcohol* **22** (6.8 mg, 47%) (eluted first); and (iii) the *bis-epoxide* **23** (4.1 mg, 27%) (eluted third).

**(*E*)-(3*S*,5*R*,12*S*,13*R*)-16-(4-Methoxybenzyloxymethyl)-5,9,12,13-tetramethyl-4-oxatricyclo[10.3.1.0$^{3,5}$]hexadeca-1(16),8-dien-2-one 25.** Dess–Martin periodinane[8] (8.5 mg, 0.02 mmol) was added to a mixture of the β-epoxy alcohol **21** (3.0 mg, 7 μmol) and $NaHCO_3$ (5.7 mg, 0.07 mmol) in dichloromethane (0.5 mL) at 0 °C. The mixture was stirred at 0 °C for 30 minutes and then allowed to warm to room temperature over 3 hours. Dess–Martin periodinane (4.2 mg, 0.01 mmol) was added to the reaction mixture and stirred for an additional hour. The mixture was quenched with saturated aqueous solutions of $NaHCO_3$ (0.5 mL) and $Na_2S_2O_3$ (0.5 mL), and then diluted with diethyl ether (2 mL). The separated aqueous phase was extracted with diethyl ether (3 × 5 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 20–30% diethyl ether in pentane as eluent to give the *ketone* (3.0 mg, 99%) as a colourless film; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 2927, 1698, 1602 and 1250; $\delta_H$ (500 MHz, $CDCl_3$) 7.24 (2H, d, *J* 8.6, 2 × Ar*H*), 6.88 (2H, d, *J* 8.6, 2 × Ar*H*), 5.06 (1H, br t, *J* 5.5, C=C*H*$CH_2$), 4.51 (1H, d, *J* 11.6, ArC*H*H), 4.20 (1H, d, *J* 11.6, ArCH*H*), 4.05 (1H, ddd, *J* 14.7, 3.3 and 2.6, OC*H*HC=C), 3.95 (1H, br d, *J* 14.7, OCH*H*C=C), 3.80 (3H, s, $OCH_3$), 3.77 (1H, s, $CH_2(CH_3)C$–C*H*C=O), 2.44 (1H, ddd, *J* 17.9, 5.1 and 1.9, C=CC*H*H), 2.36 (1H, ddd, *J* 15.1, 10.5 and 3.9, C*H*H$(CH_3)$C=$CHCH_2$), 1.99–1.94 (4H, m, $CH_3CH$, C=CHC$H_2$ and CH*H*$(CH_3)$C=$CHCH_2$), 1.92–1.83 (3H, m, C=CCH*H* and C$H_2(CH_3)$C–CHC=O), 1.60–1.49 (4H, m, C(4°)–C$H_2$ and CHC$H_2$), 1.48 (3H, s, $CH_3$C=CH), 1.22 (3H, s, $CH_3$C–CHC=O), 0.96 (3H, s, $CH_3$–C(4°)), 0.88 (3H, d, *J* 6.6, $CH_3$CH); $\delta_C$ (90 MHz, $CDCl_3$) 202.4 (*C*=O), 159.4 (Ar–*C*(4°)$OCH_3$), 144.5 (*C*=CC=O), 135.5 (Ar–*C*(4°)), 133.2 (C=*C*C=O), 130.0 (Ar–*C*H), 129.1 (*C*=CH), 126.7 (C=*C*H), 113.8 (Ar–*C*H), 72.0 (Ar*C*$H_2O$), 67.2 (O*C*$H_2$C=C), 64.7 (C–*C*HC=O), 62.4 (*C*–CHC=O), 55.3 (O*C*$H_3$), 39.9 (*C*(4°)–C=C), 34.9 (*C*$H_2$C–CHC=O), 34.1 (*C*$H_2$C=CH), 33.5 ($CH_3$-*C*H), 31.8 (CH*C*$H_2$), 27.2 (C=C*C*$H_2$), 26.0 (C(4°)–*C*$H_2$), 23.5 (C=CH*C*$H_2$), 21.5 (*C*$H_3$–C(4°)), 19.2 (*C*$H_3$C–CHC=O), 16.7 (*C*$H_3$C=CH), 15.1 (*C*$H_3$CH); *m*/*z* (ES) 461.2691 ($M^+$ + Na, 100%, $C_{28}H_{38}O_4Na$ requires 461.2668).

**(±)-Phomactin G (3).** 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (3.1 mg, 14 μmol) was added to a stirred solution of the epoxy ketone **25** (3.0 mg, 7 μmol) in dichloromethane (0.33 mL) and water (0.02 mL) at 0 °C. The mixture was allowed to warm to room temperature over 3 hours. The organic layer was separated and the aqueous phase was extracted with dichloromethane (2 × 0.5 mL). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$ (1.0 mL) and the separated aqueous phase was extracted with dichloromethane (3 × 1.0 mL). The combined organic extracts were dried over $Na_2SO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 10% acetone in dichloromethane as eluent. The pure fractions were concentrated *in vacuo* and the residue was diluted with dichloromethane (2.0 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (2 × 1.0 mL), then dried over $Na_2SO_4$ and concentrated *in vacuo* to give *(±)-phomactin G* (1.5 mg, 71%) as a colourless oil; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3692, 2928, 1602, 1433, 1236 and 1021; $\delta_H$ (500 MHz, $CD_3OD$) 5.07 (1H, br d, *J* 10.0, C=C*H*$CH_2$), 4.51 (1H, app. dt, *J* 12.5 and 2.6, OC*H*HC=C), 4.37 (1H, ddd, *J* 12.5, 3.8 and 1.4, OCH*H*C=C), 2.84 (1H, s, $CH_2(CH_3)$C–C*H*), 2.48–2.42 (1H, m, C*H*H$(CH_3)$C=$CHCH_2$), 2.13 (1H, ddq, *J* 12.0, 2.5 and 7.0, $CH_3CH$), 2.04–1.98 (1H, m, C=CC*H*H), 1.95–1.93 (1H, m, CH*H*$(CH_3)$C=$CHCH_2$), 1.92–1.89 (1H, m, C*H*H$(CH_3)$C–CH), 1.89–1.87 (1H, m, C=CHC*H*H), 1.86–1.84 (1H, m, C=CCH*H*), 1.80–1.77 (1H, m, C=CHCH*H*), 1.76–1.70 (1H, m, CH*H*$(CH_3)$C–CH), 1.68–1.66 (1H, m, C(4°)–C*H*H), 1.66–1.62 (1H, m, CHC*H*H), 1.64 (3H, s, $CH_3$C=CH), 1.52 (1H, ddd, *J* 15.1, 6.2 and 2.5, C(4°)–CH*H*), 1.44 (1H, dq, *J* 12.6 and 4.5, CHCH*H*), 1.39 (3H, s, $CH_3$C–CH), 0.93 (3H, s, $CH_3$–C(4°)), 0.92 (3H, d, *J* 7.3, $CH_3$CH); $\delta_C$ (125 MHz, $CD_3OD$) 144.7 (*C*=CC(OH)$OCH_2$), 135.2 (*C*=CH), 134.5(C=*C*C(OH)$OCH_2$), 129.5(C=*C*H), 109.7(*C*(OH)-$OCH_2$), 70.5 (O*C*$H_2$C=C), 64.8 ($CH_2$C–*C*H), 61.3 ($CH_2$*C*–CH), 38.6 *C*(4°)–C=C), 36.1 (*C*$H_2$C=CH), 35.1 (*C*$H_2$C–CH), 34.5 ($CH_3$*C*H), 33.6 (C(4°)–*C*$H_2$), 29.1 (CH*C*$H_2$), 24.4 (C=CH*C*$H_2$), 24.1 (C=C*C*$H_2$), 22.2 (*C*$H_3$–C(4°)), 21.0 (*C*$H_3$C–CH), 16.9 (*C*$H_3$C=CH), 14.9 (*C*$H_3$CH); *m*/*z* (EI) 318.2184 ($M^+$, $C_{20}H_{30}O_3$ requires 318.2195).

**(*E*)-(3*R*,5*S*,12*S*,13*R*)-16-(4-Methoxybenzyloxymethyl)-5,9,12,13-tetramethyl-4-oxatricyclo[10.3.1.0$^{3,5}$]hexadeca-1(16),8-dien-2-one 26.** Dess–Martin periodinane[8] (10.2 mg, 0.024 mmol) was added to a mixture of the alcohol **18** (7.2 mg, 0.016 mmol) and $NaHCO_3$ (13.4 mg, 0.16 mmol) in dichloromethane (1.0 mL) at 0 °C. The mixture was stirred at 0 °C for 30 minutes and then allowed to warm to room temperature over 2.5 hours. The mixture was quenched with saturated aqueous solutions of $NaHCO_3$ (1.0 mL) and $Na_2S_2O_3$ (1.0 mL), and then diluted with diethyl ether (1 mL). The separated aqueous phase was extracted with diethyl ether (3 × 5 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 30% diethyl ether in pentane as eluent to give the *ketone* (5.2 mg, 74%) as a colourless oil; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 2936, 1709, 1610 and 1249; $\delta_H$ (500 MHz, $CDCl_3$) 7.24 (2H, d, *J* 8.8, 2 × Ar*H*), 6.87 (2H, d, *J* 8.8, 2 × Ar*H*), 5.00 (1H, d, *J* 9.9, C=C*H*$CH_2$), 4.33 (2H, s, Ar*C*$H_2$), 3.80 (3H, s, $OCH_3$), 3.53 (1H, d, *J* 10.9, OC*H*HC=C), 3.53 (1H, s, $CH_2(CH_3)$C–C*H*C=O), 3.21 (1H, d, *J* 10.9, OCH*H*C=C), 2.38 (1H, ddd, *J* 17.4, 11.4 and 6.0, C=CC*H*H), 2.28 (1H, dd, *J* 14.3 and 12.6, C*H*H$(CH_3)$C=$CHCH_2$), 2.24–2.10 (4H, m, C=CHC$H_2$, C=CCH*H* and C*H*H$(CH_3)$C–CHC=O), 1.98–1.91 (2H, m, $CH_3CH$ and CH*H*$(CH_3)$C=$CHCH_2$), 1.76 (1H, dd, *J* 15.1 and 12.6, C(4°)–C*H*H), 1.63–1.52 (3H, m, CHC$H_2$ and C(4°)–CH*H*), 1.54 (3H,

s, $CH_3$C=CH), 1.29–1.22 (1H, m, CH*H*($CH_3$)C–CHC=O), 1.07 (3H, s, $CH_3$C–CHC=O), 0.95 (3H, s, $CH_3$–C(4°)), 0.90 (3H, d, *J* 7.1, $CH_3$CH); $\delta_C$ (125 MHz, $CDCl_3$) 203.3 (*C*=O), 159.2 (Ar–*C*(4°)$OCH_3$), 140.4 (*C*=CC=O), 138.6 (Ar–*C*(4°)), 135.3 (C=*C*C=O), 130.2 (*C*=CH), 129.8 (Ar–*C*H), 125.5 (C=*C*H), 113.7 (Ar–*C*H), 72.0 (Ar*C*$H_2$O), 66.8 (O*C*$H_2$C=C), 64.5 (C–*C*HC=O), 64.4 (*C*–CHC=O), 55.3 (O*C*$H_3$), 40.6 (*C*(4°)–C=C), 38.2 (*C*$H_2$C–CHC=O), 34.8 (*C*$H_2$C=CH), 33.4 ($CH_3$-*C*H), 31.9 (C(4°)–*C*$H_2$), 28.5 (C=C*C*$H_2$), 26.3 (CH*C*$H_2$), 24.5 (C=CH*C*$H_2$), 21.3 (*C*$H_3$–C(4°)), 16.0 (*C*$H_3$CH), 15.6 (*C*$H_3$C=CH), 15.1 (*C*$H_3$C–CHC=O); *m*/*z* (ES) 439.2856 ($M^+$ + H, 100%, $C_{28}H_{39}O_4$ requires 439.2848).

**Epoxy cyclic hemiacetal 27.** 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (3.4 mg, 0.015 mmol) was added to a stirred solution of the epoxy ketone **26** (5.2 mg, 0.012 mmol) in dichloromethane (1.05 mL) and water (0.15 mL) at 0 °C. The mixture was allowed to warm to 10 °C over 4 hours. The organic layer was separated and the aqueous phase was extracted with dichloromethane (2 × 0.5 mL). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$ (1.0 mL) and the separated aqueous phase was extracted with dichloromethane (3 × 1.0 mL). The combined organic extracts were dried over $Na_2SO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 20–30% diethyl ether in pentane as eluent to give the *epoxy cyclic hemiacetal* (3.6 mg, 95%) as a colourless oil; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3554, 2967, 2935, 2880, 1605 and 1027; $\delta_H$ (500 MHz, $CD_3OD$) 5.04 (1H, br d, *J* 12.0, C=C*H*$CH_2$), 4.44 (1H, dt, *J* 12.3 and 2.5, OC*H*HC=C), 4.09 (1H, ddd, *J* 12.3, 4.0 and 1.5, OCH*H*C=C), 2.70 (1H, s, $CH_2(CH_3)$C–C*H*), 2.48–2.38 (2H, m, C*H*H($CH_3$)C=$CHCH_2$ and C=CHC*H*H), 2.22–2.10 (3H, m, C=C$CH_2$ and $CH_3$C*H*), 2.05 (1H, br d, *J* 15.5, C=CHCH*H*), 2.00–1.96 (1H, obs. m, CH*H*($CH_3$)C=$CHCH_2$), 1.98 (1H, dt, *J* 12.6 and 3.8, C*H*H-($CH_3$)C–CH), 1.75 (3H, s, $CH_3$C=CH), 1.75–1.71 (1H, m, CHC*H*H), 1.65–1.62 (2H, m, C(4°)–C$H_2$), 1.57–1.49 (1H, m, CHCH*H*), 1.53 (3H, s, $CH_3$C–CH), 1.19 (1H, td, *J* 12.6 and 4.5, CH*H*($CH_3$)C–CH), 0.96 (3H, s, C*H*$_3$–C(4°)), 0.95 (3H, d, *J* 7.0, $CH_3$CH); $\delta_C$ (125 MHz, $CD_3OD$) 144.4 (*C*=CC(OH)-$OCH_2$), 135.5 (C=*C*C(OH)$OCH_2$), 135.1 (*C*=CH), 126.0 (C=*C*H), 109.7 (*C*(OH)$OCH_2$), 71.1 (O*C*$H_2$C=C), 67.3 ($CH_2$C–*C*H), 65.5 ($CH_2$*C*–CH), 39.4 (*C*$H_2$C–CH), 38.5 (*C*(4°)–C=C), 35.8 (*C*$H_2$C=CH), 34.7 ($CH_3$*C*H), 33.7 (C(4°)–*C*$H_2$), 29.2 (CH*C*$H_2$), 26.0 (C=CH*C*$H_2$), 22.7 (C=C*C*$H_2$), 22.4 (*C*$H_3$–C(4°)), 18.4 (*C*$H_3$C–CH), 16.0 (*C*$H_3$C=CH), 15.1 (*C*$H_3$CH); *m*/*z* (ES) 382.2392 ($M^+$ + Na + $CH_3CN$, 100%, $C_{22}H_{33}NO_3Na$ requires 382.2358).

**(3*E*,7*E*)-(1*S*,11*S*,12*R*,16*S*)-16-(4-Methoxybenzyloxymethyl)-4,8,11,12-tetramethyl-15-oxatricyclo[9.3.2.0$^{1,16}$]hexadeca-3,7-dien-2-one 28.** Dess–Martin periodinane[8] (4.3 mg, 0.01 mmol) was added to a mixture of the epoxy alcohol **22** (3.0 mg, 6.8 μmol) and $NaHCO_3$ (5.7 mg, 0.07 mmol) in dichloromethane (1.0 mL) at 0 °C. The mixture was stirred at 0 °C for 30 minutes and then allowed to warm to room temperature over 2 hours. The mixture was quenched with saturated aqueous solutions of $NaHCO_3$ (1.0 mL) and $Na_2S_2O_3$ (1.0 mL), and then diluted with diethyl ether (4 mL). The separated aqueous phase was extracted with diethyl ether (3 × 10 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo* to leave the *ketone* (3.0 mg, 99%) as a colourless film; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 2960, 2931, 2856, 1696, 1610 and 1261; $\delta_H$ (500 MHz, $CDCl_3$) 7.25 (2H, d, *J* 8.8, 2 × Ar*H*), 6.87 (2H, d, *J* 8.8, 2 × Ar*H*), 6.33 (1H, s, C=C*H*C=O), 5.10 (1H, br d, *J* 9.8, C=C*H*$CH_2$), 4.59 (1H, d, *J* 11.6, ArC*H*H), 4.34 (1H, d, *J* 11.6, ArCH*H*), 3.81 (3H, s, O$CH_3$), 3.62 (1H, d, *J* 11.6, OC*H*HC–C), 2.59 (1H, d, *J* 11.6, OCH*H*C–C), 2.46 (1H, app. t, *J* 13.0, C*H*H($CH_3$)C=$CHCH_2$), 2.34 (1H, dd, *J* 15.5 and 13.0, C(4°)–C*H*H), 2.30–2.05 (6H, m, C=CHC$H_2$, C$H_2$($CH_3$)C=CHC=O and C–CC$H_2$), 2.00 (1H, br dd, *J* 15.5 and 8.4, CH*H*-($CH_3$)C=C$HCH_2$), 1.80 (1H, ddq, *J* 12.3, 6.7 and 2.1, $CH_3$C*H*), 1.75 (3H, s, $CH_3$C=CHC=O), 1.61–1.56 (1H, m, C(4°)–CH*H*), 1.54 (3H, s, $CH_3$C=CH), 1.49 (1H, app. dt, *J* 12.3 and 5.6, CHC*H*H), 1.25–1.21 (1H, m, CHCH*H*), 1.05 (3H, s, $CH_3$–C(4°)), 0.79 (3H, d, *J* 6.7, $CH_3$CH); $\delta_C$ (125 MHz, $CDCl_3$) 198.8 (*C*=O), 159.0 (Ar–*C*(4°)$OCH_3$), 150.0 (*C*=CHC=O), 136.1 (Ar–*C*(4°)), 130.7 (*C*=CH), 129.1 (Ar–*C*H), 126.3 (C=*C*H), 125.1 (C=*C*HC=O), 113.6 (Ar–*C*H), 73.0 (Ar*C*$H_2$O and O*C*$H_2$C–C), 71.2 (C–*C*$CH_2$), 69.2 (*C*–C$CH_2$), 55.3 (O*C*$H_3$), 39.4 (*C*$H_2$C=CHC=O), 38.7 (*C*(4°)–C–C), 34.6 (*C*$H_2$C=CH), 33.7 ($CH_3$*C*H), 32.0 (C(4°)–*C*$H_2$), 27.5 (C–C*C*$H_2$), 25.2 (C=CH*C*$H_2$), 23.6 (CH*C*$H_2$), 19.4 (*C*$H_3$–C(4°)), 17.6 (*C*$H_3$C=CHC=O), 16.1 (*C*$H_3$C=CH), 15.0 (*C*$H_3$CH); *m*/*z* (ES) 461.2693 ($M^+$ + Na, 100%, $C_{28}H_{38}O_4Na$ requires 461.2668).

**Epoxy cyclic hemiacetal 29.** 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (1.8 mg, 8 μmol) was added to a stirred solution of the epoxy ketone **28** (2.5 mg, 6 μmol) in dichloromethane (1.0 mL) and water (0.1 mL) at 0 °C. The mixture was stirred at 0 °C for 1 hour, then allowed to warm to 10 °C and stirred for 7 hours. The organic layer was separated and the aqueous phase was extracted with dichloromethane (2 × 0.5 mL). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$ (1.0 mL) and the separated aqueous phase was extracted with dichloromethane (3 × 1.0 mL). The combined organic extracts were dried over $Na_2SO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 1% triethylamine and 20–30% diethyl ether in pentane as eluent to give the *epoxy cyclic hemiacetal* (1.5 mg, 79%) as a colourless film; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3547, 2930, 2856, 1602, 1438, 1330, 1260 and 1033; $\delta_H$ (500 MHz, $CD_3OD$) 5.19 (1H, s, $CH_2(CH_3)$C=C*H*C(OH)$OCH_2$), 5.03 (1H, br d, *J* 11.4, C=C*H*$CH_2$), 3.74 (1H, d, *J* 9.8, OC*H*HC–C), 3.29 (1H, d, *J* 9.8, OCH*H*C–C), 2.48–2.33 (2H, m, C*H*H-($CH_3$)C=$CHCH_2$ and C=CHC*H*H), 2.31–2.22 (1H, m, C*H*H-($CH_3$)C=CHC(OH)$OCH_2$), 2.14 (1H, dd, *J* 12.8 and 4.0, CH*H*($CH_3$)C=CHC(OH)$OCH_2$), 2.05–1.93 (3H, m, C–C$CH_2$ and CH*H*($CH_3$)C=$CHCH_2$), 1.85 (3H, s, $CH_3$C=CHC(OH)-$OCH_2$), 1.81–1.74 (1H, m, $CH_3$C*H*), 1.73–1.60 (2H, m, C(4°)–C$H_2$), 1.66 (3H, s, $CH_3$C=CH), 1.37–1.30 (3H, m, CHC$H_2$ and C=CHCH*H*), 0.96 (3H, s, C*H*$_3$–C(4°)), 0.82 (3H, d, *J* 7.1, $CH_3$CH); $\delta_C$ (125 MHz, $CD_3OD$) 141.9 (*C*=CHC(OH)$OCH_2$), 135.2 (*C*=CH), 128.7 (C=*C*H), 121.8 (C=*C*HC(OH)$OCH_2$), 111.4 (*C*(OH)$OCH_2$), 71.1 (C–*C*$CH_2$), 71.0 (*C*–C$CH_2$), 65.5 (O*C*$H_2$C–C), 41.4 (*C*$H_2$C=CHC(OH)$OCH_2$), 36.9 (*C*(4°)–C–C), 35.8 (*C*$H_2$C=CH), 34.3 ($CH_3$*C*H), 33.5 (C(4°)–*C*$H_2$), 26.4 (C=CH*C*$H_2$), 26.2 (CH*C*$H_2$), 23.0 (C–C*C*$H_2$), 21.3 (*C*$H_3$–C(4°)), 17.6 (*C*$H_3$C=CHC(OH)$OCH_2$), 16.1 (*C*$H_3$C=CH), 14.6 (*C*$H_3$CH); *m*/*z* (ES) 341.2119 ($M^+$ + Na, 100%, $C_{20}H_{30}O_3Na$ requires 341.2093).

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## References

1 M. Sugano, A. Sato, Y. Iijima, K. Furuya, H. Kuwano and T. Hata, *J. Antibiot.*, 1995, **48**, 1188–1190.
2 M. Sugano, A. Sato, Y. Iijima, T. Oshima, K. Furuya, H. Kuwano, T. Hata and H. Hanzawa, *J. Am. Chem. Soc.*, 1991, **113**, 5463–5464.
3 M. Chu, I. Truumees, I. Gunnarsson, W. R. Bishop, W. Kreutner, A. C. Horan, M. G. Patel, V. P. Gullo and M. S. Puar, *J. Antibiot.*, 1993, **46**, 554–563.
4 (*a*) W. P. D. Goldring and G. Pattenden, *Chem. Commun.*, 2002, 1736–1737; (*b*) C. M. Diaper, W. P. D. Goldring and G. Pattenden, *Org. Biomol. Chem.*, 2003, **1**, 3949–3956.
5 J. W. C. Cheing, W. P. D. Goldring and G. Pattenden, *Chem. Commun.*, 2003, 2788–2789.

6 M. Sugano, A. Sato, Y. Iijima, K. Furuya, H. Haruyama, K. Yoda and T. Hata, *J. Org. Chem.*, 1994, **59**, 564–569. For a synthesis of phomactin D see: H. Miyaoka, Y. Saka, S. Miura and Y. Yamada, *Tetrahedron Lett.*, 1996, **37**, 7107–7110.
7 (*a*) K. M. Foote, M. John and G. Pattenden, *Synlett*, 2001, 365–368; (*b*) K. M. Foote, C. J. Hayes, M. P. John and G. Pattenden, *Org. Biomol. Chem.*, 2003, **1**, 3917–3948.
8 D. B. Dess and J. C. Martin, *J. Am. Chem. Soc.*, 1991, **113**, 7277–7287.
9 Selective NOE enhancements measured for **16** were observed between H-16a and H-2, and H-7 and H-3.
10 F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson and W. C. Still, *J. Comput. Chem.*, 1990, **11**, 440–467.
11 K. B. Sharpless and R. C. Michaelson, *J. Am. Chem. Soc.*, 1973, **95**, 6136–6137.
12 W. Adam, Y.-Y. Chan, D. Cremer, J. Gauss, D. Scheutzow and M. Schindler, *J. Org. Chem.*, 1987, **52**, 2800–2803.