Available online at www.sciencedirect.com

ScienceDirect

Tetrahedron

Tetrahedron 63 (2007) 5379–5385

# Synthesis of indole analogues of the anti-*Helicobacter pylori* compounds CJ-13,015, CJ-13,102, CJ-13,104 and CJ-13,108

Zoe E. Wilson, Amanda M. Heapy and Margaret A. Brimble*

*Department of Chemistry, University of Auckland, 23 Symonds Street, Private Bag 92019, Auckland 1142, New Zealand*

Received 8 February 2007; revised 28 March 2007; accepted 19 April 2007
Available online 25 April 2007

**Abstract**—Racemic syntheses of indole analogues of four phthalide-containing anti-*Helicobacter pylori* agents CJ-13,015, CJ-13,102, CJ-13,104 and CJ-13,108 are reported via manipulation of a common intermediate. This intermediate was formed by the N-alkylation of 4,6-dimethoxyindole with a long chain bromide followed by further chain extension. Oxidation, acetylation, or Barton–McCombie deoxygenation of the intermediate followed by Wacker oxidation afforded three analogues whilst further reduction of one analogue afforded the final analogue.

## 1. Introduction

*Helicobacter pylori* has been shown by epidemiologic studies to have an etiological role in several diseases, including gastric and duodenal ulcers, distal gastric cancer and mucosal-associated lymphoid tissue (MALT) lymphoma (cancer of the B cell lymphocytes). It has been estimated that *H. pylori* was the cause of 5.6% of all cancers worldwide in 2002.[1] The microaerophilic, Gram negative bacteria[2] have been estimated to infect the stomach of over half of the world's population[3] and in most cases infection will persist for the lifetime of an individual without medical intervention.[4]

The currently available treatments for *H. pylori* infections are complex, involving multiple broad spectrum antibiotics in combination with proton pump inhibitors and/or bismuth salts and less than 80% of patients will be successfully treated by first line therapy.[5] Patient compliance can be a serious problem due to the complicated nature of the treatment programme as well as the sometimes unpleasant side effects. *H. pylori* is also becoming increasingly resistant to currently used antibiotics such as clarithromycin and metronidazole.[5] Consequently, there is considerable need for the development of a novel, specific antibiotic against *H. pylori*, preferably which can be used effectively as a monotherapy, allowing widespread eradication of the bacteria and a reduction in the incidence of their associated diseases.[6]

In 1997, Dekker et al.[7] reported the isolation of seven new antibiotics from the basidiomycete *Phanerochaete velutina* CL6387 (Fig. 1). These compounds exhibited selective, bactericidal activity against *H. pylori*.[7]

A six-step racemic synthesis of CJ-13,015 **1** was reported[8] by Mondal and Argade in 2004. The synthetic strategy was based on the union of 3,5-dimethoxyphthalide with 8-bromo-1-octanol and 5-methyl furfural.[8] The synthetic strategy used lacked flexibility for the synthesis of any other members of the CJ family.

The racemic synthesis of CJ-13,015 **1**, CJ-13,102 **2**, CJ-13,104 **3**, CJ-13,108 **4** and CJ-13,103 **5** was reported[9] in 2005. The flexible synthetic route involved coupling of a common phthalide aldehyde fragment with one of three appropriate ylides.[9] The enantioselective synthesis of the more complex spiroacetal-containing phthalides CJ-12,954 **6** and CJ-13,014 **7** has also recently been reported.[10] In this case a phthalide aldehyde was coupled with two heterocycle-activated spiroacetal sulfones using a modified Julia–Kocienski olefination.[10]

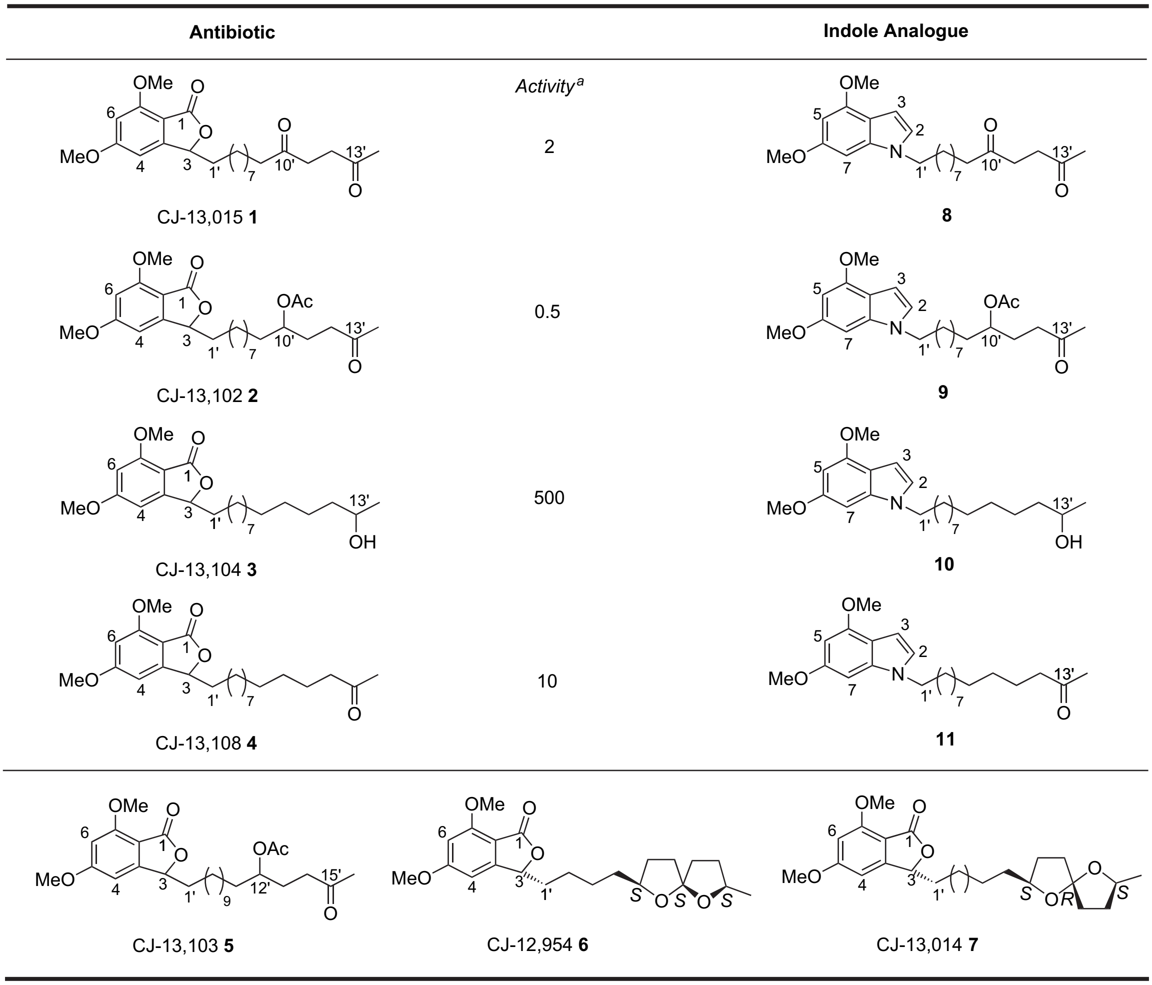
The 4,6-dimethoxyindole ring is a good bioisosteric replacement for the 5,7-dimethoxyphthalide ring system. Thus it was decided to prepare 4,6-dimethoxyindole analogues **8**, **9**, **10** and **11** of the 5,7-dimethoxyphthalides **1**, **2**, **3** and **4** in an attempt to increase activity against *H. pylori* (Fig. 1).

---

*Keywords*: Indole; *Helicobacter pylori*; Analogues.

* Corresponding author. Tel.: +64 9 3737599x88259; fax: +64 9 3737599; e-mail: m.brimble@auckland.ac.nz

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.04.067

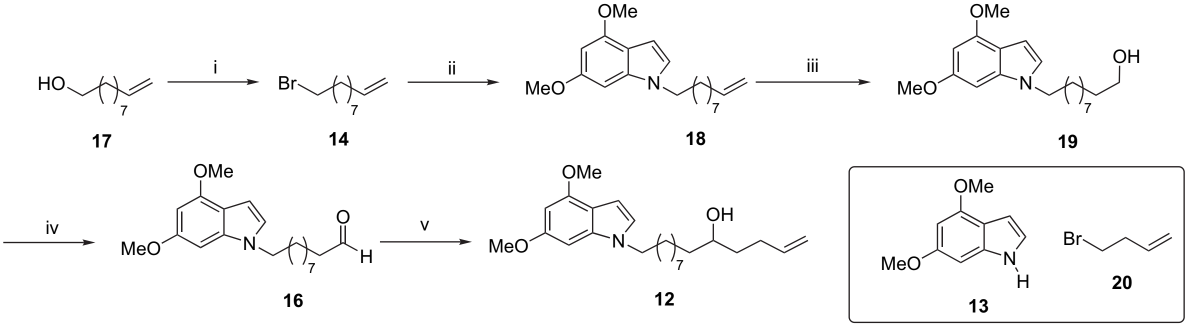


[a] mg/disk that gives a 15 mm zone of inhibition

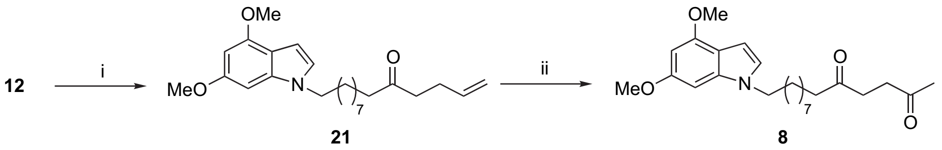
**Figure 1**. Structures of phthalide antibiotics (**1**–**7**) isolated from *Phanerochaete velutina*, the anti-*Helicobacter pylori* activity of antibiotics **1**–**4** and the structures of indole analogues synthesized (**8**–**11**).

## 2. Results and discussion

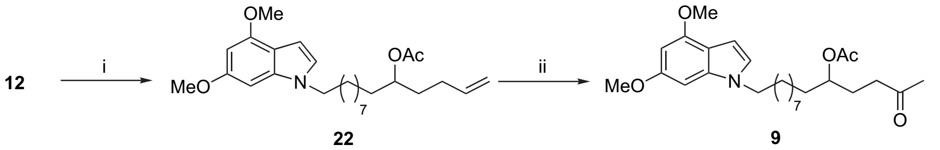
The work reported herein, describes the racemic synthesis of indole analogues (**8**–**11**) of four members of the CJ-13 family of antibiotics (**1**–**4**, respectively). The economical synthetic strategy adopted involved the synthesis of all four analogues from a common advanced intermediate **12** (Scheme 1). Oxidation (in the case of **8**), acetylation (for **9**) or Barton–McCombie deoxygenation (for **11**) of intermediate **12** was followed by Wacker oxidation to install the 13′ ketone common to these analogues (Schemes 2–4). Reduction of **11** afforded the final analogue, **10** (Scheme 4).



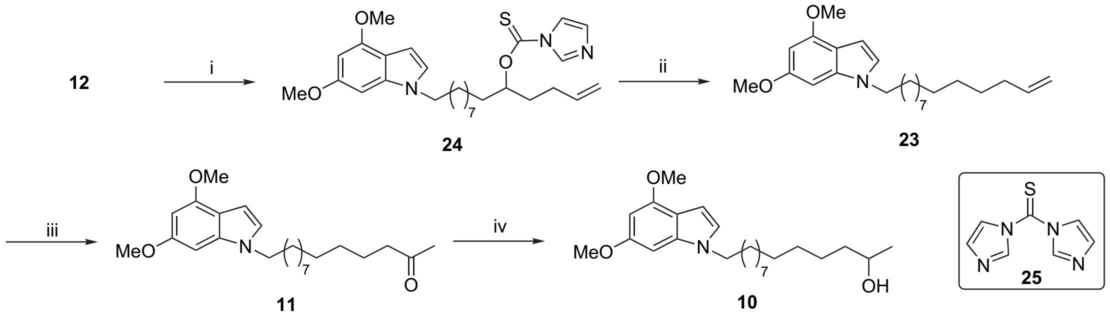
**Scheme 1**. Reagents and conditions: (i) $CBr_4$, $PPh_3$, $CH_2Cl_2$, 0 °C, 1 h, 85%; (ii) $KOH_{(s)}$, DMSO, **13**, rt, 45 min, then **14**, rt, 45 min, 82%; (iii) $BH_3\cdot SMe_2$, THF, rt, 18 h, then MeOH, NaOH, $H_2O_2$, rt, 6 h, 57%; (iv) tetrapropylammonium perruthenate, 4-methylmorpholine-*N*-oxide, 4 Å molecular sieves, $CH_2Cl_2$, rt, 3 h, 71%; (v) Mg, $CH_2BrCH_2Br$, $I_2$, **20**, $Et_2O$, then $Et_2O$, **16**, −78 °C, 15 min, 75%.



**Scheme 2**. Reagents and conditions: (i) tetrapropylammonium perruthenate, 4-methylmorpholine-*N*-oxide, 4 Å molecular sieves, $CH_2Cl_2$, rt, 3 h, 63%; (ii) $PdCl_2$, CuCl, $O_2$, DMF–$H_2O$ (3:1), 2 h, 90%.



**Scheme 3**. Reagents and conditions: (i) pyridine, $Ac_2O$, *N*,*N*-4-dimethylaminopyridine, rt, 5 h, 90%; (ii) $PdCl_2$, CuCl, $O_2$, DMF–$H_2O$ (3:1), 2 h, 99%.



**Scheme 4**. Reagents and conditions: (i) **25**, THF, reflux, 2 h, 87%; (ii) *n*-$Bu_3SnH$, azobisisobutyronitrile, toluene, reflux, 1 h, 84%; (iii) $PdCl_2$, CuCl, $O_2$, DMF–$H_2O$ (3:1), 2 h, 25%; (iv) $NaBH_4$, MeOH, rt, 10 min, 83%.

### 2.1. Synthesis of unsaturated alcohol intermediate 12

The common intermediate unsaturated alcohol **12** was prepared by N-alkylation of commercially available 4,6-dimethoxyindole **13** with bromide **14**, that in turn was prepared from alcohol **17** using an Appel reaction.[11] Selective N-alkylation was achieved in 82% yield using the method of Heaney and Ley,[12] with no evidence of substitution on the indole ring being observed. Hydroboration of the resultant alkene **18** using borane–dimethylsulfide complex gave alcohol **19**, which was then oxidized to aldehyde **16** using tetrapropylammonium perruthenate (TPAP) with *N*-methylmorpholine-*N*-oxide (NMO) as a co-oxidant. Grignard extension of the alkyl chain using 3-buten-1-yl magnesium bromide **15** then afforded unsaturated alcohol intermediate **12** in an overall 21% yield (five steps).

### 2.2. Synthesis of analogue 8

For the synthesis of indole analogue **8** TPAP oxidation of alcohol intermediate **12** afforded ketone **21** in a 63% yield (unoptimized). Wacker oxidation was then used to install the second ketone functionality, completing the synthesis of analogue **8**.

### 2.3. Synthesis of analogue 9

Alcohol intermediate **12** was acetylated under standard conditions to give acetate **22** in 90% yield. Wacker oxidation of the terminal alkene then gave analogue **9** in 99% yield, providing this indole analogue in an overall yield of 19% (seven steps).

### 2.4. Synthesis of analogues 10 and 11

The synthesis of indole analogues **10** and **11** required deoxygenation of intermediate **12**. Here Barton–McCombie deoxygenation of alcohol intermediate **12** afforded alkene **23**, in 86% yield. An imidazole thiocarbonate was used as the leaving group for the Barton–McCombie deoxygenation as this could be introduced under neutral conditions, which was vital due to the presence of the sensitive 4,6-dimethoxyindole moiety.[13] Any residual tin was quenched by passing the mixture through a column of powdered potassium fluoride in silica (10% w/w) and washing with dichloromethane, as described by Harrowven and Guy.[14]

Subsequent Wacker oxidation of the terminal olefin in **23** to a ketone afforded analogue **11**. A portion of this ketone was then reduced using sodium borohydride to give analogue **10** in 83% yield.

## 3. Conclusion

4,6-Dimethoxyindole analogues of four phthalide-containing natural products that exhibit anti-*H. pylori* activity have been synthesized. The use of common intermediate **12** enabled the flexible synthesis of indole analogues **8**, **9**,

**10** and **11**. Evaluation of these compounds for their anti-*H. pylori* activity awaits further collaborative research.

## 4. Experimental

### 4.1. General

All reactions were carried out in flame or oven dried glassware under a dry nitrogen atmosphere. Tetrahydrofuran, toluene and diethyl ether were dried over sodium wire. Dichloromethane, pyridine, dimethylsulfoxide and dimethylformamide were dried over calcium hydride and methanol was dried over magnesium methoxide. All solvents were distilled prior to use. Flash chromatography was carried out using 0.063–0.1 mm silica gel with the desired solvent. Thin layer chromatography was performed using silica coated aluminium plates (60 $F_{254}$). Compounds were identified using UV fluorescence and/or staining with vanillin in methanolic sulfuric acid or a solution of ammonium heptamolybdate and cerium sulfate in aqueous sulfuric 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 a 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. $^1$H NMR data are reported as chemical shift, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quint., quintet), coupling constant (*J* Hz) and assignment. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected.

#### 4.1.1. Procedure for the synthesis of alcohol intermediate 12.

**4.1.1.1. 10-Bromodec-1-ene 14.** A solution of 9-decen-1-ol (4.9 mL, 27.4 mmol) in dichloromethane (50 mL) was cooled to 0 °C. Carbon tetrabromide (13.6 g, 41.1 mmol) and ground triphenylphosphine (10.8 g, 41.1 mmol) were added and the mixture was stirred at 0 °C for 1 h. Pentane (150 mL) was then added and the resulting orange precipitate (triphenylphosphine oxide) was filtered off and washed with ethyl acetate (20 mL). The solvent was removed from the filtrate in vacuo and the resulting oil purified by flash chromatography using hexane–ethyl acetate (4:1, $R_f$ 0.92) as eluent to afford the *title compound* **14** (4.7 g, 85%) as a clear yellow oil. The $^1$H NMR data obtained were in agreement with those reported in the literature.[11]

**4.1.1.2. 1-(9′-Decen-1′-yl)-4,6-dimethoxy-1*H*-indole 18.** A solution of 4,6-dimethoxyindole **13** (0.25 g, 1.4 mmol) in dimethylsulfoxide (5 mL) was added dropwise to a stirred solution of crushed potassium hydroxide pellets (0.32 g, 5.6 mmol) in dimethylsulfoxide (2 mL) and the mixture stirred for 45 min at room temperature. Bromoalkene **14** (0.43 mL, 2.1 mmol) was added dropwise and the reaction mixture stirred for a further 45 min. Water (4 mL) was added and the aqueous phase extracted with diethyl ether (3×20 mL) and ethyl acetate (3×20 mL). The combined organic extracts were dried over magnesium sulfate and the solvent removed in vacuo. The resulting oil was purified via flash chromatography using hexane–diethyl ether (3:2, $R_f$ 0.79) as eluent to afford the *title compound* **18** (0.11 g, 82%) as a clear yellow oil; $\nu_{max}$ (film) 2928, 2854, 1738, 1622, 1587, 1500, 1464, 1251, 1209, 1147, 1069 cm$^{-1}$; $^1$H NMR (300 MHz; $CDCl_3$) $\delta$ 1.26–1.36 (10H, m, 3′-H, 4′-H, 5′-H, 6′-H, 7′-H), 1.77 (2H, quint., *J*=7.0 Hz, 2′-H), 2.00 (2H, q, *J*=6.7 Hz, 8′-H), 3.83 (3H, s, $OCH_3$), 3.88 (3H, s, $OCH_3$), 3.96 (2H, t, *J*=7.0 Hz, 1′-H), 4.90–5.00 (2H, m, 10′-H), 5.71–5.83 (1H, m, 9′-H), 6.21 (1H, d, *J*=1.7 Hz, 5-H), 6.38 (1H, br s, 7-H), 6.48 (1H, d, *J*=3.1 Hz, 3-H), 6.85 (1H, d, *J*=3.1 Hz, 2-H); $^{13}$C NMR (75 MHz; $CDCl_3$) $\delta$ 26.8 ($CH_2$, C-3′), 28.8 ($CH_2$, C-4′), 28.9 ($CH_2$, C-7′), 29.1 ($CH_2$, C-5′), 29.3 ($CH_2$, C-6′), 30.0 ($CH_2$, C-2′), 33.7 ($CH_2$, C-8′), 46.4 ($CH_2$, C-1′), 55.2 (6-OMe), 55.6 (4-OMe), 85.5 (CH, C-7), 91.0 (CH, C-5), 98.0 (CH, C-3), 113.5 ($CH_2$, C-10′), 114.1 (quat., C-3a), 124.9 (CH, C-2), 137.2 (quat., C-7a), 139.0 (CH, C-9′), 153.7 (quat., C-4), 157.2 (quat., C-6); *m/z* (EI+, %) 316 (28), 315 ($M^+$, 100), 191 (13), 190 (22), 176 (8), 55 (6), 41 (8); HRMS (EI+): found $M^+$, 315.2195. $C_{20}H_{29}NO_2$ requires 315.2198.

**4.1.1.3. 10-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)decan-1-ol 19.** Alkene **18** (83 mg, 0.26 mmol) was dissolved in dry tetrahydrofuran (1.5 mL) at 0 °C. Borane–dimethylsulfide complex ($BH_3 \cdot SMe_2$) (0.6 mL, 10 mmol) was then added dropwise to the solution over 30 min. The reaction mixture was allowed to warm to room temperature and stirred for 18 h. The reaction was quenched by the addition of methanol (1 mL) followed by sodium hydroxide (3 M, 0.7 mL) and hydrogen peroxide (27% in water, 0.7 mL), then left to stir for 6 h. The mixture was extracted with diethyl ether (3×20 mL). The combined organic extracts were washed with brine (50 mL), dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography using hexane–ethyl acetate (7:3, $R_f$ 0.35) as eluent to afford the *title compound* **19** (63 mg, 57%) as a colourless viscous liquid; $\nu_{max}$ (film) 3392, 2927, 2853, 1623, 1587, 1499, 1465, 1251, 1210, 1147, 1068, 1048, 935, 805, 758, 708 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.14–1.42 (12H, m, 3-H, 4-H, 5-H, 6-H, 7-H, 8-H), 1.48–1.54 (2H, m, 2-H), 1.72–1.78 (2H, m, 9-$CH_2$), 3.59 (2H, t, *J*=6.6 Hz, $CH_2OH$), 3.85 (3H, s, $OCH_3$), 3.90 (3H, s, $OCH_3$), 3.99 (2H, t, *J*=7.1 Hz, $NCH_2$), 6.21 (1H, s, 5′-H), 6.39 (1H, s, 7′-H), 6.48 (1H, d, *J*=3.2 Hz, 3′-H), 6.86 (1H, d, *J*=3.2 Hz, 2′-H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 23.4, 26.8, 29.1, 29.3, 29.3, 29.4, 29.9, 32.6 ($CH_2$, C-9, C-8, C-7, C-6, C-5, C-4, C-3, C-2), 46.4 ($NCH_2$), 55.2 ($OCH_3$), 55.6 ($OCH_3$), 62.8 ($CH_2OH$), 85.4 (CH, C-7′), 90.9 (CH, C-5′), 97.9 (CH, C-3′), 113.4 (quat., C-3a′), 124.9 (CH, C-2′), 137.1 (quat., C-7a′), 153.6 (quat., C-4′), 157.1 (quat., C-6′); *m/z* (EI+, %), 335 (11), 334 (53), 333 ($M^+$, 100), 332 (9), 191 (5), 190 (12), 176 (6), 120 (4), 91 (4), 89 (7); HRMS (FAB+): found $M^+$, 333.2309. $C_{20}H_{31}NO_3$ requires 333.2304.

**4.1.1.4. 10-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)decanal 16.** Tetrapropylammonium perruthenate (3 mg, 0.01 mmol) was added to a mixture of dry dichloromethane (2 mL), 4-methylmorpholine-*N*-oxide (30 mg, 0.25 mmol), powdered 4 Å molecular sieves (0.300 mg) and alcohol **19** (55 mg, 0.16 mmol). The reaction mixture was stirred at room temperature for 3 h, then filtered through silica and the residue washed with hexane (100 mL) and ethyl acetate (100 mL). The solvents were removed in vacuo and the resultant residue was purified by flash chromatography using hexane–ethyl acetate (1:1, $R_f$ 0.81) as eluent to afford the *title compound* **16** (39 mg, 71%) as a colourless viscous liquid; $\nu_{max}$ (film) 2929, 2854, 1723, 1621, 1586, 1499, 1456, 1250, 1210, 1147, 1047, 935, 806, 758, 710 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.20–1.27 (10H, m, 8-H, 7-H, 6-H, 5-H, 4-H), 1.57–1.60 (2H, m, 9-H), 1.77–1.82 (2H, m, 3-H), 2.36–2.42 (2H, m, CH$_2$C=O), 3.86 (3H, s, OCH$_3$), 3.91 (3H, s, OCH$_3$), 4.00 (2H, t, $J$=7.1 Hz, NCH$_2$), 6.21 (1H, s, 5′-H), 6.39 (1H, s, 7′-H), 6.49 (1H, d, $J$=3.1 Hz, 3′-H), 6.87 (1H, d, $J$=3.1 Hz, 2′-H), 9.74 (1H, t, $J$=1.8 Hz, CHO); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 22.0, 26.8, 29.0, 29.1, 29.2, 29.7, 30.0 (CH$_2$, C-9, C-8, C-7, C-6, C-5, C-4, C-3), 43.8 (CH$_2$C=O), 46.4 (NCH$_2$), 55.3 (OCH$_3$), 55.7 (OCH$_3$), 85.4 (CH, C-7′), 91.0 (CH, C-5′), 98.1 (CH, C-3′), 113.6 (quat., C-3a′), 125.0 (CH, C-2′), 137.3 (quat., C-7a′), 153.7 (quat., C-4′), 157.2 (quat., C-6′), 202.8 (C=O); *m/z* (EI+, %) 332 (57), 331 (M$^+$, 100), 330 (10), 316 (7), 302 (10), 190 (25), 177 (8), 176 (10), 91 (7), 89 (11); HRMS (EI+): found M$^+$, 331.2140. C$_{20}$H$_{29}$NO$_3$ requires 331.2147.

**4.1.1.5. 14-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)tetradec-1-en-5-ol 12.** Magnesium turnings (81 mg, 3.3 mmol) were stirred under argon overnight before dibromoethane (catalytic) and a solution of diethyl ether (4 mL) containing a crystal of iodine were added alternatively in portions, with heating to initiate the reaction. 4-Bromo-1-butene **20** (0.31 mL, 3.0 mmol) was then added dropwise, with gentle heating with a heat gun to maintain gaseous evolution. The reaction mixture changed colour from pale brown to colourless, indicating formation of the Grignard reagent, at which point the reaction mixture was cooled to −78 °C. Aldehyde **16** (0.10 g, 0.3 mmol) was then added dropwise and the mixture stirred for 15 min at −78 °C before addition of a saturated ammonium chloride solution (12 mL). The reaction mixture was filtered through a layer of silica that was washed with diethyl ether (10 mL). The layers were separated and the aqueous layer extracted with diethyl ether (3×5 mL). The combined organic extracts were washed with brine (20 mL), dried over magnesium sulfate and the solvent removed in vacuo. The resulting yellow oil was purified via flash chromatography using hexane–ethyl acetate (3:2, $R_f$ 0.77) as eluent to afford the *title compound* **12** (88 mg, 75%) as a yellow oil; $\nu_{max}$ (film) 3418, 3073, 2928, 2853, 1736, 1622, 1587, 1499, 1456, 1251, 1210, 1147, 1069 cm$^{-1}$; $^1$H NMR (400 MHz; CDCl$_3$) $\delta$ 1.23–1.29 (12H, m, 7-H, 8-H, 9-H, 10-H, 11-H, 12-H), 1.41 (2H, m, 6-H), 1.47–1.55 (2H, m, 4-H), 1.78–1.80 (2H, m, 13-H), 2.12–2.19 (2H, m, 3-H), 3.57–3.59 (1H, m, 5-H), 3.84 (3H, s, OCH$_3$), 3.90 (3H, s, OCH$_3$), 3.99 (2H, t, $J$=7.1 Hz, 14-H), 4.94–5.06 (2H, m, 1-H), 5.80–5.86 (1H, m, 2-H), 6.21 (1H, d, $J$=1.7 Hz, 5′-H), 6.39 (1H, d, $J$=1.7 Hz, 7′-H), 6.48 (1H, d, $J$=3.2 Hz, 3′-H), 6.87 (1H, d, $J$=3.2 Hz, 2′-H); $^{13}$C NMR (100 MHz; CDCl$_3$) $\delta$ 21.9 (CH$_2$, C-7), 25.5 (CH$_2$, C-12), 29.0 (CH$_2$, C-3), 29.2 (CH$_2$, C-11), 29.3 (CH$_2$, C-9), 29.4 (CH$_2$, C-10), 29.5 (CH$_2$, C-8), 30.0 (CH$_2$, C-13), 36.4 (CH$_2$, C-6), 37.4 (CH$_2$, C-4), 46.4 (CH$_2$, C-14), 55.2 (6-OMe), 55.7 (4-OMe), 71.4 (CHOH, C-5), 85.5 (CH, C-7′), 91.0 (CH, C-5′), 98.0 (CH, C-3′), 113.5 (quat., C-3a′), 114.6 (CH$_2$, C-1), 125.0 (CH, C-2′), 137.2 (quat., C-7a′), 138.6 (CH, C-2), 153.7 (quat., C-4′), 157.2 (quat., C-6′); *m/z* (EI+, %) 388 (26), 387 (M$^+$, 100), 369 (14), 332 (14), 331 (6), 191 (9), 190 (16), 41 (7); HRMS (EI+): found M$^+$, 387.2772. C$_{24}$H$_{37}$NO$_3$ requires 387.2773.

### 4.1.2. Procedure for the synthesis of analogue 8.

**4.1.2.1. 14-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)tetradec-1-en-5-one 21.** Using a similar method to that described above for the preparation of aldehyde **16**, alkene **12** (45 mg, 0.12 mmol) was oxidized using tetrapropylammonium perruthenate (2 mg, 0.006 mmol) to afford the *title compound* **21** (15 mg, 63%) as a colourless liquid; $\nu_{max}$ (film) 2927, 2853, 1713, 1587, 1499, 1455, 1251, 1210, 1147, 1069, 935, 736; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.18–1.29 (10H, m, 12-H, 11-H, 10-H, 9-H, 8-H), 1.52 (2H, m, 7-H), 1.78 (2H, m, 13-H), 2.30–2.40 (4H, m, 2×CH$_2$C=O), 2.46–2.49 (2H, CH$_2$CH=CH$_2$), 3.47 (3H, s, OCH$_3$), 3.91 (3H, s, OCH$_3$), 4.00 (2H, t, $J$=7.1 Hz, NCH$_2$), 4.98–5.05 (2H, m, CH=CH$_2$), 5.80 (1H, m, CH=CH$_2$), 6.21 (1H, s, 5′-H), 6.39 (1H, s, 7′-H), 6.48 (1H, d, $J$=3.2 Hz, 3′-H), 6.88 (1H, d, $J$=3.2 Hz, 2′-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 23.7, 26.9, 27.8, 29.2, 29.3, 29.35, 29.7, 30.0 (CH$_2$, C-13, C-12, C-11, C-10, C-9, C-8, C-7, C-3), 41.8 (CH$_2$C=O), 42.8 (CH$_2$C=O), 46.5 (NCH$_2$), 55.3 (OCH$_3$), 55.8 (OCH$_3$), 85.6 (CH, C-7′), 91.1 (CH, C-5′), 98.1 (CH, C-3′), 113.6 (quat., C-3a′), 115.1 (CH$_2$, C-1), 125.0 (CH, C-2′), 137.2 (quat., C-7a′), 137.3 (CH, C-2), 153.8 (quat., C-4′), 157.2 (quat., C-6′), 210.4 (quat., C=O); *m/z* (EI+, %) 387 (16), 386 (64), 385 (M$^+$, 100), 190 (10), 124 (8), 123 (7), 120 (11), 91 (11), 80 (14), 89 (18); HRMS (EI+): found M$^+$, 385.2602. C$_{24}$H$_{35}$NO$_3$ requires 385.2617.

**4.1.2.2. 14-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)tetradecane-2,5-dione 8.** A solution of alkene **21** (15 mg, 0.039 mmol) in dimethylformamide (1.5 mL) was added to a mixture of palladium(II) chloride (4 mg, 0.02 mmol), copper(I) chloride (10 mg, 0.05 mmol) in dimethylformamide (3 mL) and water (1 mL). Oxygen gas was bubbled through the solution for 2 h. The reaction mixture was filtered through silica and the residue washed with ethyl acetate (100 mL) and hexane (50 mL). The volatile solvents were removed in vacuo and the dimethylformamide was removed under high vacuum at 40 °C to afford the *title compound* **8** (14 mg, 90%) as a dark solid; mp 79–82 °C; $\nu_{max}$ (film) 2924, 2853, 1722, 1714, 1620, 1615, 1463, 1267, 1153, 1059, 738 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.25–1.68 (14H, m, 13-H, 12-H, 11-H, 10-H, 9-H, 8-H, 7-H), 2.19 (3H, s, CH$_3$C=O), 2.04–2.06 (2H, m, 6-H), 2.46–2.48 (4H, m, 4-H, 3-H), 2.88 (3H, s, OCH$_3$), 2.96 (3H, s, OCH$_3$), 4.17–4.26 (2H, m, NCH$_2$), 6.23 (1H, s, 5′-H), 6.29 (1H, s, 7′-H), 7.53 (1H, d, $J$=3.3 Hz, 3′-H), 7.71 (1H, d, $J$=3.3 Hz, 2′-H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 23.7, 28.9, 29.1, 29.3, 29.7, 29.7, 30.3 (CH$_2$, C-13, C-12, C-11, C-10, C-9, C-8, C-7), 36.0 (CH$_3$C=O), 36.9 (CH$_2$, C-4), 38.7 (CH$_2$, C-3), 42.7 (CH$_2$, C-6), 55.3 (OCH$_3$), 55.7 (OCH$_3$), 68.1 (NCH$_2$), 88.8 (CH, C-7′), 94.8 (CH, C-5′), 98.0 (quat., C-3a′), 128.8 (CH, C-3′), 130.9 (CH, C-2′), 132.4 (quat., C-7a′), 156.6 (quat., C-4′), 167.7 (quat., C-6′), 207.4 (quat., C-2), 209.7 (quat., C-5); *m/z* (EI+, %) 402 (1), 401 (M$^+$, 2), 273 (3), 219 (5), 165 (6), 124 (8), 120 (11), 87 (11), 88 (12), 89 (21); HRMS (EI+): found M$^+$, 401.2574. C$_{24}$H$_{35}$NO$_4$ requires 401.2566.

### 4.1.3. Procedure for the synthesis of analogue 9.

**4.1.3.1. 14-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)tetradec-1-en-5-yl acetate 22.** To a solution of alcohol **12** (45 mg, 0.12 mmol) in pyridine (5 mL) were added acetic anhydride (0.1 mL, 10 mmol) and *N*,*N*-4-dimethylaminopyridine (10 mg, 0.82 mmol). The reaction mixture was stirred at room temperature for 5 h, then extracted with diethyl ether (3×20 mL), washed with brine (20 mL) and dried over magnesium sulfate. The combined organic extracts were concentrated in vacuo and the crude product was purified by flash chromatography using hexane–ethyl acetate (7:3, $R_f$ 0.64) as eluent to afford the *title compound* **22** (45 mg, 90%) as a yellow oil; $\nu_{\max}$ (film) 2928, 2854, 1731, 1587, 1500, 1455, 1250, 1210, 1069, 936, 737 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.22–1.81 (20H, m, 13-H, 12-H, 11-H, 10-H, 9-H, 8-H, 7-H, 6-H, 4-H, 3-H), 2.03 (3H, s, OCOCH$_3$), 3.85 (3H, s, OCH$_3$), 3.90 (3H, s, OCH$_3$), 3.99 (2H, t, $J$=7.0 Hz, NCH$_2$), 4.10–4.12 (1H, m, 5-H), 4.94–5.04 (2H, m, CH=CH$_2$), 5.70–5.80 (1H, m, CH=CH$_2$), 6.21 (1H, s, 7′-H), 6.39 (1H, s, 5′-H), 6.47 (1H, d, $J$=2.7 Hz, 3′-H), 6.86 (1H, d, $J$=2.7 Hz, 2′-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 21.1 (OCOCH$_3$), 25.1, 26.8, 29.1, 29.3, 29.4, 29.45, 29.5, 30.0 (CH$_2$, C-13, C-12, C-11, C-10, C-9, C-8, C-7, C-3), 33.2 (CH$_2$, C-6), 34.0 (CH$_2$, C-4), 46.4 (NCH$_2$), 55.2 (OCH$_3$), 55.7 (OCH$_3$), 73.7 (CHO), 85.5 (CH, C-7′), 91.0 (CH, C-5′), 98.0 (CH, C-3′), 113.5 (quat., C-3a′), 114.7 (CH$_2$, C-1), 124.9 (CH, C-2′), 137.2 (CH, C-2), 137.9 (quat., C-7a′), 153.7 (quat., C-4′), 157.2 (quat., C-6′), 170.7 (quat., C=O); *m*/*z* (EI+, %) 430 (28), 429 (M$^+$, 100), 370 (5), 369 (12), 332 (2), 191 (4), 190 (6), 176 (3), 43 (6), 41 (2); HRMS (EI+): found M$^+$, 429.2870. C$_{26}$H$_{39}$NO$_4$ requires 429.2879.

**4.1.3.2. 14-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)-2-oxo-tetradecan-5-yl acetate 9.** Using a similar method to that described above for the preparation of analogue **8**, Wacker oxidation of alkene **22** (45 mg, 0.12 mmol) afforded the *title compound* **9** (45 mg, 99%) as a dark wax; $\nu_{\max}$ (film) 2926, 2853, 1730, 1715, 1614, 1456, 1373, 1249, 1150, 1047, 937, 734 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.19–2.04 (16H, m, 13-H, 12-H, 11-H, 10-H, 9-H, 8-H, 7-H, 6-H), 2.14–2.16 (2H, m, 4-H), 2.45 (2H, t, $J$=7.4 Hz, 3-H), 2.88 (3H, s, CH$_3$CO), 2.96 (3H, s, OCOCH$_3$), 3.86 (3H, s, OCH$_3$), 3.91 (3H, s, OCH$_3$), 4.01 (2H, t, $J$=7 Hz, NCH$_2$), 4.73–4.84 (1H, m, CHOAc), 6.21 (1H, s, 5′-H), 6.37 (1H, s, 7′-H), 6.48 (1H, s, 3′-H), 6.88 (1H, s, 2′-H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.1 (OCOCH$_3$), 25.2, 26.8, 27.9, 29.1, 29.3, 29.6, 29.9, 30.0 (CH$_2$, C-13, C-12, C-11, C-10, C-9, C-8, C-7, C-4), 34.2 (CH$_2$, C-6), 36.5 (CH$_3$, C-1), 39.4 (CH$_2$, C-3), 46.4 (NCH$_2$), 55.2 (OCH$_3$), 55.7 (OCH$_3$), 73.5 (CHOAc), 85.4 (CH, C-7′), 90.9 (CH, C-5′), 97.9 (CH, C-3′), 113.4 (quat., C-3a′), 125.0 (CH, C-2′), 137.2 (quat., C-7a′), 153.6 (quat., C-4′), 157.1 (quat., C-6′), 170.8 (quat., OC=O), 207.9 (C=O); *m*/*z* (EI+, %) 446 (5), 445 (M$^+$, 9), 273 (3), 219 (40), 165 (7), 124 (9), 120 (13), 91 (14), 90 (16), 89 (24); HRMS (EI+): found M$^+$, 445.2817. C$_{26}$H$_{39}$NO$_5$ requires 445.2828.

### 4.1.4. Procedure for the synthesis of analogues 10 and 11.

**4.1.4.1. 4,6-Dimethoxy-1-(10′-(*N*-imidazolylthiocarbonyloxy)-tetradec-13′-enyl)-1*H*-indole 24.** 1,1′-Thiocarbonyldiimidazole **25** (0.10 g, 0.6 mmol) was added to a solution of alcohol **12** (0.088 g, 0.2 mmol) in tetrahydrofuran (1.5 mL) and the mixture heated to reflux for 2 h. The reaction mixture was poured into a separating funnel containing water (5 mL) and shaken. The aqueous layer was extracted with dichloromethane (6×5 mL) and the organic extracts were combined and washed with saturated sodium bicarbonate solution (10 mL) and brine (10 mL), then dried over magnesium sulfate. The solvent was removed in vacuo and the resulting bright yellow oil purified via flash chromatography using hexane–ethyl acetate (4:1, $R_f$ 0.31) as eluent to afford the *title compound* **24** (98 mg, 87%) as a colourless oil; $\nu_{\max}$ (film) 3130, 2928, 2850, 1725, 1622, 1587, 1499, 1465, 1384, 1326, 1283, 1250, 1147, 1096, 971 (C–O); $^1$H NMR (400 MHz; CDCl$_3$) $\delta$ 1.25–1.34 (12H, m, 3′-H, 4′-H, 5′-H, 6′-H, 7′-H, 8′-H), 1.71–1.81 (4H, m, 9′-H, 11′-H), 1.83–1.93 (2H, m, 2′-H), 2.13–2.17 (2H, m, 12′-H), 3.86 (3H, s, OCH$_3$), 3.91 (3H, s, OCH$_3$), 4.00 (2H, t, $J$=7.1 Hz, 1′-H), 4.97–5.06 (2H, m, 14′-H), 5.62–5.63 (1H, m, 10′-H), 5.76–5.83 (1H, m, 13′-H), 6.22 (1H, d, $J$=1.5 Hz, 5-H), 6.40 (1H, d, $J$=1.5 Hz, 7-H), 6.48 (1H, d, $J$=3.2 Hz, 3-H), 6.87 (1H, d, $J$=3.2 Hz, 2-H), 7.03 (1H, d, $J$=1.6 Hz, 5″-H), 7.63 (1H, d, $J$=1.6 Hz, 4″-H), 8.34 (1H, s, 2″-H); $^{13}$C NMR (100 MHz; CDCl$_3$) $\delta$ 24.9 (CH$_2$, C-8′), 26.9 (CH$_2$, C-3′), 29.2 (CH$_2$, C-12′), 29.3 (CH$_2$, C-4′, C-5′, C-6′, C-7′), 30.0 (CH$_2$, C-2′), 32.5 (CH$_2$, C-9′), 33.2 (CH$_2$, C-11′), 46.4 (CH$_2$, C-1′), 55.3 (6-OMe), 55.7 (4-OMe), 84.6 (CH, C-7), 85.5 (CH, C-5), 91.0 (CH, C-10′), 98.0 (CH, C-3), 113.5 (quat., C-3a), 115.5 (CH$_2$, C-14′), 117.8 (CH, C-5″), 125.0 (CH, C-2), 130.6 (CH, C-4″), 136.7 (CH, C-2″), 137.1 (CH, C-13′), 137.2 (quat., C-7a), 153.7 (quat., C-4), 157.2 (quat., C-6), 183.9 (quat., C=S); *m*/*z* (EI+, %) 497 (M$^+$, 1), 370 (28), 369 (M$^+$−C$_4$H$_4$N$_2$OS, 100), 367 (25), 307 (18), 257 (16), 190 (12), 179 (13), 111 (22), 68 (12), 41 (14); HRMS (EI$^+$): found M$^+$, 497.2708. C$_{28}$H$_{39}$N$_3$O$_3$S requires 497.2712.

**4.1.4.2. 4,6-Dimethoxy-1-(tetradec-13′-enyl)-1*H*-indole 23.** Tributyltin hydride (0.053 mL, 0.2 mmol) and azobisisobutyronitrile (catalytic) were added to a solution of Barton–McCombie precursor **24** in toluene (2 mL) and the mixture heated to reflux for 1 h. The reaction was then filtered through a column of silica gel containing powdered potassium fluoride (10% w/w) and washed with dichloromethane (100 mL). The solvent was removed in vacuo and the resultant oil dissolved in diethyl ether (10 mL) and washed with saturated sodium bicarbonate (5 mL), water (5 mL) and brine (5 mL). The combined aqueous layers were then extracted with diethyl ether (4×5 mL) before the organic layers were combined and dried over magnesium sulfate and the solvent removed in vacuo. The resulting bright yellow oil was purified via flash chromatography using hexane–ethyl acetate (4:1, $R_f$ 0.90) eluent to afford the *title compound* **23** (62 mg, 84%) as a colourless oil; $\nu_{\max}$ (film) 3074, 2926, 2853, 1740, 1623, 1589, 1500, 1463, 1372, 1249, 1148, 1048; $^1$H NMR (400 MHz; CDCl$_3$) $\delta$ 1.29–1.43 (4H, m, 6′-H, 7′-H), 1.56–1.59 (14H, m, 3′-H, 4′-H, 5′-H, 8′-H, 9′-H, 10′-H, 11′-H), 1.78–1.79 (2H, m, 2′-H), 2.03 (2H, q, $J$=7.7 Hz, 12′-H), 3.86 (3H, s, OCH$_3$), 3.91 (3H, s, OCH$_3$), 4.00 (2H, t, $J$=7.1 Hz, 1′-H), 4.90–5.01 (2H, m, 14′-H), 5.76–5.84 (1H, m, 13′-H), 6.22 (1H, d, $J$=1.5 Hz, 5-H), 6.40 (1H, d, $J$=1.5 Hz, 7-H), 6.49 (1H, d, $J$=3.2 Hz, 3-H), 6.88 (1H, d, $J$=3.2 Hz, 2-H); $^{13}$C NMR (100 MHz; CDCl$_3$) $\delta$ 27.5 (CH$_2$, C-3′), 28.9 (CH$_2$, C-4′), 29.1 (CH$_2$, C-5′), 29.2 (CH$_2$, C-6′), 29.5 (CH$_2$, C-7′, C-8′), 29.8 ($CH_2$, C-11′), 30.1 ($CH_2$, C-9′), 30.3 ($CH_2$, C-10′), 30.6 ($CH_2$, C-2′), 33.8 ($CH_2$, C-12′), 46.5 ($CH_2$, C-1′), 55.3 (6-OMe), 55.7 (4-OMe), 85.5 (CH, C-7), 91.0 (CH, C-5), 98.0 (CH, C-3), 113.5 (quat., C-3a), 114.1 ($CH_2$, C-14′), 125.0 (CH, C-2), 137.3 (quat., C-7a), 139.2 (CH, C-13′), 153.7 (quat., C-4), 157.2 (quat., C-6); *m/z* (EI+, %) 372 (28), 371 ($M^+$, 100), 199 (6), 190 (12), 132 (6), 129 (6), 44 (8); HRMS (EI+): found $M^+$, 371.2828. $C_{24}H_{37}NO_2$ requires 371.2824.

**4.1.4.3. 14-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)tetradecan-2-one 11.** Using a similar method to that described above for the preparation of analogue **8**, Wacker oxidation of alkene **23** (62 mg, 0.2 mmol) afforded the *title compound* **11** (16 mg, 25%) as a pale yellow solid; mp 58–59 °C; $\nu_{max}$ (film) 3053, 2929, 2855, 1712, 1618, 1586, 1499, 1457, 1373, 1265, 1211, 1148, 1069; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 1.19–1.31 (16H, m, 5-H, 6-H, 7-H, 8-H, 9-H, 10-H, 11-H, 12-H), 1.54–1.57 (2H, m, 4-H), 1.78–1.82 (2H, m, 13-H), 2.12 (3H, s, 1-H), 2.40 (2H, t, $J$=7.5 Hz, 3-H), 3.86 (3H, s, $OCH_3$), 3.91 (3H, s, $OCH_3$), 4.01 (2H, t, $J$=7.2 Hz, 14-H), 6.22 (1H, d, $J$=1.5 Hz, 5′-H), 6.40 (1H, d, $J$=1.5 Hz, 7′-H), 6.49 (1H, d, $J$=3.1 Hz, 3′-H), 6.88 (1H, d, $J$=3.1 Hz, 2′-H); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 23.8 ($CH_2$, C-4), 26.9 ($CH_2$, C-12), 29.1 ($CH_2$, C-5), 29.2 ($CH_2$, C-6, C-11), 29.4 ($CH_2$, C-7, C-10), 29.5 ($CH_2$, C-8, C-9), 29.8 ($CH_3$, C-1), 30.1 ($CH_2$, C-13), 43.8 ($CH_2$, C-3), 46.5 ($CH_2$, C-14), 55.3 (6′-OMe), 55.7 (4′-OMe), 85.5 (CH, C-7′), 91.0 (CH, C-5′), 98.0 (CH, C-3′), 113.5 (quat., C-3a′), 125.0 (CH, C-2′), 137.2 (quat., C-7a′), 153.7 (quat., C-4′), 157.2 (quat., C-6′), 209.4 (quat., C-2); *m/z* (EI+, %) 388 (28), 387 ($M^+$, 100), 190 (11), 176 (5), 43 (12); HRMS (EI+): found $M^+$, 387.2777. $C_{24}H_{37}NO_3$ requires 387.2773.

**4.1.4.4. 14-(4′,6′-Dimethoxy-1′*H*-indol-1′-yl)tetradecan-2-ol 10.** Sodium borohydride (18 mg, 0.5 mmol) was added to a solution of ketone **11** (12 mg, 0.031 mmol) in methanol (5 mL) resulting in the evolution of heat and gas. The reaction mixture was stirred at room temperature for 10 min before pouring into water (8 mL) and extracting with dichloromethane (9×5 mL). The combined organic extracts were dried over magnesium sulfate, and the solvent removed in vacuo. The resulting bright yellow oil was purified via flash chromatography using hexane–ethyl acetate (3:2, $R_f$ 0.81) as eluent to afford the *title compound* **10** (10 mg, 83%) as a pale yellow oil; $\nu_{max}$ (film) 3400, 2925, 2853, 1723, 1622, 1588, 1500, 1463, 1372, 1251, 1210, 1147, 1069; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 1.18 (3H, d, $J$=6.1 Hz, 1-H), 1.24–1.31 (18H, m, 4-H, 5-H, 6-H, 7-H, 8-H, 9-H, 10-H, 11-H, 12-H), 1.36–1.41 (2H, m, 3-H), 1.80 (2H, quint., $J$=7.1 Hz, 13-H), 3.78 (1H, q, $J$=6.2 Hz, 2-H), 3.87 (3H, s, $OCH_3$), 3.92 (3H, s, $OCH_3$), 4.01 (2H, t, $J$=7.1 Hz, 14-H), 6.22 (1H, d, $J$=1.7 Hz, 5′-H), 6.40 (1H, br s, 7′-H), 6.49 (1H, d, $J$=3.2 Hz, 3′-H), 6.88 (1H, d, $J$=3.2 Hz, 2′-H); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 23.5 ($CH_3$, C-1), 25.8 ($CH_2$, C-4), 26.9 ($CH_2$, C-12), 29.2 ($CH_2$, C-11), 29.5 ($CH_2$, C-6, C-7, C-10), 29.6 ($CH_2$, C-8, C-9), 29.6 ($CH_2$, C-5), 30.1 ($CH_2$, C-13), 39.4 ($CH_2$, C-3), 46.5 ($CH_2$, C-14), 55.3 (6-OMe), 55.8 (4-OMe), 68.2 (CHOH, C-2), 85.6 (CH, C-7′), 91.1 (CH, C-5′), 98.0 (CH, C-3′), 113.5 (quat., C-3a′), 125.0 (CH, C-2′), 137.3 (quat., C-7a′), 153.7 (quat., C-4′), 157.2 (quat., C-6′); *m/z* (EI+, %) 390 (24), 389 ($M^+$, 95), 372 (25), 371 ($M^+-H_2O$, 100), 190 (22), 55 (13), 45 (9), 41 (12), 40 (12); HRMS (EI+): found $M^+$, 389.2921. $C_{24}H_{39}NO_3$ requires 389.2930.

## References and notes

1. Mackay, J.; Jemal, A.; Lee, N. C.; Parkin, D. M. *The Cancer Atlas*, 2nd ed.; American Cancer Society: New York, NY, 2006.
2. Marshall, B. J.; Warren, J. R. *Lancet* **1984**, *323*, 1311–1315.
3. Montecucco, C.; de Bernard, M. *Microbes Infect.* **2003**, *5*, 715–721.
4. Stoicov, C.; Saffari, R.; Cai, X.; Hasyagar, C.; Houghton, J. *Gene* **2004**, *341*, 1–17.
5. Calvet, X. *Digestion* **2006**, *73*, 119–128.
6. Trust, T. J.; Alm, R. A.; Pappo, J. *Eur. J. Surg.* **2001**, *586*, 82–88.
7. Dekker, K. A.; Inagake, T.; Gootz, T. D.; Kaneda, K.; Nomura, E.; Sakakibara, T.; Sakemi, S.; Sugie, Y.; Yamauchi, Y.; Yoshikawa, N.; Kojima, N. *J. Antibiot.* **1997**, *50*, 833–839.
8. Mondal, M.; Argade, N. P. *Tetrahedron Lett.* **2004**, *45*, 5693–5695.
9. Brimble, M. A.; Flowers, C. L.; Hutchinson, J. K.; Robinson, J. E.; Sidford, M. *Tetrahedron* **2005**, *61*, 10036–10047.
10. Brimble, M. A.; Bryant, C. J. *Chem. Commun.* **2006**, 4506–4508.
11. Kobayashi, Y.; Okui, H. *J. Org. Chem.* **2000**, *65*, 612–615.
12. Heaney, H.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1973**, 499–500.
13. Hartwig, W. *Tetrahedron* **1983**, *39*, 2609–2645.
14. Harrowven, D. C.; Guy, I. L. *Chem. Commun.* **2004**, 1968–1969.