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Total Synthesis of (−)-Cinatrin C_1 Based on an $In(OTf)_3$-Catalyzed Conia-Ene Reaction

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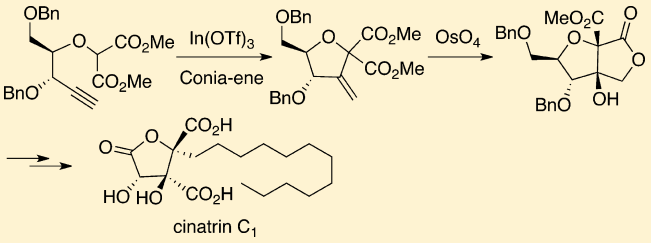
Supporting Information

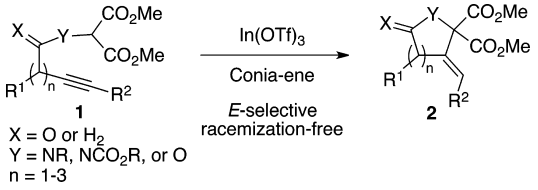
ABSTRACT: The stereocontrolled total synthesis of (−)-cinatrin C_1, a phospholipase A_2 inhibitor, has been accomplished. The key feature includes the stereoselective construction of the highly substituted tetrahydrofuran core by $In(OTf)_3$-catalyzed Conia−ene reaction of the oxygen-tethered acetylenic malonic ester followed by dihydroxylation with concomitant lactonization.



INTRODUCTION

Recently, in connection with a project directed toward the synthesis of biologically intriguing natural products having a highly functionalized heterocyclic core such as lactacystin, salinosporamide A, and oxazolomycin,[1] we have developed a new methodology for heterocycle synthesis that relies upon $In(OTf)_3$-catalyzed Conia−ene reaction[2−5] of heteroatom-tethered acetylenic malonic ester **1** giving **2** (Scheme 1). This

Scheme 1. $In(OTf)_3$-Catalyzed Conia−Ene Reactions



method is applicable to chiral terminal and nonterminal alkynes giving various five- to seven-membered nitrogen- or oxygen-containing heterocyclic compounds stereoselectively without significant amounts of racemization. To further demonstrate the synthetic utility of this methodology, we became interested in the synthesis of the cinatrins[6] possessing highly functionalized γ-lactone cores, which structurally belong to the alkyl citrate family of natural products. The reason we focused on the cinatrins arose from our continuing study on the synthesis of this family of natural products (Figure 1).[7]

In 1992, Itazaki and co-workers reported the isolation of cinatrins A, B, C_1, C_2, and C_3 from the fermentation broth of *Circinotrichum falcatisporum* RF-641.[6] The cinatrins were found to be potent inhibitors of rat platelet phospholipase A_2 (PLA_2) with maximal inhibition shown by cinatrin C_3 (IC_{50} 70 μM). Since PLA_2 plays a key role in biosynthesis of eicosanoids such as the prostanoids,[8] this class of natural products are expected to be potential anti-inflammatory agents. The intriguing biological activities and molecular architectures make the

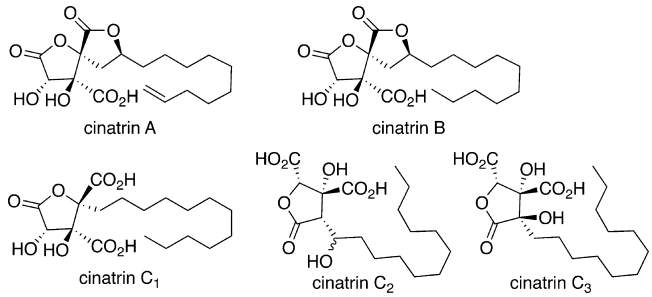


Figure 1. Cinatrin family.

cinatrins good targets for synthesis. In 1997, Evans and co-workers reported the first synthesis of (+)-cinatrin C_1 and (−)-cinatrin C_3 using a tartrate aldol methodology,[9] thus establishing the absolute structures of natural cinatrins to be enantiomeric to those originally reported.[6] Then Rizzacasa and co-workers achieved the first enantiospecific synthesis of (−)-cinatrin B,[10a] (−)-cinatrin C_1,[10b] and (+)-cinatrin C_3[10b] in naturally occurring forms from D-arabinose via Ireland−Claisen rearrangement of the tetrahydrofuran-2-carboxylic acid dodec-1-en-3-yl ester derivative.[10] Recently, Yakura and co-workers reported the synthesis of 2-*epi*-cinatrin C_1 dimethyl ester via [2,3]-sigmatropic rearrangement of the in situ generated oxonium ylide from the 5-(allyloxy)-2-diazo-3-oxopentanoic acid ester derivative.[11] Herein we report a novel total synthesis of (−)-cinatrin C_1, which features the stereoselective construction of the highly substituted tetrahydrofuran core by $In(OTf)_3$-catalyzed Conia-ene cyclization of the oxygen-tethered acetylenic malonic ester followed by dihydroxylation with concomitant lactonization.

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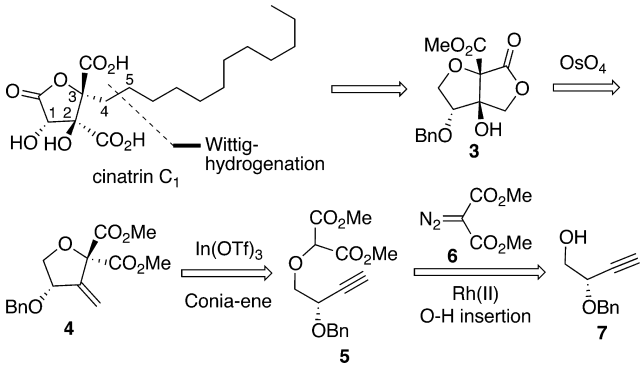
RESULTS AND DISCUSSION

From a retrosynthetic perspective, we envisioned lactone **3** as a precursor of cinatrin C_1 by the disconnection at the C4–C5 bond via Wittig olefination–hydrogenation and functional group interconversions involving oxidation of the tetrahydrofuran ring (Scheme 2). To stereoselectively access **3** we

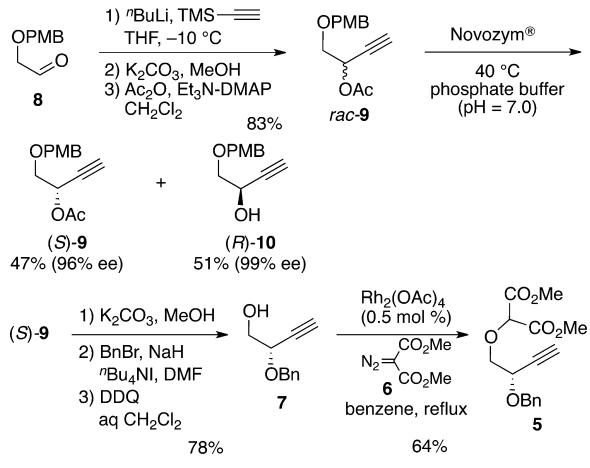
Scheme 2. Retrosynthetic Analysis



envisioned an approach from alkyne **7** via Rh(II)-catalyzed O–H insertion reaction of dimethyl diazomalonate (**6**), $In(OTf)_3$-catalyzed Conia–ene reaction of **5**, and stereoselective dihydroxylation of **4** accompanied by lactonization leading to the discrimination of the geminal esters. This approach is appealing since the two contiguous quaternary centers could be created stereoselectively by one dihydroxylation process under the influence of the C1 stereochemistry.

Following the above-mentioned retrosynthetic analysis, the route toward cinatrin C_1 began with the preparation of enantiopure **5** (Scheme 3). Thus, racemic acetate **9**, derived

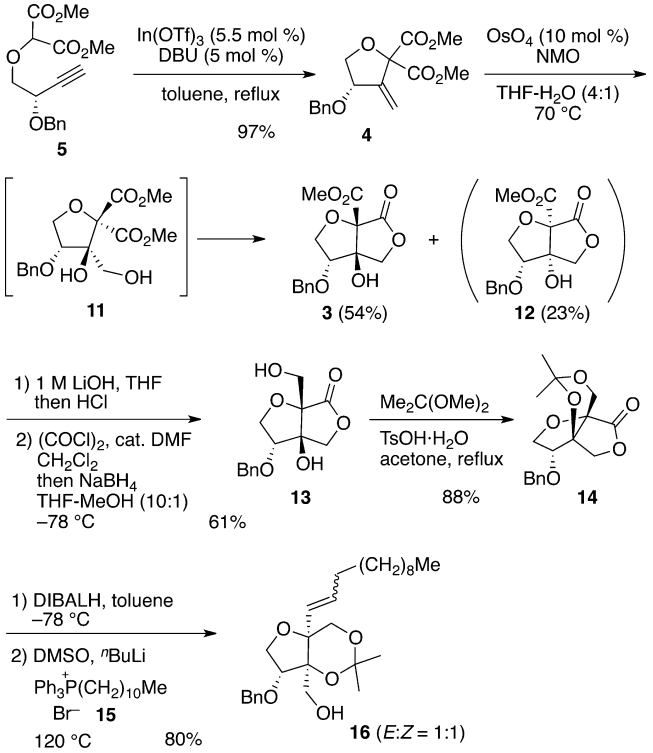
Scheme 3. Preparation of O-Tetherd Acetylenic Malonic Ester 5



from known aldehyde **8**[12] in three steps, was subjected to lipase-mediated kinetic resolution under hydrolytic conditions using Novozym[13] to give (*S*)-**9** and (*R*)-**10**[14] both in almost enantiopure forms. (*S*)-Acetate **9** was then converted to alcohol **7** via methanolysis, benzylation, and removal of the *p*-methoxybenzyl protecting group. O–H insertion reaction[15] between **7** and methyl diazomalonate (**6**) was conducted in the presence of a catalytic amount of $Rh_2(OAc)_4$ in boiling benzene to furnish compound **5** required for the crucial $In(OTf)_3$-catalyzed Conia-ene reaction.

Upon treatment of **5** with a catalytic amount of $In(OTf)_3$ in the presence of DBU in boiling toluene, regio- and stereoselective cyclization took place cleanly to produce tetrahydrofuran **4** in excellent yield (Scheme 4). It is important to note

Scheme 4. Preparation of Tetrahydrofuran Intermediate 16



that in this particular case the reaction again occurred without racemization.[16] The subsequent dihydroxylation of **4** turned out to be very sluggish at room temperature, thus requiring the reaction to be heated in order to proceed at a reasonable rate. The diastereoselectivity therefore became moderate although the lactonization of **11** took place simultaneously as expected to produce a 70:30 mixture of the desired compound **3** and its diastereomer **12**. Since the selective reduction of the γ-lactone in the presence of the methyl ester turned out to be difficult, the latter functionality was converted to the primary alcohol by alkaline hydrolysis followed by $NaBH_4$ reduction of the corresponding acid chloride to give alcohol **13**. At this point, **13** became a crystalline solid, the X-ray analysis of which allowed us to unambiguously determine its stereostructure.[17] After protection of **13** as its acetonide, DIBALH reduction of **14** afforded the corresponding lactol which was then subjected to Wittig reaction using the ylide, generated from phosphonium bromide **15**[18] by the action of *n*-butyllithium, in DMSO at 120 °C,[19] to afford **16** as an inseparable 1:1 *E*/*Z*-mixture in good yield.

With compound **16** possessing the carbon framework of cinatrin C_1 in hand, we then investigated the remaining transformations including oxidation of the tetrahydrofuran ring (Scheme 5). Thus, the primary alcohol of **16** was converted to the methyl ester by a three-step sequence involving Dess–Martin oxidation, Pinnick–Kraus oxidation,[20] and esterification to give **17** in good yield. Hydrogenation of **17** followed by removal of the acetonide group afforded diol **18**, the

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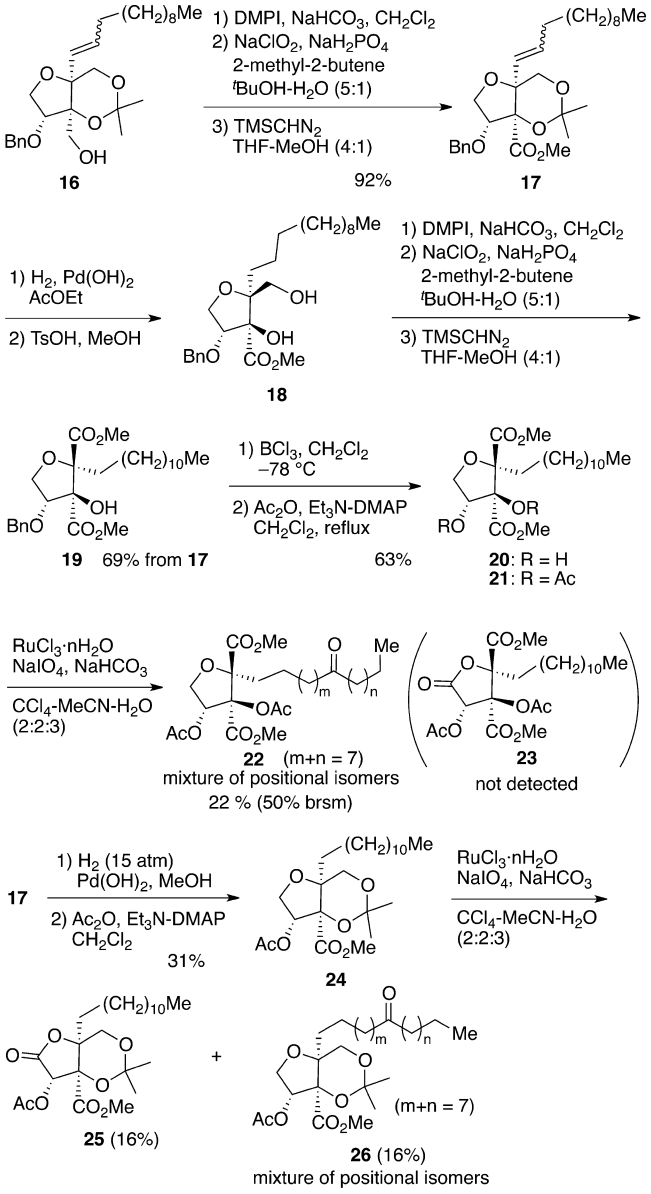
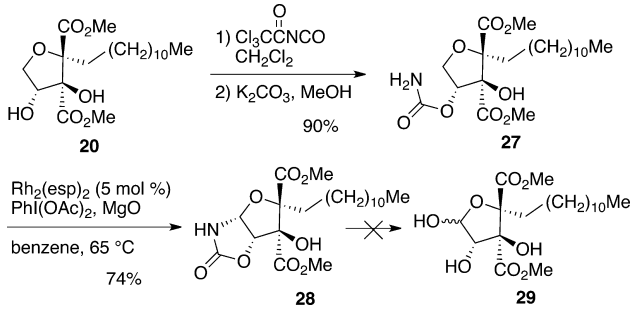
Scheme 5. Attempts toward the Synthesis of γ-Lactone Intermediates via Oxidation of the Tetrahydrofuran Rings



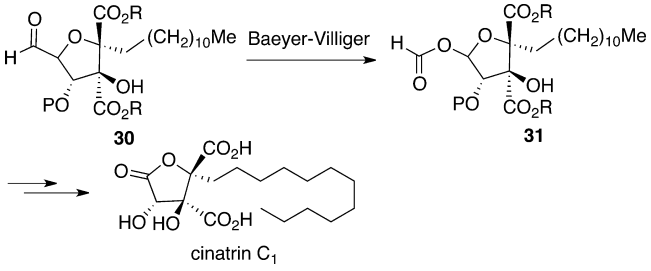
We also attempted to oxidize the tetrahydrofuran ring of **20** using the C−H amination methodology reported by Du Bois and co-workers[22,23] (Scheme 6). Thus, diol **20** was first converted to carbamate **27** by the reaction with trichloroacetyl isocyanate followed by methanolysis. Upon treatment of **27** with a catalytic amount of $Rh_2(esp)_2$ in the presence of iodosobenzene diacetate and MgO in benzene at 65 °C, the C−H amination took place cleanly to afford cyclic carbamate **28** in acceptable yield. However, the subsequent conversion of **28** to hemiacetal **29** failed under various acidic and basic hydrolysis conditions.

Scheme 6. Alternative Approach via Du Bois' C−H Amination



In order to overcome the encountered problem in the oxidation of a tetrahydrofuran ring, we envisioned an alternative approach centered around Baeyer−Villiger oxidation of aldehyde **30** giving formate **31**, from which cinatrin C_1 would be accessible (Scheme 7).

Scheme 7. Approach via a Baeyer−Villiger Oxidation



hydroxymethyl group of which was then transformed to the methyl ester in the same manner as described for the conversion of **16** to **17** giving rise to diester **19**. After BCl_3-promoted debenzylation of **19**, the resulting diol **20** was acetylated to give diacetate **21** possessing all requisite functionalities besides a γ-lactone carbonyl group. However, oxidation of **21** to γ-lactone **23** turned out to be very difficult after we had examined various oxidation conditions.[21] For example, RuO_4[21a] oxidation of **21** under conventional conditions produced ketone **22** in which some position of the alkyl chain was oxidized in low yield. It was assumed that the unexpected difficulty in the oxidation of **21** would be attributed to the highly electron deficient nature of the tetrahydrofuran ring having four electron-withdrawing ester substituents. In fact, RuO_4 oxidation of **24** with two ester groups was found to produce the desired γ-lacone **25** along with ketone **26**, although the yields of both compounds were very low.

To realize this approach, the investigation began with the preparation of compound **41** from aldehyde **33**[24] available by D-proline-catalyzed self-aldolization of **32**, following the methodology developed for the synthesis of **16** (Scheme 8). Thus, Ohira−Bestmann reaction[25] of **33** gave alkyne **34** which was then subjected to $Rh_2(OAc)_4$-catalyzed O−H insertion reaction using **6** to provide **35**. $In(OTf)_3$-catalyzed Conia−ene reaction of **35** again proceeded cleanly to afford tetrahydrofuran **36** in excellent yield. Although dihydroxylation of **36** under the conditions employed for **4** exhibited somewhat lower diastereoselectivity (dr = 2:1), Narasaka's modified procedure[26] remarkably improved this dihydroxylation-lactonization step. Thus, when **36** was treated with a catalytic amount of OsO_4 in the presence of NMO and phenylboronic acid in CH_2Cl_2 at room temperature, lactone **37** and **38** were obtained in a ratio of 5:1 in good yield.[27] Following the procedure shown in Scheme 4, compound **37** was then transformed to **41** via **39** and **40**.

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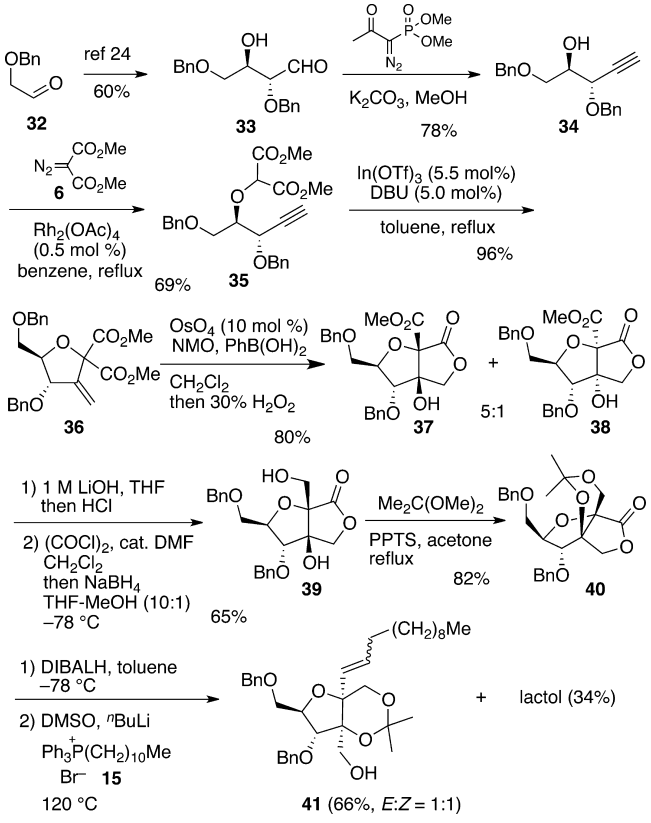
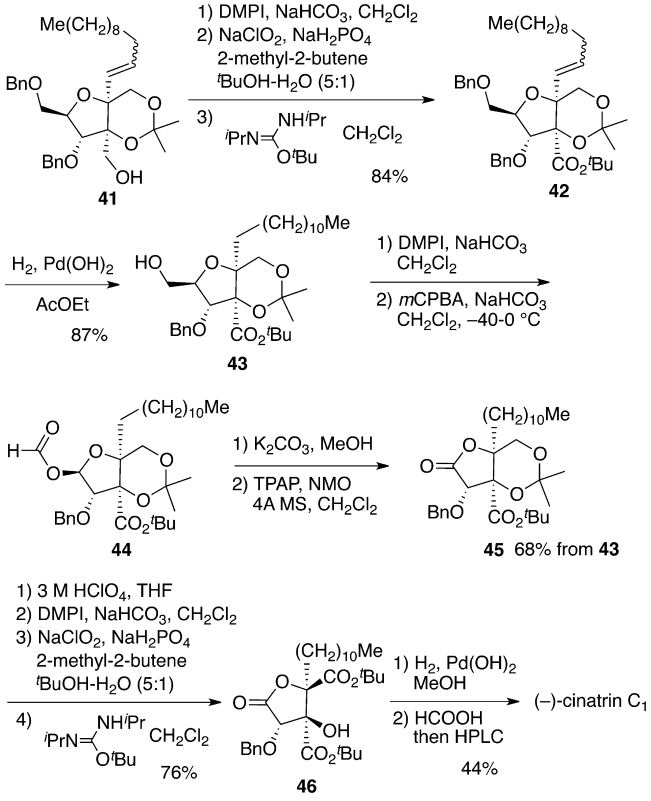
Scheme 8. Synthesis of Tetrahydrofuran Intermediate 41



Scheme 9. Completion of the Total Synthesis of Cinatrin C_1



Because all attempts to simultaneously oxidize two C2- and C3-hydroxymethyl groups were unsuccessful, we were obliged to adopt a stepwise oxidation sequence. The primary alcohol of **41** was first converted to the *tert*-butyl ester by successive Dess–Martin oxidation, Pinnick–Kraus oxidation, and esterification using *N*,*N*′-diisopropyl-*O*-2-*tert*-butylisourea[28] (Scheme 9) to afford **42** in good yield. $Pd(OH)_2$-catalyzed reaction of **42** under hydrogen atmosphere allowed hydrogenation of the olefinic double bond and hydrogenolytic removal of the primary benzyl group to give alcohol **43**. After Dess–Martin oxidation of **43**, the resulting aldehyde was subjected to Baeyer–Villiger oxidation using *m*-chloroperbenzoic acid to afford formate **44**. Methanolytic removal of the formyl group of **44** followed by TPAP oxidation[29] of the lactol led to the formation of γ-lactone **44**, which was converted to diester **46** by removal of the acetonide followed by the above-mentioned three-step conversion of the hydroxymethyl group to the *tert*-butyl ester. Finally, removal of the benzyl group and two *tert*-butyl groups, followed by HPLC purification completed the total synthesis of (−)-cinatrin C_1. The spectroscopic data and the specific rotation of the synthetic substance were in accord with those reported[6,9,10b] for natural cinatrin C_1. Since saponification of cinatrin C_1 are known to produce cinatrin C_3,[6,10b] our present synthesis constitutes the formal synthesis of (+)-cinatrin C_3.

CONCLUSION

We have accomplished the total synthesis of (−)-cinatrin C_1 in 24 steps and 2% overall yield from benzyloxyacetaldehyde (**32**). The present synthesis illustrates the synthetic utility of the methodology based on an $In(OTf)_3$-catalyzed Conia–ene reaction for heterocycle synthesis which we have previously developed.[1c]

EXPERIMENTAL SECTION

General Methods. Where appropriate, reactions were performed in flame-dried glassware under argon atmosphere. All extracts were dried over $MgSO_4$ or Na_2SO_4 and concentrated by rotary evaporation below 30 °C at 25 Torr unless otherwise noted. Commercial reagents and solvents were used as supplied with the following exceptions. *N*,*N*-Dimethylformamide (DMF), dichloromethane (CH_2Cl_2), acetonitrile (MeCN), benzene, and triethylamine (Et_3N) were distilled from CaH_2. Thin-layer chromatography (TLC) was performed using glass-packed silica gel plates (0.25 or 0.5 mm thickness). Column chromatography was performed using silica gel (particle size 100–210 μm (regular), 40–50 μm (flush)). Optical rotations were recorded on a digital polarimeter at ambient temperature. Infrared spectra were measured on a Fourier transform infrared spectrometer. ^{1}H NMR and ^{13}C NMR spectra were measured using $CDCl_3$ or CD_3OD as solvent, and chemical shifts are reported as δ values in ppm based on internal $(CH_3)_4Si$ (0.00 ppm, ^{1}H) or solvent peak. HRMS spectra were taken in EI (dual focusing sector field), ESI (TOF) or FAB (dual-focusing sector field) mode.

1-(4-Methoxybenzyloxy)-4-(trimethylsilyl)but-3-yn-2-ol. To a stirred solution of ethynyltrimethylsilane (0.60 mL, 4.34 mmol) in THF (9.0 mL) at −10 °C was added *n*-BuLi (1.66 M in hexane; 2.20 mL, 3.65 mmol). After the solution was stirred at −10 °C for 30 min, a solution of **8**[12] (551 mg, 3.06 mmol) in THF (6.0 mL) was added, and the mixture was stirred at −10 °C for 1.5 min. The reaction was quenched with saturated NH_4Cl, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 30 g, hexane/AcOEt = 6:1) to give the title compound as a pale yellow oil (731 mg, 86%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 9.0 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 4.54–4.53 (m, 3H), 3.81 (s, 3H), 3.62 (dd, J = 10.0, 3.4 Hz, 1H), 3.52 (dd, J = 10.0, 7.8 Hz, 1H), 2.49 (d, J = 3.4 Hz, 1H), 0.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 129.7, 129.4, 113.8, 103.0, 90.4, 73.2,

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73.0, 62.0, 55.2, −0.2; FTIR (neat) 3427, 2958, 1611, 1513, 1460, 1249, 1175, 1099, 1033 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{21}O_3Si$ [$(M - H)^+$] 277.1260, found 277.1275.

1-(4-Methoxybenzyloxy)but-3-yn-2-yl Acetate (*rac*-9). To an ice-cooled solution of 1-(4-methoxybenzyloxy)-4-(trimethylsilyl)but-3-yn-2-ol (1.00 g, 3.59 mmol) in MeOH (36 mL) was added K_2CO_3 (500 mg, 3.62 mmol). After the mixture was stirred at room temperature for 2 h, saturated NH_4Cl was added and the mixture was extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give the corresponding terminal alkyne (*rac*-**10**) (800 mg). This product was dissolved into CH_2Cl_2 (78 mL), and Et_3N (0.830 mL, 5.95 mmol), Ac_2O (0.440 mL, 4.65 mmol), and DMAP (24.4 mg, 0.20 mmol) were added at room temperature. After being stirred at room temperature for 3 h, the mixture was diluted with hexane, washed with 1 M HCl, H_2O, saturated $NaHCO_3$, and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 30 g, hexane:AcOEt = 4:1) gave *rac*-**9** (858 mg, 96%) as a pale yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 5.55 (m, 1H), 4.55 (d, J = 11.7 Hz, 1H), 4.51 (d, J = 11.7 Hz, 1H), 3.81 (s, 3H), 3.66 (m, 2H), 2.46 (d, J = 2.4 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 159.2, 129.4, 129.3, 113.7, 78.5, 74.4, 72.8, 70.3, 62.5, 55.1, 20.8; FTIR (neat) 3277, 2938, 2866, 1738, 1516, 1233, 1027 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{16}O_4$ (M^+) 248.1049, found 248.1049.

(*S*)-1-(4-Methoxybenzyloxy)but-3-yn-2-yl Acetate ((*S*)-9). To a mixture of *rac*-**9** (200 mg, 0.806 mmol) in phosphate buffer (NaH_2PO_4/Na_2HPO_4, pH 7.7, 5.4 mL) was added Novozym (100 mg) at room temperature. After being stirred at 40 °C for 7 h, the mixture was filtered through Celite, extracted with AcOEt, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 8 g, hexane/AcOEt = 8:1 to 3:1) gave (*S*)-**9** (98.3 mg, 49%) and (*R*)-**10** (84 mg, 51%) each as a colorless oil. The enantiopurities of (*S*)-**9**, $[\alpha]^{24}_D$ +53.9 (c 1.35, $CHCl_3$), and (*R*)-**10**, $[\alpha]^{24}_D$ −4.8 (c 1.61, $CHCl_3$) (lit.[14] $[\alpha]_D$ −4.6 (c 2.22, $CHCl_3$)), were determined to be 96% ee and 99% ee, respectively, by HPLC analysis: CHIRALCEL OD-H, hexane/*i*-PrOH = 10:1 (0.5 mL/min), t_R = 30.4 min ((*R*)-**10**) and 34.8 min ((*S*)-**10**).

(*S*)-1-(4-Methoxybenzyloxy)but-3-yn-2-ol ((*S*)-10). To an ice-cooled solution of (*S*)-**9** (354 mg, 1.43 mmol) in MeOH (14 mL) was added K_2CO_3 (193 mg, 1.40 mmol). After the mixture was stirred at room temperature for 2 h, saturated NH_4Cl was added, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 10 g, hexane/AcOEt = 3:1) to give (*S*)-**10** (248 mg, 84%) as a colorless oil: $[\alpha]^{24}_D$ +4.9 (c 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 4.58−4.51 (m, 3H), 3.81 (s, 3H), 3.63 (dd, J = 9.8, 3.6 Hz, 1H), 3.55 (dd, J = 9.8, 6.8 Hz, 1H), 2.52 (brs, 1H), 2.45 (d, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 129.51, 129.48, 113.9, 81.6, 73.6, 73.1, 73.0, 61.3, 55.2; FTIR (neat) 3438, 3279, 2933, 2860, 1610, 1510, 1240, 1105, 1028 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{14}O_3$ (M^+) 206.0943, found 206.0936.

1-(((*S*)-2-(Benzyloxy)but-3-ynyloxy)methyl)-4-methoxybenzene. To an ice-cooled solution of (*S*)-**10** (2.00 g, 9.70 mmol) in DMF (32 mL) was added NaH (60% in mineral oil, 480 mg, 12.0 mmol), and the mixture was stirred at the same temperature for 10 min. Benzyl bromide (14.0 mL, 11.8 mmol) and tetra-*n*-butylammonium iodide (72.0 mg, 0.20 mol) were added at 0 °C, and the mixture was stirred at room temperature for 5 h. The mixture was diluted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 10 g, hexane/AcOEt = 3:1) to give the corresponding benzyl ether (2.66 g, 93%) as a colorless oil: $[\alpha]^{25}_D$ +69.1 (c 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.26 (m, 7H), 6.87, (d, J = 7.8 Hz, 2H), 4.83, (d, J = 11.7 Hz, 1H), 4.59−4.53 (m, 3H), 4.32 (brs, 1H), 3.80 (s, 3H), 3.69−3.66 (m, 2H), 2.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 137.5, 130.0, 129.4, 128.4, 128.0, 127.8, 113.7, 80.4, 74.8, 73.1, 71.9, 70.8, 68.2, 55.2; FTIR (neat) 3283, 2862, 1612, 1513, 1455, 1247, 1091, 1034 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{20}O_3$ (M^+) 296.1399, found 296.1412.

(*S*)-2-(Benzyloxy)but-3-yn-1-ol (7). The benzyl ether (100 mg, 0.334 mmol) was dissolved in a mixture of CH_2Cl_2 (3.2 mL) and H_2O (0.2 mL). DDQ (309 mg, 1.36 mmol) was added at 0 °C, and the mixture was stirred at 0 °C for 1.5 h. The mixture was filtered through Celite, and the filter cake was washed thoroughly with CH_2Cl_2. The combined filtrate and washings were washed with saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 5 g, hexane/AcOEt = 9:1) to give **7** (57.6 mg, 100%) as a colorless oil: $[\alpha]_D^{26}$ +145.9 (c 0.99, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.33 (m, 5H), 4.87 (d, J = 11.2 Hz, 1H), 4.54 (d, J = 11.2 Hz, 1H), 4.23 (brs, 1H), 3.77 (t, J = 5.4 Hz, 2H), 2.52 (s, 1H), 2.15 (t, J = 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 128.5, 128.2, 128.0, 79.7, 75.6, 71.0, 69.4, 65.2; FTIR (neat) 3286, 2871, 1455, 1375, 1073 cm^{-1}; HRMS (FAB) calcd for $C_{11}H_{13}O_2$ [$(M + H)^+$] 177.0916, found 177.0930.

Dimethyl 2-((*S*)-2-(Benzyloxy)but-3-ynyloxy)malonate (5). To a stirred solution of **7** (3.20 g, 18.3 mmol) and methyl diazomalonate (**6**) (3.50 g, 22.0 mmol) in benzene (37 mL) was added $Rh_2(OAc)_4$ (40 mg, 0.091 mmol). After the solution was heated under reflux for 1 h, most of the solvent was evaporated, and the residue was subjected to column chromatography (SiO_2 200 g, toluene/AcOEt = 6:1) to give **5** (3.58 g, 64%) as a colorless oil: $[\alpha]^{26}_D$ +54.2 (c 0.90, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.26 (m, 5H), 4.83 (d, J = 11.7 Hz, 1H), 4.81 (s, 1H), 4.52 (d, J = 11.7 Hz, 1H), 4.42−4.40 (m, 1H), 3.95 (dd, J = 11.7, 3.4 Hz, 1H), 3.83 (dd, J = 7.8, 3.4 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 2.51 (d, J = 3.4 Hz, 1H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 166.9, 166.7, 137.3, 128.4, 127.9, 127.8, 79.6, 79.2, 75.6, 73.3, 71.0, 68.8, 52.9, 52.8; FTIR (neat) 3272, 2953, 2114, 1738, 1435, 1088 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{18}O_6$ (M^+) 306.1103, found 306.1091.

(*S*)-Dimethyl 4-(Benzyloxy)-dihydro-3-methylenefuran-2,2(3*H*)-dicarboxylate (4). To a solution of **5** (3.60 g, 11.7 mmol) in toluene (129 mL) were added DBU (106 μL, 0.68 mmol) and $In(OTf)_3$ (361 mg, 0.64 mmol). After the solution was heated under reflux for 3 h, most of the solvent was evaporated, and the residue was subjected to column chromatography (SiO_2 = 200 g, hexane/AcOEt = 4:1) to give **4** (3.50 g, 97%) as a colorless oil: $[\alpha]^{28}_D$ +11.1 (c 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.31 (m, 5H), 5.78 (s, 1H), 5.65 (s, 1H), 4.63 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 4.40 (brs, 1H), 4.15−4.13 (m, 2H), 3.80 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 167.4, 143.1, 137.4, 128.3, 127.8, 127.7, 116.9, 86.2, 78.5, 73.7, 70.0, 53.2; FTIR (neat) 2952, 1743, 1434, 1232, 1094, 1059 cm^{-1}; HRMS (FAB) calcd for $C_{16}H_{19}O_6$ [$(M + H)^+$] 307.1181, found 307.1203. The enantiomeric purity was determined to be 94% ee by HPLC analysis: CHIRALCEL OD-H, hexane/*i*-PrOH = 9:1 (0.5 mL/min), t_R = 33.1 min (enantiomer of **4**) and 42.3 min (compound **4**).

Methyl (3*R*,3a*S*,6a*R*)-3-(Benzyloxy)hexahydro-3a-hydroxy-6-oxofuro[3,4-*b*]-furan-6a-carboxylate (3). To a solution of **4** (3.50 g, 11.3 mmol) in THF (189 mL) and H_2O (63 mL) at room temperature were added NMO (3.98 g, 34.0 mmol) and OsO_4 (0.15 M in H_2O, 7.60 mL, 1.13 mmol), and the mixture was heated at 70 °C for 7 h. The mixture was diluted with 20% $Na_2S_2O_3$ and AcOEt. The organic layer was washed with H_2O and brine, dried, concentrated, and chromatographed (SiO_2 200 g, hexane/AcOEt = 2:1) to give **3** (1.87 g, 54%) and its diastereomer **12** (798 mg, 23%) each as a white solid.

Compound **3**: $[\alpha]^{24}_D$ −14.2 (c 0.90, MeOH); mp 115−117 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.26 (m, 5H), 4.81 (d, J = 9.3 Hz, 1H), 4.66 (d, J = 11.7 Hz, 1H), 4.54 (d, J = 11.7 Hz, 1H), 4.29 (dd, J = 10.2, 4.4 Hz, 1H), 4.22 (d, J = 9.3 Hz, 1H), 4.14 (m, 1H), 4.01 (dd, J = 10.2, 4.4 Hz, 1H), 3.87 (s, 3H), 3.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 166.3, 136.6, 128.7, 128.2, 127.6, 88.5, 87.5, 84.0, 72.5, 72.2, 70.6, 53.6; FTIR (neat) 3437, 2955, 1768, 1457, 1247, 1119, 1018 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{16}O_7$ (M^+) 308.0896, found 308.0883.

Compound **12**: $[\alpha]^{24}_D$ −76.6 (c 1.34, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.33 (m, 3H), 7.32−7.30 (m, 2H), 4.73 (d, J = 11.7 Hz, 1H), 4.63 (d, J = 11.7 Hz, 1H), 4.35 (d, J = 9.8 Hz, 1H), 4.20 (d, J = 9.8 Hz, 1H), 4.16 (dd, J = 9.8, 4.8 Hz, 1H), 4.09−4.02 (m, 1H), 3.86 (s, 3H), 3.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0,

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165.0, 135.8, 128.88, 128.85, 128.2, 88.0, 84.3, 81.0, 73.4, 73.1, 72.2, 53.2; FTIR (neat) 3468, 2956, 1791, 1458, 1303, 1123, 1025 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{16}O_7$ (M^+) 308.0896, found 308.0890.

(3*R*,3a*S*,6a*S*)-3-(Benzyloxy)tetrahydro-3a-hydroxy-6a-(hydroxymethyl)furo[3,4-*b*]furan-6(6a*H*)-one (13). To an ice-cooled solution of **3** (1.90 g, 6.10 mmol) in THF (97 mL) was added 1 M LiOH (24 mL). After being stirred at room temperature for 30 min, the mixture was diluted with Et_2O, acidified (pH = 1) with 1 M HCl, and extracted with AcOEt. The extract was dried and concentrated to give the carboxylic acid as a white solid (1.92 g). The product was dissolved in CH_2Cl_2 (10 mL) and THF (0.5 mL), and oxalyl chloride (1.60 mL, 18.7 mmol) and DMF (47.0 μL, 0.61 mmol) were added at 0 °C. After the solution was stirred at room temperature for 1 h, the most of the solvent was evaporated, and THF (61 mL) and MeOH (6 mL) were added to the residue. The resulting solution was cooled to −78 °C, and $NaBH_4$ (688 mg, 18.2 mmol) was added. After being stirred at −78 °C for 1 h, the mixture was acidified by the addition of 0.5 M HCl (10 mL), extracted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 100 g, CH_2Cl_2/AcOEt = 6:1) gave **13** as a white solid (1.04 g, 61%), which was recrystallized from AcOEt for X-ray analysis: $[\alpha]^{24}_D$ +11.0 (*c* 1.02, MeOH); mp 106−109 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.30 (m, 5H), 4.85 (d, *J* = 9.8 Hz, 1H), 4.63 (d, *J* = 12.2 Hz, 1H), 4.61 (d, *J* = 12.2 Hz, 1H), 4.19−4.11 (m, 3H), 4.12 (d, *J* = 11.7 Hz, 1H), 3.97 (d, *J* = 11.7 Hz, 1H), 3.70 (d, *J* = 6.8 Hz, 1H), 3.68 (d, *J* = 6.8 Hz, 1H), 2.61 (brs, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 137.0, 128.6, 128.2, 127.7, 85.5, 85.0, 85.0, 72.5, 71.7, 70.3, 61.6; FTIR (neat) 3419, 2877, 1766, 1461, 1382, 1017 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{16}O_6$ (M^+) 280.0947, found 280.0946.

(4a*S*,7*R*,7a*S*)-7-(Benzyloxy)-2,2-dimethyldihydro-4*H*-4a,7a-(methanooxymethano)furo[3,2-*d*][1,3]dioxin-10-one (14). To a solution of **13** (1.10 g, 3.75 mmol) in acetone (37 mL) were added 2,2-dimethoxypropane (1.40 mL, 11.2 mmol) and *p*-TsOH·H_2O (72.0 mg, 0.380 mmol). After the solution was stirred at room temperature for 11 h, 2,2-dimethoxypropane (0.92 mL, 7.50 mmol) was added, and the mixture was refluxed for 1.5 h. The reaction was quenched with $NaHCO_3$ (150 mg, 1.79 mmol), and the mixture was diluted with saturated $NaHCO_3$ and extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 63 g, CH_2Cl_2/AcOEt = 6:1) to give **14** as a colorless oil (1.10 g, 88%): $[\alpha]^{24}_D$ −8.2 (*c* 1.12, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.30 (m, 5H), 4.76 (d, *J* = 10.2 Hz, 1H), 4.61 (d, *J* = 12.2 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 4.32 (d, *J* = 10.2 Hz, 1H), 4.25 (t, *J* = 6.4 Hz, 1H), 4.14−4.09 (m, 2H), 3.92 (d, *J* = 12.7 Hz, 1H), 3.71 (dd, *J* = 9.3, 6.4 Hz, 1H), 1.47 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 136.9, 128.6, 128.1, 127.7, 100.2, 84.6, 78.8, 72.4, 70.3, 70.1, 61.5, 27.3, 26.6; FTIR (neat) 2991, 1780, 1460, 1374, 1220, 1089, 1011 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{20}O_6$ (M^+) 320.1260, found 320.1263.

((4a*S*,7*R*,7a*S*)-7-(Benzyloxy)-4a-(dodec-1-enyl)tetrahydro-2,2-dimethyl-4*H*-furo[3,2-*d*][1,3]dioxin-7a-yl)methanol (16). To a solution of **14** (1.10 g, 3.31 mmol) in toluene (33 mL) at −78 °C was added dropwise DIBALH (1.02 M in hexane; 4.90 mL, 4.80 mmol) over 5 min, and the mixture was stirred at the same temperature for 1 h. MeOH (5 mL) was added at −78 °C, and the mixture was stirred at the same temperature for 10 min. Rochelle salt (20%) was then added, and the mixture was stirred at room temperature for 30 min and filtered through Celite. The filtrate was extracted with AcOEt, washed with brine, dried, and concentrated to give the corresponding lactol as a colorless oil (1.00 g).

n-BuLi (2.76 M in hexane; 8.00 mL, 22.1 mmol) was added to DMSO (23 mL) at room temperature, and the mixture was stirred at room temperature for 30 min. The resulting solution of dimsyllithium was added to **15**[18] (11.7 g, 23.6 mmol, dried at 200 °C under reduced pressure for 1.5 h), and the mixture was then stirred at room temperature for 30 min to generate the ylide. To this solution was added a solution of the lactol (1.00 g) in DMSO (9 mL) at room temperature, and the mixture was stirred at 120 °C for 4 h. The mixture was diluted with AcOEt, washed with H_2O and brine, dried, concentrated, and chromatographed (SiO_2 230 g, hexane/AcOEt = 20:1 to 0:1) to give **16** (1.3 g, 80%, 1:1 *E*/*Z*-mixture) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.26 (m, 5H), 5.81−5.73(m, 0.5H), 5.53−5.37 (m, 0.5H), 5.38 (d, *J* = 16.1 Hz, 0.5H), 5.09 (d, *J* = 12.2 Hz, 0.5H), 4.62 (d, *J* = 12.2 Hz, 1H), 4.58 (d, *J* = 12.2 Hz, 1H), 4.20−4.16 (m, 1H), 4.11−3.66 (m, 5H), 2.39−2.30 (m, 1H), 2.21−2.12 (m, 1H), 2.05−1.98 (m, 1H), 1.54 (s, 3H), 1.44−1.39(m, 1H), 1.42 (s, 3H), 1.37−1.19 (m, 16H), 0.88 (t, *J* = 5.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 138.1, 135.6, 132.3, 128.3, 128.3, 127.3, 127.5, 127.5, 127.3, 127.2, 126.8, 124.4, 98.4, 98.3, 98.3, 86.1, 85.9, 84.6, 84.2, 81.2, 79.4, 72.1, 72.0, 71.0, 70.6, 63.7, 63.7, 60.6, 60.5, 32.5, 31.9, 30.0, 29.6, 29.6, 29.6, 29.6, 29.4, 29.3, 29.2, 29.1, 29.0, 28.0, 24.6, 24.5, 22.7, 14.1; FTIR (neat) 3488, 2925, 2856, 1459, 1375, 1205, 1112, 1051 cm^{-1}; HRMS (EI) calcd for $C_{28}H_{44}O_5$ (M^+) 460.3189, found 460.3187.

Methyl (4a*S*,7*R*,7a*S*)-7-(Benzyloxy)-4a-(dodec-1-enyl)-tetrahydro-2,2-dimethyl-4*H*-furo[3,2-*d*][1,3]dioxine-7a-carboxylate (17). To an ice-cooled solution of **16** (215 mg, 0.467 mmol) in CH_2Cl_2 (9.3 mL) were added $NaHCO_3$ (216 mg, 2.57 mmol) and Dess−Martin periodinane (DMPI) (990 mg, 2.33 mmol). After being stirred at room temperature for 5 h, the reaction was quenched with saturated $Na_2S_2O_3$, and the mixture was extracted with AcOEt. The extract was washed with $NaHCO_3$ and brine, dried, and concentrated to give the corresponding aldehyde (243 mg). The crude aldehyde was dissolved in *t*-BuOH (3.9 mL) and H_2O (0.8 mL). 2-Methyl-2-butene (1.5 mL, 14.3 mmol), NaH_2PO_4 (219 mg, 1.40 mmol), and $NaClO_2$ (169 mg, 1.87 mmol) were added, and the mixture was stirred at room temperature for 2 h. The reaction was quenched with saturated NH_4Cl, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give the corresponding carboxylic acid (239 mg), which was dissolved in THF (4 mL) and MeOH (1 mL). To this solution was added trimethylsilyldiazomethane (2.0 M in Et_2O, 0.40 mL, 0.80 mmol), and the mixture was stirred at room temperature for 1 h, and then concentrated. Purification of the residue by column chromatography (SiO_2 230 g, hexane/CH_2Cl_2 = 3:1 to 1:2) gave **17** (210 mg, 92%, 1:1 *E*/*Z*-mixture) as a pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.10 (m, 5H), 6.00−5.92 (m, 1H), 5.81−5.74 (m, 0.5H), 5.50−5.38 (m, 0.5H), 4.43 (t, *J* = 11.7 Hz, 1H), 4.43 (t, *J* = 11.7 Hz, 1H), 4.19−4.11 (m, 1H), 4.01−3.95 (m, 2H), 3.88 (d, *J* = 9.3 Hz, 0.5H), 3.80 (d, *J* = 7.8 Hz, 0.5H), 3.80 (d, *J* = 13.2 Hz, 0.5H), 3.68 (s, 1.5H), 3.66 (s, 1.5H), 3.55 (d, *J* = 12.7 Hz, 0.5H), 2.35−2.25 (m, 1H), 2.00−1.90 (m, 1H), 1.34 (s, 3H), 1.31 (s, 3H), 1.20−1.15 (m, 16H), 0.80 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.3, 137.7, 137.6, 135.5, 132.3, 128.4, 128.3, 128.2, 127.7, 127.7, 127.5, 127.4, 127.1, 127.0, 125.3, 98.5, 98.4, 86.6, 85.9, 84.2, 83.8, 80.0, 79.1, 72.4, 72.3, 70.7, 70.6, 63.3, 62.2, 52.0, 52.0, 32.4, 31.9, 30.0, 29.9, 29.9, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 28.2, 22.7, 20.6, 20.4, 14.1; FTIR (neat) 2926, 1744, 1457, 1374, 1254, 1070 cm^{-1}; HRMS (EI) calcd for $C_{29}H_{44}O_6$ (M^+) 488.3138, found 488.3143.

Dimethyl (2*R*,3*S*,4*R*)-4-(Benzyloxy)-2-dodecyltetrahydro-3-hydroxyfuran-2,3-dicarboxylate (19). Under argon atmosphere, 20% $Pd(OH)_2$/C (10.0 mg) was added to a solution of **17** (72.0 mg 0.15 mmol) in AcOEt (2.0 mL), and then a hydrogen gas balloon was attached. The mixture was stirred for 30 h, filtered through Celite, and concentrated to give the corresponding hydrogenated alkane (71 mg) as a yellow oil, which was dissolved in MeOH (2.0 mL). To this solution was added *p*-TsOH·H_2O (3.0 mg, 0.016 mmol) at room temperature, and the mixture was stirred for 3 h. The mixture was diluted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, and concentrated to give **18** (65.0 mg) as a yellow oil which was used for the next reaction without purification. Pure **18**, a colorless oil, obtained by column chromatography (SiO_2, hexane/AcOEt = 3:1 to 0:1) exhibited the following spectral data: $[\alpha]^{26}_D$ −8.1 (*c* 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.24 (m, 5H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.59 (t, *J* = 8.5 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.13 (t, *J* = 8.5 Hz, 1H), 3.98 (s, 1H), 3.93 (s, 3H), 3.85 (t, *J* = 8.5 Hz, 1H), 3.67 (d, *J* = 6.5 Hz, 2H), 2.37 (t, *J* = 6.6 Hz, 1H), 1.60−1.51 (m, 1H), 1.28−1.23 (m, 21H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 137.6, 128.4, 127.9, 127.7, 87.7, 85.2, 73.1,

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68.8, 65.0, 53.2, 32.4, 31.9, 30.3, 29.6, 29.5, 29.4, 29.3, 23.2, 22.7, 14.1; FTIR (neat) 3487, 2925, 2853, 1727, 1456, 1245, 1146, 1245, 1146, 1065 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{42}NaO_6$ $[(M + Na)^+]$ 473.2879, found 473.2889.

To an ice-cooled solution of **18** (65.0 mg) in CH_2Cl_2 (5 mL) was added DMPI (188 mg, 0.444 mmol) at room temperature. After the solution was stirred at room temperature for 4 h, the reaction was quenched with saturated $Na_2S_2O_3$, and the mixture was extracted with AcOEt. The extract was washed with $NaHCO_3$ and brine, dried, and concentrated to give the corresponding aldehyde (78 mg). The aldehyde was dissolved in *t*-BuOH (3.0 mL) and H_2O (0.5 mL), and 2-methyl-2-butene (0.47 mL, 4.43 mmol), NaH_2PO_4 (69.0 mg, 0.42 mmol), and $NaClO_2$ (53.0 mg, 0.59 mmol) were added at room temperature. After being stirred at room temperature for 2 h, the mixture was diluted with saturated NH_4Cl and AcOEt, washed with brine, dried, and concentrated to give the corresponding carboxylic acid, which was dissolved in THF (1 mL) and MeOH (1 mL). To this solution was added trimethylsilyldiazomethane (2.0 M in Et_2O, 125 μL, 0.25 mmol) at room temperature. After being stirred a room temperature for 1 h, the mixture was concentrated and chromatographed (SiO_2 8 g, hexane/AcOEt = 10:1) to give **19** (49 mg, 69% from **17**) as a colorless solid: $[\alpha]^{26}_D$ −8.6 (*c* 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.23 (m, 5H), 4.64 (d, *J* = 11.7 Hz, 1H), 4.53−4.43 (m, 3H), 3.98 (d, *J* = 7.3 Hz, 1H) 3.95 (s, 3H), 3.84 (s, 1H), 3.77 (s, 3H), 1.91−1.88 (m, 1H), 1.51−1.42 (m, 2H), 1.33−1.11 (m, 20H), 0.91 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 172.0, 137.6, 128.4, 127.9, 127.6, 89.3, 86.0, 84.4, 73.1, 70.3, 53.4, 52.3, 32.5, 31.9, 29.9, 29.6, 29.5, 29.3, 24.1, 22.7, 14.1; FTIR (neat) 3488, 2925, 2856, 0738, 1453, 1370, 1243, 1145, 1072, cm^{-1}; HRMS (EI) calcd for $C_{27}H_{42}O_7$ (M^+) 478.2931, found 478.2923.

Dimethyl (2*R*,3*S*,4*R*)-3,4-Diacetoxy-2-dodecyl-tetrahydrofuran-2,3-dicarboxylate (21). To a solution of **19** (48 mg, 0.10 mmol) in CH_2Cl_2 (2.0 mL) at −78 °C was added BCl_3 (1.0 M in CH_2Cl_2; 0.30 mL, 0.30 mmol). After the solution was stirred at −78 °C for 8 h, BCl_3 (0.10 mL, 0.10 mmol) was again added, and additional BCl_3 (0.30 mL, 0.30 mmol) was added 1 h later. The mixture was stirred at −78 °C for 30 min, diluted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, and concentrated to give **20** (42 mg), which was used for the next reaction without purification. Pure **20**, a colorless oil, obtained by silica gel column chromatography (hexane/AcOEt = 2:1) exhibited the following spectral data: $[\alpha]^{24}_D$ −17.0 (*c* 0.84, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.45 (t, *J* = 4.8 Hz, 1H), 4.34 (dd, *J* = 4.8, 8.8 Hz, 1H), 4.01 (dd, *J* = 4.8, 8.8 Hz, 1H), 3.95 (s, 3H), 3.78 (s, 3H), 3.67 (s, 1H), 1.73 (m, 2H), 1.60−1.50 (m, 1H), 1.34−1.13 (m, 19H), 1.13−1.00 (m, 1H), 0.88 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 171.5, 91.6, 84.6, 78.6, 73.1, 53.5, 52.4, 34.6, 31.9, 29.8, 29.63, 29.61, 29.57, 29.47, 29.40, 29.3, 24.4, 22.7, 14.1; FTIR (neat) 3476, 2925, 2856, 1733, 1445, 1243, 1149, 1056 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{36}O_7$ (M^+) 388.2461, found 388.2466.

Crude **20** (42 mg) was dissolved in CH_2Cl_2 (3.3 mL) and cooled to 0 °C, and Et_3N (56 μL, 0.40 mmol), DMAP (4 mg, 0.033 mmol) and AcCl (21 μL, 0.30 mmol) were added. After being heated under reflux for 3 h, the mixture was diluted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 5 g, hexane/AcOEt = 6:1) to give **21** (30 mg, 0.063 mmol, 63%) as a pale yellow oil: $[\alpha]^{26}_D$ −11.5 (*c* 1.39, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.81 (dd, *J* = 5.8, 3.9 Hz, 1H), 4.45 (dd, *J* = 9.3, 5.8 Hz, 1H), 3.94 (dd, *J* = 9.3, 3.9 Hz, 1H), 3.803 (s, 3H), 3.799 (s, 3H), 2.12 (s, 3H), 2.07 (s, 3H), 1.95 (dt, *J* = 12.4, 4.2 Hz, 1H), 1.77 (dt, *J* = 12.4, 4.2 Hz, 1H), 1.56−1.45 (m, 1H), 1.33−1.20 (m, 18H), 1.15−1.03 (m, 1H), 0.91 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 169.6, 168.7, 165.2, 90.4, 87.3, 75.83, 75.79, 71.3, 52.6, 52.4, 33.6, 31.9, 29.7, 29.62, 29.60, 29.5, 29.4, 29.3, 24.0, 22.7, 20.93, 20.85, 14.1.; FTIR (neat) 2926, 2856, 1757, 1442, 1371, 1237, 1065 cm^{-1}; HRMS (EI) calcd for $C_{24}H_{40}O_9$ (M^+) 472.2671, found 472.2643.

RuO_4 Oxidation of 21. To an ice-cooled solution of **21** (30 mg, 0.064 mmol) in a mixture of CCl_4 (0.4 mL), MeCN (0.4 mL), and H_2O (0.5 mL) were added $NaIO_4$ (54 mg, 0.25 mmol) and $RuCl_3{\cdot}nH_2O$ (1 mg, 0.005 mmol). After the solution was stirred at room temperature for 1 day, additional $NaIO_4$ (27 mg, 0.13 mmol) and $RuCl_3{\cdot}nH_2O$ (1 mg, 0.005 mmol) were added, and the mixture was stirred for 3 days. The mixture was diluted with H_2O (5 mL) and extracted with CH_2Cl_2. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 1.0 g, hexane/AcOEt = 6:1 to 5:1) to give the recovered **21** (17 mg, 56%) and **22** (7 mg, 22%) as a colorless oil which was a mixture of several positional isomers of the ketone carbonyl group: ^1H NMR (400 MHz, $CDCl_3$) δ 5.81 (dd, *J* = 4.0, 6.4 Hz, 1H), 4.56 (dd, *J* = 6.4, 9.2 Hz, 1H), 3.93 (ddd, *J* = 1.6, 3.4, 6.4 Hz, 1H), 3.803 (s, 3H), 3.797 (s, 3H), 2.42−2.35 (m, 4H), 2.12 (s, 3H), 2.07 (s, 3H), 1.95 (dt, *J* = 4.4, 12.4 Hz, 1H), 1.76 (dt, *J* = 4.4, 12.4 Hz, 1H), 1.62−1.43 (m, 4H), 1.31−1.20 (m, 9H), 1.18−1.03 (m, 1H), 0.93−0.86 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.6, 211.5, 211.0, 210.5, 182.2, 170.4, 169.7, 168.7, 165.21, 165.14, 90.39, 90.35, 90.31, 90.23, 90.16, 87.4, 77.2, 75.9, 71.3, 52.8, 52.80, 52.67, 52.52, 52.48, 52.47, 50.9, 44.7, 42.9, 42.82, 42.80, 42.77, 42.70, 42.55, 42.50, 42.48, 42.43, 37.3, 35.9, 33.7, 33.63, 33.60, 33.5, 33.4, 32.8, 31.8, 31.7, 31.6, 31.5, 29.74, 29.70, 29.57, 29.4, 29.36, 29.36, 29.30, 29.26, 29.23, 29.21, 29.14, 29.09, 29.08, 28.9, 26.0, 24.1, 24.0, 23.94, 23.91, 23.87, 23.85, 23.83, 23.78, 23.7, 23.6, 22.65, 22.62, 22.50, 22.47, 22.39, 20.92, 20.85, 20.80, 18.6, 17.3, 14.09, 14.07, 14.04, 13.93, 13.87, 13.79, 7.9; FTIR (neat) 2931, 2961, 1751, 1440, 1369, 1224, 1059 cm^{-1}. HRMS (FAB) calcd for $C_{24}H_{39}O_{10}$ $[(M + H)^+]$ 487.2543, found 487.2581.

Methyl (4a*S*,7*R*,7a*S*)-7-Acetoxy-4a-dodecyl-tetrahydro-2,2-dimethyl-4*H*-furo-[3,2-*d*][1,3]dioxine-7a-carboxylate (24). Under argon atmosphere, 20% $Pd(OH)_2/C$ (12.0 mg) was added to a solution of **17** (58 mg, 0.117 mmol) in MeOH (2.4 mL), and the mixture was stirred for 15 h under 15 atm of hydrogen atmosphere. The mixture was filtered through Celite, and the filtrate was concentrated to give the corresponding alcohol (19 mg) as a colorless oil, which was dissolved in CH_2Cl_2 (1.2 mL). This solution was cooled to 0 °C and Et_3N (15 μL, 0.11 mmol), DMAP (4 mg, 0.033 mmol), and Ac_2O (7 μL, 0.074 mmol) were added. After the solution was stirred at room temperature for 4 h, additional Et_3N (5 μL, 0.036 mmol) and Ac_2O (3 μL, 0.032 mmol) were added, and the mixture was stirred at room temperature for 1 h. The mixture was diluted AcOEt, washed saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 6 g, hexane/AcOEt = 12:1) to give **24** (16 mg, 31%) as a colorless oil: $[\alpha]^{23}_D$ +4.0 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.21 (dd, *J* = 5.6, 2.2 Hz, 1H), 4.43 (dd, *J* = 10.5, 5.6 Hz, 1H), 3.96 (d, *J* = 12.8 Hz, 1H), 3.94 (d, *J* = 12.8 Hz, 1H), 3.75 (s, 3H), 3.70 (dd, *J* = 10.5, 2.2 Hz, 1H), 2.03 (s, 3H), 1.97−1.88 (m, 1H), 1.59−1.40 (m, 1H), 1.42 (s, 3H), 1.36 (s, 3H), 1.35−1.20 (m, 20H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 169.1, 99.0, 83.3, 80.6, 79.5, 77.2, 70.7, 62.7, 52.1, 31.9, 31.4, 30.2, 29.68, 29.65, 29.63, 29.61, 29.44, 29.36, 22.7, 22.3, 20.8, 14.1; FTIR (neat) 2925, 2854, 1747, 1459, 1374, 1230, 1144, 1082, 1046 cm^{-1}. HRMS (FAB) calcd for $C_{24}H_{43}O_7$ $[(M + H)^+]$ 443.3009, found 443.3026.

Methyl (4a*S*,7*S*,7a*S*)-7-Acetoxy-4a-dodecyltetrahydro-2,2-dimethyl-6-oxo-4*H*-furo[3,2-*d*][1,3]dioxine-7a-carboxylate (25). To a solution of **24** (12 mg, 0.028 mmol) in CCl_4 (200 μL) were added MeCN (200 μL), H_2O (300 μL), and $NaIO_4$ (24 mg, 0.11 mmol), $NaHCO_3$ (15 mg, 0.18 mmol), and $RuCl_3{\cdot}nH_2O$ (3 mg, 0.014 mmol) at room temperature. After the solution was stirred at room temperature for 22 h, additional $NaIO_4$ (24 mg, 0.11 mmol) and $RuCl_3{\cdot}nH_2O$ (3 mg, 0.014 mmol) were added, and the mixture was stirred at room temperature for 27 h. The mixture was diluted with H_2O (5 mL) and extracted with CH_2Cl_2. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 = 1.5 g, hexane/AcOEt = 10:1 to 4:1) to give **25** (2 mg, 16%) and **26** (2 mg, 16%) each as a colorless oil.

Compound 25: $[\alpha]^{24}_D$ +9.9 (*c* 0.22, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.40 (s, 1H), 4.08 (d, *J* = 13.4 Hz, 1H), 4.02 (d, *J* = 13.4 Hz, 1H), 3.82 (s, 3H), 2.15 (s, 3H), 1.90−1.83 (m, 1H), 1.76−1.68 (m, 1H), 1.55 (s, 3H), 1.48 (s, 3H), 1.38−1.20 (m, 20H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 168.4, 166.9, 101.9, 83.3, 82.4, 71.6, 65.1, 52.6, 34.0, 31.9, 30.0, 29.63, 29.59, 29.47, 29.3, 28.5, 23.8, 22.7, 22.3, 20.5, 14.1; FTIR (neat) 2925, 2855, 1799, 1762,

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1457, 1376, 1205, 1065 cm^{-1}; HRMS (EI) calcd for $C_{24}H_{40}O_8$ (M^+) 456.2723, found 456.2702.

Compound ***26***. A mixture of several positional isomers of the ketone carbonyl group: ^1H NMR (400 MHz, $CDCl_3$) δ 5.21 (dd, J = 2.2, 5.9 Hz, 1H), 4.46−4.41 (m, 1H), 3.97−3.92 (m, 2H), 3.75 (s, 1H), 3.70 (dd, J = 2.2, 10.2 Hz, 1H), 2.43−2.35 (m, 5H), 2.04 (s, 3H), 1.97−1.85 (m, 1H), 1.41 (s, 3H), 1.36 (s, 3H), 1.33−1.10 (m, 16H), 1.03 (t, J = 7.6 Hz, 0.4H), 0.93−0.85 (m, 2.6H); FTIR (neat) 2926, 2857 1745, 1457, 1375, 1240, 1088 cm^{-1}; HRMS (FAB) calcd for $C_{24}H_{41}O_8$ [$(M + H)^+$] 457.2802, found 457.2800.

Dimethyl (2*R*,3*S*,4*R*)-4-(Carbamoyloxy)-2-dodecyl-3-hydroxytetrahydrofuran-2,3-dicarboxylate (27). To an ice-cooled solution of **20** (36 mg, 0.093 mmol) in CH_2Cl_2 (2 mL) was added trichloroacetyl isocyanate (11 μL, 0.093 mmol). After the solution was stirred at room temperature for 2 h, additional trichloroacetyl isocyanate (22 μL, 0.187 mmol) was added. After the solution was stirred at room temperature for 11 h, most of the solvent was evaporated. The residue was dissolved in MeOH (2 mL), and K_2CO_3 (4 mg, 0.029 mmol) was added. After being stirred at room temperature for 3 h, saturated NH_4Cl was added, and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 5 g, hexane/AcOEt = 1:1) to give **27** (36 mg, 90%) as a pale yellow oil: $[\alpha]^{25}_D$ −14.4 (*c* 0.84, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.23 (t, J = 4.4 Hz, 1H), 4.74 (brs, 2H), 4.58 (dd, J = 9.4, 6.4 Hz, 1H), 4.23 (s,1H), 4.02 (dd, J = 9.4, 4.4 Hz, 1H), 3.90 (s, 3H), 3.77 (s, 3H), 1.91 (dt, J = 12.4, 4.4 Hz, 1H), 1.65 (dt, J = 12.4, 4.4 Hz, 1H), 1.60−1.48 (m, 1H), 1.32−1.20 (m, 18H), 1.18−1.04 (m, 1H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 170.3, 155.9, 91.2, 83.9, 80.5, 70.7, 53.4, 52.3, 33.6, 31.9, 29.9, 29.65, 29.61, 29.60, 29.5, 29.4, 29.3, 24.3, 22.3, 14.1; FTIR (neat) 3369, 2924, 2853, 1828, 1732, 1601, 1440, 1362, 1243, 1068 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{37}NO_8$ (M^+) 431.2519, found 431.2530.

Dimethyl (3a*R*,5*R*,6*S*,6a*S*)-5-Dodecyl-6-hydroxy-2-oxohexahydrofuro[2,3-*d*]-oxazole-5,6-dicarboxylate (28). To a solution of **27** (22 mg, 0.051 mmol) in benzene (2 mL) were added $PhI(OAc)_2$ (20 mg, 0.062 mmol), MgO (5.0 mg, 0.124 mmol), and $Rh_2(esp)_2$ (2.0 mg, 0.003 mmol) at room temperature. After being heated at 65 °C for 2 h, the mixture was concentrated and chromatographed (SiO_2 5 g, hexane/AcOEt = 2:1) to give **28** (16 mg, 74%) as a pale yellow oil: $[\alpha]^{23}_D$ −29.5 (*c* 0.80, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.08 (d, J = 6.1 Hz, 1H), 5.82 (brs, 1H), 4.97 (d, J = 6.1 Hz, 1H), 4.17 (s, 1H), 4.00 (s, 3H), 3.77, (s, 3H), 2.00−1.93 (m, 1H), 1.68−1.62 (m, 1H), 1.35−1.20 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) d 170.4, 169.8, 156.2, 91.8, 86.0, 85.4, 83.9, 54.2, 52.6, 33.3, 31.9, 29.7, 29.65, 29.61, 29.58, 29.47, 29.3, 24.5, 22.7, 14.1; FTIR (neat) 3352, 2923, 2853, 1740, 1438, 1239, 1146, 1034; HRMS (EI) calcd for $C_{21}H_{35}NO_8$ (M^+) 429.2362, found 429.2351.

(2*R*,3*S*)-1,3-Bis(benzyloxy)pent-4-yn-2-ol (34). To a solution of dimethyl (1-diazo-2-oxopropyl)phosphonate (516 mg, 2.69 mmol) in MeOH (10 mL) was added K_2CO_3 (369 mg, 2.67 mmol) at room temperature. After the solution was stirred at room temperature for 15 min, a solution of aldehyde **33**[24] (519 mg, 1.79 mmol) in MeOH (7 mL) was added. The mixture was stirred at room temperature for 9 h. Saturated NH_4Cl was added, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 18 g, hexane/AcOEt = 8:1) to give **34** (391 mg, 78%) as a pale yellow oil: $[\alpha]^{25}_D$ +70.2 (*c* 1.08, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.27 (m, 10H), 4.84 (d, J = 11.7 Hz, 1H), 4.54 (s, 2H), 4.52 (d, J = 11.7 Hz, 1H), 4.27 (dd, J = 5.0, 2.2 Hz, 1H), 4.01 (quint, J = 5.0 Hz, 1H), 3.68 (m, 2H), 2.53 (d, J = 2.2 Hz, 1H), 2.50 (d, J = 5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 137.2, 128.4, 128.4, 128.1, 127.9, 127.7, 79.6, 75.9, 73.5, 72.0, 71.0, 70.2, 69.9; FTIR (neat) 3450, 3288, 3030, 2867, 2111, 1603, 1454, 1210, 1093 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{20}NaO_3$ [$(M + Na)^+$] 319.1310, found 319.1280.

Dimethyl 2-((2*R*,3*S*)-1,3-Bis(benzyloxy)pent-4-yn-2-yloxy)-malonate (35). To a solution of **34** (4.20 g, 14.2 mmol) in benzene (29 mL) was added $Rh_2(OAc)_4$ (31 mg, 0.070 mmol). Dimethyl diazomalonate (**6**) (2.70 g, 17.1 mmol) was added dropwise at 70 °C over 10 min, and then additional **6** (448 mg, 2.83 mmol) was added 20 min later. After being heated under reflux for 30 min, the mixture was concentrated and chromatographed (SiO_2 250 g, toluene/AcOEt = 30:1) to give **35** (4.17 g, 69%) as a colorless oil: $[\alpha]^{27}_D$ +46.7 (*c* 0.96, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.26 (m, 10H), 5.06 (s, 1H), 4.81 (d, J = 11.7 Hz, 1H), 4.54 (s, 2H), 4.53 (d, J = 11.7 Hz, 1H), 4.49−4.43 (m, 1H), 4.01−3.08 (m, 1H), 3.84−3.77 (m, 2H), 3.73 (s, 3H), 3.70 (s, 3H), 2.51 (d, J = 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 166.8, 137.9, 137.2, 128.31, 128.30, 127.9, 127.8, 127.6, 81.2, 79.4, 79.0, 76.0, 73.4, 71.1, 69.82, 69.79, 52.6; FTIR (neat) 3652, 3277, 3031, 2923, 2861, 2115, 1741, 1446, 1021 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{26}NaO_7$ [$(M + Na)^+$] 449.1576, found 449.1589.

Dimethyl (4*S*,5*R*)-4-(Benzyloxy)-5-((benzyloxy)methyl)-dihydro-3-methylene-furan-2,2-(3*H*)-dicarboxylate (36). To a solution of **35** (139 mg, 0.326 mmol) in toluene (3.3 mL) were added DBU (2.4 μL, 0.016 mmol) and $In(OTf)_3$ (10 mg, 0.018 mmol) at room temperature. The mixture was heated under reflux for 3 h, concentrated, and chromatographed (SiO_2 9 g, toluene/AcOEt = 20:1) to give **36** (134 mg, 96%) as a colorless oil: $[\alpha]^{27}_D$ +13.2 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.26 (m, 10H), 5.74 (s, 1H), 5.59 (s, 1H), 4.63 (d, J = 11.7 Hz, 1H), 4.53 (s, 2H), 4.48 (d, J = 11.7 Hz, 1H), 4.42−4.39 (m, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.63 (dd, J = 10.6, 3.9 Hz, 1H), 3.54−3.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 167.8, 143.1, 137.9, 137.6, 128.4, 128.3, 127.9, 127.8, 127.63, 127.57, 116.8, 83.4, 83.3, 80.33, 80.28, 73.4, 70.6, 69.1, 53.2; FTIR (neat) 3643, 3030, 2866, 1743, 1444, 1270, 1036 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{26}NaO_7$ [$(M + Na)^+$] 449.1576, found 449.1579.

Methyl (2*R*,3*R*,3a*S*,6a*R*)-3-(Benzyloxy)-2-((benzyloxy)-methyl)-3a-hydroxy-6-oxohexahydrofuro[3,4-*b*]furan-6a-carboxylate (37). To a stirred solution of **36** (3.5 g, 8.21 mmol) in CH_2Cl_2 (80 mL) at room temperature were added NMO (1.92 g, 16.4 mmol), $PhB(OH)_2$ (2.0 g, 16.4 mmol), and OsO_4 (0.157 M in CH_2Cl_2, 5.2 mL, 0.816 mmol). After the solution was stirred at room temperature for 19 h, the reaction was quenched with saturated $Na_2S_2O_3$, and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried, and concentrated. The residue was dissolved in acetone (41 mL) and AcOEt (41 mL), and 30% H_2O_2 (2.5 mL) was added at room temperature. After 8 h, 30% H_2O_2 (3.2 mL) was again added, and the mixture was stirred at room temperature for 4 h. The reaction was quenched with 10% $Na_2S_2O_3$ and the mixture was extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 120 g, hexane/AcOEt = 4:1) to give an inseparable 5:1 mixture of **37** and **38** (2.80 g, 80%) as a pale yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.23 (m, 10H), 5.18 (s, 0.83H), 4.71−4.63 (m, 3H), 4.59 (d, J = 9.0 Hz, 0.17H), 4.54−4.45 (m, 2H), 4.40 (dt, J = 10.2, 2.9 Hz, 0.17H), 4.25 (d, J = 9.0 Hz, 0.83H), 4.18 (dd, J = 9.5, 13.2 Hz, 0.17H), 4.02 (d, J = 0.1 Hz, 0.83H), 3.92−3.82 (dd, J = 2.0, 11.0 Hz, 0.83H), 3.84 (s, 0.51H), 3.82 (s, 2.49H), 3.76 (dd, J = 3.2, 11.5 Hz, 0.17H), 3.64−3.57 (m, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 165,6, 165.2, 137.6, 136.3, 136.2, 136.0, 128.9, 128.8, 128.6, 128.5, 128.40, 128.38, 128.27, 128.15, 127.9, 127.8, 127.6, 89.3, 87.4, 86.3, 85.5, 84.9, 83.9, 80.6, 74.4, 73.8, 73.7, 73.0, 72.4, 70.9, 69.0, 67.6, 53.1; FTIR (neat) 3338, 3032, 2872, 1790, 1452, 1293, 1124 cm^{-1}; HRMS (EI) calcd for $C_{23}H_{24}O_8$ (M^+) 428.1471, found 428.1460.

(2*R*,3*R*,3a*S*,6a*S*)-3-(Benzyloxy)-2-((benzyloxy)methyl)-tetrahydro-3a-hydroxy-6a-(hydroxymethyl)furo[3,4-*b*]furan-6-(6a*H*)-one (39). To an ice-cooled solution of a 5:1 mixture of **37** and **38** (2.80 g, 6.54 mmol) in THF (52 mL) and H_2O (23 mL) was added LiOH (1.10 g, 26.22 mmol), and the mixture was stirred at 0 °C for 3 h. The mixture was diluted with Et_2O (30 mL) and H_2O (60 mL). The aqueous layer was acidified with 1 M HCl (pH = 1) and then extracted with AcOEt. The extract was dried and concentrated to give the corresponding carboxylic acid as a colorless solid (2.76 g). The carboxylic acid thus obtained was dissolved in CH_2Cl_2 (65 mL), and oxalyl chloride (1.7 mL, 19.8 mmol) and DMF (50 μL, 0.646 mmol) were added at room temperature. After being stirred at room temperature for 4 h, the mixture was concentrated and the residue was dissolved in THF (60 mL). To this solution was added $NaBH_4$ (742

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mg, 19.6 mmol) at −78 °C, and then MeOH (6 mL) was added dropwise over 5 min. After being stirred at −78 °C for 1 h, the mixture was diluted with 1 M HCl (5 mL) and H_2O (50 mL) and extracted with AcOEt. The extract was washed with saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 100 g, hexane/AcOEt = 5:1) to give **39** (1.70 g, 65%) and its diastereomer derived from **38** (421 mg, 16%) each as a colorless oil.

Compound ***39****:* $[\alpha]^{27}_D$ +57.4 (*c* 1.16, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.23 (m, 10H), 4.77 (d, *J* = 11.5 Hz, 1H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.42 (d, *J* = 11.5 Hz, 1H), 4.34 (d, *J* = 7.3 Hz, 1H), 4.27 (d, *J* = 10.8 Hz, 1H), 4.02 (dt, *J* = 7.3, 2.0 Hz, 1H), 3.96 (d, *J* = 11.5 Hz, 1H), 3.79 (dd, *J* = 10.8, 2.0 Hz, 1H), 3.75 (d, *J* = 10.8 Hz, 1H), 3.60 (d, *J* = 10.8 Hz, 1H), 3.55 (s, 1H), 3.47 (dd, *J* = 10.8, 2.0 Hz, 1H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 137.0, 136.5, 128.7, 128.6, 128.4, 128.2, 128.0, 127.9, 86.1, 85.7, 84.3, 80.8, 73.6, 72.8, 71.5, 68.5, 62.0; FTIR (neat) 3427, 3032, 2872, 1777, 1457, 1371, 1081, 1021 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{24}NaO_7$ [(M + Na)$^+$] 423.1420, found 423.1425.

Diastereomer of ***39*** *derived from* ***38****:* $[\alpha]^{24}_D$ −26.9 (*c* 0.71, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (m, 10H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.27−4.24 (m, 1H), 4.12−4.04 (m, 3H), 3.99 (d, *J* = 11.6 Hz, 1H), 3.95 (d, *J* = 11.6 Hz, 1H), 3.78 (s, 1H), 3.58 (dd, *J* = 3.6, 11.6 Hz, 1H), 3.51 (dd, *J* = 3.6, 11.6 Hz, 1H), 2.38 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 174.0, 137.5, 136.3, 128.9, 128.8, 128.5, 128.3, 128.0, 127.9, 85.5, 84.0, 82.3, 82.1, 74.0, 73.8, 73.7, 68.7, 61.5; FTIR (neat) 3471, 3032, 2874, 1782, 1459, 1366, 1080 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{24}O_7$ (M$^+$) 400.1522, found 400.1537.

(4a*R*,6*R*,7*R*,7a*S*)-7-(Benzyloxy)-6-((benzyloxy)methyl)-2,2-dimethyldihydro-4*H*-4a,7a-(methanooxymethano)furo[3,2-*d*][1,3]dioxin-10-one (40). To a solution of **39** (81 mg, 0.202 mmol) in acetone (2 mL) were added 2,2-dimethoxypropane (125 μL, 1.02 mmol) and *p*-TsOH·H_2O (8 mg, 0.03 mmol), and the mixture was heated under reflux for 16 h. Saturated $NaHCO_3$ was added and the mixture was extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 5 g, hexane/AcOEt = 5:1) to give **40** (73 mg, 82%) as a colorless oil: $[\alpha]^{27}_D$ +41.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.26 (m, 10H), 4.76 (d, *J* = 10.7 Hz, 1H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.59 (d, *J* = 10.7 Hz, 1H), 4.56 (d, *J* = 11.7 Hz, 1H), 4.51 (d, *J* = 7.3 Hz, 1H), 4.42 (d, *J* = 7.3 Hz, 1H), 4.29 (d, *J* = 10.8 Hz, 1H), 4.11 (d, *J* = 10.8 Hz, 1H), 3.90 (d, *J* = 12.0 Hz, 1H), 3.90−3.87 (m, 1H), 3.70 (dd, *J* = 12.0, 2.7 Hz, 1H), 3.55 (dd, *J* = 12.0, 2.7 Hz, 1H), 1.42 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 137.8, 137.0, 128.5, 128.4, 128.1, 127.9, 127.7, 127.7, 100.3, 84.8, 84.0, 80.6, 77.7, 73.6, 72.8, 71.6, 68.3, 61.2, 27.8, 26.1; FTIR (neat) 2993, 2870, 1788, 1456, 1376, 1221, 1089 cm^{-1}; HRMS (EI) calcd for $C_{25}H_{28}O_7$ (M$^+$) 440.1835, found 440.1828.

((4a*S*,6*R*,7*R*,7a*S*)-7-(Benzyloxy)-6-((benzyloxy)methyl)-4a-(dodec-1-enyl)tetrahydro-2,2-dimethyl-4*H*-furo[3,2-*d*][1,3]-dioxin-7a-yl)methanol (41). To a solution of **40** (72 mg, 0.163 mmol) in toluene (2 mL) at −78 °C was added dropwise DIBALH (1.02 M in hexane; 0.25 mL, 0.255 mmol) over 5 min, and the mixture was stirred at −78 °C for 1 h. Rochelle salt (20%) was added, and the mixture was stirred at room temperature for 3 h and filtered through Celite. The filtrate was extracted with AcOEt, washed with brine, dried, and concentrated to give the corresponding lactol (0.11 g) as a colorless oil, which was used for the next reaction without further purification. Pure lactol (1:1 epimeric mixture) obtained by silica gel column chromatography exhibited the following data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.22 (m, 10H), 5.32−4.47 (m, 6H), 4.29−4.22 (m, 1.5H), 4.05 (d, *J* = 9.5 Hz, 0.5H), 4.00 (d, *J* = 8.0 Hz, 0.5 H), 3.97−3.90 (m, 0.5 Hz), 3.84 (d, J = 12.4, 0.5 Hz), 3.80 (s, 0.5 H), 3.72−3.65 (m, 1.5H), 3.57 (m, 1.5H), 1.45 (s, 3H), 1.43 (s, 1.5 H), 1.43 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 137.9, 137.6, 137.4, 128.4, 128.33, 128.29, 127.9, 127.81, 127.75, 127.71, 127.66, 127.64, 127.57, 104.2, 100.5, 99.6, 99.5, 87.9, 87.6, 84.5, 83.3, 83.0, 82.0, 80.6, 78.8, 77.2, 73.49, 73.46, 72.2, 72.1, 71.7, 69.6, 69.3, 69.2, 62.4, 62.2, 27.74, 27.71, 27.3, 27.1; FTIR (neat) 3422, 2992, 2892, 1455, 1376, 1234, 1086 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{30}NaO_7$ [(M + Na)$^+$] 465.1889 found 465.1865.

n-BuLi (2.69 M in hexane, 1.1 mL, 2.96 mmol) was added to DMSO (3 mL) at room temperature, and the mixture was stirred at room temperature for 30 min. The resulting solution of dimsyl lithium was added to **15**[18] (782 mg, 1.63 mmol, dried at 140 °C under reduced pressure for 2 h), and the mixture was stirred at room temperature for 30 min to generate the ylide. To this solution was added a solution of the lactol (0.11 g) in DMSO (2 mL), and the mixture was stirred for 4 h at 120 °C. The mixture was diluted with AcOEt, washed with H_2O and brine, dried, concentrated, and chromatographed (SiO_2 10 g, hexane/AcOEt = 15:1 to 3:1) to give the unreacted lactol (25 mg, 34%) and **41** (63 mg, 66%; 1:1 *E*/*Z* mixture) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.25 (m, 10H), 5.81 (dt, *J* = 15.6, 6.8 Hz, 0.5H), 5.53 (dt, *J* = 12.0, 7.3 Hz, 0.5H), 5.29 (d, *J* = 15.6 Hz, 0.5H), 5.08 (d, *J* = 12.0 Hz, 0.5H), 4.65−4.52 (m, 4H), 4.29 (dt, *J* = 1.5, 6.8 Hz, 0.5H), 4.19−4.10 (m, 1H), 4.00 (dd, *J* = 8.6, 11.5 Hz, 0.5H), 3.86−3.79 (m, 2H) 3.75−3.64 (m, 3H), 3.58−3.52 (m, 1H), 2.42−2.32 (m, 1H), 2.21 (d, *J* = 6.4 Hz, 0.5H), 2.13 (d, *J* = 7.3 Hz, 0.5H), 2.03−1.99 (m, 1H), 1.52 (s, 3H), 1.37 (s, 1.5H), 1.36 (s, 1.5H), 1.37−1.20 (m, 16H), 0.88 (t, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 138.2, 138.1, 136.3, 128.3, 128.3, 128.2, 127.7, 127.7, 127.6, 127.5, 127.5, 127.5, 127.4, 125.6, 123.8, 98.1, 98.1, 86.7, 86.1, 85.7, 85.6, 82.2, 81.9, 81.6, 80.3, 73.3, 73.3, 72.0, 72.0, 71.4, 71.2, 63.3, 63.1, 60.6, 60.5, 32.5, 31.9, 30.0, 29.6, 29.6, 29.5, 29.4, 29.3, 29.3, 29.1, 29.0, 29.0, 28.7, 28.0, 24.4, 24.2, 22.7, 14.1; FTIR (neat) 3491, 2925, 2857, 1728, 1458, 1374, 1249, 1200, 1109 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{52}NaO_6$ [(M + Na)$^+$] 603.3662 found 603.3632.

***tert*-Butyl (4aS,6R,7R,7aS)-7-(Benzyloxy)-6-((benzyloxy)-methyl)-4a-(dodec-1-enyl)tetrahydro-2,2-dimethyl-4*H*-furo-[3,2-*d*][1,3]dioxine-7a-carboxylate (42).** To an ice-cooled solution of **41** (402 mg, 0.692 mmol) in CH_2Cl_2 (7 mL) were added $NaHCO_3$ (581 mg, 6.92 mmol) and DMPI (594 mg, 1.40 mmol). After the solution was stirred at room temperature for 5 h, saturated $Na_2S_2O_3$ was added, and the mixture was extracted with AcOEt. The extract was washed with saturated $NaHCO_3$ and brine, dried, and concentrated to give the corresponding aldehyde (400 mg). The aldehyde was dissolved in *t*-BuOH (5.5 mL) and H_2O (1.1 mL), and 2-methyl-2-butene (2.2 mL, 20.8 mmol), NaH_2PO_4 (324 mg, 2.08 mmol), and $NaClO_2$ (250 mg, 2.76 mmol) were added at room temperature. After being stirred at room temperature for 2 h, saturated NH_4Cl was added, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give the corresponding carboxylic acid (474 mg), which was dissolved in CH_2Cl_2 (7 mL). To this solution was added 2-*tert*-butyl-1,3-diisopropylisourea (1.55 mL, 6.92 mmol) at room temperature, and the mixture was stirred at room temperature for 1 h. The mixture was filtered through Celite, concentrated, and chromatographed (SiO_2 15 g, hexane/AcOEt = 15:1 to 10:2) to give **42** (379 mg, 84%; 1:1 *E*/*Z*-mixture) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.20 (m, 10H), 6.03 (d, *J* = 14.4 Hz, 1H), 5.91−5.85 (m, 0.5H), 5.57−5.51 (m, 0.5H), 4.60−4.44 (m, 4H), 4.28−4.23 (m, 0.5H), 4.18−4.13 (m, 0.5H), 4.02 (t, *J* = 13.2 Hz, 1H), 3.87−3.84 (m, 1.5H), 3.72−3.67 (m, 1H), 3.62 (d, *J* = 12.7 Hz, 0.5H), 3.53 (t, *J* = 7.8 Hz, 1H), 2.40−2.35 (m, 1H), 2.08−2.03 (m, 1H), 1.44−1.24 (m, 31H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 168.7, 138.3, 138.3, 138.0, 135.3, 132.1, 128.3, 128.3, 128.1, 127.7, 127.6, 127.5, 127.5, 127.4, 127.4, 127.2, 127.2, 98.6, 98.4, 88.6, 88.0, 85.0, 84.5, 82.0, 81.9, 80.9, 80.5, 79.9, 77.2, 73.4, 73.3, 71.9, 71.8, 71.3, 71.1, 63.2, 62.1, 32.5, 31.9, 30.1, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 29.3, 29.2, 29.1, 28.3, 27.9, 22.7, 21.7, 21.6, 14.1; FTIR (neat) 2925, 2857, 1732, 1457, 1372, 1253, 1111 cm^{-1}; HRMS (ESI) calcd for $C_{40}H_{58}NaO_7$ [(M + Na)$^+$] 673.4080, found 673.4064.

***tert*-Butyl (4aS,6R,7R,7aS)-7-(Benzyloxy)-4a-dodecyltetrahydro-6-(hydroxymethyl)-2,2-dimethyl-4*H*-furo[3,2-*d*][1,3]-dioxine-7a-carboxylate (43).** Under argon atmosphere, 20% $Pd(OH)_2$/C (140 mg) was added to a solution of **42** (467 mg 0.717 mmol) in AcOEt (7.2 mL), and then a hydrogen gas balloon was attached to the flask. The mixture was stirred at room temperature for

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2 h, filtered through Celite, concentrated, and chromatographed (SiO_2 15 g, hexane/AcOEt = 6:1) to give **43** (353 mg, 87%) as a yellow oil: $[\alpha]^{22}_D$ +34.1 (*c* 1.16, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.28 (m, 5H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 3.96 (q, *J* = 3.7 Hz, 1H), 3.93 (s, 2H), 3.88 (d, *J* = 3.7 Hz, 1H), 3.62 (dt, *J* = 11.7, 3.7 Hz, 1H), 3.35 (quint, *J* = 5.4 Hz, 1H), 2.32 (t, *J* = 5.4 Hz, 1H), 2.18–2.10 (m, 1H), 1.94–1.86 (m, 1H), 1.47 (s, 9H), 1.43 (s, 3H), 1.41 (s, 3H), 1.35–1.19 (m, 20H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 137.5, 128.4, 127.9, 127.8, 98.9, 88.1, 84.9, 82.6, 82.1, 79.8, 76.8, 76.7, 73.7, 62.9, 62.4, 31.9, 30.6, 30.2, 29.7, 29.6, 29.3, 27.95, 27.91, 27.8, 22.7, 22.2, 21.2, 14.1; FTIR (neat) 3482, 2924, 2856, 1732, 1460, 1373, 1252 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{54}NaO_7$ $[(M + Na)^+]$ 585.3767, found 585.3744.

***tert*-Butyl (4a*S*,7*S*,7a*S*)-7-(Benzyloxy)-4a-dodecyltetrahydro-2,2-dimethyl-6-oxo-4*H*-furo[3,2-*d*][1,3]dioxine-7a-carboxylate (45).** To an ice-cooled solution of **43** (352 mg, 0.625 mmol) in CH_2Cl_2 (6.3 mL) were added $NaHCO_3$ (525 mg, 6.25 mmol) and DMPI (594 mg, 1.40 mmol). After the solution was stirred at room temperature for 1 h, additional $NaHCO_3$ (79 mg, 0.94 mmol) and DMPI (881 mg, 2.08 mmol) were added at 0 °C, and the mixture was stirred at room temperature for 1 h. $Na_2S_2O_3$ (10%) was added, and the mixture was extracted with AcOEt. The extract was washed with saturated $NaHCO_3$ and brine, dried, and concentrated to give the aldehyde (361 mg). The aldehyde was dissolved in CH_2Cl_2 (6.3 mL), and $NaHCO_3$ (263 mg, 3.13 mmol) and *m*-chloroperbenzoic acid (*m*-CPBA) (75%; 216 mg, 0.939 mmol) were added at −40 °C. After being stirred at −40 °C for 1 h, additional *m*-CPBA (75%, 144 mg, 0.626 mmol) was added, and the mixture was stirred at 0 °C for 1 h. $Na_2S_2O_3$ (10%) was added, and the mixture was extracted with AcOEt. The extract was washed with saturated $NaHCO_3$, dried, and concentrated to give formate **44** (353 mg), which was used for the next reaction without purification. Pure **44**, a colorless oil, obtained by silica gel column chromatography (hexane/AcOEt = 15:1) exhibited the following spectral data: $[\alpha]^{21}_D$ +50.5 (*c* 0.23, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 0.5 Hz, 1H), 7.45–7.26 (m, 5H), 6.22 (s, 1H), 4.79 (d, *J* = 11.5 Hz, 1H), 4.65 (d, *J* = 11.5 Hz, 1H), 4.08 (s, 1H), 3.97 (s, 2H), 2.08–2.00 (m, 1H), 1.96–1.89 (m, 1H), 1.45 (s, 3H), 1.44 (s, 12H), 1.34–1.25 (m, 20H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 160.1, 137.2, 128.4, 127.8, 127.3, 99.4, 98.9, 90.5, 83.0, 82.8, 82.3, 73.8, 62.7, 33.3, 31.9, 30.2, 29.67, 29.64, 29.52, 29.34, 27.9, 22.7, 22.5, 21.6, 14.1; FTIR (neat) 2926, 2856, 1732, 1460, 1374, 1254, 1119 cm^{-1}; HRMS (EI) calcd for $C_{33}H_{51}O_8$ $[(M - H)^+]$ 575.3584, found. 575.3564.

Crude formate **44** (353 mg) was dissolved in MeOH (6.3 mL), and K_2CO_3 (37 mg, 0.268 mmol) was added at 0 °C. After stirring at 0 °C for 15 min, saturated NH_4Cl was added, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give the lactol (363 mg), which was dissolved in CH_2Cl_2 (6.3 mL). To this solution were added 4A molecular sieves, NMO (146 mg, 1.25 mmol), and TPAP (22 mg, 0.063 mmol) at room temperature. After being stirred at room temperature for 1 h, the mixture was filtered through Celite, concentrated, and chromatographed (SiO_2 15 g, hexane/AcOEt = 20:1) to give lactone **45** (234 mg, 68% from **43**) as a yellow oil: $[\alpha]^{22}_D$ −22.9 (*c* 0.97, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 5H), 4.97 (d, *J* = 11.5 Hz, 1H), 4.72 (d, *J* = 11.5 Hz, 1H), 4.33 (s, 1H), 4.03 (d, *J* = 13.2 Hz, 1H), 3.98 (d, *J* = 13.2 Hz, 1H), 2.06–2.01 (m, 2H), 1.45 (s, 3H), 1.43 (s, 9H), 1.36 (s, 3H), 1.36–1.20 (m, 20H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 166.1, 136.5, 128.3, 128.1, 128.0, 100.1, 83.4, 82.6, 81.6, 80.3, 73.1, 63.2, 33.5, 31.9, 30.0, 29.61, 29.59, 29.5, 29.35, 29.32, 29.2, 27.8, 22.7, 22.5, 22.4, 14.1; FTIR (neat) 2926, 2856, 1785, 1735, 1461, 1376, 1253, 1146 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{51}O_7$ $[(M + H)^+]$ 547.3635, found 547.3636.

Di-*tert*-butyl (2*R*,3*S*,4*S*)-2-Dodecyltetrahydro-3,4-dihydroxy-5-oxofuran-2,3-dicarboxylate (46). To a solution of **45** (18 mg, 0.033 mmol) in THF (1 mL) was added 3 M $HClO_4$ (0.11 mL, 0.33 mmol) at room temperature. After the solution was stirred at room temperature for 24 h, saturated $NaHCO_3$ was added, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give the corresponding diol (18 mg). This diol was then dissolved in CH_2Cl_2 (2 mL), and $NaHCO_3$ (28 mg, 0.33 mmol) and DMPI (42 mg, 0.099 mmol) were added at 0 °C. After the solution was stirred at room temperature for 1 h, 10% $Na_2S_2O_3$ was added, and the mixture was extracted with AcOEt. The extract was washed with saturated $NaHCO_3$ and brine, dried, and concentrated to give the aldehyde (17 mg). The aldehyde was dissolved in *t*-BuOH (1 mL) and H_2O (0.3 mL), 2-methyl-2-butene (75 μL, 1.65 mmol), NaH_2PO_4 (20 mg, 0.128 mmol), and $NaClO_2$ (15 mg, 0.166 mmol) were added at room temperature. After stirring at room temperature for 2 h, saturated NH_4Cl was added, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give the corresponding carboxylic acid (17 mg), which was dissolved in CH_2Cl_2 (2 mL). To this solution was added 2-*tert*-butyl-1,3-diisopropylisourea (75 μL, 0.313 mmol) at room temperarure, and the mixture was stirred at room temperature for 4 h. The mixture was filtered through Celite, concentrated, and chromatographed (SiO_2 3 g, hexane/AcOEt = 15:1) to give **46** (14 mg, 76% from **45**) as a colorless oil: $[\alpha]^{25}_D$ −22.7 (*c* 1.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 5H), 4.97 (d, *J* = 11.6 Hz, 1H), 4.75 (d, *J* = 11.6 Hz, 1H), 4.68 (s, 1H), 3.87 (s, 1H), 2.05–1.98 (m, 1H), 1.63–1.50 (m, 1H), 1.46 (s, 9H), 1.42 (s, 9H), 1.38–1.20 (m, 20H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 168.4, 166.9, 136.7, 128.3, 128.2, 128.0, 86.3, 86.1, 83.8, 83.4, 78.1, 73.4, 31.9, 30.8, 29.8, 29.6, 29.6, 29.4, 29.3, 29.1, 27.8 (6C), 23.5, 22.7, 14.1; FTIR (neat) 3477, 2927, 1809, 1739, 1461, 1373, 1254, 1152 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{53}O_8$ $[(M + H)^+]$ 577.3740, found 577.3770.

(−)-Cinatrin C_1. Under argon atmosphere, 20% $Pd(OH)_2/C$ (5 mg) was added to a solution of **46** (14 mg 0.026 mmol) in MeOH (1 mL), and then a hydrogen gas balloon was attached to the flask. The mixture was stirred at room temperature for 2 h, filtered through Celite, and concentrated to give the corresponding diol (11 mg). The diol was dissolved in HCO_2H (1 mL) at 0 °C, and the mixture was stirred at 40 °C for 7 h. After most of the HCO_2H was azeotropically removed using toluene, the residue was purified by HPLC (COSMOSIL $5C_{18}$-MS-II 20 × 250 mm, MeCN–H_2O–TFA (80:20:0.1), 4 mL/min, UV 210 nm, t_R = 22.5 min) and lyophilized to give cinatrin C_1 as a white powder (4.2 mg, 44%): $[\alpha]^{25}_D$ −5.9 (*c* 0.30, MeOH) [lit. $[\alpha]^{24}_D$ −11.2 (*c* 0.31, MeOH),[6a] $[\alpha]^{26}_D$ −1.6 (*c* 0.11, MeOH),[10b] $[\alpha]^{23}_D$ +9.7 (*c* 0.319, MeOH)[9] for (+)-cinatrin C_1]; mp 163–164 °C (lit.[6a] mp 162–164 °C); ^1H NMR (400 MHz, CD_3OD) δ 4.67 (s, 1H), 2.08 (appt, *J* = 13.2 Hz, 1H), 1.67–1.58 (m, 1H), 1.48–1.37 (m, 1H), 1.36 (m, 1H), 1.27 (m, 22H), 0.80 (appt, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 175.3, 171.7, 88.5, 74.5, 33.1, 32.5, 30.81, 30.77, 30.75, 30.6, 30.5, 30.4, 25.0, 23.7, 14.4; FTIR (KBr) 3416, 2924, 2856, 1781, 1722, 1389, 1268, 1131, 1034 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{29}O_8$ $[(M - H)^-]$ 373.1862, found 373.1853.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

X-ray analysis of **13** and ^1H and ^{13}C NMR spectra of synthetic intermediates and cinatrin C_1. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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