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Synthesis of the phthalide-containing anti-*Helicobacter pylori* agents CJ-13,015, CJ-13,102, CJ-13,103, CJ-13,104 and CJ-13,108

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Abstract—Flexible racemic syntheses of the phthalide-containing antibiotics CJ-13,015, CJ-13,102, CJ-13,103, CJ-13,104 and CJ-13,108 that inhibit *Helicobacter pylori* have been carried out in a convergent fashion by Wittig coupling of a phthalide-containing aldehyde fragment with an appropriate phosphorous ylide.

1. Introduction

Helicobacter pylori is a microaerophilic Gram-negative bacterium that infects over 50% of the human population worldwide. Infection has been associated with chronic superficial gastritis, chronic active gastritis, peptic ulcer disease and gastric cancer in humans.[1] As a result of the latter, the International Agency for Research in Cancer classified *H. pylori* as a class I carcinogen in 1994.[2]

The current first-line triple-therapy for *H. pylori*-associated gastrointestinal diseases, using a combination of antibiotics with a proton-pump inhibitor, fails to fully eradicate *H. pylori* in approximately 10–23% of patients. As a result, second-line or rescue treatments are often required.[3] Treatment failure is associated with the emergence of *H. pylori* strains that are resistant to the broad-spectrum antibiotics used.[2]

Consequently, there is an urgent need for the development of more effective and selective anti-*H. pylori* agents. In a screening program designed to discover such compounds, Dekker et al.[4] isolated seven new phthalide antibiotics with specific anti-*H. pylori* activity (**1**–**7**) from the basidiomycete *Phanerochaete velutina* CL6387 (Fig. 1). Two structurally related compounds, spirolaxine **8a**[5a] and its methyl ether **8b**,[5b] isolated from *Sporotrichum laxum*, *S. pruinosum* and *Phanerochaete*, *chrysosporium* have also been reported. These phthalide-containing compounds provide promising new leads for the treatment of *H. pylori*-related diseases.

To date, CJ-13,015 **3** is the only member of the *P. velutina* series of antibiotics to have been synthesized.[6] The synthetic strategy used a 5-methylfuranyl bromide as a latent 1,4-dicarbonyl system and was efficient requiring only six steps. However, the synthetic route did not possess the intrinsic flexibility necessary to access the other compounds in the series. We herein report a flexible synthetic strategy that has been used to prepare five of these antibiotics **3**–**7** as racemates.

Our recent enantioselective total synthesis of spirolaxine methyl ether **8b**[7] unequivocally established the absolute stereochemistry at C-3 of the phthalide unit to be of the (*R*)-configuration. It is therefore, likely that C-3 of the phthalide unit in compounds **1**–**7** will also exhibit the (*R*)-configuration. To this end the enantioselective total syntheses of the more complex and helicobactericidal spiroacetal containing antibiotics CJ-12,954 **1** and CJ-13,014 **2**, are currently being investigated.

2. Results and discussion

The work reported herein, describes the racemic total syntheses of five of the *P. velutina* series of phthalide antibiotics (**3**–**7**). The highly convergent and flexible synthetic strategy adopted hinged on the Wittig reaction of a key phthalide aldehyde **9**, derived from 2,4-dimethoxybenzoic acid **10**, with the ylide generated from the appropriate phosphonium salt **11**, **12** or **13** (Scheme 1).

Keywords: Phthalides; *Helicobacter pylori*; Wittig reaction.
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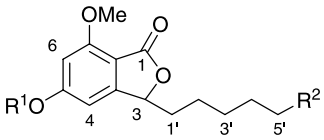
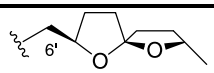
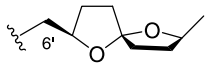
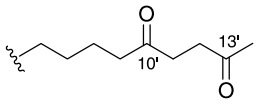
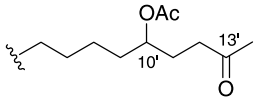
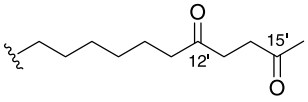
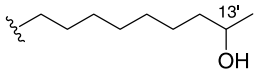
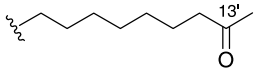
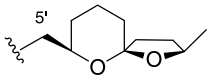


Antibiotic	R^1	R^2	Activity[a]
CJ-12,954 **1**	Me		0.02
CJ-13,014 **2**	Me		0.02
CJ-13,015 **3**	Me		2
CJ-13,102 **4**	Me		0.5
CJ-13,103 **5**	Me		50
CJ-13,104 **6**	Me		500
CJ-13,108 **7**	Me		10
Spirolaxine **8a**	H		0.01
Spirolaxine methyl ether **8b**	Me		No data

a. μg/disk that gives a 15 mm zone of inhibition.

Figure 1. Structure and anti-*H. pylori* activity of phthalide antibiotics (**1–7**) and spirolaxine **8** isolated from *P. velutina*.

The alcohol functionality in CJ-13,104 **6** was easily obtained from reduction of the ketone in CJ-13,108 **7**, that in turn was derived from the 11-carbon phosphonium salt **13**, (Scheme 3). CJ-13,015 **3** and CJ-13,102 **4** were prepared from a common hydroxyketone intermediate **14** starting from the 11-carbon phosphonium salt **11** (Scheme 4). CJ-13,103 **5** was available from the union of the ylide derived from the 13-carbon phosphonium salt **12** with phthalide aldehyde **9** (Scheme 5).

2.1. Synthesis of phthalide aldehyde 9

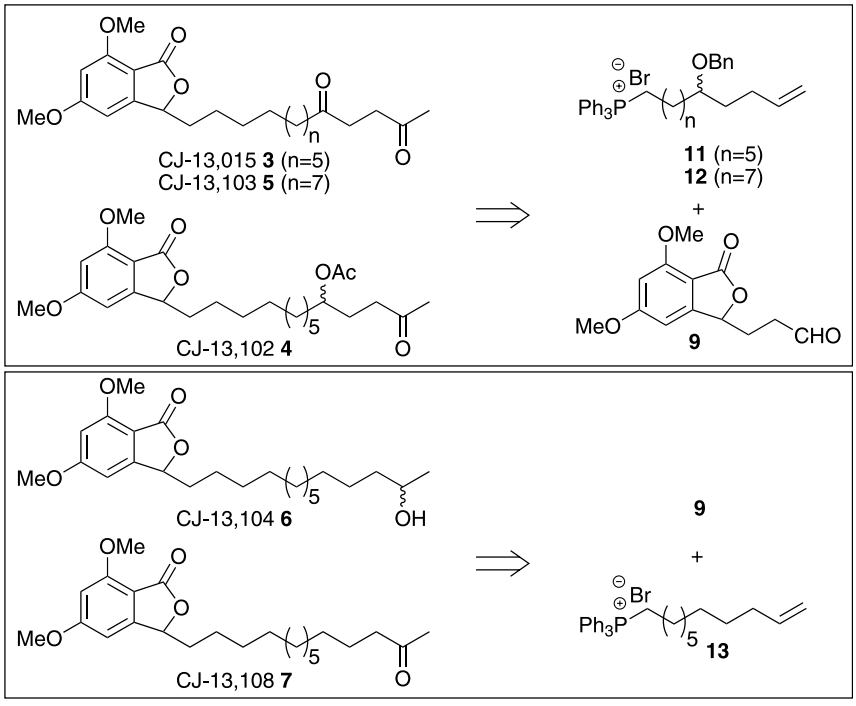
Phthalide aldehyde **9** was the core building block used to prepare all five of the desired compounds. It was prepared from commercially available 2,4-dimethoxybenzoic acid **10** (Scheme 2) firstly by conversion to the corresponding amide **15**. *ortho*-Lithiation followed by formylation provided aldehyde **16**, which furnished alkene **17** upon treatment with but-3-en-1-ylmagnesium bromide. Acid-catalysed cyclisation furnished phthalide **18** that upon ozonolysis of the terminal olefin gave the desired phthalide aldehyde **9** in 65% overall yield.

2.2. Synthesis of CJ-13,104 6 and CJ-13,108 7

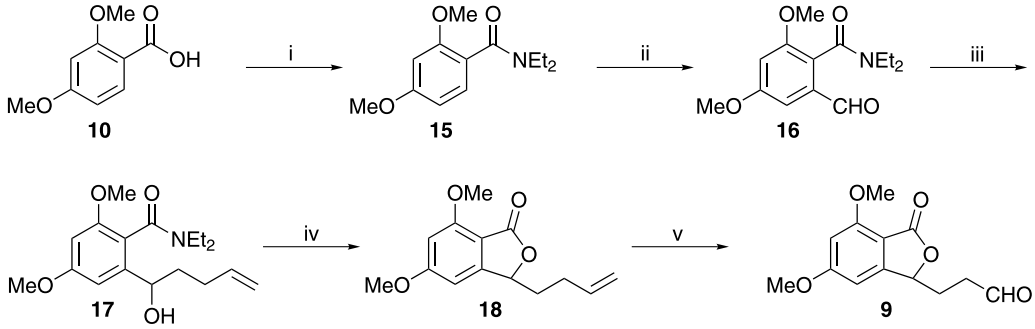
The synthesis of CJ-13,104 **6** and CJ-13,108 **7** (Scheme 3) began with the preparation of phosphonium salt **13**, obtained from commercially available 10-undecen-1-yl bromide **19** in 96% yield. Wittig reaction of the ylide generated from phosphonium salt **13**, with aldehyde **9** gave the desired olefin **20** in 86% yield, as a mixture of (*E*)- and (*Z*)-isomers, the relative ratios of which were unable to be determined. Selective Wacker oxidation of the terminal olefin afforded methyl ketone **21**, which upon hydrogenation of the internal olefin furnished CJ-13,108 **7** in 62% yield. Reduction of the C-13′ ketone in CJ-13,108 **7** with sodium borohydride gave CJ-13,104 **6** in 95% yield.

2.3. The synthesis of CJ-13,015 3 and CJ-13,102 4

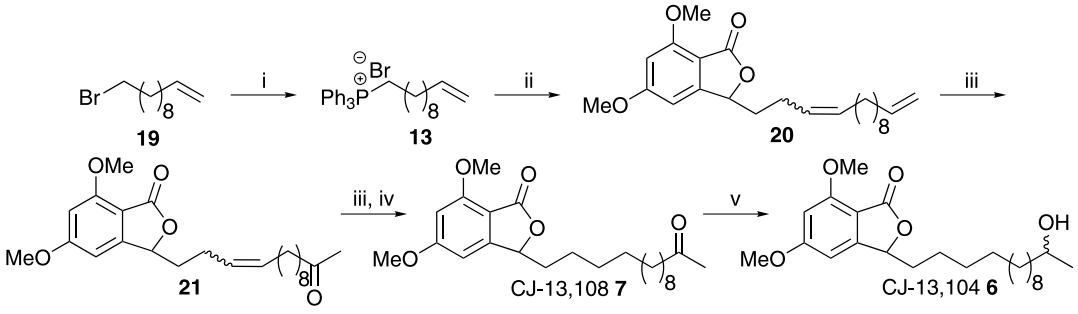
The synthesis of CJ-13,015 **3** and CJ-13,102 **4** (Scheme 4) started from a common hydroxyketone intermediate **14** that was prepared from commercially available 7-octen-1-ol **22**. Protection of the alcohol as a *tert*-butyldimethylsilyl ether **23** followed by epoxidation of the terminal olefin provided oxirane **24** in quantitative yield. Ring-opening of the epoxide using a higher-order allyl-cuprate afforded alcohol **25**, which was protected as a benzyl ether **26**. Cleavage of the *tert*-butyldimethylsilyl ether yielded alcohol **27** that underwent conversion to bromide **28** followed by reaction with triphenylphosphine to furnish the desired phosphonium



Scheme 1. Retrosynthetic analysis of CJ-13,015, CJ-13,102, CJ-13,103, CJ-13,104 and CJ-13,108.

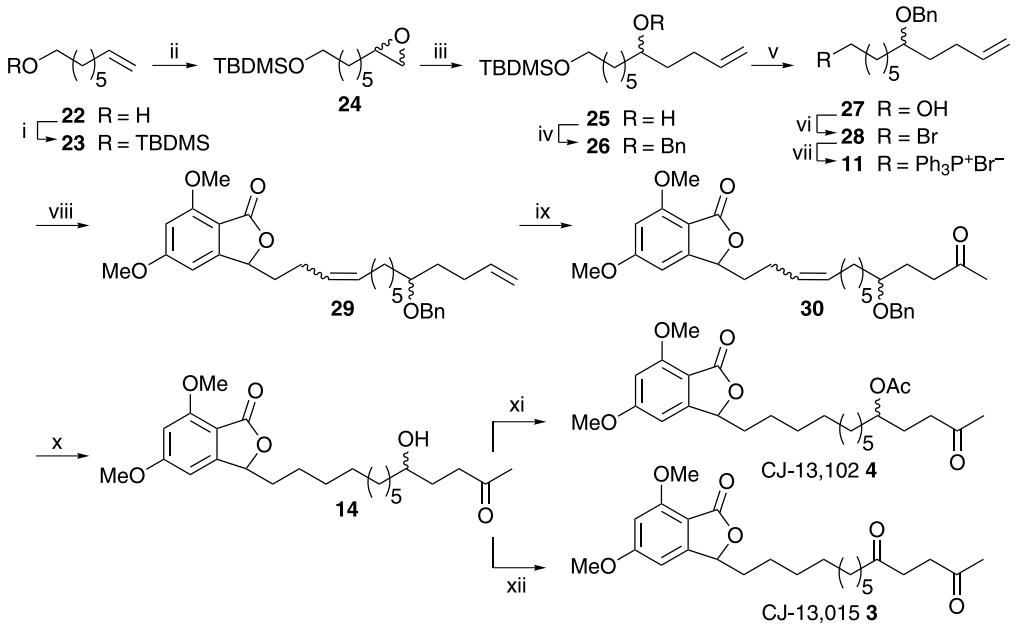


Scheme 2. Reagents and conditions: (i) $SOCl_2$, reflux, 2.5 h, then Et_2NH, CH_2Cl_2, rt, 12 h, 96%; (ii) *t*-BuLi (1.1 equiv), THF, −78 °C, 15 min, then DMF, rt, 16 h, 99%; (iii) but-3-en-1-ylmagnesium bromide, Et_2O, rt, 30 min; (iv) *p*TSA, PhMe, reflux, 6 h, 87% from **16**; (v) O_3, MeOH, −50 °C, 10 min, then Me_2S, rt, 1 h, 79%.

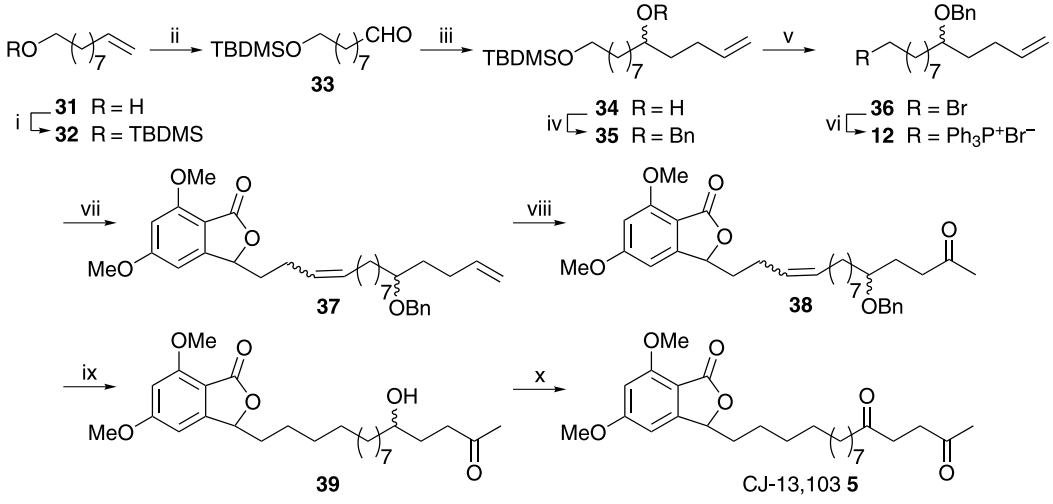


Scheme 3. Reagents and conditions: (i) PPh_3, MeCN, reflux, 24 h, 96%; (ii) *n*-BuLi, THF, −78 °C to rt, 30 min, then **9**, −78 °C to rt, 2 h, 86% (iii) $PdCl_2$, CuCl, DMF–H_2O (8/1), O_2, rt, 3 h, 62%; (iv) 10% Pd/C, H_2, EtOAc, rt, 1 h, 100% (v) $NaBH_4$, MeOH, rt, 10 min, 95%.

salt **11** in 34% overall yield (seven steps). Wittig reaction of the ylide generated from phosphonium salt **11** with phthalide aldehyde **9** gave olefin **29** in 72% yield, as a mixture of (*E*)- and (*Z*)-isomers, the relative ratios of which were unable to be determined. Selective Wacker oxidation of the terminal olefin afforded ketone **30** which, upon simultaneous hydrogenation of the internal olefin and hydrogenation of the benzyl ether, furnished hydroxyketone **14**. Direct acetylation of alcohol **14** provided CJ-13,102 **4**, whereas TPAP oxidation furnished the diketone CJ-13,015 **3**.



Scheme 4. Reagents and conditions: (i) TBDMSCl, imidazole, DMAP, CH_2Cl_2, 0 °C, 3 h, 99%; (ii) *m*CPBA, NaOAc, CH_2Cl_2, rt, 18 h, 99%; (iii) 5% CuCN, allylmagnesium bromide, Et_2O, −78 °C, 10 h, 55%; (iv) NaH, TBAI, DMF, 0 °C, 75 min, then BnBr, rt, 18 h, 81%; (v) TBAF, THF, 0 °C, 2 h, 97%; (vi) CBr_4, PPh_3, MeCN, 0 °C, 30 min, 100%; (vii) PPh_3, MeCN, reflux, 26 h, 80%; (viii) *n*-BuLi, THF, −78 °C to rt, 30 min, then **9**, −78 °C to rt, 2 h, 72%; (ix) $PdCl_2$, CuCl, DMF–H_2O (8/1), O_2, rt, 3 h, 54%; (x) 10% Pd/C, H_2, EtOAc, rt, 3 h; (xi) Ac_2O, DMAP, pyridine, rt, 8 h, 83% from **30**; (xii) TPAP, NMO, CH_2Cl_2, rt, 30 min, 37% over two steps.



Scheme 5. Reagents and conditions: (i) TBDMSCl, imidazole, DMAP, CH_2Cl_2, 0 °C, 3 h, 96%; (ii) O_3, MeOH, −50 °C, 10 min, then Me_2S, rt, 1 h, 95%; (iii) but-3-en-1-ylmagnesium bromide, Et_2O, rt, 30 min, 96%; (iv) NaH, TBAI, DMF, 0 °C, 75 min, then BnBr, rt, 18 h, 95%; (v) PPh_3Br_2, CH_2Cl_2, rt, 24 h, 91%; (vi) PPh_3, MeCN, reflux, 24 h, 80%; (vii) *n*-BuLi, THF, −78 °C to rt, 30 min, then **9**, −78 °C to rt, 2 h, 73%; (viii) $PdCl_2$, CuCl, DMF–H_2O (8/1), O_2, rt, 3 h, 61% (ix) 10% Pd/C, H_2, EtOAc, rt, 3 h; (x) TPAP, NMO, CH_2Cl_2, rt, 30 min, 44% over two steps.

2.4. Synthesis of CJ-13,103 5

Following a similar strategy to that used for the synthesis of CJ-13,015 **3**, the preparation of CJ-13,103 **5** started with commercially available 9-decen-1-ol **31** (Scheme 5). Protection of the alcohol as a *tert*-butyldimethylsilyl ether **32** followed by ozonolysis of the terminal olefin provided aldehyde **33**. Treatment of **33** with but-3-en-1-ylmagnesium bromide afforded alcohol **34** in quantitative yield. Protection of the alcohol as a benzyl ether **35** followed by a one-pot desilylation–bromination procedure[8] using triphenylphosphine–bromine complex, afforded bromide **36**, that furnished the desired phosphonium salt **12** upon reaction with triphenylphosphine. Wittig reaction of the ylide generated from phosphonium salt **12** with phthalide aldehyde **9** gave olefin **37** in 73% yield, as a mixture of (*E*) and (*Z*) isomers, the relative ratios of which were unable to be determined. Selective Wacker oxidation of the terminal olefin afforded ketone **38** which, upon simultaneous hydrogenation of the internal olefin and

hydrogenation of the benzyl ether, furnished hydroxyketone **39**. Finally, oxidation of alcohol **39** afforded CJ-13,103 **5**.

3. Conclusions

An efficient and flexible strategy has been developed to prepare five anti-*Helicobacter pylori* agents (**3**–**7**). The convergent strategy developed, involving union of phthalide aldehyde **9** with an appropriately functionalized ylide, is readily amenable to the construction of analogues.

4. Experimental

4.1. General

All reactions were carried out in flame dried or oven dried glassware under a dry nitrogen atmosphere. Tetrahydrofuran was distilled from sodium benzophenone while dichloromethane and *N*,*N*-dimethylformamide were dried over calcium hydride and distilled prior to use. Flash chromatography was carried out using 0.063–0.1 mm silica gel with the appropriate solvent. Thin-layer chromatography was performed using silica coated aluminium plates (60 F254). Compounds were identified using UV fluorescence and or staining with vanillin in ethanolic sulphuric acid. Low resolution mass spectra were recorded using a VG-70SE spectrometer operating at a nominal accelerating voltage of 70 eV. High resolution mass spectra were recorded at a nominal resolution of 5000–10,000. Infrared spectra were obtained using a Perkin-Elmer Spectrum 1000 series Fourier Transform IR spectrometer as a thin film between sodium chloride plates. NMR spectra were recorded on either the Bruker DRX300 spectrometer operating at 300 MHz for ^{1}H nuclei and 75 MHz for ^{13}C nuclei or using a Bruker DRX400 spectrometer operating at 400 MHz for ^{1}H nuclei and 100 MHz for ^{13}C nuclei. Melting points were determined on a Kofler hot-stage apparatus, and are uncorrected.

4.2. Procedure for the synthesis of phthalide aldehyde 9

4.2.1. *N*,*N*-Diethyl 2,4-dimethoxybenzamide 15. A solution of 2,4-dimethoxybenzoic acid **10** (5.15 g, 28.27 mmol) in thionyl chloride (20 mL) was heated at reflux for 2.5 h. The solvent was removed in vacuo. Benzene (3×10 mL) was added to the residue then removed in vacuo. A solution of diethylamine (9 mL, 87.00 mmol) in dichloromethane (10 mL) was added dropwise to a stirred solution of the crude acid chloride in dichloromethane (40 mL) at 0 °C. After stirring at room temperature for 12 h, the reaction mixture was diluted with dichloromethane (50 mL), washed with 10% w/v aqueous sodium bicarbonate (3×10 mL), brine (3×10 mL), and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using diethyl ether–hexane (3/1) as eluent gave the title compound **15** (6.71 g, 96%) as a viscous yellow oil. The ^{1}H NMR data obtained were in agreement with the literature values.[9]

4.2.2. *N*,*N*-Diethyl 2-formyl-4,6-dimethoxybenzamide 16. *tert*-Butyllithium (23 mL of a 1.05 M solution in hexanes, 24.15 mmol) was added dropwise to a stirred solution of *N*,*N*-diethyl 2,4-dimethoxybenzamide **15** (5.20 g, 21.91 mmol) in tetrahydrofuran (193 mL) at −78 °C. After stirring for 25 min, *N*,*N*-dimethylformamide (6.7 mL, 86.16 mmol) was added dropwise. The reaction mixture was warmed to room temperature, stirred for 12 h and the solvent removed in vacuo. The residue was dissolved in dichloromethane (30 mL), washed with brine (3×15 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using diethyl ether as eluent gave the title compound **16** (5.71 g, 99%) as a viscous yellow oil. ν_{max} (film) 2971, 1702, 1633, 1602, 1461, 1320, 1290, 1223, 1201, 1155, 1097, 1045, 955, 936 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 0.96 (3H, t, J=7.1 Hz, NCH_2CH_3), 1.22 (3H, t, J=7.1 Hz, NCH_2CH_3), 3.07 (2H, q, J=7.1 Hz, NCH_2CH_3), 3.41–3.55 (1H, m, $NCH_AH_BCH_3$), 3.58–3.70 (1H, m, $NCH_AH_BCH_3$), 3.78 (3H, s, OMe), 3.81 (3H, s, OMe), 6.65 (1H, d, J=2.3 Hz, 5-H), 6.97 (1H, d, J=2.3 Hz, 6-H), 9.90 (1H, s, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) 12.6 (CH_3, NCH_2CH_3), 13.7 (CH_3, NCH_2CH_3), 39.0 (CH_2, NCH_2CH_3), 42.8 (CH_2, NCH_2CH_3), 55.6 (CH_3, OMe), 55.9 (CH_3, OMe), 102.4 (CH, C-5), 104.7 (CH, C-3), 123.3 (quat., C-1), 134.2 (quat., C-2), 156.8 (quat., C-6), 160.9 (quat., C-4), 165.7 (quat., $CONEt_2$), 190.2 (CH, CHO); *m*/*z* (FAB+, %) 266 (M^+, 65), 238 (12), 236 (23), 193 (100), 167 (13), 165 (16), 154 (15), 71 (19); HRMS (FAB+): found MH^+, 266.1383. $C_{14}H_{19}NO_4$ requires 266.1392.

4.2.3. *N*,*N*-Diethyl 4,6-dimethoxy-2-(1′-hydroxypent-4′-en-1′-yl)benzamide 17. A solution of aldehyde **16** (900 mg, 3.39 mmol) in diethyl ether (15 mL) was added dropwise to the stirred solution of but-3-en-1-ylmagnesium bromide (11.75 mL of a 0.63 M solution in diethyl ether, 7.41 mmol) at 0 °C and the reaction mixture allowed to warm to room temperature. After stirring for 30 min, saturated aqueous ammonium chloride (20 mL) was added, the reaction mixture extracted with diethyl ether (3×10 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (1/1) as eluent afforded the title compound **17** (1.01 g) as a 1:1 mixture of rotamers and as a viscous yellow oil. ν_{max} (film) 3390, 2937, 1614, 1455, 1317, 1202, 1154, 1049, 912, 732, 635 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 1.04 (3H, t, J=7.0 Hz, NCH_2CH_3), 1.23 (3H, t, J=7.0 Hz, NCH_2CH_3), 1.70–2.30 (4H, m, 2′-H, 3′-H), 3.15 (2H, q, J=7.0 Hz, NCH_2CH_3), 3.47 (2H, t, J=7.0 Hz, NCH_2CH_3), 3.77 (3H, s, OMe), 3.82 (3H, s, OMe), 4.45–4.59 (1H, m, 1′-H), 4.92–5.15 (2H, m, 5′-H), 5.74–5.88 (1H, m, 4′-H), 6.36 (1H, d, J=2.2 Hz, 5-H), 6.59 (1H, d, J=2.2 Hz, 3-H), 6.64 (1H, d, J=2.2 Hz, 3-H); ^{13}C NMR (75 MHz, $CDCl_3$) 12.5, 12.6 (CH_3, NCH_2CH_3), 13.6, 15.2 (CH_3, NCH_2CH_3), 30.4 (CH_2, C-3′), 37.3 (CH_2, C-2′) 38.7 (CH_2, NCH_2CH_3), 42.8 (CH_2, NCH_2CH_3), 55.3 (CH_3, OMe), 55.4 (CH_3, OMe), 69.6, 73.1 (CH, C-1′), 97.4, 97.5 (CH, C-5), 102.0, 103.4 (CH, C-3), 114.7, 114.8 (CH_2, C-5′), 117.0 (quat., C-1), 138.1, 138.3 (CH, C-4′), 144.0 (quat., C-2), 156.1 (quat., C-6), 161.0, 161.2 (quat., C-4), 168.5 (quat., C=O); *m*/*z* (EI+, %) 321 (M^+, 17), 266 (18), 249 (38), 236 (11), 231 (25), 207 (59), 193 (100), 165 (29), 74 (32), 58 (33), 41 (12); HRMS (EI+): found M^+, 321.1938. $C_{18}H_{27}NO_4$ requires 321.1940.

4.2.4. 3-(But-3′-en-1′-yl)-5,7-dimethoxy-(3*H*)-isobenzofuran-1-one 18. To a crude sample of alcohol **17** (1.10 g, 3.42 mmol) in toluene (20 mL) was added *p*-toluenesulfonic acid monohydrate (100 mg, 0.50 mmol). The mixture was heated under reflux for 6 h. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (1/1) as eluent yielded the title compound **18** (800 mg, 87% over two steps) as a yellow oil. ν_{max} (film) 2942, 1739, 1606, 1463, 1340, 1218, 1160, 1033, 913, 816, 732, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.72–1.85 (1H, m, 1′-H_A), 2.02–2.14 (1H, m, 1′-H_B), 2.20–2.30 (2H, m, 2′-H), 3.90 (3H, s, OMe), 3.95 (3H, s, OMe), 5.00–5.12 (2H, m, 4′-H), 5.28–5.35 (1H, m, 3-H), 5.75–5.89 (1H, m, 3′-H), 6.43 (1H, s, 6-H), 6.43 (1H, s, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) 28.8 (CH_2, C-2′), 34.0 (CH_2, C-1′), 55.8 (CH_3, OMe), 55.8 (CH_3, OMe), 78.9 (CH, C-3), 97.4 (CH, C-6), 98.6 (CH, C-4), 105.8 (quat., C-7a), 115.7 (CH_2, C-4′), 136.8 (CH, C-3′), 154.8 (quat., C-3a), 159.5 (quat., C-7), 166.6 (quat., C-5), 168.2 (quat., C=O); *m/z* (EI+, %) 248 (M^+, 7), 194 (34), 193 (100), 165 (31), 91 (12); HRMS (EI+): found M^+, 248.1055. $C_{13}H_{14}O_4$ requires 248.1049.

4.2.5. 5,7-Dimethoxy-3-(3′-oxoprop-1′-yl)-(3*H*)-isobenzofuran-1-one 9. A solution of olefin **18** (200 mg, 0.81 mmol) in methanol (15 mL) was cooled to −50 °C under nitrogen. Ozone was bubbled through the solution for 10 min at a rate of 1 L/min. The mixture was flushed with nitrogen and dimethyl sulfide (3 mL) was added. The resulting mixture was warmed to room temperature, further dimethyl sulfide added (1 mL) and the mixture stirred for 1 h. The solvent was removed in vacuo and the resulting yellow residue dissolved in water (5 mL), extracted with diethyl ether (3×10 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (1/1) as eluent afforded the title compound **9** (160 mg, 79%) as a yellow oil. ν_{max} (film) 2928, 2951, 1755, 1602, 1463, 1338, 1218, 1158, 1028, 837, 734 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.88 (1H, dddd, J=14.4, 8.3, 8.3, 5.1 Hz, 1′-H_A), 2.44 (1H, dddd, J=14.4, 7.4, 7.4, 3.2 Hz, 1′-H_B), 2.54 (1H, ddd, J=18.7, 8.2, 5.1 Hz, 2′-H_A), 2.75 (1H, td, J=18.7, 7.4 Hz, 2′-H_B), 3.88 (3H, s, OMe), 3.94 (3H, s, OMe), 5.34 (1H, dd, J=8.3, 3.2 Hz, 3-H), 6.42 (1H, s, 4-H), 6.43 (1H, s, 6-H), 9.80 (1H, apparent s, 3′-H); ^{13}C NMR (75 MHz, $CDCl_3$) 26.9 (CH_2, C1′), 38.9 (CH_2, C2′), 56.0 (CH_3, OMe), 56.0 (CH_3, OMe), 78.4 (CH, C3), 97.4 (CH, C6), 99.1 (CH, C4), 106.7 (quat., C7a), 154.3 (quat., C3a), 159.7 (quat., C7), 167.0 (quat., C5), 168.0 (quat., C1), 200.7 (CH, C3′); *m/z* (EI+, %) 250 (M^+, 30), 206 (61), 193 (100), 165 (21), 135 (20) and 77 (10); HRMS (EI+): found M^+, 250.0833. $C_{13}H_{14}O_5$ requires 250.0841.

4.3. Procedure for the synthesis of CJ-13,104 6 and (±)-CJ-13,108 7

4.3.1. Triphenyl(undec-10-en-1-yl)phosphonium bromide 13. Triphenylphosphine (3.2 g, 12.3 mmol) was added in one portion to a solution of 11-bromoundec-1-ene **19** (2.8 mL, 12.9 mmol) in benzene (20 mL). The solution was heated under nitrogen at reflux for 24 h. The solvent was removed in vacuo leaving a viscous white residue that was triturated with diethyl ether (2×5 mL). Removal of the solvent in vacuo afforded the title compound **13** (6.15 g, 96%) as a viscous colourless oil. The ^{31}P NMR data obtained was in agreement with the literature value. ^{31}P NMR (300 MHz, $CDCl_3$) 24.2 (lit. ^{31}P 24.3).[10]

4.3.2. 5,7-Dimethoxy-3-(tetradec-3′,13′-dien-1′-yl)-(3*H*)-isobenzofuran-1-one 20. *n*-Butyllithium (0.56 mL of a 1.6 M solution in hexanes, 0.90 mmol) was added dropwise to a stirred solution of triphenyl(undec-10-en-1-yl)-phosphonium bromide **13** (370 mg, 0.75 mmol) in tetrahydrofuran (10 mL) at −78 °C. The resulting deep orange solution was warmed to room temperature, re-cooled to −78 °C and a solution of phthalide aldehyde **9** (150 mg, 0.60 mmol) in tetrahydrofuran (5 mL) added dropwise with stirring. The mixture was warmed to room temperature, stirred for 2 h and the solvent removed in vacuo. The resulting residue was dissolved in dichloromethane (20 mL), washed with brine (3×5 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (4/1) as eluent afforded the title compound **20** (200 mg, 86%) as a greasy colourless oil. ν_{max} (film) 2926, 2853, 1759, 1614, 1463, 1433, 1338, 1217, 1158, 1056, 1029, 910, 837, 732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.25–1.42 (12H, m, 6′-H, 7′-H, 8′-H, 9′-H, 10′-H, 11′-H), 1.62–1.78 (1H, m, 1′-H_A), 1.91–2.08 (5H, m, 1′-H_B, 5′-H, 12′-H), 2.09–2.36 (2H, m, 2′-H), 3.89 (3H, s, OMe), 3.94 (3H, s, OMe), 4.90–5.01 (2H, m, 14′-H), 5.27–5.48 (3H, m, 3-H, 3′-H, 4′-H), 5.73–5.87 (1H, m, 13′-H), 6.42 (1H, s, 6-H), 6.42 (1H, s, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) 22.5 (CH_2, C-2′), 27.0 (CH_2, C-5′), 28.7 (CH_2, C-11′), 28.9 (CH_2, C-6′), 29.1 (CH_2, C-10′), 29.3 (CH_2, C-9′), 29.3 (CH_2, C-8′), 29.4 (CH_2, C-7′), 33.6 (CH_2, C-12′), 34.8 (CH_2, C-1′), 55.7 (CH_3, OMe), 55.8 (CH_3, OMe), 79.1 (CH, C-3), 97.3 (CH, C-6), 98.5 (CH, C-4), 106.7 (quat., C-7a), 113.9 (CH_2, C-14′), 127.4 (CH, C-3′), 131.6 (CH, C-4′), 139.0 (CH, C-13′), 154.9 (quat., C-3a), 159.4 (quat., C-7), 166.6 (quat., C-5), 168.2 (quat., C=O); *m/z* (EI+, %) 386 (M^+, 23), 261 (25), 247 (24), 208 (100), 193 (50); HRMS (EI+): found M^+, 386.2457. $C_{24}H_{34}O_4$ requires 386.2451.

4.3.3. 5,7-Dimethoxy-3-(13′-oxotetradec-3′-en-1′-yl)-(3*H*)-isobenzofuran-1-one 21. Palladium(II) chloride (46 mg, 0.26 mmol) and copper(I) chloride (61 mg, 0.62 mmol) were added to a stirred solution of diene **20** (200 mg, 0.52 mmol) in *N*,*N*-dimethylformamide–water (4 mL/0.5 mL) at room temperature. The reaction mixture was bubbled with oxygen gas with stirring for 3 h. The mixture was filtered through a pad of Celite® and the solvent removed in vacuo. The resulting residue was dissolved in dichloromethane (10 mL), washed with brine (3×2 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (1/1) as eluent afforded the title compound **21** (130 mg, 62%) as a greasy colourless oil. ν_{max} (film) 3498, 2926, 2853, 1756, 1712, 1613, 1464, 1432, 1338, 1217, 1158, 1054, 1028, 837, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.22–1.36 (10H, m, 6′-H, 7′-H, 8′-H, 9′-H, 10′-H), 1.49–1.62 (2H, m, 11′-H), 1.68–1.79 (1H, m, 1′-H_A), 1.90–2.07 (3H, m, 1′-H_B, 5′-H), 2.12 (3H, s, 14′-H), 2.15–2.33 (2H, m, 2′-H), 2.41 (2H, t, J=7.3 Hz, 12′-H), 3.89 (3H, s, OMe), 3.94 (3H, s, OMe), 5.26–5.50 (3H, m, 3-H, 3′-H, 4′-H), 6.42 (1H, s, 6-H), 6.42

(1H, s, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) 22.6 (CH_2, C-2′), 23.7 (CH_2, C-11′), 27.1 (CH_2, C-5′), 29.0 (CH_2, C-10′), 29.0 (CH_2, C-9′), 29.2 (CH_2, C-6′), 29.2 (CH_2, C-8′), 29.5 (CH_2, C-7′), 29.7 (CH_2, C-14′), 34.9 (CH_2, C-1′), 43.7 (CH_2, C-12′), 55.8 (CH_3, OMe), 55.9 (CH_3, OMe), 79.1 (CH, C-3), 97.4 (CH, C-6), 98.6 (CH, C-4), 106.8 (quat., C-7a), 127.5 (CH, C-3′), 131.6 (CH, C-4′), 155.0 (quat., C-3a), 159.5 (quat., C-7), 166.6 (quat., C-5), 168.3 (quat., C-1), 209.3 (quat., C-13′); *m/z* (EI+, %) 402 (M^+, 25), 384 (18), 345 (14), 208 (100), 207 (88), 194 (75), 193 (72), 43 (46); HRMS (EI+): found M^+, 402.2403. $C_{24}H_{34}O_5$ requires 402.2406.

4.3.4. (±)-CJ-13,108 7. Palladium 10% on carbon (20 mg, 0.036 mmol) was added in one portion to a stirred solution of olefin **21** (130 mg, 0.32 mmol) in ethyl acetate (5 mL) at room temperature. The reaction mixture was stirred under an atmosphere of hydrogen for 1 h and filtered through a pad of Celite®. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (1/1) as eluent afforded the title compound **7** (130 mg, 100%) as a colourless solid. The ^{1}H and ^{13}C NMR data obtained were in agreement with the literature values.[4] Mp 104–106 °C; ν_{max} (film) 3462, 2915, 1758, 1701, 1600, 1469, 1336, 1220, 1162, 1053, 1026, 837 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 1.22–1.36 (16H, m, 3′-H, 4′-H, 5′-H, 6′-H, 7′-H, 8′-H, 9′-H, 10′-H), 1.41–1.46 (2H, m, 2′-H), 1.52–1.59 (2H, m, 11′-H), 1.64–1.73 (1H, m, 1′-H_A), 1.94–1.99 (1H, m, 1′-H_B), 2.13 (3H, s, 14′-H), 2.42 (2H, t, J=7.4 Hz, 12′-H), 3.90 (3H, s, OMe), 3.95 (3H, s, OMe), 5.30 (1H, dd, J=7.8, 3.9 Hz, 3-H), 6.42 (1H, s, 6-H), 6.42 (1H, s, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$) 23.7 (CH_2, C-11′), 24.5 (CH_2, C-2′), 29.0 (CH_2), 29.2 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.7 (CH_2, C-14′), 34.7 (CH_2, C-1′), 43.6 (CH_2, C-12′), 55.8 (CH_3, OMe), 55.8 (CH_3, OMe), 79.8 (CH, C-3), 97.3 (CH, C-6), 98.4 (CH, C-4), 106.7 (quat., C-7a), 155.1 (quat., C-3a), 159.4 (quat., C-7), 166.5 (quat., C-5), 168.4 (quat., C-1), 209.3 (quat., C-13′); *m/z* (EI+, %) 404 (M^+, 32), 347 (65), 207 (57), 193 (100), 43 (19); HRMS (EI+): found M^+, 404.2559. $C_{24}H_{36}O_5$ requires 404.2563.

4.3.5. CJ-13,104 6. Sodium borohydride (116 mg, 3.07 mmol) was added in one portion to a stirred solution of CJ-13,108 **7** (310 mg, 0.77 mmol) in methanol (10 mL) at 0 °C. The reaction mixture was stirred at room temperature under an atmosphere of nitrogen for 10 min and the solvent removed in vacuo. The residue was dissolved in dichloromethane (10 mL), washed with brine (3×2 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (1/1) as eluent afforded the title compound **6** (296 mg, 95%) as a colourless solid. The ^{1}H and ^{13}C NMR data obtained were in agreement with the literature values.[4] Mp 100–102 °C; ν_{max} (film) 3413, 3054, 2928, 2854, 1752, 1604, 1495, 1463, 1422, 1337, 1265, 1219, 1159, 1058, 896, 840, 737, 704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 1.18 (3H, d, J=6.2 Hz, 14′-H), 1.20–1.38 (18H, m, 3′-H, 4′-H, 5′-H, 6′-H, 7′-H, 8′-H, 9′-H, 10′-H, 11′-H), 1.38–1.45 (4H, m, 2′-H, 12′-H), 1.67–1.71 (1H, m, 1′-H_A), 2.00–1.96 (1H, m, 1′-H_B), 3.81 (1H, sextet, J=6.1 Hz, 13′-H), 3.89 (3H, s, OMe), 3.95 (3H, s, OMe), 5.30 (1H, dd, J=7.9, 3.7 Hz, 3-H), 6.41 (1H, s, 6-H), 6.41 (1H, s, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$) 23.4 (CH_3, C-14′), 24.6 (CH_2, C-2′), 25.7 (CH_2, C-11′), 29.3 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.5 (CH_2) 29.5 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 34.8 (CH_2, C-1′), 39.3 (CH_2, C-12′), 55.9 (CH_3, OMe), 55.9 (CH_3, OMe), 68.1 (CH, C-13′), 79.9 (CH, C-3), 97.3 (CH, C-6), 98.5 (CH, C-4), 106.9 (quat., C-7a), 155.2 (quat., C-3a), 159.5 (quat., C-7), 166.6 (quat., C-5), 168.5 (quat., C=O); *m/z* (EI+, %) 406 (M^+, 1), 388 (38), 362 (48), 207 (60), 193 (100), 165 (13), 55 (19), 45 (16), 41 (18); HRMS (EI+): found M^+, 406.2713. $C_{24}H_{38}O_5$ requires 406.2719.

4.4. Procedure for the synthesis of (±)-CJ-13,015 3 and CJ-13,102 4

4.4.1. 1-(*tert*-Butyldimethylsilyloxy)-oct-7-ene 23. A solution of 7-octen-1-ol **22** (1.51 g, 11.8 mmol) in dichloromethane (10 mL) was added dropwise to a stirred mixture of imidazole (850 mg, 12 mmol), 4-dimethylaminopyridine (69 mg, 0.57 mmol) and *tert*-butyldimethylsilyl chloride (1.88 g, 12.4 mmol) in dry dichloromethane (30 mL) at 0 °C. After stirring at for 3 h, saturated aqueous sodium bicarbonate (10 mL) was added, the reaction mixture extracted with dichloromethane (3×5 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using heptane–diethyl ether (99/1) as eluent afforded the title compound **23** (2.74 g, 100%) as a colourless oil. ν_{max} (film) 2955, 2929, 2857, 1641, 1471, 1463, 1414, 1387, 1361, 1255, 1102, 1030, 1005, 993, 937, 909, 836, 811, 775, 660 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 0.05 (6H, s, Si^{t}Bu*Me*$_2$), 0.90 (9H, s, Si^t*Bu*Me$_2$), 1.27–1.32 (4H, m, 3-H, 4-H), 1.36–1.46 (2H, m, 5-H), 1.50 (2H, quintet, J=6.8 Hz, 2-H), 2.05 (2H, dt, J=7.0, 7.0 Hz, 6-H), 3.60 (2H, t, J=6.5 Hz, 1-H), 4.96 (1H, d, J=11.4 Hz, 8-H_A), 4.99 (1H, d, J=19.2 Hz, 8-H_B), 5.76–5.84 (1H, m, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) −5.3 (CH_3, Si^{t}Bu*Me*$_2$), 17.5 (quat., Si^t*Bu*Me$_2$) 25.0 (CH_2, C-3), 25.3 (CH_3, Si^t*Bu*Me$_2$), 28.3 (CH_2, C-4), 28.3 (CH_2, C-5), 32.2 (CH_2, C-2), 33.2 (CH_2, C-6), 63.1 (CH_2, C-1), 114.7 (CH_2, C-8), 140.0 (CH, C-7); *m/z* (CI, NH_3, %) 243 (MH^+, 100), 202 (4), 185 (29), 132 (12), 91 (13), 71 (12); HRMS (CI, NH_3): found MH^+, 243.2144. $C_{14}H_{30}OSi$ requires 243.2144.

4.4.2. 1-(*tert*-Butyldimethylsilyloxy)-7-epoxyoctane 24. A solution of 1-(*tert*-butyldimethylsilyloxy)-oct-7-ene **23** (2.79 g, 11.5 mmol) in dry dichloromethane (5 mL) was added dropwise to a stirred mixture of 3-chloroperoxybenzoic acid (3.40 g, 20 mmol) and sodium acetate (2.00 g, 23 mmol) in dichloromethane (50 mL) at 0 °C and the mixture stirred for 1 h. After stirring at room temperature for 18 h, the reaction mixture was filtered, washed with saturated aqueous sodium sulfite (3×10 mL), extracted with dichloromethane (3×5 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using hexane–diethyl ether (3/1) as eluent afforded the title compound **24** (2.77 g, 99%) as a pale yellow oil. ν_{max} (film): 2928, 2856, 1471, 1463, 1409, 1387, 1361, 1255, 1098, 1006, 938, 917, 835, 812, 775, 659 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 0.03 (6H, s, Si^{t}Bu*Me*$_2$), 0.88 (9H, s, Si^t*Bu*Me$_2$), 1.32–1.34 (4H, m, 3-H, 4-H), 1.43–1.54 (6H, m, 2-H, 5-H, 6-H), 2.45 (1H, dd, J=5.0, 2.7 Hz, 8-H_A), 2.73 (1H, dd, J=5.0, 4.1 Hz, 8-H_B), 2.85–2.88 (1H, m, 7-H),

3.59 (2H, t, J=6.5 Hz, 1-H); ^{13}C NMR (100 MHz, $CDCl_3$) −5.3 (CH_3, Si^{t}Bu*Me*$_2$), 18.3 (quat., Si^t*Bu*Me$_2$), 25.8 (CH_2), 26.0 (CH_3, Si^t*Bu*Me$_2$), 26.1 (CH_2), 29.3 (CH_2, C-4), 32.5 (CH_2, C-6), 32.8 (CH_2, C-2), 47.0 (CH_2, C-8), 52.3 (CH, C-7), 63.2 (CH_2, C-1); *m/z* (CI, NH_3, %) 259 (MH^+, 100), 243 (6), 127 (19), 109 (13), 92 (12), 71 (7); HRMS (CI, NH_3): found MH^+, 259.2087. $C_{14}H_{30}O_2Si$ requires 259.2093.

4.4.3. 1-(*tert*-Butyldimethylsilyloxy)undec-10-en-7-ol 25. A solution of allylmagnesium bromide (1.53 mL of a 1 M solution in diethyl ether, 1.53 mmol) was added dropwise to a stirred suspension of copper(I) cyanide (37.6 mg, 0.33 mmol) in diethyl ether (4 mL) at −78 °C. To the resulting stirred cuprate reagent was added a solution of epoxide **24** (198 mg, 0.77 mmol) in diethyl ether (6 mL) at −78 °C. After stirring for 10 h, saturated aqueous ammonium chloride (30 mL) was added and the mixture allowed to warm to room temperature. The reaction mixture was extracted with diethyl ether (3×20 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using hexane–diethyl ether (4/1) as eluent gave the title compound **25** (1.02 g, 55%) as a pale yellow oil. ν_{max} (film) 3350, 3077, 2929, 2856, 1641, 1471, 1463, 1412, 1388, 1360, 1255, 1100, 1005, 938, 910, 836, 812, 775, 710, 661 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 0.03 (6H, s, Si^{t}Bu*Me*$_2$), 0.88 (9H, s, Si^t*Bu*Me$_2$), 1.26–1.37 (6H, m, 3-H, 4-H, 5-H), 1.38–1.61 (6H, m, 2-H, 6-H, 8-H), 2.09–2.23 (2H, m, 9-H), 3.59 (2H, t, J=6.6 Hz, 1-H), 3.53–3.62 (1H, m, 7-H), 4.96 (1H, dd, J=10.2, 1.7 Hz, 11-H$_A$), 5.04 (1H, dd, J=17.1, 1.7 Hz, 11-H$_B$), 5.78–5.89 (1H, m, 10-H); ^{13}C NMR (100 MHz, $CDCl_3$) −5.3 (CH_3, Si^{t}Bu*Me*$_2$), 18.4 (quat., Si^t*Bu*Me$_2$), 25.6 (CH_2), 25.8 (CH_2) 26.0 (CH_3, Si^t*Bu*Me$_2$), 29.5 (CH_2), 30.1 (CH_2, C-9), 32.8 (CH_2, C-2), 36.5 (CH_2), 37.4 (CH_2), 63.2 (CH_2, C-1), 71.5 (CH, C-7), 114.7 (CH_2, C-11), 138.6 (CH, C-10); *m/z* (CI, NH_3, %) 301 (MH^+, 18), 283 (20), 151 (14), 109 (50), 95 (100), 83 (20), 81 (42), 75 (49); HRMS (CI, NH_3): found MH^+, 301.2561. $C_{17}H_{36}O_2Si$ requires 301.2563.

4.4.4. 7-(Benzyloxy)-1-(*tert*-butyldimethylsilyloxy) undec-10-ene 26. A solution of alcohol **25** (161 mg, 0.53 mmol) in *N*,*N*-dimethylformamide (1 mL) was added dropwise to a stirred suspension of sodium hydride (15 mg, 0.64 mmol) and tetrabutylammonium iodide (51 mg, 0.15 mmol) in *N*,*N*-dimethylformamide (1 mL) at 0 °C. After stirring for 75 min, benzyl bromide (0.08 mL, 0.64 mmol) was added dropwise and the reaction mixture stirred at room temperature for 18 h. Saturated aqueous ammonium chloride (5 mL) was added, the reaction mixture extracted with diethyl ether (3×5 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using hexane–diethyl ether (49/1) as eluent gave the title compound **26** (170 mg, 81%) as a yellow oil. ν_{max} (film) 3065, 3030, 2929, 2857, 1640, 1496, 1471, 1462, 1454, 1387, 1360, 1254, 1206, 1098, 1071, 1028, 1005, 994, 938, 910, 836, 813, 775, 734, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 0.05 (6H, s, Si^{t}Bu*Me*$_2$), 0.90 (9H, s, Si^t*Bu*Me$_2$), 1.25–1.43 (6H, m, 3-H, 4-H, 5-H), 1.46–1.65 (6H, m, 2-H, 6-H, 8-H), 2.01–2.17 (2H, m, 9-H), 3.39 (1H, quintet, J=5.9 Hz, 7-H), 3.60 (2H, t, J=6.6 Hz, 1-H), 4.49 (2H, s, OC*H*$_2$Ph), 4.94 (1H, dd, J=8.8, 2.0 Hz, 11-H$_A$), 5.00 (1H, dd, J=17.2, 2.0 Hz, 11-H$_B$), 5.77–5.87 (1H, m, 10-H), 7.24–7.38 (5H, m, OCH$_2$*Ph*); ^{13}C NMR (100 MHz, $CDCl_3$) −5.3 (CH_3, Si^{t}Bu*Me*$_2$), 18.4 (quat., Si^t*Bu*Me$_2$), 25.3 (CH_2), 25.8 (CH_2), 26.0 (CH_3, Si^t*Bu*Me$_2$), 29.6 (CH_2), 29.6 (CH_2), 32.8 (CH_2), 33.1 (CH_2, C-8), 33.7 (CH_2), 63.3 (CH_2, C-1), 70.8 (CH_2, O*C*H$_2$Ph), 78.4 (CH, C-7), 114.4 (CH_2, C-11), 127.4 (CH, OCH$_2$*Ph*), 127.7 (CH, OCH$_2$*Ph*), 128.3 (CH, OCH$_2$*Ph*), 138.8 (CH, C-10), 139.0 (quat., OCH$_2$*Ph*); *m/z* (CI, NH_3, %) 391 (MH^+, 7), 283 (17), 216 (28), 108 (18), 92 (45), 91 (100); HRMS (CI, NH_3): found MH^+, 391.3034. $C_{24}H_{42}O_2Si$ requires 391.3032.

4.4.5. 7-(Benzyloxy)undec-10-en-1-ol 27. Tetrabutylammonium fluoride (4.13 mL of a 1 M solution in tetrahydrofuran, 4.13 mmol) was added dropwise to a stirred mixture of silyl ether **26** (1.08 g, 2.75 mmol) and 4 Å molecular sieves (200 mg) in tetrahydrofuran (15 mL) at 0 °C. After stirring for 2 h, saturated aqueous ammonium chloride (10 mL) was added, the reaction mixture extracted with diethyl ether (3×5 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using hexane–diethyl ether (4/1) as eluent gave the title compound **27** (613 mg, 97%) as a yellow oil. ν_{max} (film): 3368, 3065, 3030, 2931, 2857, 1640, 1496, 1454, 1414, 1396, 1350, 1307, 1257, 1206, 1067, 1028, 994, 910, 735, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 1.30–1.44 (6H, m, 3-H, 4-H, 5-H), 1.50–1.70 (6H, m, 2-H, 6-H, 8-H), 2.11–2.15 (2H, m, 9-H), 3.40 (1H, quintet, J=5.8 Hz, 7-H), 3.63 (2H, t, J=6.6 Hz, 1-H), 4.50 (2H, s, OC*H*$_2$Ph), 4.95 (1H, dd, J=10.2, 1.6 Hz, 11-H$_A$), 5.01 (1H, dd, J=17.2, 1.6 Hz, 11-H$_B$), 5.77–5.85 (1H, m, 10-H), 7.25–7.36 (5H, m, OCH$_2$*Ph*); ^{13}C NMR (100 MHz, $CDCl_3$) 25.2 (CH_2), 25.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2, C-9), 32.7 (CH_2), 33.1 (CH_2, C-8), 33.7 (CH_2), 63.0 (CH_2, C-1), 70.8 (CH_2, O*C*H$_2$Ph), 78.3 (CH, C-7), 114.4 (CH_2, C-11), 127.4 (CH, OCH$_2$*Ph*), 127.8 (CH, OCH$_2$*Ph*), 128.3 (CH, OCH$_2$*Ph*) 138.8 (CH, C-10), 139.0 (quat., OCH$_2$*Ph*); *m/z* (EI+, %) 276 (M^+, 1), 175 (4), 107 (9), 92 (10), 91 (100), 65 (4), 55 (5), 41 (4); HRMS (EI+): found M^+, 276.2089. $C_{18}H_{28}O_2$ requires 276.2089.

4.4.6. 7-(Benzyloxy)-1-bromoundec-10-ene 28. A solution of carbon tetrabromide (1.44 g, 4.34 mmol) in acetonitrile (2 mL) was added dropwise to a stirred mixture of alcohol **27** (0.60 g, 2.17 mmol) and triphenylphosphine (1.14 g, 4.34 mmol) in acetonitrile (20 mL) at 0 °C. After stirring the reaction mixture at room temperature for 30 min, saturated aqueous sodium bicarbonate (10 mL) was added and the reaction mixture extracted with diethyl ether (3×5 mL). The organic layer was washed with brine (2×10 mL) and dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using hexane–diethyl ether (49/1) as eluent gave the title compound **28** (0.72 g, 98%) as a colourless oil. ν_{max} (film): 3064, 3029, 2933, 2857, 1640, 1496, 1453, 1349, 1306, 1260, 1206, 1093, 1067, 1028, 993, 910, 734, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 1.25–1.47 (6H, m, 3-H, 4-H, 5-H), 1.48–1.70 (4H, m, 6-H, 8-H), 1.83 (2H, quintet, J=7.2 Hz, 2-H), 2.08–2.22 (2H, m, 9-H), 3.37–3.43 (3H, m, 1-H, 7-H), 4.49 (2H, s, OC*H*$_2$Ph), 4.95 (1H, dd, J=10.2, 1.6 Hz, 11-H$_A$), 5.01 (1H, dd, J=17.2, 1.6 Hz, 11-H$_B$), 5.77–5.85 (1H, m, 10-H), 7.25–7.36 (5H, m, OCH$_2$*Ph*);

^{13}C NMR (100 MHz, $CDCl_3$) 25.1 (CH_2), 28.1 (CH_2), 28.9 (CH_2), 29.6 (CH_2, C-9), 32.7 (CH_2), 33.1 (CH_2, C-8), 33.6 (CH_2), 33.9 (CH_2, C-1), 70.8 (CH_2, O*C*H_2Ph), 78.3 (CH, C-7), 114.5 (CH_2, C-11), 127.4 (CH, OCH$_2$*Ph*), 127.7 (CH, OCH$_2$*Ph*), 128.3 (CH, OCH$_2$*Ph*), 138.7 (CH, C-10), 139.0 (quat., OCH$_2$*Ph*); *m/z* (EI+, %) 339 (M^+, 0.1), 175 (9), 107 (9), 92 (10), 91 (100), 65 (4), 55 (5), 41 (5); HRMS (EI+): found M^+, 338.1243, 340.1219. $C_{18}H_{27}BrO$ requires 338.1245, 340.1225.

4.4.7. [7-(Benzyloxy)undec-10-en-1-yl]triphenylphosphonium bromide 11. Triphenylphosphine (1.18 g, 4.51 mmol) was added in one portion to a stirred solution of bromide **28** (765 mg, 2.26 mmol) in acetonitrile (10 mL) at room temperature. The mixture was heated under an atmosphere of nitrogen at reflux for 26 h. Removal of the solvent in vacuo followed by flash column chromatography using dichloromethane–methanol (19/1) as eluent gave the title compound **11** (1.08 g, 80%) as a wax. ν_{max} (film) 3377, 3055, 3031, 3007, 2989, 2934, 2859, 2791, 1639, 1618, 1587, 1495, 1485, 1453, 1438, 1413, 1344, 1315, 1273, 1190, 1161, 1113, 1066, 1027, 996, 912, 788, 725, 693 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 1.20–1.36 (4H, m, 4-H, 5-H), 1.41–1.68 (8H, m, 2-H, 3-H, 6-H, 8-H), 2.04–2.17 (2H, m, 9-H), 3.35 (1H, quintet, J=5.8 Hz, 7-H), 3.84–3.91 (2H, m, 1-H), 4.45 (2H, s, O*CH*$_2$Ph) 4.94 (1H, dd, J=10.2, 1.6 Hz, 11-H$_A$), 4.99 (1H, dd, J=17.1, 1.6 Hz, 11-H$_B$), 5.74–5.85 (1H, m, 10-H), 7.25–7.31 (5H, m, OCH$_2$*Ph*), 7.65–7.89 (15H, m, P*Ph*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) 22.5 (CH_2, d, J=7 Hz, C-2), 22.7 (CH_2, d, J=49 Hz, C-1), 24.8 (CH_2, C-5), 29.4 (CH_2, C-4), 29.6 (CH_2, C-9), 30.3 (CH_2, d, J=15 Hz, C-3), 33.0 (CH_2, C-8), 33.6 (CH_2, C-6), 70.7 (CH_2, O*C*H$_2$Ph), 78.2 (CH, C-7), 114.4 (CH_2, C-11), 118.4 (quat., d, J=85 Hz, P*Ph*$_3$), 127.4 (CH, OCH$_2$*Ph*), 127.7 (CH, OCH$_2$*Ph*), 128.3 (CH, OCH$_2$*Ph*), 130.4 (CH, d, J=12 Hz, P*Ph*$_3$), 133.7 (CH, d, J=10 Hz, P*Ph*$_3$), 134.9 (CH, P*Ph*$_3$) 138.7 (CH, C-10), 139.0 (quat., OCH$_2$*Ph*); *m/z* (FAB+, %) 521 (M^+−Br, 100), 429 (4), 413 (5), 373 (6), 275 (4), 262 (8), 183 (6), 91 (15); HRMS (FAB): found M^+−Br, 521.2965. $C_{36}H_{42}BrOP$ requires 521.2973.

4.4.8. 3-(10′-Benzyloxytetradec-3′,13′-dien-1′-yl)-5,7-dimethoxy-(3*H*)-isobenzofuran-1-one 29. *n*-Butyllithium (0.23 mL of a 1.6 M solution in hexanes, 0.37 mmol) was added dropwise to a stirred solution of phosphonium salt **11** (200 mg, 0.33 mmol) in dry tetrahydrofuran (5 mL) at −78 °C. The resulting deep orange solution was warmed to room temperature, re-cooled to −78 °C, and a solution of phthalide aldehyde **9** (69 mg, 0.28 mmol) in dry tetrahydrofuran (2 mL) was added dropwise with stirring. The mixture was warmed to room temperature, stirred for 2 h and the solvent removed in vacuo. The resulting residue was dissolved in dichloromethane (20 mL), washed with brine (3×5 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using hexane–diethyl ether (4/6) as eluent gave the title compound **29** (98 mg, 72%) as a viscous colourless oil. ν_{max} (film) 3505, 3065, 3005, 2931, 2855, 1759, 1639, 1613, 1495, 1462, 1455, 1432, 1360, 1338, 1216, 1158, 1108, 1062, 1028, 911, 837, 735, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 1.23–1.46 (6H, m, 6′-H, 7′-H, 8′-H), 1.48–1.66 (4H, m, 9′-H, 11′-H), 1.67–1.78 (1H, m, 1′-H$_A$), 1.94–2.05 (3H, m, 1′-H$_B$, 5′-H), 2.09–2.21 (3H, m, 2′-H$_A$, 12′), 2.22–2.35 (1H, m, 2′-H$_B$), 3.40 (1H, quintet, J=5.8 Hz, 10′-H), 3.86 (3H, s, OMe), 3.92 (3H, s, OMe), 4.49 (2H, s, O*CH*$_2$Ph), 4.94 (1H, dd, J=10.2, 1.8 Hz, 14′-H$_A$), 5.00 (1H, dd, J=17.2, 1.8 Hz, 14′-H$_B$), 5.22–5.28 (1H, m, 3-H), 5.30–5.47 (2H, m, 3′-H, 4′-H), 5.72–5.88 (1H, m, 13′-H), 6.40 (2H, br s, 4-H, 6-H), 7.21–7.36 (5H, m, OCH$_2$*Ph*); ^{13}C NMR (100 MHz, $CDCl_3$) 22.8 (CH_2, C-2′), 25.2 (CH_2, C-8′), 27.2 (CH_2, C-5′), 29.4 (CH_2), 29.6 (CH_2), 29.6 (CH_2, C-12′), 33.1 (CH_2, C-11′), 33.7 (CH_2, C-9′), 35.0 (CH_2, C-1′), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 70.8 (CH_2, O*C*H$_2$Ph), 78.4 (CH, C-10′), 79.3 (CH, C-3), 97.3 (CH, C-6), 98.7 (CH, C-4), 106.9 (quat., C-7a), 114.4 (CH_2, C-14′), 127.4 (CH, OCH$_2$*Ph*), 127.6 (CH, C-3′), 127.7 (CH, OCH$_2$*Ph*), 128.3 (CH, OCH$_2$*Ph*), 131.7 (CH, C-4′), 138.8 (quat., OCH$_2$*Ph*), 139.0 (CH, C-13′), 155.1 (quat., C-3a), 159.6 (quat., C-7), 166.7 (quat., C-5), 168.5 (quat., C=O); *m/z* (FAB+, %) 493 (MH^+, 9), 385 (8), 219 (5), 120 (11), 91 (22); HRMS (FAB): found MH^+, 493.2953. $C_{31}H_{40}O_5$ requires 493.2954.

4.4.9. 3-(10′-Benzyloxy-13′-oxotetradec-3′-en-1′-yl)-5,7-dimethoxy-(3*H*)-isobenzofuran-1-one 30. Palladium(II) chloride (11 mg, 0.06 mmol) and copper(I) chloride (15 mg, 0.16 mmol) were added in one portion to a stirred solution of diene **29** (64 mg, 0.13 mmol) in *N*,*N*-dimethylformamide–water (4 mL/0.5 mL) at room temperature. The reaction mixture was bubbled with oxygen gas with stirring for 3 h. The mixture was filtered through Celite® and the solvent removed in vacuo. The resulting residue was dissolved in dichloromethane (10 mL), washed with brine (3×2 mL) and dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using hexane–ethyl acetate (1/1) as eluent afforded the title compound **30** (35 mg, 54%) as a viscous colourless oil. ν_{max} (film) 3503, 3061, 3005, 2930, 2855, 1755, 1713, 1605, 1494, 1456, 1432, 1359, 1338, 1271, 1217, 1158, 1108, 1062, 1028, 972, 837, 735, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 1.20–1.50 (6H, m, 6′-H, 7′-H, 8′-H), 1.53–1.65 (2H, m, 9′-H), 1.67–1.78 (2H, m, 1′-H$_A$, 11′-H$_A$), 1.82–1.93 (1H, m, 11′-H$_B$), 1.94–2.05 (3H, m, 1′-H$_B$, 5′-H), 2.11 (3H, s, 14′-H), 2.13–2.23 (1H, m, 2′-H$_A$,), 2.23–2.35 (1H, m, 2′-H$_B$), 2.48–2.53 (2H, m, 12′-H), 3.38–3.40 (1H, m, 10′-H), 3.89 (3H, s, OMe), 3.95 (3H, s, OMe), 4.43 (1H, d, J=11.5 Hz, O*CH*$_A$H$_B$Ph), 4.51 (1H, d, J=11.5 Hz, OCH$_A$*H*$_B$Ph), 5.28–5.30 (1H, m, 3-H), 5.35–5.45 (2H, m, 3′-H, 4′-H), 6.41 (1H, s, 4-H), 6.42 (1H, s, 6-H), 7.30–7.34 (5H, m, OCH$_2$*Ph*); ^{13}C NMR (100 MHz, $CDCl_3$) 22.8 (CH_2, C-2′), 25.2 (CH_2, C-8′), 27.2 (CH_2, C-5′), 27.5 (CH_2, C-11′), 29.4 (CH_2), 29.6 (CH_2), 30.0 (CH_3, C-14′), 33.7 (CH_2, C-9′), 35.0 (CH_2, C-1′), 39.3 (CH_2, C-12′), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 70.8 (CH_2, O*C*H$_2$Ph), 77.9 (CH, C-10′), 79.3 (CH, C-3), 97.3 (CH, C-6), 98.7 (CH, C-4), 106.9 (quat., C-7a), 127.5 (CH, OCH$_2$*Ph*), 127.6 (CH, C-3′), 127.8 (CH, OCH$_2$*Ph*), 128.3 (CH, OCH$_2$*Ph*), 131.7 (CH, C-4′), 138.8 (quat., OCH$_2$*Ph*), 155.1 (quat., C-3a), 159.6 (quat., C-7), 166.7 (quat., C-5), 168.5 (quat., C-1), 209.1 (quat., C-13′); *m/z* (FAB+, %) 509 (MH^+, 2), 401 (9), 219 (4), 124 (7), 120 (8), 91 (19), 89 (22); HRMS (FAB+): found MH^+, 509.2904. $C_{31}H_{40}O_6$ requires 509.2903.

4.4.10. 5,7-Dimethoxy-3-(10′-hydroxy-13′-oxotetradec-1′-ly)-(3*H*)-isobenzofuran-1-one 14. Palladium 10% on

carbon (20 mg, 0.036 mmol) was added in one portion to a stirred solution of benzyl ether **30** (35 mg, 0.07 mmol) in ethyl acetate (5 mL) at room temperature. The reaction mixture was bubbled with hydrogen gas for 3 h and filtered through a pad of Celite®. Removal of the solvent in vacuo afforded the title compound **14** as a colourless oil (25 mg) that was not purified further before use in the subsequent steps.

4.4.11. (±)-CJ-13,015 3. Tetra-*n*-propylammonium perruthenate (5 mg, 0.01 mmol) and *N*-methylmorpholine *N*-oxide (10 mg, 0.09 mmol) were added to a stirred solution of crude alcohol **14** (11 mg) in dichloromethane (2 mL) at room temperature. The reaction mixture was stirred for 30 min then filtered through a pad of silica. Removal of the solvent in vacuo followed by flash column chromatography using hexane–ethyl acetate (1/1) as eluent afforded the title compound **3** (4 mg, 37% over two steps) as a colourless solid. The ^{1}H and ^{13}C NMR data obtained were in agreement with the literature values.[4] Mp 103–104 °C; ν_{max} (film) 3584, 2925, 2852, 1756, 1710, 1603, 1494, 1465, 1431, 1413, 1360, 1337, 1218, 1159, 1099, 1053, 1028, 836, 689 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 1.18–1.39 (10H, m, 3′-H, 4′-H, 5′-H, 6′-H, 7′-H), 1.37–1.52 (2H, m, 2′-H), 1.52–1.74 (3H, m, 1′-H_A, 8′-H), 1.92–2.03 (1H, m, 1′-H_B), 2.19 (3H, s, 14′-H), 2.44 (2H, t, J=7.4 Hz, 9′-H), 2.67–2.72 (4H, m, 11′-H, 12′-H), 3.90 (3H, s, OMe), 3.95 (3H, s, OMe), 5.30 (1H, dd, J=7.9, 3.7 Hz, 3-H), 6.41 (1H, s, 4-H), 6.42 (1H, s, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$) 23.8 (CH_2, C-8′), 24.6 (CH_2, C-2′), 29.1 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 30.0 (CH_3, C-14′), 34.8 (CH_2, C-1′), 36.0 (CH_2, C-12′), 36.9 (CH_2, C-11′), 42.8 (CH_2, C-9′), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 79.9 (CH, C-3), 97.3 (CH, C-6), 98.6 (CH, C-4), 106.9 (quat., C-7a), 155.2 (quat., C-3a), 159.6 (quat., C-7), 166.6 (quat., C-5), 168.6 (quat., C-1), 207.4 (quat., C-13′), 209.7 (quat., C-10′); *m/z* (FAB+, %) 419 (MH^+, 5), 403 (73), 120 (14), 89 (19); HRMS (FAB+): found MH^+, 419.2431. $C_{24}H_{34}O_6$ requires 419.2434.

4.4.12. CJ-13,102 4. Acetic anhydride (2 mL, 21.16 mmol) was added dropwise to a stirred mixture of crude alcohol **14** (11 mg) and *N*,*N*-dimethyl-4-aminopyridine (5 mg, 0.04 mmol) in pyridine (2 mL) at room temperature. The reaction mixture was stirred for 8 h and the solvent removed in vacuo. Flash column chromatography using hexane–ethyl acetate (1/1) as eluent afforded the title compound **4** (10 mg, 83% over two steps) as a colourless oil. ^{1}H and ^{13}C NMR data obtained were in agreement with the literature values.[4] ν_{max} (film) 3504, 2927, 2853, 1756, 1718, 1603, 1494, 1464, 1432, 1359, 1337, 1241, 1218, 1159, 1104, 1052, 1028, 837, 732, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 1.20–1.35 (10H, m, 3′-H, 4′-H, 5′-H, 6′-H, 7′-H), 1.35–1.58 (4H, m, 8′-H, 2′-H), 1.61–1.80 (3H, m, 1′-H_A, 9′-H), 1.84–2.02 (3H, m, 1′-H_B, 11′-H), 2.05 (3H, s, O*Ac*) 2.15 (3H, s, 14′-H), 2.45 (2H, t, J=7.4 Hz, 12′-H), 3.90 (3H, s, OMe), 3.95 (3H, s, OMe), 4.82–4.88 (1H, m, 10′-H), 5.29 (1H, dd, J=7.8, 3.7 Hz, 3-H), 6.41 (1H, s, 4-H), 6.42 (1H, s, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$) 21.2 (CH_3, O*Ac*), 24.6 (CH_2, C-2′), 25.2 (CH_2, C-8′), 27.9 (CH_2, C-11′), 29.3 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.4 (CH_2) 30.0 (CH_3, C-14′), 34.2 (CH_2, C-9′), 34.8 (CH_2, C-1′), 39.5 (CH_2, C-12′), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 73.5 (CH, C-10′), 80.0 (CH, C-3), 97.3 (CH, C-6), 98.6 (CH, C-4), 106.9 (quat., C-7a), 155.2 (quat., C-3a), 159.6 (quat., C-7), 166.6 (quat., C-5), 168.6 (quat., C-1), 170.9 (quat., O*Ac*), 208.0 (quat., C-13′); *m/z* (FAB+, %) 463 (MH^+, 3), 403 (11), 120 (15), 89 (23), 73 (12); HRMS (FAB+): found MH^+, 463.2703. $C_{26}H_{38}O_7$ requires 463.2696.

4.5. Procedure for the synthesis of (±)-CJ-13,103 5

4.5.1. 1-(*tert*-Butyldimethylsilyloxy)dec-9-ene 32. Using a similar method to that described above for the preparation of sily ether **23**, alcohol **31** (3.6 g, 23.04 mmol) was reacted with *tert*-butyldimethylsilyl chloride (5.53 g, 29.90 mmol) to afford the the title compound **32** (6.00 g, 96%) as a colourless oil. The ^{1}H and ^{13}C NMR data obtained were in agreement with the literature values.[11]

4.5.2. 9-(*tert*-Butyldimethylsilyloxy)nonanal 33. A solution of alkene **32** (5.00 g, 18.5 mmol) in methanol (20 mL) was cooled to −50 °C under nitrogen. Ozone was bubbled through the solution for 10 min at a rate of 1 L/min. The mixture was flushed with nitrogen and dimethyl sulfide (5 mL) was added. The resulting mixture was warmed to room temperature, further dimethyl sulfide added (2 mL) and the mixture stirred for 1 h. The solvent was removed in vacuo and the resulting yellow residue dissolved in water (5 mL), extracted with diethyl ether (3×10 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (1/1) as eluent afforded the title compound **33** (4.80 g, 95%) as an oil. The ^{1}H NMR data obtained was in agreement with the literature values.[12]

4.5.3. 1-(*tert*-Butyldimethylsilyloxy)tridec-12-en-9-ol 34. A solution of aldehyde **33** (5.00 g, 18.3 mmol) in diethyl ether (15 mL) was added dropwise to a stirred solution of but-3-en-1-ylmagnesium bromide (56 mL of 0.5 M solution in diethyl ether, 28 mmol) at 0 °C and the reaction mixture allowed to warm to room temperature. After stirring for 30 min, saturated aqueous ammonium chloride (20 mL) was added, the reaction mixture extracted with diethyl ether (3× 10 mL) and the organic layer dried over magnesium sulfate. Removal of the solvent in vacuo followed by flash column chromatography using ethyl acetate–hexane (1/1) as eluent afforded the title compound **34** as a yellow oil. ν_{max} (film) 3361, 2929, 2856, 1641, 1471, 1463, 1387, 1361, 1255, 1100, 1006, 938, 909, 835, 775 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 0.02 (6H, s, Si^{t}Bu*Me*$_2$), 0.87 (9H, s, Si^{t}*Bu*Me$_2$), 1.22–1.34 (8H, m, 3-H, 4-H, 5-H, 6-H), 1.38–1.66 (8H, m, 2-H, 7-H, 8-H, 10-H), 2.10–2.20 (2H, m, 11-H), 3.56–3.59 (3H, m, 1-H, 9-H), 4.94 (1H, d, J=10.2 Hz, 13-H_A), 5.02 (1H, d, J=17.2 Hz, 13-H_B), 5.78–5.85 (1H, m, 12-H); ^{13}C NMR (100 MHz, $CDCl_3$) −5.3 (CH_3, Si^{t}Bu*Me*$_2$), 18.3 (quat., Si^{t}*Bu*Me$_2$), 25.6 (CH_2), 25.7 (CH_2), 25.9 (CH_3, Si^{t}*Bu*Me$_2$), 29.3 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 30.0 (CH_2, C-11), 32.8 (CH_2, C-2), 36.4 (CH_2), 37.4 (CH_2), 63.2 (CH_2, C-1), 71.5 (CH, C-7), 114.7 (CH_2, C-11), 138.6 (CH, C-10); *m/z* (FAB+, %) 329 (MH^+, 27), 311 (17), 123 (14), 115 (16), 109 (21), 95 (40), 89 (27), 81 (37), 75 (83); HRMS (FAB+): found MH^+, 329.2883. $C_{19}H_{40}O_2Si$ requires 329.2876.

4.5.4. 9-Benzyloxy-1-(*tert*-butyldimethylsilyloxy)tridec-12-ene 35. Using a similar method to that described above

for the preparation of benzyl ether **26**, alcohol **34** (944 mg, 2.87 mmol) was reacted with benzyl bromide (0.48 mL, 4.02 mmol) to afford the title compound **35** (1.14 g, 95%) as a yellow oil. ν_{max} (film) 3065, 3031, 2929, 2856, 1641, 1496, 1471, 1462, 1454, 1387, 1360, 1306, 1254, 1207, 1098, 1071, 1028, 1005, 938, 909, 835, 814, 775, 733, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 0.05 (6H, s, Si^{t}BuMe_2), 0.90 (9H, s, Si^t*Bu*Me$_2$), 1.22–1.38 (8H, m, 3-H, 4-H, 5-H, 6-H), 1.44–1.70 (8H, m, 2-H, 7-H, 8-H, 10-H), 2.10–2.29 (2H, m, 11-H), 3.38–3.47 (1H, m, 9-H), 3.59–3.67 (2H, m, 1-H), 4.53 (2H, s, *OCH*$_2$Ph) 4.88–5.05 (2H, m, 13-H), 5.87–5.92 (1H, m, 12-H), 7.27–7.38 (5H, m, OCH$_2$*Ph*); ^{13}C NMR (100 MHz, $CDCl_3$) −5.3 (CH_3, Si^{t}Bu*Me*$_2$), 18.3 (quat., Si^t*Bu*Me$_2$), 25.2 (CH_2), 25.7 (CH_2), 25.9 (CH_3, Si^t*Bu*Me$_2$), 29.3 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 32.8 (CH_2), 33.1 (CH_2), 33.7 (CH_2), 63.2 (CH_2, C-1), 70.7 (CH_2, O*C*H$_2$Ph), 78.3 (CH, C-9), 114.4 (CH_2, C-13), 127.3 (CH, OCH$_2$*Ph*), 127.7 (CH, OCH$_2$*Ph*), 128.2 (CH, OCH$_2$*Ph*), 138.7 (CH, C-12), 139.0 (quat., OCH$_2$*Ph*); *m/z* (FAB+, %) 419 (MH^+, 5), 311 (11), 95 (13), 91 (100), 89 (14), 81 (13), 75 (81); HRMS (FAB+): found MH^+, 419.3341. $C_{26}H_{46}O_2Si$ requires 419.3345.

4.5.5. 1-Bromo-9-(benzyloxy)tridec-12-ene 36. Bromine (1.71 mL, 33.4 mmol) was added dropwise to a stirred solution of triphenylphosphine (8.89 g, 33.9 mmol) in dichloromethane (100 mL) at 0 °C. The mixture was warmed to room temperature resulting in formation of a white suspension to which was added a solution of silyl ether **35** (2.00 g, 4.78 mmol) in dichloromethane dropwise with stirring. The resulting mixture was stirred for 24 h at room temperature then filtered through a plug of silica using hexane–ethyl acetate (9/1) as eluent, affording the title compound **36** (1.60 g, 4.40 mmol) as a colourless oil. ν_{max} (film) 3064, 3029, 2929, 2854, 1639, 1496, 1453, 1349, 1305, 1252, 1206, 1093, 1067, 1027, 994, 910, 733, 696, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 1.25–1.32 (6H, m, 4′-H, 5′-H, 6′-H), 1.34–1.45 (4H, m, 3′-H, 7′-H), 1.46–4.70 (4H, m, 8′-H, 10′-H), 1.84 (2H, quintet, J=7.2 Hz, 2-H), 2.06–2.20 (2H, m, 11-H), 3.35–3.43 (3H, m, 1-H, 9-H), 4.49 (2H, s, OC*H*$_2$Ph), 4.93–4.96 (1H, m, 13-H$_A$), 5.01 (1H, dd, J=17.2, 1.6 Hz, 13-H$_B$), 5.78–5.85 (1H, m, 10-H), 7.22–7.36 (5H, m, OCH$_2$*Ph*); ^{13}C NMR (100 MHz, $CDCl_3$) 25.1 (CH_2), 28.1 (CH_2), 28.6 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 32.7 (CH_2), 33.0 (CH_2), 33.6 (CH_2), 34.0 (CH_2, C-1), 70.7 (CH_2, O*C*H$_2$Ph), 78.3 (CH, C-9), 114.4 (CH_2, C-13), 127.3 (CH, OCH$_2$*Ph*), 127.7 (CH, OCH$_2$*Ph*), 128.2 (CH, OCH$_2$*Ph*), 138.7 (CH, C-12), 139.0 (quat., OCH$_2$*Ph*); *m/z* (EI+, %) 368 (M^+, 0.1), 366 (M^+, 0.1), 175 (11), 92 (11), 91 (100); HRMS (EI+): found M^+, 366.1550, 368.1537. $C_{20}H_{31}BrO$ requires 366.1558, 368.1538.

4.5.6. [9-(Benzyloxy)tridec-12-en-1-yl]triphenylphosphonium bromide 12. Using a similar method to that described above for the preparation of phosphonium salt **11**, bromide **36** (730 mg, 1.99 mmol) was reacted with triphenylphosphine (680 mg, 2.58 mmol) to afford the title compound **12** (1.0 g, 80%) as a wax. ν_{max} (film) 3390, 3056, 3007, 2989, 2928, 2856, 2792, 2174, 1639, 1615, 1587, 1485, 1463, 1454, 1439, 1413, 1340, 1317, 1271, 1190, 1162, 1113, 1069, 1027, 996, 923, 787, 723, 691, 638 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.16–1.36 (8H, m, 3′-H, 4′-H, 5′-H, 6′-H), 1.41–1.56 (2H, m, 7′-H), 1.57–1.71 (4H, m, 2′-H, 8′-H), 1.72–2.36 (4H, m, 10′-H, 11′-H), 3.35–3.45 (1H, m, 9-H), 3.64–3.82 (2H, m, 1-H), 4.48 (2H, s, OC*H*$_2$Ph), 4.89–5.07 (2H, m, 13-H), 5.71–5.89 (1H, m, 12-H), 7.20–7.40 (5H, m, OCH$_2$*Ph*), 7.65–7.94 (15H, m, P*Ph*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) 22.3 (CH_2, d, J=9 Hz, C-2), 22.6 (CH_2, d, J=46 Hz, C-1), 24.8 (CH_2), 27.1 (CH_2), 28.7 (CH_2), 28.8 (CH_2), 29.3 (CH_2, d, J=5 Hz, C-4), 30.1 (CH_2, d, J=16 Hz, C-3), 32.8 (CH_2), 33.4 (CH_2), 70.4 (CH_2, O*C*H$_2$Ph), 78.1 (CH, C-9), 114.1 (CH_2, C-13), 118.0 (quat., d, J=86 Hz, P*Ph*$_3$), 127.0 (CH, OCH$_2$*Ph*), 127.4 (CH, OCH$_2$*Ph*), 127.9 (CH, OCH$_2$*Ph*), 130.2 (CH, d, J=13 Hz, P*Ph*$_3$), 133.3 (CH, d, J=10 Hz, P*Ph*$_3$), 134.8 (CH, d, J=3 Hz, P*Ph*$_3$), 138.4 (CH, C-12), 138.7 (quat., OCH$_2$*Ph*); *m/z* (FAB+, %) 549 (M^+−Br, 100), 523 (28), 521 (28), 459 (18), 441 (92), 401 (51), 275 (12), 262 (27), 183 (15), 91 (14).

4.5.7. 3-(12′-Benzyloxyhexadec-3′,15′-dien-1′-yl)-5,7-dimethoxy-(3*H*)-isobenzofuran-1-one 37. Using a similar method to that described above for the preparation of diene **29**, phosphonium salt **12** (300 mg, 0.48 mmol) was reacted with phthalide aldehyde **9** (120 mg, 0.48 mmol) to afford the title compound **37** (181 mg, 73%) as a viscous colourless oil. ν_{max} (film) 3514, 3075, 3006, 2927, 2853, 1759, 1640, 1614, 1495, 1463, 1455, 1434, 1360, 1338, 1217, 1158, 1109, 1061, 1029, 912, 837, 735, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.22–1.42 (10H, m, 6′-H, 7′-H, 8′-H, 9′-H, 10′-H), 1.45–1.88 (5H, m, 1′-H$_A$, 11′-H, 13′-H), 1.92–2.07 (3H, m, 1′-H$_B$, 5′-H), 2.08–2.21 (3H, m, 2′-H$_A$, 14′-H), 2.22–2.37 (1H, m, 2′-H$_B$), 3.37–3.43 (1H, m, 12′-H), 3.89 (3H, s, OMe), 3.95 (3H, s, OMe), 4.49 (2H, OC*H*$_2$Ph), 4.89–5.11 (2H, m, 16′-H$_A$), 5.29 (1H, dd, J=8.5, 3.3 Hz, 3-H), 5.33–5.48 (2H, m, 3′-H, 4′-H), 5.71–5.87 (1H, m, 15′-H), 6.41 (2H, br s, 4-H, 6-H), 7.22–7.37 (5H, m, OCH$_2$*Ph*); ^{13}C NMR (75 MHz, $CDCl_3$) 22.7 (CH_2), 25.2 (CH_2), 27.2 (CH_2), 27.4 (CH_2), 29.2 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 31.6 (CH_2), 33.1 (CH_2), 33.7 (CH_2), 34.9 (CH_2, C-1′), 55.8 (CH_3, OMe), 55.9 (CH_3, OMe), 70.7 (CH_2, O*C*H$_2$Ph), 78.4 (CH, C-12′), 79.2 (CH, C-3), 97.3 (CH, C-6), 98.6 (CH, C-4), 106.9 (quat., C-7a), 114.3 (CH_2, C-16′), 127.3 (CH, OCH$_2$*Ph*), 127.5 (CH, C-3′), 127.7 (CH, OCH$_2$*Ph*), 128.2 (CH, OCH$_2$*Ph*), 131.7 (CH, C-4′), 138.7 (CH, C-15′), 139.0 (quat., OCH$_2$*Ph*), 155.0 (quat., C-3a), 159.6 (quat., C-7), 166.6 (quat., C-5), 168.3 (quat., C=O); *m/z* (FAB+, %) 521 (MH^+, 12), 413 (24), 373 (10), 207 (10), 193 (10), 120 (12), 91 (30); HRMS (FAB+): found MH^+, 521.3260. $C_{33}H_{44}O_5$ requires 521.3267.

4.5.8. 3-(12′-Benzyloxy-15′-oxohexadec-3′-en-1′-yl)-5,7-dimethoxy-(3*H*)-isobenzofuran-1-one 38. Using a similar method to that described above for the preparation of methyl ketone **30**, Wacker oxidation of alkene **37** (111 mg, 0.21 mmol) afforded the title compound **38** (70 mg, 61%) as a viscous colourless oil. ν_{max} (film) 2928, 2853, 1755, 1713, 1676, 1613, 1494, 1463, 1433, 1339, 1217, 1159, 1059, 1029, 914, 837, 733, 697, 500 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.20–1.48 (10H, m, 6′-H, 7′-H, 8′-H, 9′-H, 10′-H), 1.49–1.62 (2H, m, 11′-H), 1.65–1.90 (3H, m, 1′-H$_A$, 13′-H), 1.92–2.08 (3H, m, 1′-H$_B$, 5′-H), 2.10 (3H, s, 16′-H), 2.12–2.22 (1H, m, 2′-H$_A$), 2.23–2.35 (1H, m, 2′-H$_B$), 2.42–2.53 (2H, m, 14′-H), 3.35–3.42 (1H, m, 12′-H), 3.89 (3H, s, OMe), 3.95 (3H, s, OMe), 4.42 (1H, d, J=11.6 Hz, OC*H*$_A$H$_B$Ph), 4.50 (1H, d, J=11.6 Hz,

OCH_AH_BPh), 5.29 (1H, d, $J=8.6$, 3.3 Hz, 3-H), 5.33–5.48 (2H, m, 3′-H, 4′-H), 6.41 (1H, s, 4-H), 6.42 (1H, s, 6-H), 7.30–7.37 (5H, m, OCH_2Ph); ^{13}C NMR (75 MHz, $CDCl_3$) 22.7 (CH_2, C-2′), 25.3 (CH_2), 27.2 (CH_2), 27.5 (CH_2), 29.2 (CH_2), 29.5(CH_2), 29.6 (CH_2), 29.7 (CH_2), 29.9 (CH_3, C-14′), 33.7 (CH_2), 35.0 (CH_2, C-1′), 39.3 (CH_2, C-14′), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 70.7 (CH_2, CH_2Ph), 77.9 (CH, C-12′), 79.3 (CH, C-3), 97.4 (CH, C-6), 98.7 (CH, C-4), 106.9 (quat., C-7a), 127.5 (CH, OCH_2Ph), 127.5 (CH, C-3′), 127.8 (CH, OCH_2Ph), 128.3 (CH, OCH_2Ph), 131.7 (CH, C-4′), 138.8 (quat., OCH_2Ph), 155.1 (quat., C-3a), 159.6 (quat., C-7), 166.7 (quat., C-5), 168.4 (quat., C-1), 208.9 (quat., C-15′); *m/z* (FAB+, %) 537 (MH^+, 5), 429 (75), 389 (10), 207 (11), 191 (17), 165 (10), 120 (11), 91 (52), 89 (32); HRMS (FAB+): found MH^+, 537.3226. $C_{33}H_{44}O_6$ requires 537.3216.

4.5.9. 5,7-Dimethoxy-3-(12′-hydroxy-15′-oxohexadec-1-yl)-(3*H*)-isobenzofuran-1-one 39. Using a similar method to that described above for the preparation of alcohol **14**, benzyl ether **38** (60 mg, 0.11 mmol) was reacted with hydrogen over 10% palladium on charcoal to afford the title compound **39** as a colourless oil (48 mg) that was not purified further before use in the subsequent steps.

4.5.10. (±)-CJ-13,103 5. Using a similar method to that described above for the preparation of CJ-13,015 **3**, TPAP oxidation of alcohol **39** (40 mg, 0.09 mmol) afforded the title compound **5** (25 mg, 44% from **38**) as a colourless solid. ^1H and ^{13}C NMR data obtained were in agreement with the literature values.[4] Mp 103–104 °C; ν_{max} (film) 2921, 2848, 2100, 1757, 1641, 1470, 1337, 1218, 1160, 837, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 1.20–1.37 (14H, m, 3′-H, 4′-H, 5′-H, 6′-H, 7′-H, 8′-H, 9′-H), 1.38–1.49 (2H, m, 2′-H), 1.52–1.61 (2H, m, 10′-H), 1.64–1.75 (1H, m, 1′-H_A), 1.93–2.02 (1H, m, 1′-H_B) 2.19 (3H, s, 16′-H), 2.44 (2H, t, $J=7.4$ Hz, 11′-H), 22.66–2.72 (4H, m, 13′-H, 14′-H), 3.89 (3H, s, OMe), 3.95 (3H, s, OMe), 5.30 (1H, dd, $J=8.0$, 3.7 Hz, 3-H), 6.41 (1H, s, 4-H), 6.41 (1H, s, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$) 23.8 (CH_2, C-10′), 24.6 (CH_2, C-2′), 29.2 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.5 (CH_2) 30.0 (CH_3, C-16′), 34.8 (CH_2, C-1′), 36.0 (CH_2, C-14′), 36.9 (CH_2, C-13′), 42.8 (CH_2, C-11′), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 80.0 (CH, C-3), 97.4 (CH, C-6), 98.6 (CH, C-4), 107.0 (quat., C-7a), 155.2 (quat., C-3a), 159.6 (quat., C-7), 166.6 (quat., C-5), 168.6 (quat., C-1), 207.4 (quat., C-15′), 209.8 (quat., C-12′); *m/z* (EI+, %) 446 (M^+, 9), 428 (18), 375 (23), 348 (12), 333 (87), 207 (46), 193 (100), 165 (14), 99 (17), 71 (11), 57 (12), 55 (20), 43 (27); HRMS (EI+): found M^+, 446.2678. $C_{26}H_{38}O_6$ requires 446.2668.

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References and notes

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