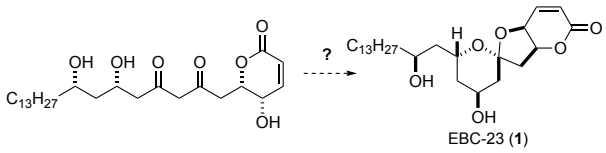
Synthetic efforts and ultimate limitation to an asymmetric Achmatowicz approach toward EBC-23

Yanping Wang[†] and George A. O'Doherty[†,*]

[†] Department of Chemistry and Chemical Biology, Northeastern University, Boston, Massachusetts 02115, US.

G.ODoherty@neu.edu

Supporting Information Placeholder



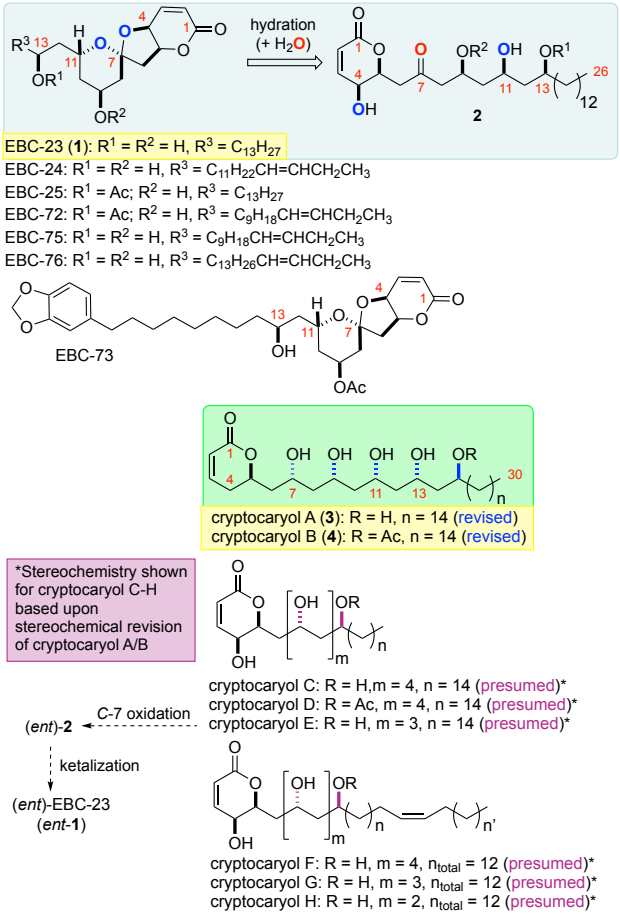
ABSTRACT: Effort toward the total synthesis of the polyketide natural product EBC-23 is reported. The asymmetric approach is convergent and uses a late stage Claisen-like enolate/acid chloride coupling to establish a key 1,3-diketone intermediate. The 1,3-diketone target is an oxidized form of the hydrated natural product, which fails to spiroketalize. The convergent asymmetric synthesis uses an asymmetric Noyori transfer hydrogenation of a β-furyl ketoester to enantioselectively form a chiral furyl alcohol. An Achmatowicz/Jones/Luche three-step reaction sequence was used to stereoselectively convert the furyl alcohol into the 5-hydroxy-pyran-2-one. The absolute stereochemistry of the 1,3-polyol fragment was established by a Leighton allylation. A subsequent Grubbs cross metathesis, and Evans acetalation were used to install the 1,3-syn-diol stereochemistry.

Introduction:

The polyketide natural product EBC-23 (**1**) was found as part of an ongoing effort to find new structures with important biological activity. The novel spiroketal natural product was isolated from the fruit of *Cinnamomum laubatii*, which is a member of the Lauraceae family found in the Australian tropical rainforests.[1] The 26 carbon δ-lactone, EBC-23 (**1**), was discovered as a member of a family of related pyranone containing spiroketal/1,3-polyol natural products (Figure 1) with *in vitro* anticancer activity against a range of cancer cell lines (*i.e.*, melanoma (MM96L), breast carcinoma (MCF7), prostate cancer (DU145)).[1] The structure of EBC-23 was confirmed by a series of NMR experiments in combination with

synthetic efforts.[2] This culminated in the successful total synthesis by Williams in 2008,[2,3] and followed by three more syntheses by Yamamoto,[4] Ghosh[5] and Yadav.[6]

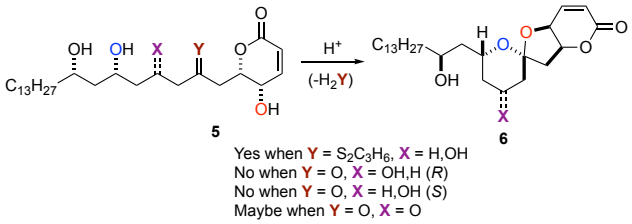
Figure 1. The structures of cryptocaryols A-H, EBCs 23-25, 72, 75, 76 and stereoisomers



Structurally, the EBCs are members of the cryptocaryol family of natural products, which have gained attention due to their interesting structures and biological activity (Figure 1).[1,2] The cryptocaryols are pyranone containing 1,3-polyol polyacetates with variable degrees of acetate oligomerization (*e.g.*, *C*-30, *C*-28, *C*-26, etc.) and oxidation. In general, the cryptocaryols oxidation includes both unsaturation along the side chain and a stereospecific hydroxylation at the *C*-4 position in the pyranone. Unique to the EBCs is the additional oxidation at *C*-7 and subsequent spiroketalization at *C*-7 ketone between the *C*-4 and *C*-11 hydroxyl groups. Thus, the hydrated form of EBC-23 can be viewed as *C*-7 keto-version of enantiomer of cryptocaryol E. Although it lacks a spiroketal, the cis-fused dioxa-[4.3.0]bicyclooctene ring system also appears in the altholactone natural products.[7]

Over the years, we have been interested in the synthesis and Stereochemical-Structure Activity Relationship (S-SAR)[8] study of the cryptocaryol class of natural products, with an emphasis on cryptocaryols A and B. As part of these studies, we have found that the cyptocaryols biological activity (*i.e.*, PDCD4 stabilization and anticancer activity) occurs independent of its stereochemistry.[9] As part of these efforts, we became interested in the de novo asymmetric synthesis of EBC-23, its stereoisomers and congeners. Herein we report our synthetic progress towards these aims and in particular, the limitations discovered with our Achmatowics/Jones/Luche furan alcohol to 5-hydroxy-pyran-2-one synthetic approach in a convergent synthesis of EBC-23. This effort builds upon the difficulties encountered by Williams *et al*. in their synthetic studies toward EBC-23 (Scheme 1).[2]

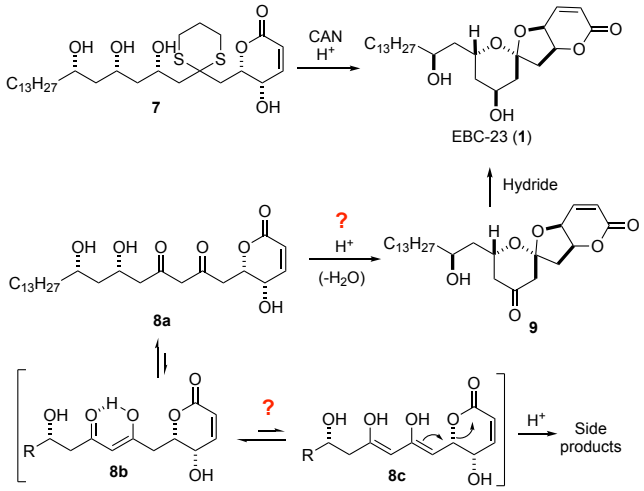
Scheme 1. Effects of C-9 and C-11 on spiroketal formation.



Specifically, Williams found great difficultly in the spiroketalization of polyols like **5** that contained the pyranone ring system. The solution that Williams found was to generate the spiroketal from a dithiane. Interestingly, Yamamoto found that a stepwise deprotection process with PMB-deprotection being the final step appeared to solve this pyranone compatibility issue. Alternatively, Gosh and Yadav found that simply installing the pyranone ring after or during the spiroketal formation solved this problem. We however wanted to re-investigate this issue with the compatibility of spiroketal formation to the pyranone as a solution would add a high degree of convergency. This convergency we believed would better enable a stereochemical-SAR type study of the EBC class of molecules. We surmised that the difficulty with the pyranone in the spiroketalization was associated with enolization and β-elimination/ring opening of these pyanone intermediates (Scheme 2). Our proposed solution to this

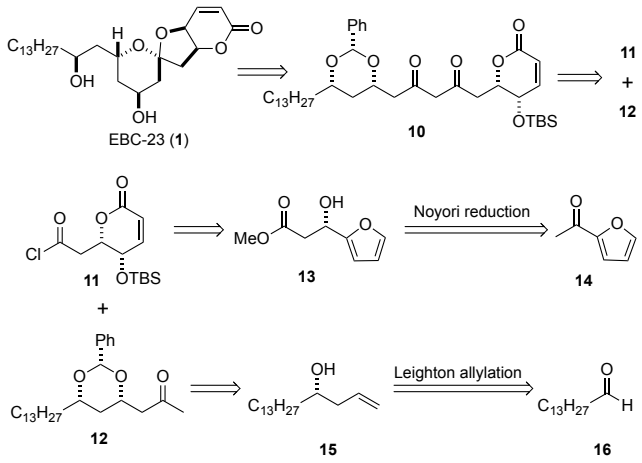
problem was based upon the supposition 1,3-diketones like **8a** would be exist primarily in enol form **8b** less likely to enolize to form **8c** and undergo the subsequent degenerative β-elimination and ring opening.

Scheme 2. Retrosynthetic Analysis of EBC-23 (1)



Retrosynthetically this led us to the desire for the synthesis of 1,3-diketone **10**, which we believed could be assembled by a Claisen condensation (Scheme 3). More specifically, a Claisen type coupling reaction between **11** and **12** to form an oxidized protected variant of the hydrated EBC-23 precursor **10**. Access to the desired acid chloride/pyranone **11**, could be arrive at by use of the Achmatowicz/Jones/Luche three step reaction sequence.[10] We have previously synthesized related pyranones from furan alcohols like **13**, which can be prepared from **14** by a methoxycarbonylation and asymmetric Noyori reduction. Finally, the ketone polyol fragment **12** could be derived from cross-metathesis/asymmetric hydration of homoallylic alcohol **15**,[11] which in turn could be arrived at by a Leighton allylation of aldehyde **16**.

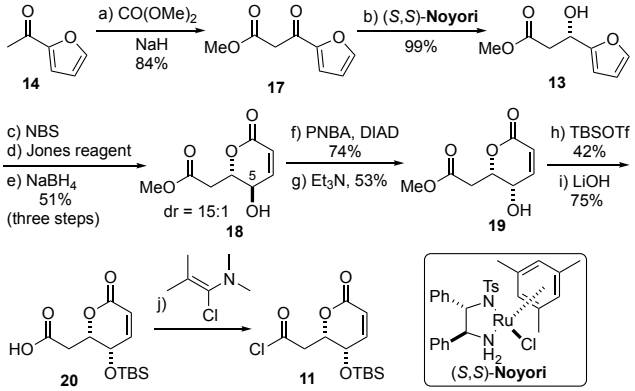
Scheme 3. Retrosynthetic Analysis of EBC-23 (1)



Results and Discussion:

Our approach to EBC-23 began with the asymmetric synthesis of the two key coupling products pyranone **11** and ketone **12**. An important aspect of these asymmetric approaches for a convergent synthesis is that the syntheses prepare the fragments in high enantiomeric purity. We found the optimal asymmetry introduction steps for the fragment syntheses were accomplished with a Noyori hydrogen transfer reduction of a furylketone **17** and a Leighton allylation of aldehyde **16**. The two asymmetric syntheses are outlined in Schemes 4 and 5.

Scheme 4. Synthesis of Acyl Chloride 11

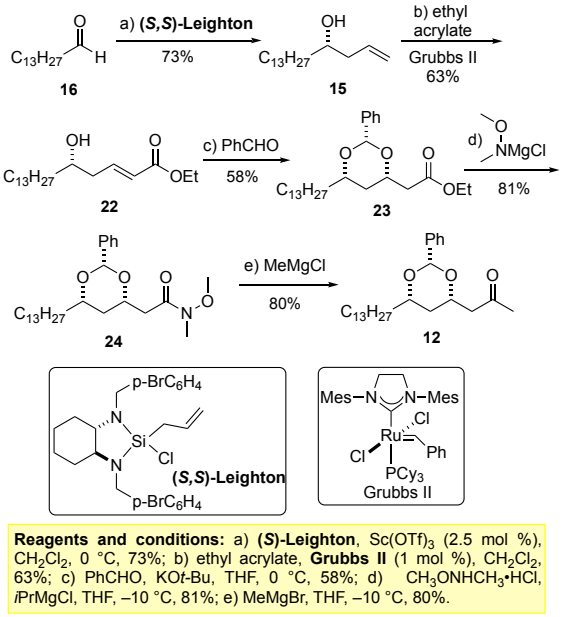


Reagents and conditions: a) dimethyl carbonate, NaH, KH (2.4 mol %), THF, reflux, 84%; b) HCO_2Na, (*S*,*S*)-**Noyori** (2.5 mol %), CTAB (10 mol %), H_2O, rt, 99%; c) NBS, $NaOAc{\cdot}3H_2O$, $NaHCO_3$, THF/H_2O (4:1), 0 °C; d) Jones reagent, acetone, 0 °C; e) $NaBH_4$, CH_2Cl_2/MeOH (1:1), 0 °C, 51% (over three steps); f) PNBA, PPh_3, DIAD, THF, 0 °C, 74%; g) EtN_3, MeOH/CH_2Cl_2 (1:3), 0 °C, 74%; h) TBSOTf, 2,6-lutidine, THF, –78 °C, 42%; i) LiOH, THF/H_2O (4:1), 0 °C, 75%; j) Ghosez's reagent, CH_2Cl_2, 0 °C (used as crude).

Our synthesis of acid chloride **11** from 2-acetyl furan **14** is outlined in Scheme 4. Recently, we reported an efficient asymmetric synthesis of **11** from commercially available **14** via a

Noyori/Achmatowicz sequence (Scheme 4).[12,13] The synthesis began with the base promoted Claisen condensation of acetylfuran **14** to form β-ketoester **17**. While we have explored many different ways to achieve this transformation,[14] this was most practically accomplished on scale with the use of NaH as base in the presence of excess dimethyl carbonate. Under these conditions ($NaH/CO(OMe)_2$ in THF) β-ketoester **17** can be prepared in very good yield (73%). The asymmetric Noyori hydrogen transfer reduction of β-ketoester **17** (HCO_2H/Et_3N, (*S,S*)-Noyori) was used to form furan alcohol **13** in excellent yield (85%) and enantiomeric excess (>95% ee).[15] The furan alcohol **13** was oxidatively hydrated under the Achmatowicz conditions (NBS in buffered THF/H_2O) to give a mixture of pyranone anomers.[16] A subsequent two-step Jones oxidation[17] and Luche reduction reaction sequence was used to convert the anomers into pyranone **18** as a 15:1 mixture of C-4 diastereomer (51%).[18] While the Luche reduction step occurred with excellent stereoselectivity, it surprisingly formed the undesired equatorial alcohol stereoisomer. The stereochemistry of *C*-5 was inverted under Mitsunobu conditions (*p*-nitrobenzoic acid, DIAD). The resulting ester was hydrolyzed with Et_3N in MeOH to give an alcohol **19**. The alcohol **19** was then protected as a TBS-ether (TBSOTf, 2,6-lutidine) and then the methyl ester was hydrolyzed (LiOH) to give carboxylic acid **20**. The carboxylic acid **20** was converted into acid chloride **11** with Ghosez reagent (1-choro-1-(dimethylamino)-2-methyl-2-propene).[19]

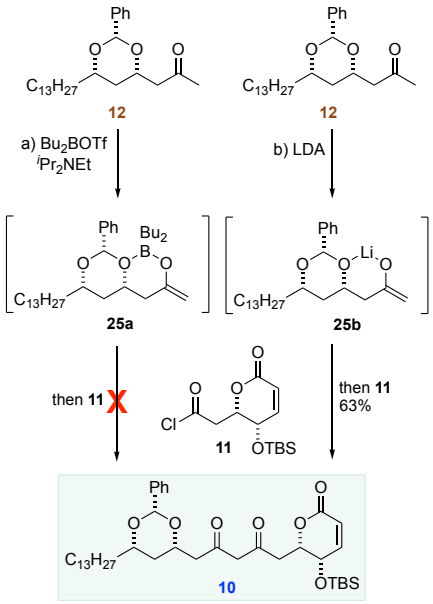
Scheme 5. Synthesis of Methyl Ketone 12



Reagents and conditions: a) **(*S*)-Leighton**, $Sc(OTf)_3$ (2.5 mol %), CH_2Cl_2, 0 °C, 73%; b) ethyl acrylate, **Grubbs II** (1 mol %), CH_2Cl_2, 63%; c) PhCHO, KO*t*-Bu, THF, 0 °C, 58%; d) CH_3ONHCH_3•HCl, *i*PrMgCl, THF, –10 °C, 81%; e) MeMgBr, THF, –10 °C, 80%.

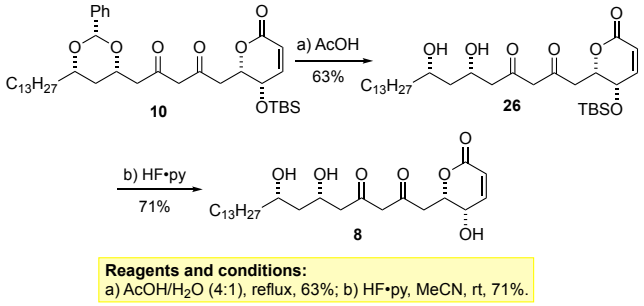
Our synthesis of the ketone fragment **12**, began with a Leighton allylation of tetradecanal **16** (Scheme 5). Leighton allylation of **16** gave homoallylic alcohol **15**,[20] which was converted into δ-hydroxy enoate **22** in a cross-metathesis reaction with ethyl acrylate using the second-generation Grubbs catalyst (Grubbs II). Enoate **22** was then diastereoselectively converted into benzylidene protected diol **23** upon its exposed to the Gauchet-Prunet/Evans hydration/acetalation conditions (PhCHO, KOt-Bu).[9,11,21] The ester moiety in **23** was transformed into methyl ketone **12** via a two-step Weinreb amide formation (**23** to **24**) and subsequent methyl Grignard addition.

Scheme 6. Synthesis of Diketone 19



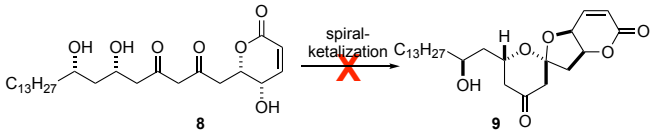
With access to the two fragments ketone **12** and acid chloride **11** we next explored their coupling (Scheme 6). This effort began with the formation of boron enolate **25a** and the exploration of its reactivity with acid chloride **11**. The formation of boron enolate **25a** began with the exposure of ketone **12** to Bu_2BOTf and Hunigs base. Unfortunately, we were not able to find conditions under which boron enolate **25a** would react with acid chloride **11**. Under various conditions, only recovery of ketone **12** was observed. We next turned to the use of lithium enoate **25b** in this coupling reaction. Exposure of ketone **12** to freshly prepared LDA readily generated lithium enoate **25b**. In contrast to the boron enolate **25a**, the lithium enolate **25b** readily reacted with acid chloride **11a** to form 1,3-diketone **10** in good yield (63%).[22]

Scheme 7. Synthesis of Diketone 19



With ready access to the desired 1,3-diketone **10**, we explored its deprotection and spiroketalization (Scheme 7). We initially looked to accomplish this in one-pot, the difficulties associated with this led use to explore this in a stepwise manner. In contract to the one-step protocol, the deprotection could be accomplished in a two-step process. This was accomplished with the removal of the benzylidene acetal group and then desilylation. Exposure of **10** to the mildly acid aqueous acetic acid conditions gave good diol **26** in good yield. Similarly, the TBS-group could be removed with exposure to HF•Py, which provided triol **8** is good overall yield (71 %). In contrast, to the deprotection steps, we were not able to find conditions to affect the spiroketalization of **8** to form **9** (Scheme 8).

Scheme 8. Attempted 1,3-Diketone Spiroketalization



entry	catalyst	solvent	temp.	time	results
1	TsOH	CH_2Cl_2	rt	2 h	intractable product
2	TsOH	$C_6D_6/CDCl_3$[a]	rt	12 h	intractable product
3	CSA	MeOH	0 °C	2 h	intractable product
4	CSA	toluene	rt	16 h	intractable product

a. ratio = 1:1

Conclusions

In conclusion, a convergent asymmetric synthesis of a *C*-9 oxidized variant of the hydrated precursor to ECB-23 was accomplished in an eighteen total steps (13 longest linear steps) from achiral starting

materials, furan **14** and aldehyde **16**. While the diketone **8** failed to spiroketalize, this effort sheds light into similar difficulties in the spiroketalization report by Williams in their successful synthesis of EBC-23.[2] The route featured a surprisingly efficient lithium enolate acid chloride convergent coupling reaction to form the key 1,3-diketone precursor of ECB-23. The asymmetry of the two fragments was introduced by the use of a Noyori hydrogen transfer reduction of an acylfuran and Leighton allylation of aldehyde **16**. Further efforts to develop this chemistry for complete total synthesis are ongoing and will be reported in due course.

Experimental Section

General Methods:

All ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a Varian 400 or 500 MHz spectrometer. Chemical shifts were reported relative to internal tetramethylsilane (δ 0.00 ppm) or $CDCl_3$ (δ 7.26 ppm) for ^{1}H NMR and $CDCl_3$ (δ 77.2 ppm) for $^{13}C\{^{1}H\}$ NMR. Infrared (IR) spectra were obtained on a FT-IR spectrometer. Optical rotations were measured with a digital polarimeter in the solvent specified. Melting points were determined with a standard melting point apparatus. Flash column chromatography was performed on 60-200 or 230-400 mesh silica gel. Analytical thin-layer chromatography was performed with precoated glass-backed plates and visualized by quenching of fluorescence and by charring after treatment with p-anisaldehyde or potassium permanganate stain. R_f values were obtained by elution in the stated solvent ratios. Diethyl ether, tetrahydrofuran, methylene dichloride and triethylamine were dried by passing through activated alumina column with argon gas pressure. Commercial reagents were used without purification unless otherwise noted. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of argon/nitrogen using oven- or flame-dried glassware and standard syringe/septa techniques. Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectra were obtained using α-cyano-4-hydroxycinnamic acid (CCA) as the matrix on a MALDITOF mass spectrometer.

Methyl 2-((2*S*)-6-hydroxy-3-oxo-3,6-dihydro-2H-pyran-2-yl)acetate (13a)

To a stirred solution of **13** (5.30 g, 31.1 mmol) in tetrahydrofuran/water at 0 °C (4:1, 60 mL) was added sodium bicarbonate (5.23 g, 62.3 mmol) and sodium acetate trihydrate (4.24 g, 31.1 mmol). Then *N*-bromosuccinimide (5.54 g, 31.1 mmol) was added in portions to the mixture. After 30 min, the reaction was quenched by adding saturated aqueous solution of sodium bicarbonate and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used directly for next step. An aliquot of the crude residue was purified by flash chromatography (20 to 60% EtOAc in hexanes) on silica gel (30 mL) to afford pure **13a** for characterization.

Data for **13a**: R_f = 0.37 (60% EtOAc in Hexanes); $[[\alpha]_D^{21}$ = –8.0 ($CHCl_3$, c = 0.80); IR (neat) 3429, 2956, 1740, 1698, 1440, 1371, 1293, 1231, 1175, 1092, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.91 (dd, J = 10.0, 3.5 Hz, 1H), 6.14 (d, J = 10.0 Hz, 1H), 5.63 (d, J = 3.5 Hz, 1H), 5.02 (dd, J = 7.5, 4.0 Hz, 1H), 3.70 (s, 3H), 3.01 (dd, J = 16.5, 3.5 Hz, 1H), 2.74 (dd, J = 16.5, 7.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 195.0, 171.6, 144.7, 127.3, 87.9, 70.9, 52.2, 35.2; MALDI-TOF/CCA-HRMS calcd for $C_8H_{10}O_3Na$ $[M + Na]^+$: 209.0420, found 209.0408.

Methyl (*S*)-2-(3,6-dioxo-3,6-dihydro-2H-pyran-2-yl)acetate (13b)

To a stirred solution of **13a** (5.80 g, 31.1 mmol) in acetone (70 mL) at 0 °C was added Jones reagent[17] (2.5 M, 18.7 mL, 46.7 mmol) slowly via syringe. The resulting mixture was stirred at the same temperature for 15 min. The reaction was quenched by adding isopropanol slowly and filtered through Celite. The filtrate was extracted with EtOAc (3 × 80 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was

used directly for next step. An aliquot of the crude residue was purified by flash chromatography (30 to 70% EtOAc in hexanes) on silica gel (30 mL) to afford pure **13b** for characterization. Data for **13b**: R_f = 0.30 (70% EtOAc in Hexanes); $[\alpha]_D^{21}$ = –41.5 ($CHCl_3$, c = 1.67); IR (neat) 3437, 3071, 2958, 1731, 1622, 1440, 1372, 1265, 1212, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.93 (d, J = 12.0 Hz, 1H), 6.85 (d, J = 12.0 Hz, 1H), 5.14 (t, J = 4.0 Hz, 1H), 3.70 (s, 3H), 3.25 (dd, J = 17.5, 4.5 Hz, 1H), 3.08 (dd, J = 17.5, 4.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.9, 169.8, 160.2, 138.4, 135.5, 79.5, 52.5, 37.5; MALDI-TOF/CCA-HRMS calcd for $C_8H_8O_5Na$ $[M + Na]^+$: 207.0264, found 207.0249.

Methyl 2-((2*S*,3*R*)-3-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)acetate (18)

To a stirred solution of **13b** (5.73 g, 31.1 mmol) in a mixed solvent of dichloromethane/methanol (1:1, 100 mL) at –78 °C was added sodium borohydride (1.77 g, 46.7 mmol). The resulting mixture was stirred at the temperature for 30 s. The reaction was quenched by adding water (50 mL) and 1 N hydrochloride acid (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (30 to 80% EtOAc in hexanes) on silica gel (80 mL) to afford **18** (2.16 g, 51%) as a white solid. Data for **18**: R_f = 0.29 (70% EtOAc in Hexanes); mp: 115–117 °C; $[\alpha]_D^{21}$ = –52.2 (MeOH, c = 0.67); IR (neat) 3435, 2956, 2926, 1735, 1440, 1378, 1334, 1228, 1155, 1082, 1039 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.86 (dd, J = 10.0, 2.0 Hz, 1H), 5.99 (dd, J = 10.0, 2.0 Hz, 1H), 4.65 (ddd, J = 10.0, 6.0, 6.0 Hz, 1H), 4.51 (ddd, J = 8.0, 2.0, 2.0 Hz, 1H), 3.75 (s, 3H), 2.98 (br s, 1H), 2.93 (dd, J = 16.0, 5.5 Hz, 1H), 2.86 (dd, J = 16.0, 6.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.1, 162.6, 149.5, 120.3, 78.4, 66.3, 52.6, 37.6; MALDI-TOF/CCA-HRMS calcd for $C_8H_{10}O_5Na$ $[M + Na]^+$: 209.0420, found 209.0407.

(2*S*,3*S*)-2-(2-Methoxy-2-oxoethyl)-6-oxo-3,6-dihydro-2H-pyran-3-yl 4-nitrobenzoate (18a)

To a stirred solution of **18** (1.96 g, 10.6 mmol) in tetrahydrofuran (40 mL) at 0 °C was added triphenylphosphine (5.71 g, 21.7 mmol) and 4-nitrobenzoic acid (3.55 g, 21.3 mmol) under N_2. A solution of diisopropyl azodicarboxylate (4.58 g, 21.3 mmol) in tetrahydrofuran (10 mL) was added slowly via syringe. The resulting mixture was stirred at the same temperature for 1.5 h. The reaction was quenched by adding saturated aqueous sodium bicarbonate (40 mL), and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (20 to 50% EtOAc in hexanes) on silica gel (80 mL) to afford **18a** (2.60 g, 74%) as a white solid. Data for **18a**: R_f = 0.24 (40% EtOAc in Hexanes); mp: 112–114 °C; $[\alpha]_D^{21}$ = +281.5 ($CHCl_3$, c = 1.89); IR (neat) 3114, 3080, 2999, 2956, 2856, 1731, 1609, 1530, 1439, 1343, 1267, 1099, 1014 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.30 (ddd, J = 8.5, 2.0, 2.0 Hz, 2H), 8.19 (ddd, J = 8.5, 2.0, 2.0 Hz, 2H), 7.13 (ddd, J = 10.0, 6.0 Hz, 1H), 7.32 (d, J = 10.0 Hz, 1H), 5.61 (dd, J = 5.5, 2.5 Hz, 1H), 5.14 (ddd, J = 7.0, 7.0, 2.5 Hz, 1H), 3.71 (s, 3H), 2.98 (dd, J = 16.5, 7.5 Hz, 1H), 2.85 (dd, J = 16.5, 7.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.5, 163.8, 161.9, 151.1, 139.6, 134.0, 131.2, 125.8, 124.0, 75.1, 64.1, 52.5, 35.3; MALDI-TOF/CCA-HRMS calcd for $C_{15}H_{13}O_8NNa$ $[M + Na]^+$: 358.0533, found 358.0560.

Methyl 2-((2*S*,3*S*)-3-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)acetate (19)

To a stirred solution of **18a** (2.40 g, 7.16 mml) in methanol/dichloromethane (3:1, 24 mL) at 0 °C was added triethylamine (2.00 mL, 14.3 mmol) in one portion via syringe under N_2. The resulting mixture was warmed to room temperature and stirred for 3 h. The mixture was concentrated, and the crude residue was purified by flash chromatography (40 to 70% EtOAc in hexanes) on silica gel (80 mL) to afford **19** (0.705 g, 53%) as a low melting white amorphous solid. Data for **19**: R_f = 0.29 (70% EtOAc in Hexanes); $[\alpha]_D^{21}$ = +11.7 ($CHCl_3$, c = 0.57); IR (neat) 3422, 2955, 1732, 1440, 1384, 1257, 1181, 1092, 1051, 1002 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.02 (dd, J = 10.0, 6.0 Hz, 1H), 6.12 (d, J = 10.0 Hz, 1H), 4.83 (ddd, J = 6.5, 6.5, 2.5 Hz, 1H), 4.26 (ddd, J = 9.0, 6.0, 2.5 Hz, 1H), 3.73 (s, 3H), 2.98 (dd, J = 17.0, 7.0 Hz, 1H),

2.92 (dd, J = 17.0, 7.0 Hz, 1H), 2.86 (d, J = 9.5 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 170.8, 163.4, 144.4, 122.8, 77.2, 61.5, 52.4, 35.0; MALDI-TOF/CCA-HRMS calcd for $C_8H_{10}O_5Na$ $[M + Na]^+$: 209.0420, found 209.0409.

Methyl 2-((2*S*,3*S*)-3-((tert-butyldimethylsilyl)oxy)-6-oxo-3,6-dihydro-2H-pyran-2-yl)acetate (19a)

To a stirred solution of **19** (0.705 g, 3.79 mmol) in dichloromethane (10 mL) at –78 °C was added 2,6-lutidine (0.50 mL, 5.05 mmol), followed by *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.02 mL, 4.42 mmol). The resulting mixture was stirred at the same temperature for 30 min. The reaction was quenched by adding 1 N hydrochloric acid (50 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (5 to 20% EtOAc in hexanes) on silica gel (70 mL) to afford **19a** (0.480 g, 42%) as a low melting white amorphous solid. Data for **19a**: R_f = 0.29 (20% EtOAc in Hexanes); $[\alpha]_D^{21}$ = +178.2 ($CHCl_3$, c = 1.76); IR (neat) 2955, 2858, 1731, 1440, 1386, 1327, 1254, 1178, 1061 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (dd, J = 9.5, 5.0 Hz, 1H), 6.08 (d, J = 9.5 Hz, 1H), 4.79 (ddd, J = 6.5, 6.5, 3.0 Hz, 1H), 4.33 (dd, J = 5.0, 2.5 Hz, 1H), 3.71 (s, 3H), 2.88 (dd, J = 17.0, 7.5 Hz, 1H), 2.84 (dd, J = 17.0, 6.5 Hz, 1H), 0.86 (s, 9H), 0.066 (s, 3H), 0.056 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 170.6, 162.9, 144.4, 122.5, 77.2, 61.9, 52.1, 34.8, 25.7, 18.1, –4.0, –4.9; MALDI-TOF/CCA-HRMS calcd for $C_{14}H_{24}O_5NaSi$ $[M + Na]^+$: 323.1285, found 323.1270.

2-((2*S*,3*S*)-3-((tert-Butyldimethylsilyl)oxy)-6-oxo-3,6-dihydro-2H-pyran-2-yl)acetic acid (20)

To a stirred solution of **19a** (115 mg, 0.383 mmol) in tetrahydrofuran/water (4:1, 5 mL) at 0 °C was added lithium hydroxide monohydrate (32.0 mg, 0.766 mmol) in one portion. The resulting mixture was stirred at the same temperature for 5 min. The reaction was quenched by adding 1 N hydrochloric acid (1 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over

anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (20 to 50% EtOAc in hexanes) on silica gel (20 mL) to afford **20** (82.0 mg, 75%) as a white solid. Data for **20**: R_f = 0.29 (1% isopropanol in EtOAc); mp: 111–113 °C; $[\alpha]_D^{21}$ = +170.9 ($CHCl_3$, c = 0.55); IR (neat) 3034, 2936, 1742, 1709, 1432, 1255, 1194, 1069, 1098, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.50 (dd, J = 12.0, 7.0 Hz, 1H), 6.06 (dd, J = 12.0, 1.0 Hz, 1H), 5.84 (ddd, J = 6.5, 4.0, 1.5 Hz, 1H), 4.81 (dd, J = 4.5, 4.5 Hz, 1H), 2.80 (dd, J = 17.0, 5.0 Hz, 1H), 2.49 (d, J = 17.0 Hz, 1H), 0.85 (s, 9H), 0.033 (s, 3H), –0.012 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.5, 170.4, 147.7, 121.3, 82.2, 71.1, 39.8, 25.7, 18.1, –4.7, –5.0; MALDI-TOF/CCA-HRMS calcd for $C_{13}H_{22}O_5NaSi$ $[M + Na]^+$: 309.1129, found 309.1143.

2-((2*S*,3*S*)-3-((tert-Butyldimethylsilyl)oxy)-6-oxo-3,6-dihydro-2H-pyran-2-yl)acetyl chloride (11)

To a stirred solution of **20** (0.684 g, 2.39 mmol) in dichloromethane (8 mL) at room temperature was added 1-chloro-*N,N*,2-trimethyl-1-propenylamine (0.49 mL, 3.58 mmol). The resulting mixture was stirred at the same temperature for 30 min. The mixture was diluted with EtOAc/hexane (1:1, 100 mL), washed with brine, over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue containing crude **11** was used directly for next step.

(*S*)-Heptadec-1-en-4-ol (15)[23]

To a stirred solution of **16** (18.5 g, 87.1 mmol) in dichloromethane (150 mL) at 0 °C was added a solution of (*S,S*)-Leighton reagent (58.3 g, 105 mmol) in dichloromethane (50 mL) via syringe, followed by followed by scandium triflate (1.07 mg, 2.18 mmol) under N_2. The resulting mixture was stirred at the same temperature for 20 h. The reaction was quenched by adding 1 N hydrochloric acid (100 mL). The formed solid was filtered through a fritted funnel, and the filtrate was extracted with EtOAc (3 × 150 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (2.5 to

10% EtOAc in hexanes) on silica gel (250 mL) to afford **15** (16.1 g, 73%) as a white solid. Data for **15**: R_f = 0.33 (10% EtOAc in Hexanes); mp: 29–30 °C; $[\alpha]_D^{21}$ = –4.0 ($CHCl_3$, c = 0.61); IR (neat) 3331, 2955, 2922, 2851, 1642, 1470, 1341, 1264, 1070 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.87–5.79 (m, 1H), 5.14–5.11 (m, 2H), 3.66–3.61 (m, 1H), 2.32–2.27 (m, 1H), 2.16–2.10 (m, 1H), 1.64–1.58 (m, 1H), 1.48–1.42 (m, 3H), 1.32–1.22 (m, 20H), 0.88 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.1, 118.3, 70.8, 42.1, 37.0, 32.1, 29.85, 29.80, 29.6, 25.9, 22.9, 14.3.

Ethyl (*S*,*E*)-5-hydroxyoctadec-2-enoate (22)

To a stirred solution of **15** (14.6 g, 57.3 mmol) in dichloromethane (20 mL) at room temperature was added ethyl acrylate (123 mL, 1.15 mol), followed by the Grubbs second-generation catalyst (486 mg, 0.573 mmol) under N_2. The resulting mixture was degassed by two freeze−pump−thaw cycles, then warmed to room temperature and stirred at the same temperature. After 16 h, the mixture was diluted with hexanes (400 mL), and purified by flash chromatography (2.5 to 20% EtOAc in hexanes) on silica gel (400 mL) to afford **22** (11.7 g, 63%) as a white solid. Data for **22**: R_f = 0.29 (20% EtOAc in Hexanes); mp: 31–33 °C; $[\alpha]_D^{21}$ = +2.5 ($CHCl_3$, c = 1.01); IR (neat) 3404, 2955, 2918, 2849, 1723, 1695, 1655, 1472, 1369, 1332, 1319, 1177, 1072 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.97 (ddd, J = 15.0, 7.5, 7.5 Hz, 1H), 5.90 (ddd, J = 15.0, 1.5, 1.5 Hz, 1H), 4.18 (q, J = 7.0 Hz, 2H), 3.75 (dddd, J = 7.5, 7.5, 5.0, 5.0 Hz, 1H), 2.40 (dddd, J = 14.0, 7.0, 4.5, 1.5 Hz, 1H), 2.31 (dddd, J = 14.0, 8.0, 8.0, 1.5 Hz, 1H), 1.65 (s, 1H), 1.50–1.39 (m, 4H), 1.33–1.22 (m, 20H), 1.28 (t, J = 7.0 Hz, 3H), 0.87 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.5, 145.4, 124.0, 70.8, 60.5, 40.4, 37.3, 32.1, 29.86, 29.83, 29.82, 29.76, 29.73, 29.53, 25.8, 22.9, 14.4, 14.3; MALDI-TOF/CCA-HRMS calcd for $C_{20}H_{38}O_3Na$ $[M + Na]^+$: 349.2713, found 349.2703.

Ethyl 2-((2*S*,4*S*,6*S*)-2-phenyl-6-tridecyl-1,3-dioxan-4-yl)acetate (23)

To a stirred solution of **22** (1.22 g, 3.74 mmol) in tetrahydrofuran (10 mL) at 0 °C was added benzaldehyde (0.38 mL, 3.73 mmol), followed by potassium tert-butoxide (42.0 mg, 0.373 mmol) under N_2. The resulting mixture was stirred for 15 min. Then the addition of benzaldehyde/ potassium tert-butoxide was repeated two more times. The mixture was passed through a pad of silica gel, and the silica gel was washed with EtOAc (30 mL). The filtrate was concentrated, and the crude residue was purified by flash chromatography (5% EtOAc in hexanes) on silica gel (80 mL) to afford **23** (0.936 g, 58%) as a white solid. Data for **23**: R_f = 0.33 (10% Et_2O in Hexanes); mp: 38–40 °C; $[\alpha]_D^{21}$ = –5.2 ($CHCl_3$, c = 3.31); IR (neat) 2925, 2854, 1738, 1466, 1456, 1372, 1346, 1177, 1149, 1114, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51–7.48 (m, 2H), 7.37–7.30 (m, 3H), 5.56 (s, 1H), 4.31 (dddd, J = 11.0, 6.5, 6.5, 2.5 Hz, 1H), 4.18 (q, J = 7.0 Hz, 2H), 3.84 (dddd, J = 11.0, 7.0, 5.0, 2.0 Hz, 1H), 2.73 (dd, J = 15.5, 7.0 Hz, 1H), 2.51 (dd, J = 15.5, 6.0 Hz, 1H), 1.73 (ddd, J = 13.0, 2.5, 2.5 Hz, 1H), 1.72–1.64 (m, 1H), 1.56–1.38 (m, 4H), 1.33–1.26 (m, 23H), 0.90 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.0, 138.8, 128.7, 128.3, 126.2, 100.7, 73.4, 60.7, 41.2, 36.7, 36.0, 32.1, 29.82, 29.78, 29.74, 29.5, 25.2, 22.9, 14.4, 14.3; MALDI-TOF/CCA-HRMS calcd for $C_{27}H_{44}O4Na$ $[M + Na]^+$: 455.3132, found 455.3162.

***N*-methoxy-*N*-methyl-2-((2*S*,4*S*,6*S*)-2-phenyl-6-tridecyl-1,3-dioxan-4-yl)acetamide (24)**

To a stirred solution of **23** (1.85 g, 4.42 mmol) in tetrahydrofuran (16 mL) at –10 °C was added N,O-dimethylhydroxylamine hydrochloride (0.647 g, 6.63 mmo), followed by a solution of isopropylmagnesium chloride in tetrahyrofuran (2 M, 6.65 mL, 13.3 mmol) via syringe slowly under N_2. The resulting mixture was stirred at the same temperature for 30 min. The reaction was quenched by adding saturated aqueous ammonium chloride (20 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (10 to 30% EtOAc in hexanes) on silica gel (80 mL) to afford **24** (1.60 g, 81%) as a colorless oil. Data for **24**: R_f = 0.32 (30%

EtOAc in Hexanes); $[\alpha]_D^{21}$ = –16.3 ($CHCl_3$, c = 1.36); IR (neat) 2924, 2853, 1667, 1458, 1388, 1342, 1117, 1027 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.50–7.48 (m, 2H), 7.37–7.28 (m, 3H), 5.57 (s, 1H), 4.38 (dddd, J = 11.0, 7.0, 7.0, 2.5 Hz, 1H), 3.85 (dddd, J = 11.0, 7.0, 5.0, 2.0 Hz, 1H), 3.67 (s, 3H), 3.20 (s, 3H), 2.98 (dd, J = 15.5, 6.0 Hz, 1H), 2.55 (dd, J = 15.5, 6.0 Hz, 1H), 1.80 (ddd, J = 13.0, 2.5, 2.5 Hz, 1H), 1.71–1.65 (m, 1H), 1.55–1.36 (m, 4H), 1.34–1.24 (m, 20H), 0.88 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.6, 138.9, 128.7, 128.3, 126.3, 100.8, 76.9, 73.7, 61.6, 38.4, 37.1, 36.1, 32.1, 29.85, 29.79, 29.76, 29.5, 25.2, 22.9, 14.3; MALDI-TOF/CCA-HRMS calcd for $C_{27}H_{45}O_4NNa$ $[M + Na]^+$: 470.3241, found 470.3250.

1-((2*S*,4*S*,6*S*)-2-Phenyl-6-tridecyl-1,3-dioxan-4-yl)propan-2-one (12)

To a stirred solution of **24** (0.776 g, 1.73 mmol) in tetrahydrofuran (5 mL) at –10 °C was added a solution of methylmagnesium bromide (3 M, 0.87 mL, 2.60 mmol) in tetrahydrofuran via syringe slowly under N2. The resulting mixture was stirred at the same temperature for 0.5 h. The reaction was quenched by adding saturated aqueous ammonium chloride (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (5 to 10% EtOAc in hexanes) on silica gel (40 mL) to afford **12** (0.558 g, 80%) as a white solid. Data for **12**: R_f = 0.26 (10% EtOAc in Hexanes); mp: 47–48 °C; $[\alpha]_D^{21}$ = –3.3 ($CHCl_3$, c = 3.4); IR (neat) 2914, 2849, 1724, 1692, 1470, 1452, 1404, 1344, 1137, 1123, 1098, 1056, 1019 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49–7.47 (m, 2H), 7.37–7.29 (m, 3H), 5.55 (s, 1H), 4.32 (dddd, J = 9.5, 8.0, 6.0, 2.5 Hz, 1H), 3.84 (dddd, J = 10.0, 7.5, 5.0, 2.5 Hz, 1H), 2.87 (dd, J = 16.0, 7.0 Hz, 1H), 2.56 (dd, J = 16.0, 6.0 Hz, 1H), 2.21 (s, 3H), 1.69 (ddd, J = 13.5, 2.5, 2.5 Hz, 1H), 1.70–1.63 (m, 1H), 1.55–1.44 (m, 2H), 1.42–1.35 (m, 2H), 1.32–1.25 (m, 20H), 0.89 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.9, 138.7, 128.7, 128.3, 126.1,

100.7, 76.9, 73.2, 49.7, 36.9, 36.0, 32.1, 31.4, 29.81, 29.76, 29.73, 29.5, 25.2, 22.8, 14.3; MALDI-TOF/CCA-HRMS calcd for $C_{26}H_{42}O_3Na$ $[M + Na]^+$: 425.3026, found 425.3055.

1-((2*S*,3*S*)-3-((tert-Butyldimethylsilyl)oxy)-6-oxo-3,6-dihydro-2H-pyran-2-yl)-5-((2*S*,4*S*,6*S*)-2-phenyl-6-tridecyl-1,3-dioxan-4-yl)pentane-2,4-dione (10)

LDA solution: To a stirred solution of diisopropylamine (0.770 mL, 4.78 mmol) in tetrahydrofuran (5 mL) at –78 °C was added *n*-butyllithium (1.8 M, 2.0 mL, 3.6 mmol) slowly. The resulting mixture was stirred at the same temperature for 15 min and used directly for next step. To a stirred solution of methyl ketone **12** (1.92 g, 4.78 mmol) in tetrahydrofuran (10 mL) at –78 °C was added LDA solution slowly. The resulting mixture was stirred at the same temperature for 15 min. A solution of acyl chloride **11** in tetrahydrofuran (5 mL) at –78 °C was slowly added the mixture. After 15 min, the reaction mixture was quenched by adding water, and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (5 to 20% EtOAc in hexanes) on silica gel (50 mL) to afford **10** (0.840 g, 52%) as a colorless oil. Data for **10**: R_f = 0.19 (20% EtOAc in Hexanes); $[\alpha]_D^{21}$ = +2.8 ($CHCl_3$, c = 0.52); IR (neat) 3417, 2926, 2855, 1787, 1724, 1636, 1461, 1347, 1260, 1147, 1094 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 14.89 (br s, 1H), 7.48–7.46 (m, 2H), 7.36–7.31 (m, 3H), 6.79 (dd, J = 15.5, 5.5 Hz, 1H), 6.17 (dd, J = 15.5, 1.5 Hz, 1H), 5.63 (s, 1H), 5.55 (s, 1H), 5.01 (ddd, J = 5.5, 4.0, 1.5 Hz, 1H), 4.60 (ddd, J = 5.5, 4.5, 2.5 Hz, 1H), 4.32 (dddd, J = 9.5, 8.5, 6.0, 2.5 Hz, 1H), 3.83 (dddd, J = 9.0, 7.5, 5.0, 2.5 Hz, 1H), 2.82 (dd, J = 15.0, 7.0 Hz, 1H), 2.76 (dd, J = 17.5, 5.5 Hz, 1H), 2.57 (dd, J = 15.0, 6.0 Hz, 1H), 2.51 (dd, J = 17.5, 2.5 Hz, 1H), 1.69 (ddd, J = 13.0, 2.0, 2.0 Hz, 1H), 1.70–1.65 (m, 1H), 1.54–1.41 (m, 3H), 1.40–1.35 (m, 1H), 1.32–1.25 (m, 20H), 0.88 (t, J = 7.0 Hz, 3H), 0.84 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 199.5, 174.8, 174.2, 138.8, 135.1, 128.8, 128.3, 127.9, 126.2, 102.2, 100.7, 83.4, 77.0, 73.6, 70.6, 47.2, 39.3, 37.0, 36.0, 32.1, 29.88, 29.86, 29.85,

29.84, 29.82, 29.81, 29.77, 29.76, 29.5, 25.7, 25.2, 22.9, 18.1, 14.3, –4.7, –4.9; MALDI-TOF/CCA-HRMS calcd for $C_{39}H_{62}O_7SiNa$ $[M + Na]^+$: 693.4157, found 693.4169.

(6*S*,8*S*)-1-((2*S*,3*S*)-3-((tert-Butyldimethylsilyl)oxy)-6-oxo-3,6-dihydro-2H-pyran-2-yl)-6,8-dihydroxyhenicosane-2,4-dione (26)

To a flask with 10 (45.3 mg, 67.5 μmol) was added a solution of acetic acid (2 mL, 80%) in water. The resulting mixture was heated in an oil bath to reflux and stirred for 1 min. The solvent was removed under reduced pressure. The crude residue was purified by flash chromatography (30 to 80% EtOAc in hexanes) on silica gel (2 mL) to afford **26** (25.0 mg, 63%) as a colorless oil. Data for **26**: R_f = 0.23 (50% EtOAc in Hexanes); $[\alpha]_D^{21}$ = –28.6 ($CHCl_3$, c = 0.22); IR (neat) 3418, 2925, 2854, 1785, 1732, 1646, 1575, 1462, 1404, 1258, 1155, 1092, 1029 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.53 (dd, J = 16.0, 6.0 Hz, 1H), 6.25 (dd, J = 16.0, 1.5 Hz, 1H), 5.45 (s, 1H), 4.97 (ddd, J = 5.5, 4.5, 1.0 Hz, 1H), 4.65 (dddd, J = 9.5, 7.0, 7.0, 7.0 Hz, 1H), 4.57 (ddd, J = 5.5, 4.0, 2.0 Hz, 1H), 3.87–3.81 (m, 1H), 2.77 (dd, J = 17.0, 5.0 Hz, 1H), 2.55–2.53 (m, 2H), 2.51 (dd, J = 17.0, 1.5 Hz, 1H), 2.03 (ddd, J = 14.5, 8.5, 6.5 Hz, 1H), 1.85 (ddd, J = 14.5, 6.5, 4.0 Hz, 1H), 1.62 (d, J = 4.5 Hz, 1H), 1.53–1.49 (m, 3H), 1.46–1.41 (m, 1H), 1.34–1.25 (m, 20H), 0.88 (t, J = 7.0 Hz, 3H), 0.84 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.4, 174.7, 166.5, 132.3, 127.2, 107.1, 83.6, 78.0, 70.8, 69.0, 42.0, 41.7, 39.4, 38.1, 32.1, 29.89, 29.87, 29.85, 29.80, 29.79, 29.6, 25.7, 22.9, 14.3, –4.6, –4.9; MALDI-TOF/CCA-HRMS calcd for $C_{32}H_{58}O_7SiNa$ $[M + Na]^+$: 605.3844, found 605.3860.

(6*S*,8*S*)-6,8-Dihydroxy-1-((2*S*,3*S*)-3-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)henicosane-2,4-dione (8)

To a plastic tube with **26** (15 mg, 25.7 mmol) was added a solution of hydrogen fluoride pyridine (1.2 M, 1.2 mL, 1.2 mmol) in acetonitrile at room temperature. The resulting mixture was stirred at the same temperature overnight. The reaction was quenched by adding saturated aqueous sodium bicarbonate (4

mL) and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (20 to 100% EtOAc in hexanes) on silica gel (2 mL) to afford **8** (8.5 mg, 71%) as a colorless oil. Data for **8**: R_f = 0.28 (90% EtOAc in Hexanes); $[\alpha]_D^{21}$ = –55.1 ($CHCl_3$, c = 0.20); IR (neat) 3385, 2924, 2854, 1777, 1732, 1640, 1573, 1460, 1407, 1265, 1159, 1081, 1024 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.52 (dd, J = 16.0, 5.0 Hz, 1H), 6.36 (dd, J = 16.0, 1.5 Hz, 1H), 5.48 (s, 1H), 5.12 (s, 1H), 5.04 (ddd, J = 5.5, 4.0, 1.5 Hz, 1H), 4.74–4.68 (m, 1H), 4.65–4.62 (m, 1H), 3.88–3.83 (m, 1H), 3.35 (s, 1H), 2.84 (dd, J = 18.0, 5.5 Hz, 1H), 2.65 (dd, J = 18.0, 1.0 Hz, 1H), 2.60–2.50 (m, 2H), 2.06 (ddd, J = 14.5, 9.0, 7.5 Hz, 1H), 1.85 (ddd, J = 14.5, 6.0, 3.5 Hz, 1H), 1.57–1.50 (m, 3H), 1.45–1.40 (m, 1H), 1.33–1.25 (m, 20H), 0.88 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.3, 174.5, 166.1, 130.5, 128.2, 107.4, 83.1, 78.4, 69.8, 69.5, 41.7, 38.7, 38.1, 32.1, 29.89, 29.87, 29.85, 29.79, 29.77, 29.6, 25.6, 22.9, 14.3; MALDI-TOF/CCA-HRMS calcd for $C_{26}H_{44}O_7Na$ $[M + Na]^+$: 491.2979, found 491.2995.

Author Information

G.ODoherty@neu.edu

Author contributions

All authors were involved with execution of the research plan and preparation of the manuscript. All authors have read and agreed to the published version of the manuscript.

Supporting Information

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^1H and $^{13}C\{^1H\}$ NMR spectra (PDF)

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