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# Catalytic Asymmetric Synthesis and Stereochemical Revision of (+)-Cryptoconcatone H

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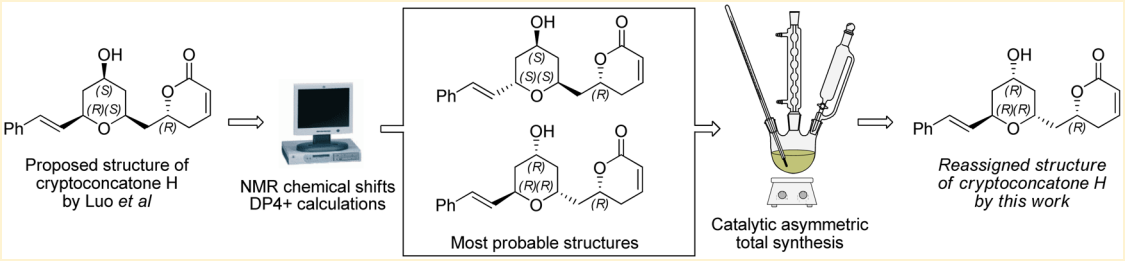
Supporting Information




**ABSTRACT:** The total synthesis and structural revision of (+)-cryptoconcatone H are described. Guided by computational studies for the final structure assignment, the stereogenic centers at the tetrahydropyran moiety of (+)-cryptoconcatone H were assembled through catalytic asymmetric methodologies: Krische allylation, cross-metathesis reaction, and THP formation via Pd(II)-catalyzed cyclization. Finally, a Krische allylation reaction established the last stereocenter, and the lactone moiety was formed by ring-closing metathesis.

The genus *Cryptocarya* (Laureceae) comprises more than 350 species distributed in tropical and subtropical areas, including South Africa, Asia, Oceania, and South America.[1] The biological profile of their secondary metabolites remains virtually underexplored. Recently, Luo and co-workers reported the isolation of eight novel $\alpha,\beta$-unsaturated $\delta$-lactones, named cryptoconcatones A−H, as well as two alkylidene butenolides, namely, cryptoconcatones I and J, from the leaves and twigs of *C. concinna* (Figure 1).[2]

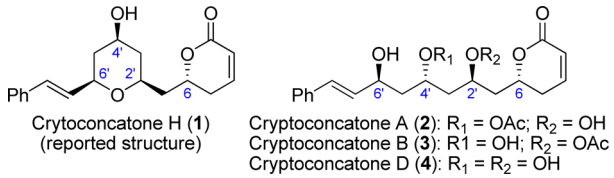



**Figure 1.** Structures of cryptoconcatones H (**1**), A (**2**), B (**3**), and D (**4**).

The chemical structures of cryptoconcatones A (**2**), B (**3**), and D (**4**) were determined by a combination of spectroscopic methods and chemical derivatization, whereas the structure of cryptoconcatone H (**1**) was proposed through an interplay of Mosher's ester methodology and ROESY experiments to assign an *S* absolute configuration at C-4′ and establish the all *cis* relationship among H-2′, H-4′, and H-6′, respectively. The absolute configuration at C-6 in these $\alpha,\beta$-dihydropyran-2-ones emerged as *R* due to a positive Cotton effect at 250−272 nm in their ECD spectra. It is noteworthy that cryptoconcatone H (**1**) was the only one in this series of $\alpha,\beta$-unsaturated lactones to display opposite absolute configurations at C-2′, C-4′, and C-6′ when compared to cryptoconcatone D (**4**).

Due to our continuing interest in the stereochemical assignment and biological activity of dihydropyran-2-ones,[3] we were attracted to unambiguously elucidating the structure of cryptoconcatone H using a combined computational/experimental approach. In this regard, quantum chemical calculations of NMR shifts have emerged as a powerful and affordable strategy to facilitate structural elucidation problems.[4] Hence, we undertook DP4+ calculations of the eight plausible diastereoisomers (compounds **1**, **5**, and **6** in Figure 2 and **19**−**23** in the Supporting Information) at the recommended PCM/

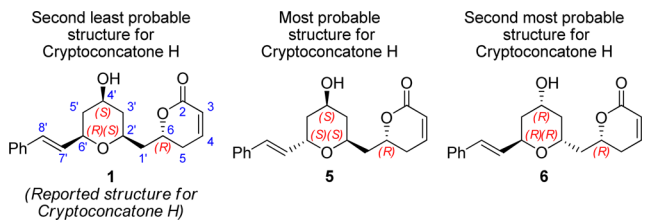



**Figure 2.** Structure **1** proposed by Luo and co-workers for cryptoconcatone H and stereoisomers **5** and **6**, which were found as the most probable structures by DP4+ calculations.

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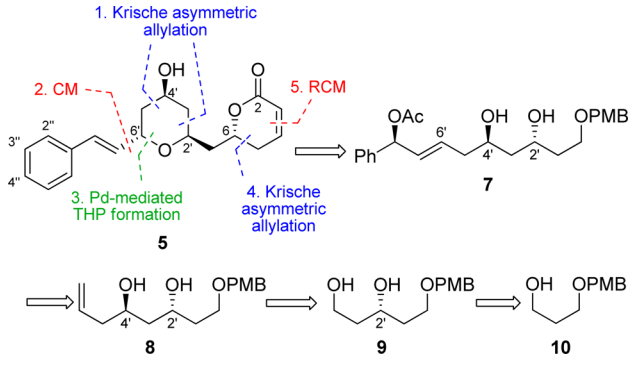
mPW1PW91/6-31+G**//B3LYP/6-31G* level of theory.[5] To our surprise, isomer **1** was not among the most likely candidates but instead was the second least probable isomer.

The agreement between the NMR data of natural cryptoconcatone H and those calculated for isomer **1** was modest, with CMAE values of 2.2 ppm ($^{13}$C) and 0.17 ppm ($^{1}$H). Moreover, we noticed serious discrepancies for most of the signals associated with the tetrahydropyran moiety, with those assigned to C-2′ ($\Delta\delta$ = 4.9 ppm), C-6′ ($\Delta\delta$ = 4.5 ppm), and H-6′ ($\Delta\delta$ = 0.68 ppm) being the most significant ones. On the other hand, isomers **5** and **6**, bearing the same relative configuration at the tetrahydropyran ring (Figure 2), displayed excellent agreement with the experimental data reported for cryptoconcatone H, with CMAE values of 1.0 and 1.3 ppm ($^{13}$C) and 0.08 and 0.10 ppm ($^{1}$H), respectively. Interestingly, all of the conflicting resonances from C-2′ to C-6′ were nicely reproduced by our calculations.

The DP4+ calculations strongly identified isomer **5** as the most likely candidate (99.9%), followed by isomer **6** (0.02%). Given the known tendency of DP4 (or DP4+) to overestimate the probability rates[4−6] and considering that the two stereoclusters of the molecule are separated by a methylene group, we recomputed the DP4+ values by taking only the NMR data of the most relevant region to differentiate among candidates (in this case, the C-2′ to the C-6′ region). Here again, the DP4+ values strongly supported isomers **5** (53%) and **6** (47%) over the remaining six candidates (<0.1%), but the difference between the first two isomers was less marked. As a result, we decided to focus our initial efforts on the synthesis of compound **5**, which was the most likely structure of cryptoconcatone H according to our calculations.

As represented in the retrosynthetic analysis (Scheme 1), we proposed the use of catalytic asymmetric transformations to

**Scheme 1. Retrosynthetic Plan for Tetrahydropyran 5**




install the stereogenic centers and the carbon backbone required for compound **5**. The tetrahydropyran ring was to be formed via palladium-catalyzed stereospecific cyclization (Tsuji−Trost reaction) involving the hydroxyl group at C-2′ and the allyl acetate moiety in intermediate diol **7**. The introduction of the allylic acetate required for the above transformation was conceived as arising from the cross-metathesis reaction of diol **8** and the acetate corresponding to (*S*)-1-phenyl allylic alcohol.[7] To implement this approach, diol **9** was expected to be formed via catalytic asymmetric allylation of 3-(4-methoxybenzyloxy)-1-propanol (**10**), according to the methodology developed by Krische and co-workers.[8]

Monoprotection of 1,3-propanediol provided alcohol **10**,[9] which was submitted to oxidative catalytic asymmetric allylation employing a chiral iridium catalyst via the transfer hydrogenative coupling of allyl acetate with *in situ* generated aldehyde from alcohol **10**.[8] In fact, this approach proved to be quite efficient as the preformed iridium-(*S*)-BINAP catalyst provided alcohol **11** in 95% yield and allowed the recovery of 90% of the catalyst (Scheme 2). The enantiomeric excess (ee) of known alcohol **11** was determined after chiral HPLC analysis, and assignment of the *S* configuration was confirmed by employing Mosher's derivatization protocol (see the Experimental Section).

Lemieux−Johnson oxidation of the terminal olefin, followed by reduction to the corresponding primary alcohol **9** set the stage for a second catalytic diastereoselective Krische allylation with either (*R*)-SEGPHOS or (*R*)-BINAP as the chiral ligand. For preparative purposes, the latter one was the ligand of choice as it provided better results as far as reproducibility is concerned. This methodology allowed stereocontrol over the absolute configuration of the newly generated stereogenic center in diol **8** (C-4′ in cryptoconcatone numbering) with a diastereoisomeric ratio superior to 20:1 in favor of the 1,3-*anti* relationship. The relative configuration was assigned after conversion of diol **8** to the corresponding acetonide and inspection of its $^{13}$C NMR spectrum which displayed two isochronous methyl groups at 24.8 ppm, in accordance with Rychnovsky's model (see the Experimental Section).[10]

The insertion of the benzylic acetate moiety required for the formation of the tetrahydropyran ring was successfully implemented via a cross-metathesis process involving diol **8** and acetate (−)-**12**, which afforded ester **7** in 89% yield when Grubbs−Hoveyda II catalyst (3 mol %) was employed. We then attempted to form the required tetrahydropyran motif via a Tsuji−Trost protocol [Pd(PPh$_3$)$_4$, THF, rt],[11] which surprisingly provided a complex mixture of products.

On the basis of previous literature data,[12] we explored the use of the allylic alcohol corresponding to **7** in a stereospecific Pd(II)-catalyzed cyclization. To our delight, a single product (assigned as **13**) was obtained in good yield (78%, two steps).[13] Its 2′,6′-*trans* relationship was initially assigned on the grounds of the rationalization proposed by Uenishi and co-workers,[12] and this was confirmed by inspection of its NOESY spectrum, which displayed correlations between H-2′ and the styrenic hydrogens (H-7′ and H-8′) as well as between H-2′ and H-4′, in addition to correlations involving H-4′ and H-7′ and H-8′, as depicted in Scheme 2.

Next, after silylation of the secondary alcohol and deprotection of the primary hydroxyl group in **13**, a third Krische allylation of the primary alcohol **14** introduced the stereogenic center at C-6 (cryptoconcatone numbering), affording **15** in 59% yield (87% based on recovered starting material) and greater than 20:1 diastereoisomeric ratio (Scheme 3). The absolute configuration of the newly created stereogenic center was later confirmed by a positive Cotton effect in the CD spectrum of tetrahydropyran **5**, which was prepared after esterification of the secondary alcohol with acryloyl chloride to afford **16**, followed by ring-closing metathesis (RCM) and deprotection of the secondary alcohol.[14] At this stage, the *trans* relationship between H-2′/H-6′ of tetrahydropyran **5** was confirmed from its NOESY spectrum, revealing the same correlations involving H-2′, H-4′, and the styrenic hydrogens (H-7′ and H-8′) as those observed for compound **13** (Scheme 2).

Inspection of the $^{1}$H and $^{13}$C NMR spectra of tetrahydropyran **5** revealed H-6 and H-6′ as two different multiplets,



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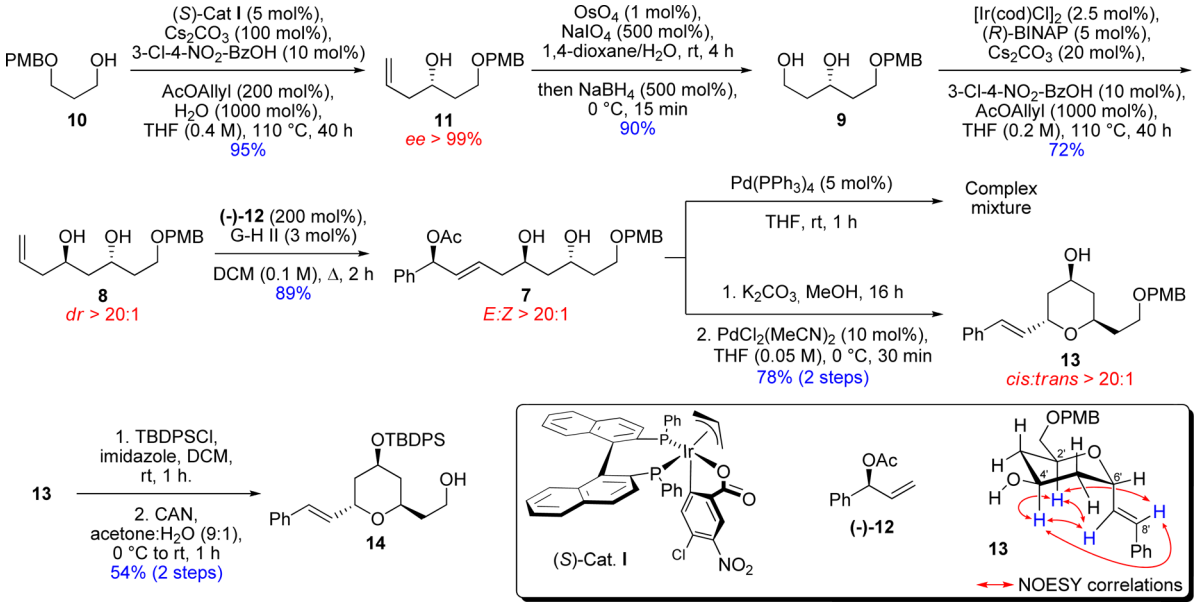
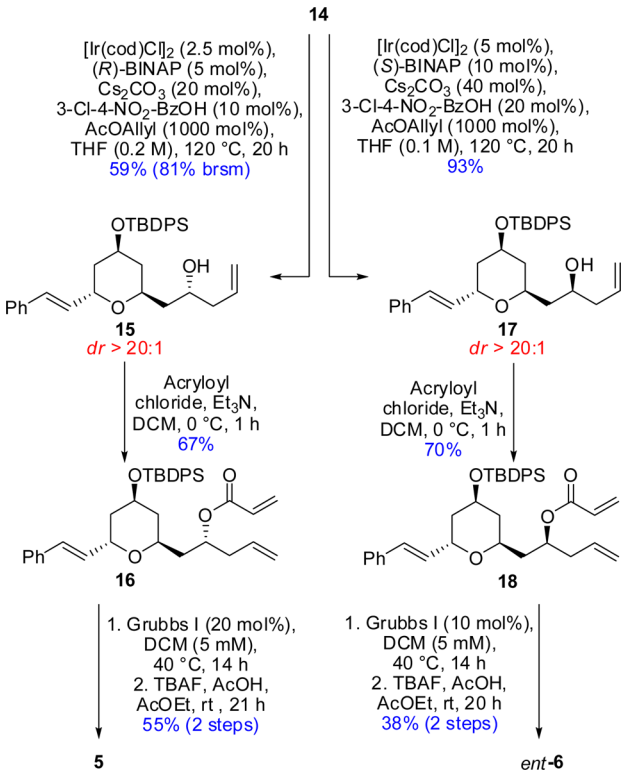
**Scheme 2. Catalytic Asymmetric Preparation of Tetrahydropyran 14**




**Scheme 3. Final Steps in the Preparation of Tetrahydropyran 5 and *ent*-6**



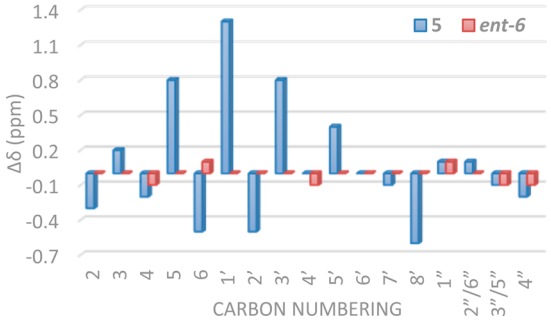




**Figure 3.** Comparison of $^{13}$C NMR data of synthetic **5** and *ent*-**6** with natural cryptoconcatone H.

as well as H-4′ being less shielded than H-2′, in contrast to the pattern found for natural cryptoconcatone H. In fact, comparison of its $^{1}$H and $^{13}$C NMR data with those available for cryptoconcatone H exposed large differences in the multiplet pattern and chemical shifts for several nuclei (differences of 0.33, 0.16, and 0.12 ppm were observed for H-1′a, H-2′, and H-6, respectively, and differences of 1.3 ppm for C-1 and 0.8 ppm for C-3′ and C-5 were observed, among others), as described in Figure 3 and in the Supporting Information. Additionally, the specific optical rotation for synthetic **5** {$[\alpha]_D^{22}$ +105 (*c* 1.0, MeOH)} differed from the one described for natural cryptoconcatone H {$[\alpha]_D^{25}$ −24 (*c* 0.1, MeOH)}.

A closer analysis of the NMR data reported by Luo and co-workers for the Mosher esters prepared from cryptoconcatone H revealed that the absolute configuration at C-4′ was misassigned. According to the model described by Riguera and co-workers,[15] the $\Delta\delta$ values should correspond to the *R* configuration at C-4′ instead of the *S* configuration assigned by those authors.

Taking into account the enantiomeric relationship at the tetrahydropyran ring between **5** and **6** and considering that the latter with an *R* configuration at C-4′ is the second best fit found in our computational studies, we then employed tetrahydropyran **14** described earlier to install the stereogenic center at C-6 with the required *S* configuration and prepare *ent*-**6**. We therefore used Krische's protocol with (*S*)-BINAP, which, after some experimentation, afforded tetrahydropyran **17** in excellent yield (93%) and diastereoisomeric ratio (>20:1) starting from alcohol **14**. After esterification with acryloyl chloride, RCM reaction, and deprotection of the secondary alcohol, tetrahydropyran *ent*-**6** was isolated in 38% overall yield (two steps) from acrylate **18** (Scheme 3). As described for compounds **5** and **13**, the *trans* configuration between H-2′/H-6′ of tetrahydropyran *ent*-**6** was likewise verified by a NOESY



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experiment, displaying similar correlations as those depicted for compound **13** in Scheme 2 (see the Supporting Information).

$^{1}H$ and $^{13}C$ NMR data of *ent*-**6** were virtually identical to those available for natural cryptoconcatone H, with the maximum deviations being 0.05 and 0.1 ppm, respectively (see Figure 3 and the Supporting Information). As expected, *ent*-**6** displayed a negative Cotton effect in the CD analysis and a positive specific optical rotation {($[\alpha]_D^{22}$ +65 (c 0.1, MeOH)}.[16]

In summary, the synthetic results reported herein guided by computational studies led to a revision of the structure assigned to cryptoconcatone H by Luo and co-workers, which can now be confidently described as the all *R* stereoisomer **6** (Figure 2).

## EXPERIMENTAL SECTION

**General Information.** Starting materials and reagents were obtained from commercial sources and used as received unless otherwise specified. DCM, triethylamine, and 2,6-lutidine were treated with calcium hydride and distilled before use. THF was treated with metallic sodium and distilled before use. Anhydrous reactions were carried out with continuous stirring under an atmosphere of dry nitrogen. Progress of the reactions was monitored by thin-layer chromatography (TLC) analysis (silica gel 60 F254 on aluminum plates) and visualized by UV light and/or staining with *p*-anisaldehyde standard solution. $^{1}H$ NMR, $^{13}C$ NMR, and 2D experiments ($^{1}H-^{1}H$ COSY, $^{1}H-^{13}C$ HSQC, $^{1}H-^{13}C$ HMBC, and NOESY) were recorded on 250, 400, or 500 MHz equipment; chemical shifts ($\delta$) are reported in parts per million (ppm) relative to deuterated solvent as the internal standard ($CDCl_3$ 7.27 ppm, 77.0 ppm) unless otherwise specified. Mass spectra were recorded on a Q-Tof spectrometer operating in electrospray mode (ESI). FT-IR spectra were recorded in $cm^{-1}$. Flash column chromatography was performed on silica gel (300−400 mesh).

**Synthesis of Alcohol 11.** To a sealable tube containing (*S*)-Cat. **I**[8] (390 mg, 0.369 mmol, 5 mol %), 4-Cl-3-$NO_2$-BzOH (142 mg, 0.688 mmol, 10 mol %), and $Cs_2CO_3$ (2.25 g, 6.88 mmol, 100 mol %) kept under a nitrogen atmosphere was added a solution of distilled alcohol **10**[9] (1.35 g, 6.88 mmol, 100 mol %) in THF (17.2 mL, 0.4 M). Water (1.24 mL, 68.8 mmol, 1000 mol %) and allyl acetate (1.50 mL, 13.8 mmol, 200 mol %) were added, and the rubber septum was replaced with a screw cap. The reaction mixture was heated in an oil bath at 110 °C for 43 h, cooled to rt, and then concentrated under reduced pressure. Purification of the residue by flash column chromatography (gradient, 20−50% AcOEt/Hex to isolate **11** and then 0−50% DCM/AcOEt for catalyst recovery) gave alcohol **11** (1.54 g, 6.52 mmol; 95% yield) as a light yellow oil and catalyst (*S*)-Cat. **I** (351 mg, 0.333 mmol; 90% recovered) as a yellow powder. TLC: 0.34 (30% AcOEt/Hex); $[\alpha]_D^{20}$ −7 (*c* 1.0, $CHCl_3$), Lit. $[\alpha]_D^{20}$ −3.0 (*c* 1.00, $CHCl_3$);[17] FTIR (ATR): 3456, 2935, 2860, 1613, 1513, 1247, 1090, 1034, 821 $cm^{-1}$; $^{1}H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.25 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.94−5.74 (m, 1H), 5.17−5.10 (m, 1H), 5.08 (s, 1H), 4.46 (s, 2H), 3.93−3.83 (m, 1H), 3.81 (s, 3H), 3.77−3.56 (m, 2H), 2.86 (br. d, *J* = 2.5 Hz, 1H), 2.25 (t, *J* = 6.6 Hz, 2H), 1.81−1.71 (m, 2H) ppm; $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ 159.2, 134.8, 130.0, 129.2, 117.4, 113.8, 72.9, 70.3, 68.5, 55.2, 41.8, 35.8 ppm; HPLC: column: Chiralpak IA (particle size: 5 $\mu$m; dimensions: 4.6 mm $\phi$ × 250 mm); eluent: hexanes (99.3)/(0.7) IPA; flow: 0.8 mL/min; detector: 225 nm (Hg lamp); $t_R$ (*R*)-**11**: 47.8 min, (*S*)-**11**: 50.1 min; ee > 99%.

*(S)-MTPA Ester of 11.* The general procedure using (*R*)-MTPACl was followed.[18] TLC: 0.78 (30% AcOEt/Hex); $^{1}H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.60−7.46 (m, 2H), 7.42−7.30 (m, 3H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.48 (dd, *J* = 1.5, 5.0 Hz, 2H), 5.85−5.64 (m, 1H), 5.42−5.29 (m, 1H), 5.13−5.06 (m, 2H), 4.38−4.26 (m, 2H), 3.79 (s, 3H), 3.53 (d, *J* = 1.1 Hz, 3H), 3.41−3.21 (m, 2H), 2.49−2.41 (m, 1H), 1.92−1.86 (m, 1H) ppm.

*(R)-MTPA Ester of 11.* The general procedure using (*S*)-MTPACl was followed.[18] TLC: 0.78 (30% AcOEt/Hex); $^{1}H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.61−7.49 (m, 2H), 7.45−7.32 (m, 3H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.49 (dd, *J* = 1.5, 5.0 Hz, 2H), 5.64 (tdd, *J* = 7.0, 9.6, 17.5 Hz, 1H), 5.33 (quin, *J* = 6.1 Hz, 1H), 5.08−4.95 (m, 2H), 4.40 (s, 2H), 3.80 (s, 3H), 3.53−3.40 (m, 5H), 2.45−2.33 (m, 2H), 1.93 (q, *J* = 6.3 Hz, 2H) ppm.

**Synthesis of Diol 9.** To a solution of olefin **11** (427 mg, 1.81 mmol, 100 mol %) in a 3:1 mixture of 1,4-dioxane/$H_2O$ (26.2 mL, 0.1 M) at 0 °C were successively added 2,6-lutidine (0.43 mL, 3.6 mmol, 200 mol %), $OsO_4$ (0.18 mL, 18 $\mu$mol, 1 mol %; 0.1 M in $^{t}$BuOH), and $NaIO_4$ (1.17 g, 5.42 mmol, 300 mol %) in portions. The thick mixture was vigorously stirred at rt for 4 h and then cooled to 0 °C when $NaBH_4$ (395 mg, 13.1 mmol, 500 mol %) was added carefully in portions (generation of gas). After 15 min of stirring, satd. aq. $Na_2S_2O_3$ (15 mL) was added to the resultant gray suspension and the mixture was stirred for 1 h. After addition of satd. aq. $NaHCO_3$ (5 mL) and stirring for 1 h, the mixture was diluted with DCM (50 mL) and the aqueous phase was extracted with AcOEt. The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (gradient, 50−100% AcOEt/Hex and then 5% MeOH/AcOEt) gave diol **9** (389 mg, 1.62 mmol; 90% yield) as a colorless oil. TLC: 0.07 (50% AcOEt/Hex), 0.43 (5% MeOH/AcOEt); $[\alpha]_D^{20}$ −10 (*c* 1.0, $CHCl_3$), Lit. $[\alpha]_D^{25}$ −8.5 (*c* 0.027, $CHCl_3$);[19] FTIR (ATR): 3375, 2939, 2865, 1613, 1513, 1302, 1247, 1174, 1086, 1034, 820, 732, 668 $cm^{-1}$; $^{1}H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.25 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 4.46 (s, 2H), 4.16−4.01 (m, 1H), 3.81 (s, 3H), 3.84 (t, *J* = 5.2 Hz, 1H), 3.77−3.59 (m, 2H), 3.52 (br. s, 1H), 2.74 (br. s, 1H), 1.95−1.67 (m, 4H) ppm; $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ 159.3, 129.9, 129.3, 113.9, 73.0, 71.5, 68.7, 61.3, 55.2, 38.5, 36.6 ppm.

**Synthesis of Diol 8.** A solution of alcohol **9** (548 mg, 2.28 mmol, 100 mol %) in anhydrous THF (11.4 mL, 0.2 M) was added to a sealed tube charged with $[Ir(cod)Cl]_2$ (39.5 mg, 57.0 $\mu$mol, 2.5 mol %), (*R*)-BINAP (71.7 mg, 0.114 mmol, 5 mol %), $Cs_2CO_3$ (149 mg, 0.456 mmol, 20 mol %), 4-Cl-3-$NO_2$-BzOH (46.9 mg, 0.228 mmol, 10 mol %), and allyl acetate (1.7 mL, 16 mmol, 1000 mol %) under a nitrogen atmosphere. The reaction mixture was allowed to stir in an oil bath at 110 °C for 44 h and then concentrated under reduced pressure. Purification of the residue by flash column chromatography (gradient, 20−100% AcOEt/Hex to isolate **8** and then 0−50% DCM/AcOEt for catalyst recovery) gave alcohol **8** (461.6 mg, 1.646 mmol; 72% yield, dr > 20:1) as a light brown oil and (*R*)-Cat. **I** (49.5 mg, 46.9 $\mu$mol; 41% recovered yield) as a yellow powder. TLC: 0.23 (50% AcOEt/Hex); $[\alpha]_D^{22}$ −14 (*c* 1.0, $CHCl_3$); FTIR (ATR): 3422, 2937, 1613, 1513, 1247, 1087, 1034, 820 $cm^{-1}$; $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.25 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.83 (tdd, *J* = 7.2, 10.1, 17.1 Hz, 1H), 5.16−5.08 (m, 2H), 4.46 (s, 2H), 4.19−4.13 (m, 1H), 4.03−3.95 (m, 1H), 3.81 (s, 3H), 3.71 (td, *J* = 4.8, 9.3 Hz, 1H), 3.65 (dt, *J* = 3.9, 9.3 Hz, 1H), 2.27 (t, *J* = 6.7 Hz, 2H), 1.89 (dtd, *J* = 4.6, 9.3, 14.1 Hz, 1H), 1.72−1.66 (m, 1H), 1.65−1.55 (m, 2H) ppm; $^{13}C$ NMR (101 MHz, $CDCl_3$): $\delta$ 159.2, 134.8, 129.8, 129.2, 117.5, 113.7, 72.8, 68.8, 68.7, 67.9, 55.1, 42.1, 41.9, 36.2 ppm; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{24}O_4$ 281.1753; found 281.1741.

*Acetonide of 8.* The general procedure using 2,2-dimethoxypropane for the preparation of isopropylidene ketals was followed.[10] TLC: 0.37 (10% AcOEt/Hex); $[\alpha]_D^{22}$ −17 (*c* 1.0, $CHCl_3$); FTIR (ATR): 2987, 2938, 2857, 1613, 1513, 1379, 1247, 1224, 1172, 1122, 1094, 1036, 993, 913, 820; $^{1}H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.26 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.80 (tdd, *J* = 6.8, 10.2, 17.1 Hz, 1H), 5.15−4.99 (m, 2H), 4.43 (s, 2H), 3.99 (td, *J* = 6.8, 14.3 Hz, 1H), 3.86 (td, *J* = 6.8, 14.3 Hz, 1H), 3.81 (s, 3H), 3.57−3.48 (m, 2H), 2.31 (br. td, *J* = 6.8, 14.4 Hz, 1H), 2.19 (br. td, *J* = 6.8, 14.2 Hz, 1H), 1.76 (br. q, *J* = 6.6 Hz, 2H), 1.64−1.57 (m, 2H), 1.34 (s, 6H) ppm; $^{13}C$ NMR (126 MHz, $CDCl_3$): $\delta$ 159.1, 134.5, 130.6, 129.3, 116.8, 113.8, 100.3, 72.7, 66.3, 66.2, 63.7, 55.3, 40.1, 38.0, 36.0, 24.8 ppm; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{19}H_{28}O_4Na$ 343.1885; found 343.1893.

**Synthesis of Ester 7.** A solution of diol **8** (200 mg, 0.713 mmol, 100 mol %), acetate (−)-**12**[7] (250 mg, 1.42 mmol, 200 mol %), and Hoveyda−Grubbs second-generation catalyst (13.8 mg, 21.4 $\mu$mol, 3 mol %) in dry DCM (7.1 mL, 0.1 M), under a nitrogen atmosphere



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was heated to reflux in an oil bath at 45 °C. After 2 h, the reaction mixture was concentrated under reduced pressure. Purification of the crude residue by flash column chromatography (gradient, 5−100% AcOEt/Hex) gave acetate (−)-**12** (128 mg 0.724 mmol; 51% recovered) as a colorless oil, followed by diol **7** (271 mg, 0.632 mmol; 89% yield) as a light brown oil. TLC: 0.17 (50% AcOEt/Hex); $[\alpha]_D^{22}$ +4 (*c* 1.0, $CHCl_3$); FTIR (ATR): 3429, 2937, 2862, 1734, 1612, 1513, 1371, 1244, 1087, 1031, 986, 821, 756, 700 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.40−7.26 (m, 5H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.31−6.11 (m, 1H), 5.85−5.65 (m, 2H), 4.44 (s, 2H), 4.18−4.06 (m, 1H), 4.04−3.89 (m, 1H), 3.79 (s, 3H), 3.74−3.56 (m, 2H), 3.53 (br. s, 1H), 2.99 (br. s, 1H), 2.36−2.14 (m, 2H), 2.08 (s, 3H), 1.92−1.81 (m, 1H), 1.70−1.63 (m, 1H), 1.62−1.53 (m, 2H) ppm; $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ 170.1, 159.3, 139.4, 131.3, 130.3, 129.8, 129.3, 128.5, 127.9, 126.8, 113.8, 76.2, 73.0, 69.2, 68.9, 68.1, 55.2, 42.1, 40.4, 36.2, 21.3 ppm; HRMS (ESI-TOF) *m*/*z*: $[M - C_2H_3O_2]^+$ calcd for $C_{23}H_{29}O_4$ 369.2066; found 369.2057.

**Synthesis of Tetrahydropyran 13.** To a solution of acetate **7** (351 mg, 0.820 mmol, 100 mol %) in MeOH (3.3 mL, 0.22 M) was added $K_2CO_3$ (567 mg, 4.10 mmol, 555 mol %) portionwise at 0 °C. After 12 h, the reaction mixture was treated with $H_2O$ (6 mL) and satd. aq. $NH_4Cl$ (6 mL) and then diluted with AcOEt (6 mL). The aqueous phase was separated, taken up to pH 7 with HCl 6 M, and extracted with AcOEt. The combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated under reduced pressure. The resulting residue was then dissolved in anhydrous THF (16.4 mL, 0.05 M) under a nitrogen atmosphere, and $PdCl_2(MeCN)_2$ (21.5 mg, 82.0 $\mu$mol, 10 mol %) was added at 0 °C. After 30 min, the reaction mixture was concentrated under reduced pressure at rt. Purification of the residue by flash column chromatography (gradient, 30−80% AcOEt/Hex) gave tetrahydropyran **13** (211 mg, 0.572 mmol; 78% yield for two steps) as a yellow-brown oil. TLC: 0.28 (50% AcOEt/Hex); $[\alpha]_D^{22}$ +46 (*c* 2.0, $CHCl_3$); FTIR (ATR): 3407, 2937, 2866, 1612, 1512, 1449, 1360, 1301, 1247, 1174, 1088, 1067, 1034, 969, 819, 755, 705, 693, 667 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.38−7.20 (m, 7H), 6.82 (d, *J* = 8.7 Hz, 1H), 6.59 (dd, *J* = 1.8, 16.3 Hz, 1H), 6.27 (dd, *J* = 4.4, 16.3 Hz, 1H), 4.85−4.75 (m, 1H), 4.46 (s, 2H), 4.10−3.99 (m, 1H), 3.96−3.86 (m, 1H), 3.78 (s, 3H), 3.68−3.55 (m, 2H), 2.17 (tdd, *J* = 2.1, 4.4, 12.8 Hz, 1H), 1.95 (tdd, *J* = 2.0, 4.4, 12.8 Hz, 1H), 1.88−1.71 (m, 3H), 1.31 (td, *J* = 10.6, 12.2 Hz, 1H) ppm; $^{13}C$ NMR (101 MHz, $CDCl_3$): $\delta$ 159.1, 136.7, 131.5, 130.5, 129.6, 129.3, 128.6, 127.6, 126.4, 113.8, 72.8, 72.4, 66.8, 66.4, 64.7, 55.2, 41.3, 38.2, 36.1 ppm; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{28}O_4Na$ 391.1885; found 391.1887.

**Synthesis of Alcohol 14.** To a solution of tetrahydropyran **13** (200 mg, 0.543 mmol, 100 mol %) and imidazole (74.7 mg, 1.09 mmol, 200 mol %) in DCM (1 mL, 0.5 M) at 0 °C was added TBDPSCl (0.22 mL, 0.81 mmol, 150 mol %) dropwise under a nitrogen atmosphere. After stirring at rt for 1 h, the reaction mixture was poured into satd. aq. $NaHCO_3$ and extracted with DCM. The combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated under reduced pressure. The resulting residue was then dissolved in a 9:1 mixture of acetone/water (5.5 mL, 0.1 M), and CAN (902 mg, 1.63 mmol, 300 mol %) was added in three equal portions every 20 min at 0 °C, with the third one added at room temperature. After 80 min, the mixture was treated with satd. aq. $NaHCO_3$ (15 mL), water (15 mL) and diluted with AcOEt (15 mL) and water (15 mL). The aqueous phase was extracted with AcOEt, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the crude mixture by flash column chromatography (gradient, 10−40% AcOEt/Hex) gave alcohol **14** (142 mg, 0.292 mmol; 54% yield for two steps) as a colorless syrup. TLC: 0.34 (30% AcOEt/Hex); $[\alpha]_D^{22}$ +34 (*c* 1.0, $CHCl_3$); FTIR (ATR): 3400, 2931, 2888, 2857, 1653, 1471, 1428, 1113, 1073, 971, 822, 742, 699 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.74−7.66 (m, 4H), 7.46−7.38 (m, 6H), 7.32−7.27 (m, 2H), 7.26−7.16 (m, 3H), 6.17 (dd, *J* = 1.8, 16.4 Hz, 1H), 5.90 (dd, *J* = 4.2, 16.4 Hz, 1H), 4.67 (br. s, 1H), 3.99 (tt, *J* = 5.0, 10.3 Hz, 1H), 3.84−3.74 (m, 3H), 2.70 (br. s, 1H), 1.93−1.80 (m, 4H), 1.70−1.60 (m, 1H), 1.55 (td, *J* = 10.5, 12.7 Hz, 2H), 1.08 (s, 9H) ppm; $^{13}C$ NMR (101 MHz, $CDCl_3$): $\delta$ 136.5, 135.8, 135.7, 134.3, 134.1, 131.4, 129.8, 129.7, 129.4, 128.4, 127.7, 127.6, 126.3, 72.3, 70.5, 65.7, 61.5, 41.2, 37.8, 37.6, 26.9, 19.1 ppm; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{31}H_{38}O_3SiNa$ 509.2488; found 509.2484.

**Synthesis of Alcohol 15.** A solution of alcohol **14** (58.7 mg, 121 $\mu$mol, 100 mol %) in anhydrous THF (0.6 mL, 0.2 M) was added to a sealed tube charged with $[Ir(cod)Cl]_2$ (2.1 mg, 3.0 $\mu$mol, 2.5 mol %), (*R*)-BINAP (3.8 mg, 6.0 $\mu$mol, 5 mol %), $Cs_2CO_3$ (7.9 mg, 24 $\mu$mol, 20 mol %), 4-Cl-3-$NO_2$-BzOH (2.5 mg, 12 $\mu$mol, 10 mol %), and allyl acetate (131 $\mu$L, 1.21 mmol, 1000 mol %) under a nitrogen atmosphere. The reaction mixture was allowed to stir in an oil bath at 120 °C for 20 h and then concentrated under reduced pressure. Purification of the resultant residue by flash column chromatography (gradient, 4−20% AcOEt/Hex) gave allyl alcohol **15** (37.0 mg, 70.2 $\mu$mol; 59% yield, dr > 20:1) as a yellow gum and alcohol **14** (16.4 mg, 33.7 $\mu$mol; 28% yield recovered) as a yellow gum. TLC: 0.16 (10% AcOEt/Hex); $[\alpha]_D^{22}$ +41 (*c* 1.0, $CHCl_3$); FTIR (ATR): 2931, 2857, 1471, 1428, 1113, 1073, 971, 915, 822, 739, 702 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.75−7.67 (m, 4H), 7.48−7.38 (m, 6H), 7.34−7.28 (m, 2H), 7.26−7.17 (m, 3H), 6.18 (dd, *J* = 1.5, 16.4 Hz, 1H), 5.92 (dd, *J* = 4.2, 16.4 Hz, 1H), 5.84 (tdd, *J* = 7.1, 10.3, 17.2 Hz, 1H), 5.15−5.06 (m, 2H), 4.71 (br. s, 1H), 4.00 (tt, *J* = 4.7, 9.8 Hz, 1H), 3.92−3.73 (m, 3H), 2.29 (qd, *J* = 7.0, 13.7 Hz, 1H), 2.20 (td, *J* = 7.0, 13.7 Hz, 1H), 1.94−1.70 (m, 4H), 1.60−1.50 (m, 2H), 1.10 (s, 9H) ppm; $^{13}C$ NMR (101 MHz, $CDCl_3$): $\delta$ 136.4, 135.8, 135.7, 134.9, 134.2, 134.0, 131.5, 129.8, 129.7, 129.2, 128.5, 128.4, 127.7, 126.3, 117.2, 72.2, 71.5, 71.4, 65.4, 41.9, 41.6, 41.5, 37.6, 26.9, 19.1 ppm; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{34}H_{42}O_3SiNa$ 549.2801; found 549.2800.

**Synthesis of Alcohol 17.** A solution of alcohol **14** (13.2 mg, 27.1 $\mu$mol, 100 mol %) in anhydrous THF (0.3 mL, 0.1 M) was added to a sealed tube charged with $[Ir(cod)Cl]_2$ (0.94 mg, 1.4 $\mu$mol, 5 mol %), (*S*)-BINAP (1.69 mg, 2.71 $\mu$mol, 10 mol %), $Cs_2CO_3$ (3.6 mg, 11 $\mu$mol, 40 mol %), 4-Cl-3-$NO_2$-BzOH (1.1 mg, 5.4 $\mu$mol, 20 mol %), and allyl acetate (29.5 $\mu$L, 271 $\mu$mol, 1000 mol %) under a nitrogen atmosphere. The reaction mixture was allowed to stir in an oil bath at 120 °C for 20 h and then concentrated under reduced pressure. Purification of the resultant residue by flash column chromatography (gradient, 4−20% AcOEt/Hex) gave allyl alcohol **17** (13.3 mg, 25.2 $\mu$mol; 93% yield, dr > 20:1) as a yellow gum. TLC: 0.16 (10% AcOEt/Hex); $[\alpha]_D^{23}$ +42 (*c* 2.0, $CHCl_3$); FTIR (ATR): $\delta$ 3453, 2931, 2857, 1428, 1113, 1069, 912, 822, 742, 702 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): 7.73−7.67 (m, 4H), 7.44−7.38 (m, 6H), 7.33−7.28 (m, 2H), 7.25−7.16 (m, 3H), 6.19 (dd, *J* = 1.5, 16.4 Hz, 1H), 5.91 (dd, *J* = 4.2, 16.4 Hz, 1H), 5.88−5.78 (m, 1H), 5.14−5.08 (m, 2H), 4.65 (br. s, 1H), 4.05−3.95 (m, 2H), 3.88 (tdd, *J* = 2.5, 8.2, 10.8 Hz, 1H), 2.62 (br. s, 1H), 2.24 (t, *J* = 6.7 Hz, 2H), 1.89−1.73 (m, 4H), 1.60−1.53 (m, 2H), 1.08 (s, 9H) ppm; $^{13}C$ NMR (126 MHz, $CDCl_3$): $\delta$ 136.6, 135.8, 135.7, 134.9, 134.3, 134.1, 131.3, 129.7, 129.7, 129.3, 128.4, 127.6, 127.5, 126.3, 117.6, 72.3, 67.7, 67.5, 65.9, 42.1, 41.5, 41.1, 37.9, 26.9, 19.1 ppm; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{34}H_{42}O_3SiNa$ 549.2801; found 549.2817.

**Synthesis of Ester 16.** Triethylamine (58 $\mu$L, 0.41 mmol, 600 mol %) was added to a solution of alcohol **15** (36.0 mg, 68.3 $\mu$mol, 100 mol %) in DCM (1 mL, 0.07 M) at 0 °C, under nitrogen atmosphere. After stirring for 10 min, acryloyl chloride (17.3 $\mu$L, 205 $\mu$mol, 300 mol %) in DCM (0.4 mL, 0.5 M) was added and the mixture was stirred for additional 10 min at 0 °C and then kept at rt for 2 h. The reaction mixture was treated with half satd. aq. $NaHCO_3$ (1 mL) and extracted with DCM. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the resultant residue by flash column chromatography (gradient, 0−9% AcOEt/Hex; 2% triethylamine) gave ester **16** (26.4 mg, 45.5 $\mu$mol; 67% yield) as a colorless oil. TLC: 0.41 (10% AcOEt/Hex); $[\alpha]_D^{23}$ +20 (*c* 1.0, $CHCl_3$); FTIR (ATR): 2930, 2957, 1722, 1428, 1405, 1295, 1271, 1195, 1112, 1070, 969, 822, 741, 702 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.74−7.67 (m, 4H), 7.46−7.38 (m, 6H), 7.36−7.17 (m, 6H), 6.36 (dd, *J* = 1.7, 17.3 Hz, 1H), 6.17 (dd, *J* = 1.4, 16.4 Hz, 1H), 6.08 (dd, *J* = 10.3, 17.2 Hz, 1H), 5.94 (dd, *J* = 4.3, 16.4 Hz, 1H), 5.75 (dd, *J* = 1.6, 10.3 Hz, 1H), 5.20 (quin, *J* = 6.2 Hz,



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1H), 5.12−5.02 (m, 2H), 4.69−4.60 (m, 1H), 4.01 (tt, $J$ = 4.4, 9.2 Hz, 1H), 3.68 (br. dddd, $J$ = 2.7, 4.7, 7.5, 9.8 Hz, 1H), 2.49−2.28 (m, 2H), 2.07 (dt, $J$ = 7.5, 14.9 Hz, 1H), 1.93−1.66 (m, 4H), 1.54−1.41 (m, 1H), 1.09 (s, 9H) ppm; $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ 165.6, 136.7, 135.8, 135.7, 134.3, 134.1, 133.5, 131.0, 130.3, 129.9, 129.7, 128.8, 128.4, 127.6, 127.4, 126.3, 117.9, 71.4, 71.1, 67.5, 65.9, 40.6, 39.4, 38.5, 37.7, 26.9, 19.1 ppm; HRMS (ESI-TOF) $m/z$: $[M + H]^+$ calcd for $C_{37}H_{45}O_4Si$ 581.3087; found 581.3070.

**Synthesis of Ester 18.** Compound **18** (15.4 mg, 26.5 μmol; 70% yield) was obtained as a colorless oil from alcohol **17** (20.0 mg, 38.0 μmol) in a similar procedure as that described for ester **16**. TLC: 0.41 (10% AcOEt/Hex); $[\alpha]_D^{22}$ +71 ($c$ 1.0, $CHCl_3$); FTIR (ATR): 2930, 2856, 1722, 1428, 1405, 1270, 1195, 1112, 1070, 982, 821, 741, 701, 668 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ 7.75−7.66 (m, 4H), 7.47−7.35 (m, 6H), 7.26−7.11 (m, 5H), 6.31 (dd, $J$ = 1.6, 17.2 Hz, 1H), 6.07−5.92 (m, 2H), 5.89−5.72 (m, 2H), 5.67 (dd, $J$ = 1.7, 10.3 Hz, 1H), 5.40−5.28 (m, 1H), 5.10 (br. d, $J$ = 4.3 Hz, 1H), 5.05 (s, 1H), 4.63 (s, 1H), 3.98 (tt, $J$ = 5.0, 10.3 Hz, 1H), 3.53 (br. tt, $J$ = 2.1, 10.3 Hz, 1H), 2.37 (br. t, $J$ = 6.2 Hz, 2H), 1.94−1.59 (m, 5H), 1.46 (td, $J$ = 10.3, 12.2 Hz, 1H), 1.08 (s, 9H) ppm; $^{13}$C NMR (63 MHz, $CDCl_3$): $\delta$ 165.7, 136.7, 135.8, 135.8, 134.3, 134.2, 133.4, 130.8, 130.5, 130.0, 129.7, 128.6, 128.2, 127.6, 127.3, 126.3, 117.9, 71.9, 70.0, 65.9, 41.7, 40.2, 39.4, 37.4, 26.9, 19.1 ppm; HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ calcd for $C_{37}H_{44}O_4SiNa$ 603.2906; found 603.2922.

**Synthesis of Tetrahydropyran 5.** To a solution of ester **16** (25.0 mg, 43.0 μmol, 100 mol %) in DCM (8.5 mL, 5 mM) was added Grubbs I catalyst (1.8 mg, 2.2 μmol, 5 mol %), and the mixture was kept under reflux in an oil bath at 45 °C. After 60 min of reaction, a second portion of Grubbs I catalyst (1.8 mg, 2.2 μmol, 5 mol %) was added. After 12 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was then dissolved in AcOEt (1 mL) and glacial AcOH (2.4 μL, 43 μmol, 100 mol %), TBAF (172 μL, 0.172 mmol, 1 M stn in THF; 400 mol %) and TBAF (172 mL, 0.172 mmol, 1 M THF soln., 400 mol%) were added at 0 °C. After stirring at rt for 21 h, the reaction mixture was treated with satd. aq $NaHCO_3$. The aqueous phase was extracted with AcOEt, and the combined organic phases were washed with brine, dried under $Na_2SO_4$, and concentrated under reduced pressure. Purification of the resultant residue by flash column chromatography (gradient, 50−100% AcOEt/Hex and then 3−9% MeOH/AcOEt) gave tetrahydropyran **5** (7.5 mg, 24 μmol; 55% yield for two steps) as a yellow gum. TLC: 0.38 (AcOEt); $[\alpha]_D^{22}$ +105 ($c$ 1.0, MeOH); FTIR (ATR): 3422, 2920, 1716, 1389, 1251, 1069, 1032, 970, 818, 759, 692, 668 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$):[20] $\delta$ 7.38−7.35 (m 2H), 7.35−7.30 (m, 2H), 7.27−7.24 (m, 1H), 6.88 (ddd, $J$ = 2.7, 5.5, 9.6 Hz, 1H), 6.57 (dd, $J$ = 1.6, 16.2 Hz, 1H), 6.28 (dd, $J$ = 5.0, 16.2 Hz, 1H), 6.03 (br. dd, $J$ = 1.6, 9.6 Hz, 1H), 4.78−4.74 (m, 1H), 4.67 (dddd, $J$ = 4.5, 6.1, 6.3, 11.0 Hz, 1H), 4.07 (tt, $J$ = 4.2, 10.3 Hz, 1H), 3.97 (dddd, $J$ = 2.2, 5.3, 7.7, 10.3 Hz, 1H), 2.46 (tdd, $J$ = 2.7, 11.0, 18.4 Hz, 1H), 2.39 (br. td, $J$ = 5.5, 18.4 Hz, 1H), 2.20 (ddd, $J$ = 6.1, 7.7, 14.3 Hz, 1H), 2.16 (tdd, $J$ = 2.0, 4.2, 12.8 Hz, 1H), 2.01 (tdd, $J$ = 2.2, 4.2, 12.1 Hz, 1H), 1.84 (ddd, $J$ = 5.3, 6.3, 14.3 Hz, 1H), 1.77 (ddd, $J$ = 5.7, 10.3, 12.8 Hz, 1H), 1.37 (td, $J$ = 10.3, 12.1 Hz, 1H) ppm; $^{13}$C NMR (126 MHz, $CDCl_3$):[20] $\delta$ 164.7, 145.4, 136.7, 132.4, 129.1, 128.9, 128.1, 126.7, 121.6, 75.3, 72.7, 66.1, 64.6, 41.0, 40.6, 38.3, 29.5 ppm; HRMS (ESI-TOF) $m/z$: $[M + H]^+$ calcd for $C_{19}H_{23}O_4$ 315.1596; found: 315.1585; ECD: positive Cotton effect, maximum at 248 nm ($c$ 0.23 mg/mL, MeOH).

**Synthesis of Tetrahydropyran *ent*-6.** Compound *ent*-**6** (3.0 mg, 9.5 μmol; 38% yield for two steps) was obtained as a light yellow gum from ester **18** (15 mg, 25 μmol) in a similar procedure as that described for tetrahydropyran **5**. TLC: 0.38 (AcOEt); $[\alpha]_D^{22}$ +65 ($c$ 0.1, MeOH); FTIR (ATR): 3419, 2925, 2854, 1711, 1385, 1253, 1062, 1030, 972, 816, 761, 710, 693 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$):[20] $\delta$ 7.42 (d, $J$ = 7.4 Hz, 2H), 7.32 (t, $J$ = 7.4 Hz, 2H), 7.23 (br. t, $J$ = 7.4 Hz, 1H), 6.89 (ddd, $J$ = 2.8, 5.8, 9.7 Hz, 1H), 6.60 (dd, $J$ = 2.0, 16.4 Hz, 1H), 6.22 (dd, $J$ = 4.2, 16.4 Hz, 1H), 6.05 (ddd, $J$ = 1.0, 2.5, 9.7 Hz, 1H), 4.83−4.76 (m, 2H), 4.14 (tt, $J$ = 2.2, 10.6 Hz, 1H), 4.04 (tt, $J$ = 4.2, 10.6 Hz, 1H), 2.44−2.32 (m, 2H), 2.16 (tdd, $J$ = 2.0, 4.2, 12.7 Hz, 1H), 1.95 (tdd, $J$ = 2.2, 4.2, 12.3 Hz, 1H), 1.92 (ddd, $J$ = 2.8, 9.4, 14.6 Hz, 1H), 1.86 (ddd, $J$ = 3.1, 9.9, 14.6 Hz, 2H), 1.76 (ddd, $J$ = 5.8, 10.6, 12.7 Hz, 1H), 1.31 (td, $J$ = 10.6, 12.3 Hz, 1H) ppm; $^{13}$C NMR (126 MHz, $CDCl_3$):[20] $\delta$ 164.4, 145.3, 136.7, 131.8, 129.0, 128.9, 128.0, 126.8, 121.8, 74.7, 72.7, 65.6, 64.7, 41.9, 41.8, 38.7, 30.3 ppm; HRMS (ESI-TOF) $m/z$: $[M + H]^+$ calcd for $C_{19}H_{23}O_4$ 315.1596; found: 315.1592; OCR: negative Cotton effect, minimum at 259 nm ($c$ 0.23 mg/mL, MeOH).

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01378.

Spectral and HPLC data (PDF)
Computational studies (PDF)

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### Notes

The authors declare no competing financial interest.

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