Hydrogen-Bonded Xanthones as Potential UV Absorbers: The Synthesis of Xanthones from Bio-Renewable Cardanol Utilizing a Ceric Ammonium Sulfate (CAS)-Mediated Oxidation Reaction

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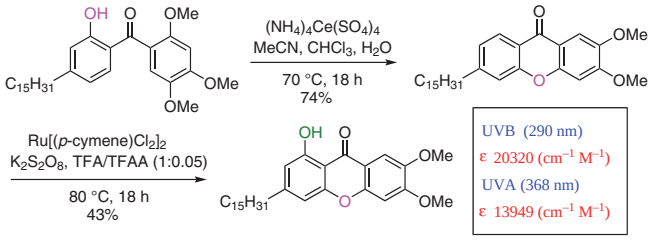

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Abstract The synthesis of hydrogen-bonded xanthones by using biorenewable hydrogenated cardanol (3-pentadecylphenol) is described. Hydrogenated cardanol was initially converted into various hydroxybenzophenones. These benzophenones were converted into xanthones by utilizing an oxidative ceric ammonium sulfate-mediated reaction. A subsequent ruthenium-mediated late-stage oxidation of the xanthones provided hydrogen-bonded xanthones, which displayed good UVA and UVB absorbing properties.

Key words cardanols, benzophenones, ceric ammonium sulfate, oxidative addition, xanthones, UV absorbers

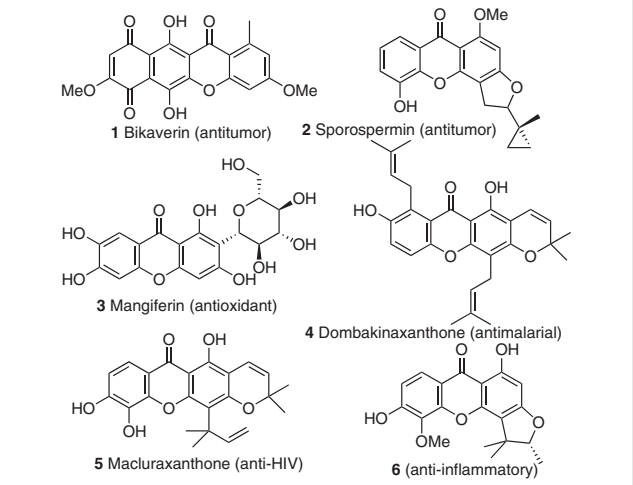


Figure 1 Examples of biologically active xanthones

Xanthones[2–4] belong to a class of compounds that display extensive biological activities, including significant antitumor,[5] antioxidant,[3] antimalarial,[6] antiinflammatory,[7] and anti-HIV activity.[8] A few examples are shown in Figure 1. These include bikaverin (**1**), sporospermin (**2**), mangiferin (**3**), dombakinaxanthone (**4**), macluraxanthone (**5**), and the antiinflammatory xanthone **6**. As a result, many synthetic approaches towards the assembly of the xanthone core have been developed.[3,9]

We have recently reported on a new method for the synthesis of xanthones and related compounds.[10] This involved the treatment of phenol-containing benzophenones with ceric ammonium sulfate (CAS) that allowed for an oxidative cyclization to form xanthones and related products.[11]

In addition, our group has demonstrated the use of bio-renewable resources for the synthesis of new UV absorbers.[12] Utilizing anacardic acids and cardanols extracted from cashew nut shells, we were able to synthesize a range of hydrogen-bonded aromatic and heteroaromatic compounds, and their UV spectra were obtained. We found that two cardanol-derived triazines **7** and **8** (Figure 2) showed excellent characteristics to be potential UV absorbers.[12] Notably, triazine **8** showed absorbance in both the UVA and UVB regions with experimental ε values of 21,452 L mol^{-1} cm^{-1} at 300 nm and 12,515 L mol^{-1} cm^{-1} at 364 nm. These results indicate that triazine **8** could be classified as a broad-spectrum UV filtering agent.

In this paper, we report on the use of our recently reported[11] ceric ammonium sulfate (CAS)-mediated oxidative cyclization reaction[13] to synthesize several hydrogen-bonded xanthones from benzophenones intermediates. The benzophenones were synthesized, in part, from the bio-

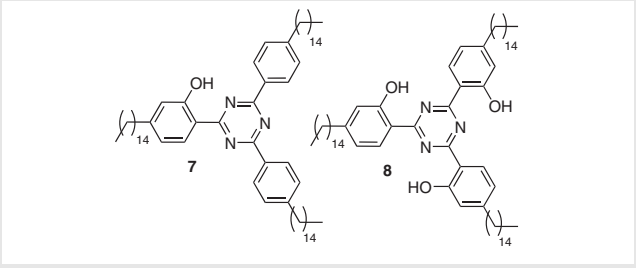
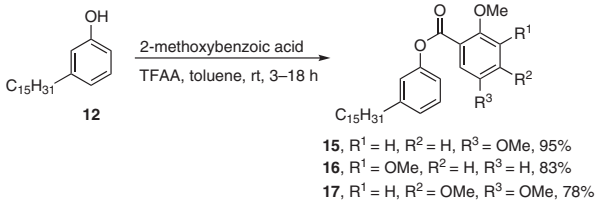


Figure 2 Hydrogen-bonded triazines synthesized from bio-renewable cardanol

renewable starting material hydrogenated cardanol (3-pentadecylphenol). We also report on the UV absorption properties of the synthesized hydrogen-bonded xanthones.

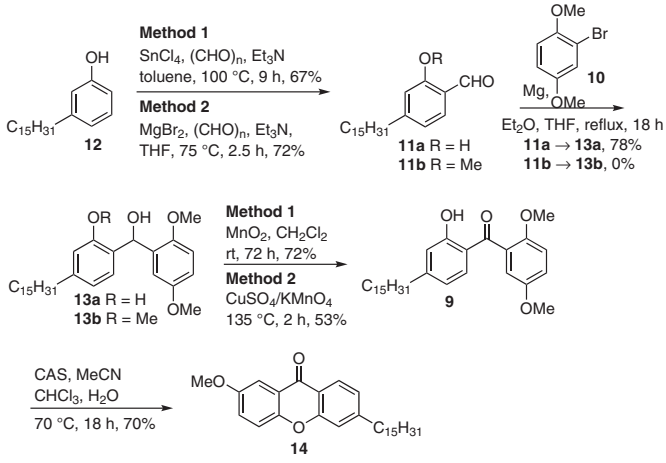
As a starting point for the construction of the desired xanthones, we chose to attempt the assembly of the hydrogen-bonded benzophenone **9** by means of the addition of the aromatic Grignard reagent derived from **10** to benzaldehyde **11a**. In turn, we anticipated that benzaldehyde **11a** could be obtained from hydrogenated cardanol (**12**). Indeed, by utilizing standard formylation conditions, or a greener $MgBr_2$-mediated protocol, hydrogenated cardanol was converted into benzaldehyde **11a** (Scheme 1). Reaction of **11a** with the Grignard reagent derived from 1-bromo-2,5-dimethoxybenzene (**10**) resulted in the formation of the secondary alcohol **13a**. The alcohol **13a** was then oxidized to the required benzophenone **9**, by utilizing MnO_2 or by an alternative solvent-free method using $CuSO_4/KMnO_4$. As our first CAS-mediated test example, benzophenone **9** was exposed to ceric ammonium sulfate to afford the desired xanthone **14** in a good yield of 70%. In this case, slightly modified reaction conditions for the CAS reaction were employed, in that the reaction mixture was heated to 70 °C instead of conducting the reaction at room temperature.[11] On repeating the Grignard reaction, we found that the reaction did not provide reproducible yields. This might be a result of the phenol on benzaldehyde **11** interfering with the reaction. Therefore, an alternative method for the synthesis of the benzophenone **9** had to be sought. Furthermore, our attempts at forming other derivatives of the secondary alcohol were unsuccessful. For example, the attempted synthesis of **13b** from benzaldehyde **11b** and **10** through a Grignard reaction met with failure.

Reacting hydrogenated cardanol (**12**) with three different benzoic acids in the presence of TFAA in the nonchlorinated solvent toluene provided the three esters **15**–**17** in good yields, as shown in Scheme 2. The same reaction could also be conducted in dichloromethane, as described in the experimental section. The conversion of the esters **15**, **16**, and **17** by means of a Fries rearrangement to furnish the desired hydroxybenzophenones **9**, **18**, and **19** proved to be problematic.



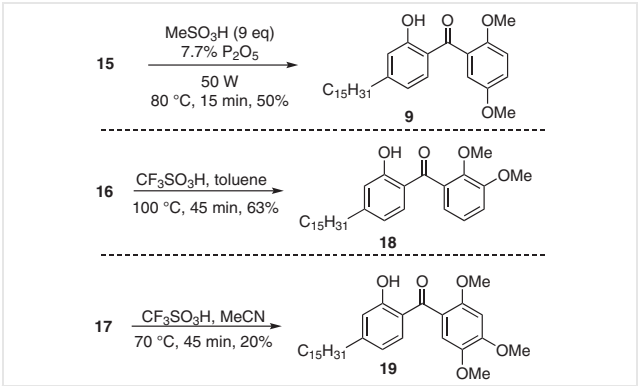
Scheme 2 Synthesis of aromatic esters as precursors for the Fries rearrangement

Experimenting with a number of conditions, such as heating with Lewis acids (e.g., $AlCl_3$), led only to decomposition. Photochemical Fries conditions disappointingly resulted in mixtures of the *ortho* and *para* products produced in low yields, while anionic Fries rearrangement conditions met with no success. The best yields for the Fries rearrangement were obtained by utilizing slightly different reaction conditions for each substrate. For example, ester **15** was



Scheme 1 Initial attempts at the synthesis of xanthones from benzophenones utilizing a ceric ammonium sulfate-mediated oxidative cyclization reaction

converted into benzophenone **9** in the presence of methanesulfonic acid and phosphorus pentoxide (Eaton's reagent[14]) in a reproducible yield of 50%, with the recovery of some starting material **15** (20%) (Scheme 3). In addition, dimethoxy aromatic ester **16** was transformed into **18** in the presence of the related stronger acid, trifluoromethanesulfonic acid in a good yield of 63%. However, the trimethoxybenzene **17** only afforded the desired benzophenone **19** in a poor yield of 20%.

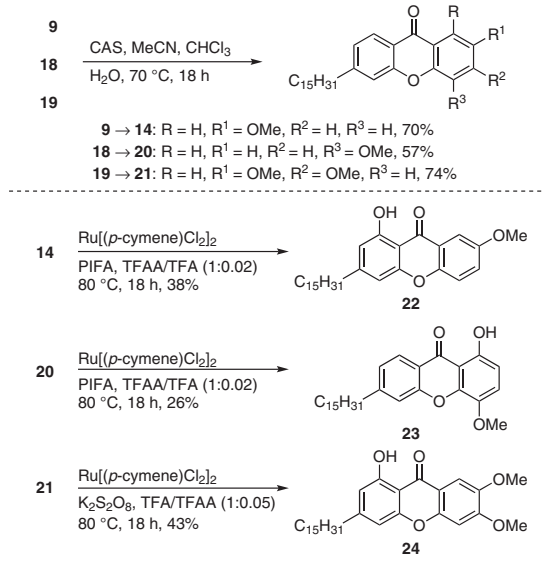


Scheme 3 Fries rearrangements for the synthesis of benzophenones

The stage was now set to conduct the oxidative-mediated CAS reaction (Scheme 4). As before benzophenone **9** yielded xanthone **14** in good yield. Benzophenone **18** furnished xanthone **20**, and benzophenone **19** afforded xanthone **21**, both in good yields. The final step of the synthesis involved the carbonyl-directed late-stage alcohol functionalization of the three xanthones **14**, **20**, and **21** with a ruthenium catalyst in the presence of [bis(trifluoroacetoxy)iodo]benzene (PIFA) or $K_2S_2O_8$, as an oxidant, and TFAA/TFA.[15] Reaction with each of the xanthones **14**, **20**, and **21** afforded the desired hydrogen-bonded xanthones **22**–**24**, albeit in poor yields. The reaction is believed to commence with a carboxylate-assisted C–H ruthenation, where the ketone of the xanthone allows for ruthenium coordination. This is followed by an oxidation-induced reductive elimination to introduce the alcohol.[15c] Interestingly, xanthones **14** and **21** exhibited similar regioselectivities, where the OH functionalization took place on the cardanol-derived half of the molecule, giving xanthones **22** and **24** respectively, whereas xanthone **20** was hydroxylated on the anisole fragment, forming xanthone **23**.

These hydroxyxanthones, together with the hydroxybenzophenones, exhibit hydrogen bonding, and are therefore potential UV absorbers.[16]

UVA and UVB rays occur at wavelengths of 315–400 and 280–315 nm respectively. Materials and human or animal skin need to be protected from these harmful rays. The six hydrogen-bonded aromatic compounds **9**, **18**, **19**, **22**–**24** that we had synthesized were examined as possible UV absorbers. The three benzophenones **9**, **18**, and **19** showed



Scheme 4 CAS-mediated oxidative cyclization reactions of benzophenones, followed by late-stage ruthenium-mediated hydroxylation

λ_{max} (nm) values in the UVA range (Table 1), while two of the hydrogen-bonded xanthones, compounds **22** and **24**, showed λ_{max} (nm) values in both the UVA and UVB ranges (Table 1 and Figure 3).

Table 1 UV Spectral Data for Hydrogen-Bonded Compounds **9**, **18**, **19**, **22**, **23**, and **24**

Compound	λ_{max} (nm)	ε (cm^{-1} M^{-1})
9	239	14997.44
	273	24839.51
	338	9045.33
18	239	19777.87
	274	30041.75
	334	10310.74
19	240	22241.57
	273	31417.47
	345	13015.81
22	240	22133.61
	265	41913.54
	290	12628.38
	384	6653.66
23	240	22405.19
	271	28470.43
	348	2896.83
	384	4118.93
24	238	26931.87
	256	40639.13
	290	20319.57
	368	13948.59

Of particular interest, xanthone **24** showed a molar absorption coefficient of 20320 L mol^{-1} cm^{-1} in the UVB range (290 nm) and a molar absorption coefficient of 13949 L mol^{-1} cm^{-1} (368 nm) in the UVA range, indicating that xanthone **24** could be potentially useful for the protection of

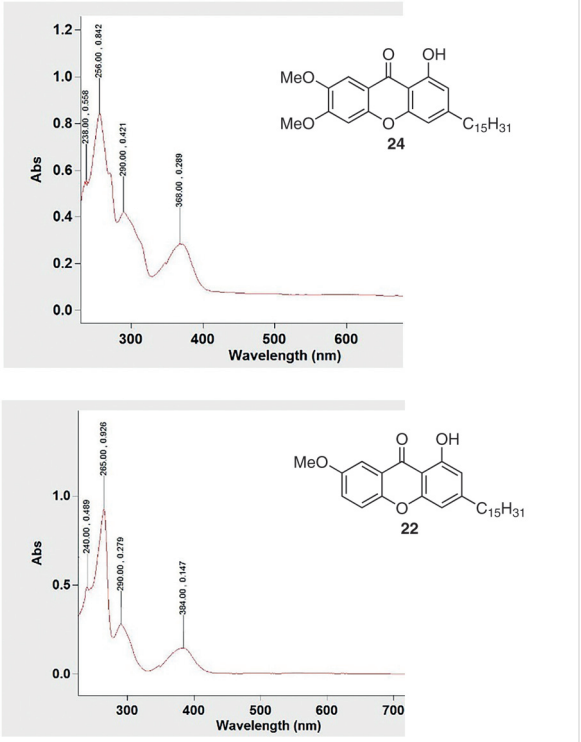


Figure 3 UV spectra of hydrogen-bonded xanthones **22** and **24**

materials or as a sunscreen. In comparison, the commercially available sunscreen agents oxybenzone (OB), 2-ethylhexyl 4-methoxycinnamate (OMC), and avobenzone are reported to show experimental molar absorption coefficients of 15150 L mol^{-1} cm^{-1} at 287 nm, 39470 L mol^{-1} cm^{-1} at 356 nm, and 31670 L mol^{-1} cm^{-1} at 310 nm, respectively.[17]

In summary, we have been able to demonstrate that utilizing the bio-renewable starting material hydrogenated cardanol allows for the assembly of xanthones through an oxidative ceric ammonium sulfate (CAS)-mediated methodology. The products were converted into hydrogen-bonded xanthones. One of the xanthones **24** synthesized showed promising UVA and UVB activities.

The solvents and reagents used for this project were purchased from ACE Chemicals or Sigma-Aldrich, and were used without purification unless otherwise stated. Acetonitrile (MeCN) was distilled over calcium hydride under nitrogen gas. Tetrahydrofuran (THF) was distilled over sodium wire and benzophenone under nitrogen gas. Thin-layer chromatography (TLC) was performed on aluminum-backed ALUGRAM Sil G/$UV_2$54 plates that were precoated with 0.25 mm silica gel 60. The compounds were detected by using an ultraviolet light source operating at 254 nm. Flash column chromatography was performed using silica gel (particle size: 0.035–0.070 mm). ^{1}H NMR spectra were recorded on spectrometers operating at 400 MHz or 300 MHz for ^{1}H NMR spectra. All ^{1}H NMR spectra were recorded in deuterated chloroform ($CDCl_3$), with all chemical shift values reported in parts per million referenced against 0.03% tetramethylsilane (TMS) as an internal standard. All ^{13}C NMR spectra were recorded at 75 or 101 MHz with chemical shifts reported on the δ scale in parts per million (ppm) relative to the central signal of $CDCl_3$ taken as 77.0 ppm. Coupling constants *J* are reported in hertz (Hz). Commonly used abbreviations in assignments include: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet. Infrared spectra were recorded where all predominant absorptions are reported in terms of wavenumbers (ν/cm^{-1}). High-resolution mass spectra (HRMS) were recorded and are quoted as the relative abundance (*m/z*). HRMS was performed only on novel compounds where no MS data were available. Melting points were recorded and are reported without correction. UV spectra were recorded using an Agilent Cary 100 UV/vis spectrophotometer, using quartz cuvettes of 1 cm path length (*l*). The data were collected over the wavelength (λ) range 200–800 nm at a scan rate of 600 nm min^{-1} and at data intervals of 1.0 nm. The data were processed using *Agilent Cary WinUV* software version 12.00, and a plot of absorption (A) versus λ was obtained. The molar absorption coefficient (ε) at each λ_{max} was determined by using the formula $A = \varepsilon^* l^* M$, where M = molarity. To prepare the hydroxybenzophenones **9**, **18**, and **19** and the hydroxyxanthones **22**, **23**, and **24** for UV absorption analysis, each compound was dissolved in 1 mL of chloroform to obtain a stock solution of 1 mg mL^{-1}. The stock solution was then appropriately diluted to a concentration of 10 ppm. All samples were thus analyzed for their UV absorption properties at a concentration of 10 ppm.

2-Hydroxy-4-pentadecylbenzaldehyde (11)[12]

Method 1: To a solution of hydrogenated cardanol (**12**; 10 g, 32.8 mmol, 1.0 equiv) in anhyd toluene (125 mL) were added $SnCl_4$ (0.854 g, 3.28 mmol, 0.4 mL, 0.1 equiv) and Et_3N (6.97 mL, 0.4 M) under N_2. The mixture was stirred at rt for 30 min. Paraformaldehyde (2.17 g, 72.16 mmol, 2.2 equiv) was then added, and the mixture stirred for another 30 min at rt, before being heated to 100 °C. The mixture was then stirred for 8 h, and the reaction was then quenched with 1 M aq HCl (100 mL). The mixture was extracted with EtOAc (3 × 100 mL), and the combined organic layers were washed sequentially with H_2O (100 mL) and brine (100 mL) then dried ($MgSO_4$), filtered, and concentrated in vacuo. The compound was purified by column chromatography (silica gel, 5% EtOAc–hexane) to give a white solid; yield: 7.4 g (67%).

Method 2: A flask purged with inert gas was charged with paraformaldehyde (295.5 mg, 9.84 mmol, 3.0 equiv) and anhyd $MgCl_2$ (624.6 mg, 6.56 mmol, 2.0 equiv) in a glovebox. Anhyd THF (20 mL) was then added, and the mixture was stirred at rt. Et_3N (663.8 mg, 0.9 mL, 6.56 mmol, 2.0 equiv) was added dropwise by syringe, and the mixture was stirred for 10 min. Hydrogenated cardanol (**12**; 1.0 g, 3.28 mmol, 1.0 equiv) was then added portionwise and the mixture was heated to 75 °C and stirred for 2.5 h. Upon completion, the reaction was quenched with 1 M aq HCl (10 mL) and extracted with EtOAc (3 × 50 mL). The organic layers were washed with H_2O (50 mL) and brine (50 mL) then dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by crystallization from MeOH to give a white solid; yield: 740 mg (72%); mp 51–52 °C; R_f = 0.86 (20% EtOAc–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.04 (s, 1 H, OH), 9.80 (s, 1 H, CHO), 7.41 (d, *J* = 7.8, 1 H, ArH-1′), 6.83–6.77 (m, 2 H, ArH-2′,3′), 2.60 (t, *J* = 7.7, 2 H), 1.61 (p, *J* = 6.9, 2 H), 1.25 (s, 24 H), 0.88 (t, *J* = 6.4, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.7 (C=O), 161.8 (ArC–OH), 153.8, 133.6, 120.5, 118.9, 117.1, 36.5, 32.0, 30.7, 29.8, 29.3, 22.8, 14.2.

2-Bromo-1,4-dimethoxybenzene (10)[18]

NBS (7.0 g, 39.8 mmol, 1.1 equiv) was added to a solution of 1,4-dimethoxybenzene (5.0 g, 36.2 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (80 mL), and the mixture was stirred at the reflux for 72 h. After cooling, the reaction was quenched with sat. aq $NaSO_3$ (40 mL) and extracted with CH_2Cl_2 (3 × 40 mL). The organic layers were washed sequentially with H_2O (50 mL) and brine (50 mL) then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20% EtOAc–hexane) to give a yellow oil; yield: 5.6 g (72%); R_f = 0.76 (20% EtOAc–hexane).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.08 (dd, *J* = 2.1, 1.3, 1 H, ArH), 6.75 (m, 2 H, ArH), 3.76 (s, 3 H, OMe), 3.68 (s, 3 H, OMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.9 (ArC–OMe), 150.2 (ArC–OMe), 119.0, 113.4, 112.8, 111.8, 56.61 (OMe), 55.69 (OMe).

2-[(2,5-Dimethoxyphenyl)(hydroxy)methyl]-5-pentadecylphenol (13)

All glassware was oven-dried for a minimum of 2 h before setting up this reaction. An oven-dried, three-necked round-bottomed flask was charged with Mg turnings (58.3 mg, 2.4 mmol, 4.0 equiv) and one granule of I_2 dissolved in anhyd Et_2O (5 mL). To this suspension was added dropwise a solution of 2-bromo-1,4-dimethoxybenzene (**10**; 520.9 mg, 2.4 mmol, 4.0 equiv) in anhyd Et_2O (1.5 mL). The mixture was gently heated for 4 h, and the surfaces of Mg turnings were repeatedly scratched using a glass rod, until the first signs of Grignard reagent formation were observed. After complete formation of the Grignard reagent, the mixture was cooled to 0 °C and a solution of 2-hydroxy-4-pentadecylbenzaldehyde (**11**; 200 mg, 0.60 mmol, 1.0 equiv) in anhyd THF (1.5 mL) was added dropwise. The resulting mixture was refluxed for 90 min, and then stirred overnight at rt. Upon completion of the reaction, the mixture was cooled to 0 °C and sat. aq NH_4Cl (20 mL) was added to quench the reaction. The organic material was extracted with EtOAc (3 × 50 mL), and the combined organic layers were washed with H_2O (50 mL) and brine (50 mL) then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 10% EtOAc–hexane) to yield a cream solid; yield: 220 mg (78%); R_f = 0.49 (20% EtOAc–hexane); mp 78–79 °C.

FTIR (solid): 3353 (O–H), 3185 (O–H), 1501 (C=C), 1252 (C–O), 1225 (C–O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.20 (s, 1 H, C–OH), 6.85–6.55 (m, 6 H, ArH), 6.12 (d, *J* = 4.5, 1 H, ArOH), 4.14 (d, *J* = 4.6, 1 H, H-1′), 3.76 (s, 3 H, OMe), 3.65 (s, 3 H, OMe), 2.52 (t, *J* = 7.7, 2 H), 1.55 (p, *J* = 7.0, 2 H), 1.26 (s, 24 H), 0.88 (t, *J* = 6.5, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9, 153.9, 150.9, 144.4, 130.8, 127.6, 122.8, 119.9, 116.9, 114.6, 113.3, 111.7, 72.8, 55.9, 55.5, 35.6, 32.0, 31.2, 29.4, 22.7.

HRMS (ESI$^+$) = *m/z* (%) = 453.3340 (100) [M – H_2O + H]$^+$, 454.3375 (30).

HRMS (ESI?): *m/z* [M – H_2O + H]$^+$ calcd for $C_{30}H_{45}O_3$: 453.3367; found: 453.3340.

(2,5-Dimethoxyphenyl)(2-hydroxy-4-pentadecylphenyl)methanone (9)

Method 1 (*Oxidation with MnO_2*): Activated MnO_2 (306 mg, 3.50 mmol, 8.0 equiv) was added to a solution of secondary alcohol **13** (200 mg, 0.44 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL), and the mixture was stirred for 5 d at rt. Upon completion of the reaction, the mixture was filtered through Celite, concentrated in vacuo under reduced pressure, and purified by column chromatography (silica gel, 15% EtOAc–hexane) to give a white solid; yield: 145 mg (73%).

Method 2 (*Solvent-free oxidation*): Secondary alcohol **3** (200 mg, 0.44 mmol, 1.0 equiv) was ground to a fine powder with a pestle and mortar, then transferred to a round-bottomed flask. Using the same pestle and mortar, $KMnO_4$ (243 mg, 1.54 mmol, 3.5 equiv) and $CuSO_4$·5 H_2O (384.5 mg, 1.54 mmol, 3.5 equiv) were ground together until they formed a fine homogeneous powder. This was then added to the round-bottomed flask containing compound **13**, and the mixture was stirred until homogeneous. The mixture was heated at 135 °C for 2 h, then cooled. EtOAc (20 mL) was added, and the reaction was quenched with sat. aq $Na_2S_2O_3$ (10 mL). The organic material was extracted with EtOAc (3 × 20 mL), and the combined organic layers were washed sequentially with H_2O (20 mL) and brine (20 mL) then dried ($MgSO_4$), filtered, and concentrated in vacuo under reduced pressure. The crude product was purified by column chromatography (silica gel, 15% EtOAc–hexane) to give a white solid; yield: 110 mg (53%).

Method 3 (*Fries rearrangement*): A microwave tube was carefully charged with P_2O_5 (65.1 mg, 0.46 mmol, 7.7% of $MeSO_3H$) to minimize exposure to the atmosphere. This was quickly followed by the addition of $MeSO_3H$ (573 mg, 5.96 mmol, 9.2 equiv) and benzoate ester **15** (305 mg, 0.65 mmol, 1.0 equiv). The tube was placed in a 50 W microwave oven and the mixture was heated at 80 °C for 15 min. The reaction was quenched with H_2O (10 mL) and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed sequentially with sat. aq $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL), then dried ($MgSO_4$) and filtered. After concentration in vacuo, the product was purified by column chromatography (silica gel, 5% EtOAc–hexane) to give a white solid; yield: 153 mg [50% (63% based on recovered starting material)]; R_f = 0.66 (20% EtOAc–hexane); mp 61–62 °C.

FTIR (solid): = 3001 (O–H), 2914 (C–H), 2849 (C–H), 1632 (C=O), 1574 (C=C), 1307 (C–O), 1229 (C–O), 1099 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.16 (s, 1 H, OH), 7.24 (d, *J* = 8.3, 1 H, ArH-3′), 7.01–6.97 (m, 1 H), 6.95–6.91 (m, 1 H), 6.83 (s, 2 H, ArH-1′,4′), 6.62 (d, *J* = 8.2, 1 H, ArH-2′), 3.77 (s, 3 H, OMe), 3.72 (s, 3 H, OMe), 2.58 (t, *J* = 7.7, 2 H), 1.61 (p, *J* = 7.2, 2 H), 1.26 (s, 24 H), 0.88 (t, *J* = 6.6, 3 H, Me).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.9 (C=O), 163.1 (C–OH), 153.1 (ArC–OMe), 153.3, 150.5 (ArC–OMe), 133.7, 128.1, 119.4, 118.0, 117.4, 116.9, 113.9, 113.0, 56.4 (OMe), 55.9 (OMe), 36.3, 31.9, 30.1, 29.7, 29.6, 29.5, 29.4, 29.3, 22.7, 14.1.

HRMS (ESI$^+$): *m/z* (%) = 469.3297 (90) [M + H]$^+$, 470.3340 (30).

HRMS (ESI?): *m/z* [M + H]$^+$ calcd for $C_{30}H_{45}O_4$: 469.3318; found: 469.3297.

2-Methoxy-6-pentadecyl-9*H*-xanthen-9-one (14)

In a round-bottomed flask, $CHCl_3$ (3 mL) and MeCN (12 mL) were used to dissolve benzophenone **9** (145 mg, 0.32 mmol, 1.0 equiv). H_2O (6 mL) was added to form a suspension to which CAS (810 mg, 1.28 mmol, 4.0 equiv) was added in portions. The mixture was then heated to 70 °C and stirred for 18 h. Upon completion of the reaction, the mixture was transferred to a separatory funnel, and EtOAc (50 mL) and H_2O (20 mL) were added. The organic layer was separated, washed sequentially with sat. aq $NaHCO_3$ (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 10% EtOAc–hexane) to give a white solid; yield: 98 mg (70%); R_f = 0.71 (20% EtOAc–hexane); mp 94–95 °C.

FTIR (solid): = 2920 (C–H), 2848 (C–H), 1651 (C=O), 1483 (C=C), 1346 (C–O), 1315, 1226 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.2, 1 H, ArH-1′), 7.71 (s, 1 H, ArH-3′), 7.42 (d, *J* = 9.2, 1 H), 7.33–7.25 (m, 2 H), 7.20 (d, *J* = 8.2, 1 H, ArH-2′), 3.92 (s, 3 H, OMe), 2.75 (t, *J* = 7.8, 2 H), 1.69 (p, *J* = 7.4, 2 H), 1.25 (s, 24 H), 0.88 (t, *J* = 6.6, 3 H, Me).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.9 (C=O), 156.3, 155.9, 151.0, 151.0, 126.5, 124.6, 124.6, 122.2, 119.3, 119.2, 117.0, 105.9, 55.9 (OMe), 36.2, 31.9, 30.9, 29.7, 29.7, 29.5, 29.4, 29.4, 29.2, 22.7, 14.1.

HRMS (ESI?): *m/z* (%) = 437.3024 (100) $[M + H]^+$, 438.3057 (30), 439.3085 (5).

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{29}H_{41}O_3$: 437.3056; found: 437.3024.

3-Pentadecylphenyl 2,5-Dimethoxybenzoate (15)

Method 1: To a two-necked flask containing 2,5-dimethoxybenzoic acid (657 mg, 3.61 mmol, 1.1 equiv) was added TFAA (1.8 mL, 13.12 mmol, 4.0 equiv) under N_2, and the solution was stirred for 15 min at rt. A solution of hydrogenated cardanol (**12**; 1.0 g, 3.28 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (20 mL) was added and the mixture was stirred at rt. for 8 h. The reaction was quenched with sat. aq $NaHCO_3$ (20 mL), and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with H_2O (50 mL) and brine (50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20% EtOAc–hexane) to give a pale-yellow low-melting solid; yield: 1.4 g (93%).

Method 2: To a two necked flask containing 2,5-dimethoxybenzoic acid (40 mg, 0.22 mmol, 1.2 equiv) was added TFAA (0.18 mL, 1.29 mmol, 7 equiv) under N_2, and the solution was stirred for 15 min at rt. A solution of hydrogenated cardanol (**12**; 55 mg, 0.18 mmol, 1.0 equiv) in anhyd toluene (3 mL) was added, and the mixture stirred at rt for 3 h. The reaction was quenched with sat. aq $NaHCO_3$ (5 mL) and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (silica gel, 20% EtOAc–hexane) to give a pale-yellow low-melting solid; yield: 80 mg (95%); R_f = 0.60 (20% EtOAc–hexane); mp 43–44.5 °C.

FTIR (solid): 2917 (C–H), 2850 (C–H), 1715 (C=O), 1584 (C=C), 1286 (C–O), 1232 (C–O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 3.2, 1 H, ArH-3′), 7.33–7.26 (m, 1 H, ArH-5′), 7.09 (dd, *J* = 9.0, 3.1, 2 H, ArH-2′,7′), 7.03 (dd, *J* = 7.8, 1.6, 2 H, ArH-4′,6′), 6.96 (d, *J* = 9.1, 1 H, ArH-1′), 3.88 (s, 3 H, OMe), 3.81 (s, 3 H, OMe), 2.62 (dd, *J* = 8.8, 6.7, 2 H), 1.62 (p, *J* = 7.3, 2 H), 1.31 (s, 24 H), 0.93 (t, *J* = 6.8, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.3 (C=O), 154.3, 153.1, 151.0, 144.6, 129.1, 125.9, 121.7, 120.3, 119.7, 119.0, 116.3, 114.1, 56.8 (OMe), 55.9 (OMe), 35.8, 32.0, 31.3, 29.7, 29.7, 29.6, 29.5, 29.4, 29.4, 22.7, 14.2.

HRMS (ESI?): *m/z* (%) = 469.3299 (100) $[M + H]^+$, 470.3334 (30), 471.3362 (5).

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{30}H_{45}O_4$: 469.3318; found: 469.3299.

3-Pentadecylphenyl 2,3-dimethoxybenzoate (16)

Method 1: TFAA (2.74 mL, 19.7 mmol, 4.0 equiv) was added to a two-necked flask containing 2,3-dimethoxybenzoic acid (987 mg, 5.41 mmol, 1.1 equiv) under N_2, and the solution was stirred for 15 min at rt. A solution of hydrogenated cardanol (**12**; 1.5 g, 4.92 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (25 mL) was then added and the mixture was stirred at rt for 18 h. The reaction was quenched with a sat. aq $NaHCO_3$ (20 mL), and the mixture was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with H_2O (20 mL) and brine (20 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20% EtOAc–hexane) to give a white solid; yield: 2.2 g (96%).

Method 2: TFAA (0.18 mL, 1.29 mmol, 7 equiv) was added to a two-necked flask containing 2,3-dimethoxybenzoic acid (40 mg, 0.22 mmol, 1.2 equiv) under N_2, and the solution was stirred for 15 min at rt. A solution of hydrogenated cardanol (**12**; 55 mg, 0.18 mmol, 1.0 equiv) in anhyd toluene (3 mL) was then added, and the mixture was stirred at rt for 18 h. The reaction was quenched with sat. aq $NaHCO_3$ (10 mL), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with H_2O (10 mL) and brine (10 mL) then dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (silica gel, 20% EtOAc–hexane) to give a white solid; yield: 70 mg (83%); R_f = 0.64 (20% EtOAc–hexane); mp 65.6–66.4 °C.

FTIR (solid): 2921 (C–H), 1731 (C=O), 1583 (C=C), 1307 (C–O), 1251 (C–O), 1210 (C–O), 1096 (C–O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (dd, *J* = 6.9, 2.5, 1 H, ArH), 7.35–7.28 (m, 1 H, ArH), 7.19–7.11 (m, 2 H, ArH), 7.10–7.02 (m, 3 H, ArH), 3.96 (s, 3 H, OMe), 3.92 (s, 3 H, OMe), 2.62 (t, *J* = 7.7, 2 H), 1.62 (p, *J* = 8.7, 3 H), 1.26 (s, 24 H), 0.88 (t, *J* = 6.8 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.6 (C=O), 153.7, 150.9, 149.7, 144.8, 129.1, 126.0, 125.5, 123.9, 122.6, 121.6, 118.9, 116.4, 61.6 (OMe), 56.1 (OMe), 35.8, 31.9, 31.3, 30.9, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 22.7, 14.1.

HRMS (ESI?): *m/z* (%) = 469.3304 (100) $[M + H]^+$, 470.3339 (30), 471.3369 (5).

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{30}H_{45}O_4$: 469.3318; found: 469.3304.

3-Pentadecylphenyl 2,4,5-Trimethoxybenzoate (17)

Method 1: TFAA (2.74 mL, 19.7 mmol, 4.0 equiv) was added to a two-necked flask containing 2,4,5-trimethoxybenzoic acid (1.15 g, 5.41 mmol, 1.1 equiv) under N_2, and the solution was stirred for 15 min at rt. A solution of hydrogenated cardanol (**12**; 1.5 g, 4.92 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (20 mL) was added, and the mixture was stirred at rt for 18 h. The reaction was quenched with a sat. aq $NaHCO_3$ (20 mL) and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with H_2O (20 mL) and brine (20 mL) then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20% EtOAc–hexane) to give a white solid; yield: 2.3 g (94%).

Method 2: TFAA (0.18 mL, 1.29 mmol, 7 equiv) was added to a two-necked flask containing 2,4,5-trimethoxybenzoic acid (47 mg, 0.22 mmol, 1.2 equiv) under N_2, and the solution was stirred for 15 min at rt. A solution of hydrogenated cardanol (**12**; 55 mg, 0.18 mmol, 1.0 equiv) in anhyd toluene (3 mL) was added and the mixture was stirred at rt for 18 h. The reaction was quenched with sat. aq $NaHCO_3$ (10 mL), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with H_2O (10 mL) and brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20% EtOAc–hexane) to give a white solid; yield: 70 mg (78%); R_f = 0.24 (20% EtOAc–hexane); mp 62.3–62.6 °C.

FTIR (solid): 2919 (C–H), 2850 (C–H), 1707 (C=O), 1578 (C=C), 1268 (C–O), 1238 (C–O), 1205 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (s, 1 H, ArH-1′), 7.29 (dd, *J* = 15.3, 7.6, 1 H, ArH), 7.08–6.99 (m, 3 H, ArH), 6.58 (s, 1 H, ArH-2′), 3.97 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 2.62 (t, *J* = 7.7, 2 H), 1.62 (p, *J* = 8.7, 3 H), 1.26 (s, 24 H), 0.88 (t, *J* = 6.8, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.9 (C=O), 156.6 (ArC–OMe), 154.2 (ArC–OMe), 151.0, 144.6, 142.6 (ArC–OMe), 129.0, 125.7, 121.8, 119.1, 114.6, 109.8, 97.8, 57.1 (OMe), 56.5 (OMe), 56.1 (OMe), 35.8, 31.9, 31.3, 29.7, 29.7, 29.6, 29.5, 29.4, 22.7, 14.1.

HRMS: (ESI?): *m/z* (%) = 499.3402 (100) $[M + H]^+$, 500.3429 (30).

HRMS: (ESI?): *m/z* $[M + H]^+$ calcd for $C_{31}H_{47}O_5$: 499.3423; found: 499.3402.

(2,3-Dimethoxyphenyl)(2-hydroxy-4-pentadecylphenyl)methanone (18)

A one-necked round-bottomed flask was charged with benzoate ester **16** (1.0 g, 2.13 mmol, 1.0 equiv). This was then dissolved in anhyd toluene (8.5 mL), placed in an oil bath, and heated to 100 °C with stirring for 5 min. Triflic acid (0.32 mL) was then added, and the mixture was stirred at 100 °C for 45 min. The reaction was quenched with H_2O (10 mL) followed by sat. aq $NaHCO_3$ (10 mL), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with H_2O (15 mL) and brine (15 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 5% EtOAc–hexane) to yield a clear low-melting solid; yield: 630 mg (63%); R_f = 0.70 (20% EtOAc–hexane); mp 38–39 °C.

FTIR (solid): 2917 (C–H), 2849 (C–H), 1634 (C=O), 1580 (C=C), 1364 (C–O), 1269 (C–O), 1229 (C–O), 1075 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.20 (s, 1 H, OH), 7.23 (d, *J* = 8.2, 1 H, ArH-1′), 7.13 (td, *J* = 7.9, 1.8, 1 H, ArH), 7.04 (d, *J* = 8.2, 1 H, ArH), 6.86 (s, 1 H, ArH), 6.84 (s, 1 H, ArH-3′), 6.61 (d, *J* = 8.3, 1 H, ArH-2′), 3.91 (s, 3 H, OMe), 3.79 (s, 3 H, OMe), 2.58 (t, *J* = 7.8, 2 H), 1.60 (p, *J* = 7.7, 2 H), 1.26 (s, 24 H), 0.87 (t, *J* = 7.1, 3 H, Me).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.0 (C=O), 163.1 (ArC–OH), 153.4 (ArC–OMe), 152.8 (ArC–OMe), 146.2, 133.8 (ArC–1′), 133.3, 124.0, 119.9, 119.5, 118.1, 117.4, 114.1, 61.8 (OMe), 55.9 (OMe), 36.3, 32.0, 30.6, 29.7, 29.6, 29.5, 29.4, 29.3, 22.7, 14.2.

HRMS (ESI?): *m/z* (%) = 469.3292 (100) $[M + H]^+$, 470.3327 (30), 471.3355 (5).

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{30}H_{45}O_4$: 469.3318; found: 469.3292.

(2-Hydroxy-4-pentadecylphenyl)(2,4,5-trimethoxyphenyl)methanone (19)

A small reaction tube was charged with benzoate ester **17** (300 mg, 0.60 mmol). Anhyd MeCN (2.5 mL) was added and the mixture was stirred at 70 °C until the solid completely dissolved. Triflic acid (0.09 mL) was then added and the resulting mixture was stirred for 45 min at 70 °C. The reaction was quenched with H_2O (5 mL) followed by sat. aq $NaHCO_3$ (5 mL), and mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (5 mL) and brine (5 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20% EtOAc–hexane) to give a white solid; yield: 60 mg (20%); R_f = 0.36 (20% EtOAc–hexane); mp 62.8–63.8 °C.

FTIR (solid): 2915 (C–H), 2849 (C–H), 1662 (C=O), 1508 (C=C), 1307 (C–O), 1263 (C–O), 1218 (C–O), 1097 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.25 (s, 1 H, OH), 7.31 (d, *J* = 8.2, 1 H, ArH-5′), 6.87 (s, 1 H, ArH-2′), 6.84 (s, 1 H, ArH-3′), 6.63 (d, *J* = 8.3, 1 H, ArH-4′), 6.59 (s, 1 H, ArH-1′), 3.97 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 3.76 (s, 3 H, OMe), 2.59 (t, *J* = 7.8, 2 H), 1.62 (m, 2 H), 1.25 (s, 24 H), 0.88 (t, *J* = 6.6, 3 H, Me).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.4 (C=O), 163.0 (C–OH), 152.9 (ArC–OMe), 151.9 (ArC–OMe), 151.8 (ArC–OMe), 143.0, 133.7, 119.3, 118.3, 117.4 (C–3′), 112.6 (C–2′), 97.5 (C–1′), 56.7 (OMe), 56.5 (OMe), 56.2 (OMe), 36.3, 31.9, 31.0, 30.6, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 22.7, 14.1.

HRMS (ESI?): *m/z* (%) = 499.3412 (100) $[M + H]^+$, 500.3445 (30), 501.3470 (5).

HRMS (ESI?): *m/z* calcd $[M + H]^+$ for $C_{31}H_{47}O_5$: 499.3423; found: 499.3412.

5-Methoxy-3-pentadecyl-9*H*-xanthen-9-one (20)

Benzophenone **18** (113 mg, 0.24 mmol, 1.0 equiv) was dissolved in $CHCl_3$ (2.5 mL) and MeCN (10 mL). H_2O (5 mL) was then added to form a suspension to which CAS (607 mg, 0.96 mmol, 4.0 equiv) was added in portions. The mixture was heated to 70 °C and stirred for 18 h. Upon completion of the reaction, the mixture was transferred to a separatory funnel and EtOAc (20 mL) and H_2O (10 mL) were added. The separated organic layer was washed with sat. aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 15% EtOAc–hexane) to give a white solid; yield: 60 mg (57%); R_f = 0.52 (20% EtOAc–hexane); mp 103–104.8 °C.

FTIR (solid): 2916 (C–H), 2849 (C–H), 1661 (C=O), 1508 (C=C), 1270 (C–O), 1198 (C–O), 1110 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.2, 1 H, ArH-1′), 7.91 (d, *J* = 7.9, 1 H, ArH-3′), 7.44 (s, 1 H, ArH-2′), 7.32–7.18 (m, 3 H), 4.05 (s, 3 H, OMe), 2.75 (t, *J* = 7.7 Hz, 2 H), 1.69 (p, *J* = 7.6, 2 H), 1.25 (s, 24 H), 0.90–0.84 (m, 3 H, Me).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.0 (C=O), 156.1, 151.3, 148.6 (ArC–OMe), 146.5, 126.4, 125.1, 123.3, 122.8, 119.6, 117.7, 117.4, 115.1, 56.4 (OMe), 36.2, 31.9, 30.8, 29.7, 29.7, 29.6, 29.5, 29.4, 29.2, 22.7, 14.2.

HRMS (ESI?): *m/z* (%) = 437.3050 (100) $[M + H]^+$, 438.3071 (30).

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{29}H_{41}O_3$: 437.3056; found: 437.3050.

2,3-Dimethoxy-6-pentadecyl-9*H*-xanthen-9-one (21)

Benzophenone **19** (159 mg, 0.32 mmol, 1.0 equiv) was dissolved in $CHCl_3$ (3 mL) and MeCN (12 mL) in a round-bottomed flask. H_2O (6 mL) was added to form a suspension to which CAS (810 mg, 1.28 mmol, 4.0 equiv) was added in portions. The mixture was then heated to 70 °C and stirred for 18 h. Upon completion of the reaction, the mixture was transferred to a separatory funnel and EtOAc (20 mL) and H_2O (10 mL) were added. The organic layer was washed with sat. aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 15% EtOAc–hexane) to give a white solid; yield: 110 mg (74%); R_f = 0.33 (20% EtOAc–hexane); mp 96.5–97.7°C.

FTIR (solid): 2916 (C–H), 2849 (C–H), 1646 (C=O), 1508 (C=C), 1270 (C–O), 1208 (C–O), 1170 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.1, 1 H, ArH-5′), 7.67 (s, 1 H, ArH-1′), 7.26 (d, *J* = 7.3, 1 H, ArH-3′), 7.20 (d, *J* = 8.2, 1 H, ArH-4′), 6.90 (s, 1 H, ArH-2′), 4.02 (s, 3 H, OMe), 4.00 (s, 3 H, OMe), 2.75 (t, *J* = 7.7, 2 H), 1.69 (p, *J* = 7.5, 2 H), 1.25 (s, 24 H), 0.88 (t, *J* = 6.6, 3 H, Me).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.0 (C=O), 156.2, 155.2 (ArC–OMe), 152.4, 150.4, 146.6 (ArC–OMe), 126.3, 124.7, 119.5, 116.8, 115.0, 105.4, 99.6, 56.5 (OMe), 56.3 (OMe), 36.2, 31.9, 31.0, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 22.7, 14.1.

HRMS (ESI?): *m/z* (%) = 467.3145 (100) $[M + H]^+$, 468.3178 (30), 469.3209 (5).

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{30}H_{43}O_4$: 467.3161; found: 467.3145.

1-Hydroxy-7-methoxy-3-pentadecyl-9*H*-xanthen-9-one (22)

A tube was charged with xanthone **14** (30 mg, 0.069 mmol, 1.0 equiv), PIFA (36 mg, 0.084 mmol, 1.2 equiv), Ru[(*p*-cymene)Cl_2]$_2$ (4 mg, 0.0069 mmol, 10 mol%), TFAA (0.18 mL), and TFA (0.004 mL). The tube was then sealed and heated to 80 °C for 18 h. After cooling, the reaction mixture was added to sat. aq $NaHCO_3$ (10 mL) and then extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (10 mL) and brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 5% EtOAc–hexane) to give a pale-yellow solid; yield: 12 mg (38%); R_f = 0.86 (20% EtOAc–hexane); mp 98–99 °C.

FTIR (solid): 3080 (O–H), 2918 (C–H), 2849 (C–H), 1652 (C=O), 1484 (C=C), 1277 (C–O), 1207 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.57 (s, 1 H, OH), 7.62 (d, *J* = 2.9, 1 H, ArH-5′), 7.40 (d, *J* = 9.1, 1 H, ArH-3′), 7.33 (dd, *J* = 9.1, 2.9, 1 H, ArH-4′), 6.76 (s, 1 H, ArH-2′), 6.64 (s, 1 H, ArH-1′), 3.92 (s, 3 H, OMe), 2.66 (t, *J* = 7.7, 2 H), 1.66 (p, *J* = 7.4 Hz, 2 H), 1.26 (s, 24 H), 0.88 (t, *J* = 6.7, 3 H, Me).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 181.6 (C=O), 161.5 (C–OH), 156.3, 156.0, 153.7, 151.0, 125.4, 120.9, 119.2, 110.3, 106.9, 106.8, 105.1, 55.9 (OMe), 36.8, 31.9, 30.6, 29.7, 29.7, 29.5, 29.5, 29.4, 29.2, 22.7, 14.1.

HRMS (ESI?): *m/z* (%) = 453.2978 (100) $[M + H]^+$, 454.3009 (30), 455.3047 (5)

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{29}H_{41}O_4$: 453.3005; found: 453.2978.

1-Hydroxy-4-methoxy-6-pentadecyl-9*H*-xanthen-9-one (23)

A tube was charged with xanthone **20** (50 mg, 0.11 mmol, 1.0 equiv), PIFA (57 mg, 0.132 mmol, 1.2 equiv), Ru[(*p*-cymene)Cl_2]$_2$ (7 mg, 0.0114 mmol, 10 mol%), TFAA (1 mL), and TFA (0.02 mL). The tube was then sealed and heated to 80 °C for 18 h. After cooling, the mixture was added to sat. aq $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with H_2O (10 mL) and brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 5% EtOAc–hexane) to give a yellow solid; yield: 13 mg (26%); R_f = 0.73 (20% EtOAc–hexane); mp 81–83 °C.

FTIR (solid): = 2919 (C–H), 2852 (C–H), 1625 (C=O), 1511 (C=C), 1273 (C–O), 1120 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.09 (s, 1 H, OH), 8.11 (d, *J* = 8.1, 1 H, ArH-1′), 7.34 (s, 1 H, ArH-3′), 7.21–7.14 (m, 2 H, ArH-2′,4′), 6.66 (d, *J* = 8.7, 1 H, ArH-5′), 3.90 (s, 3 H, OMe), 2.69 (t, *J* = 7.9, 2 H), 1.61 (m, 2 H), 1.18 (s, 24 H), 0.80 (m, 3 H, Me).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.3 (C=O), 156.2, 154.6 (ArC–OH), 152.4, 145.9, 140.0 (ArC–OMe), 125.7, 125.3, 120.2, 118.5, 117.3, 109.5, 108.7, 57.5 (OMe), 36.3, 31.9, 30.9, 30.7, 29.6, 29.5, 29.4, 29.4, 29.2, 22.7, 14.1.

HRMS (ESI?): *m/z* (%) = 453.2995 (100) $[M + H]^+$, 454.3034 (30).

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{29}H_{41}O_4$: 453.3005; found: 453.2995.

1-Hydroxy-6,7-dimethoxy-3-pentadecyl-9*H*-xanthen-9-one (24)

A tube was charged with xanthone **21** (45 mg, 0.096 mmol, 1.0 equiv), $K_2S_2O_8$ (52 mg, 0.192 mmol, 2.0 equiv), Ru[(*p*-cymene)Cl_2]$_2$ (6 mg, 0.0096 mmol, 10 mol%), TFA (1 mL), and TFAA (0.05 mL). The tube was then sealed and heated to 80 °C for 18 h. After cooling, the mixture was added to sat. aq $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with H_2O (10 mL) and brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 5% EtOAc–hexane) to give a pale-yellow solid; yield: 20 mg (43%); R_f = 0.45 (20% EtOAc–hexane); mp 104–105.8 °C.

FTIR (solid): 2918 (C–H), 2851 (C–H), 1645 (C=O), 1510 (C=C), 1272 (C–O), 1172 (C–O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.72 (s, 1 H, OH), 7.57 (s, 1 H, ArH-1′), 6.88 (s, 1 H, ArH-2′), 6.73 (s, 1 H, ArH-3′), 6.63 (s, 1 H, ArH-4′), 4.02 (s, 3 H, OMe), 4.00 (s, 3 H, OMe), 2.66 (t, *J* = 7.7, 2 H), 1.66 (p, *J* = 7.7, 2 H), 1.25 (s, 24 H), 0.88 (t, *J* = 6.7 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 180.6 (C=O), 161.3 (ArC–OH), 156.2, 155.9 (ArC–OMe), 152.9, 152.6, 146.8 (ArC–OMe), 113.5, 110.4, 106.8, 106.6, 104.5, 99.5, 56.6 (OMe), 56.4 (OMe), 36.7, 31.9, 30.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.2, 22.7, 14.1.

HRMS (ESI?): *m/z* (%) = 483.3098 (100) $[M + H]^+$, 484.3128 (30).

HRMS (ESI?): *m/z* $[M + H]^+$ calcd for $C_{30}H_{43}O_5$: 483.3110; found: 483.3098.

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1719903.

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