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Asymmetric synthesis of Goniothalesdiol A from (*R*)-2,3-*O*-cyclohexylidine glyceraldehyde

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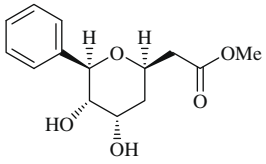
ABSTRACT

Goniothalesdiol A **1** has been synthesized from (*R*)-2,3-*O*-cyclohexylidine glyceraldehyde with high stereoselectivity and 22% overall yield in 11 simple steps. The key features of the synthetic strategy include the stereocontrolled allylation of (*R*)-2,3-*O*-cyclohexylidine glyceraldehydes; the cross-metathesis with a Grubbs's second generation catalyst, and the intramolecular base-catalyzed oxy-Michael addition for the formation of the tetrahydropyran ring.

1. Introduction

The synthesis of substituted tetrahydropyrans is of considerable interest due to the prevalence of these structures in natural products and biologically active compounds. Tetrahydropyrans bearing substituents at the 2- and 6-positions on the ring are often observed in a large number of biologically important natural products, such as zampanolide,[1a] leucascandrolide,[1b] phorboxazole,[1c] ratjadone,[1d] lasonolide,[1e] misakinolides,[1f] scytophycins,[1g] sorangicin A,[1h] swinholides,[1i] and laulimalide.[1j] The stereoselective synthesis of 2,6-disubstituted tetrahydropyrans is an important task since the *cis*- or *trans*-configuration of the 2,6-substituents on the hydropyran ring can affect the three dimensional molecular shape, as well as the biological activity of the natural product.[2] Several strategies have already been employed for the synthesis of these tetrahydropyran scaffolds:[3] The majority of approaches involve Prins' cyclization,[3a] palladium-catalyzed cyclization of non-3-ene-2,8-diols,[3b] reductive cyclizations of hydroxysulfinyl ketones,[3c] or hydroxy-epoxide cyclization, and intramolecular conjugate addition.[3d]

Recently, Goniothalesdiol A **1** (Fig. 1) isolated from the *Goniothalamus* sp. has been shown to possess a 2,3,4,6-tetrasubstituted pyran ring,[4] only one synthesis based on Sharpless kinetic resolution has been reported.[5] Application of the known synthetic strategies for the synthesis of **1** requires the intermediates to be prepared via a complex set of reactions. Furthermore, the kinetic resolution strategy suffers from the drawback of a maximum yield of 50%. We have thus devised an alternative route to **1** using (*R*)-2,3-*O*-cyclohexylidine glyceraldehyde as a starting chiral template.



Goniothalesdiol A **1**

Figure 1.

2. Results and discussion

(*R*)-2,3-*O*-Cyclohexylidine glyceraldehyde **2** can be readily prepared from D-mannitol on a multi-gram scale.[6] Compared to the corresponding acetonide, cyclohexylidine glyceraldehyde is stable, and provides the appropriate steric hindrance when allylation with allyl bromide is carried out to give *anti*-homoallylic alcohol **3**, almost exclusively[7] (91%, de 94%). The diastereomers are easily separated by column chromatography. To obtain homoallylic alcohol **8** with a free primary alcohol group, compound **3** was subjected to a series of simple protection and deprotection steps with high yields. The secondary alcohol function was first protected by benzylation to obtain **4,** the cyclohexylidine protecting group was removed with 90% TFA in water to obtain diol **5**, and the primary hydroxy group of **5** was selectively protected as a TBDMS ether followed by protection of the resulting secondary alcohol as a benzyl derivative. Treatment of the dibenzyl ether **7** with TBAF in THF afforded the primary alcohol **8** (overall yield 52% from **3**). The alcohol **8** was oxidized to aldehyde by Swern oxidation protocol and the crude aldehyde was directly used for Grignard reaction with phenyl magnesium bromide in dry ether at −78 °C. The corresponding *anti*-alcohol **9** was obtained in 59% yield after column chromatography (Scheme 1).

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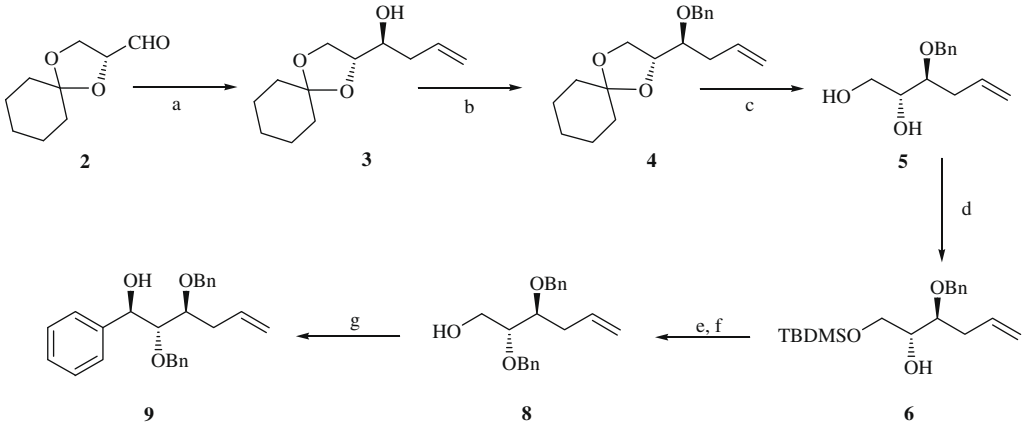


Scheme 1. Reagents and conditions: (a) Allyl bromide, Zn, aq NH_4Cl, 0 °C, 4 h, 91%; (b) NaH, BnBr, THF, 0 °C to rt, 6 h, 93%; (c) 90% CF_3COOH in water, 0 °C, 2 h, 80%; (d) TBDMSCl, imidazole, CH_2Cl_2, 0 °C to rt, 6 h, 82%; (e) NaH, BnBr, TBAI (cat), THF, 0 °C to rt, 6 h; (f) TBAF, THF, rt, 2 h, 85% (for steps e and f); (g) (i) $(COCl)_2$,DMSO, Et_3N, CH_2Cl_2, −78 °C, 0.5 h; (ii) phenyl magnesium bromide, dry ether −78 °C, 3 h, 59%.

Cross-metathesis[8] of **9** with methyl acrylate in DCM using Grubbs's second generation catalyst (5 mol %) gave exclusively *trans*-**10** in 91% yield. Base-catalyzed intramolecular oxa-Michael addition reaction gave **11** as a single diastereomer (90%).[9] The reaction apparently proceeds via formation of stable chair conformer. Finally, debenzylation of **11** using Pd–C in EtOAc gave the target molecule **1** (98%) (Scheme 2). The stereochemistry of the substituents on the tetrahydropyran ring was confirmed by comparing the physical and spectroscopic data of **1** with the literature data.[5]

3. Conclusion

In conclusion, we have developed a simple, convenient, and efficient approach for Goniothalesdiol A **1** from a D-glyceraldehyde template in 22% overall yield using stereoselective allylation, Grignard reaction, cross-metathesis, and base-catalyzed intramolecular oxa-Michael addition as the key steps.

4. Experimental

4.1. General

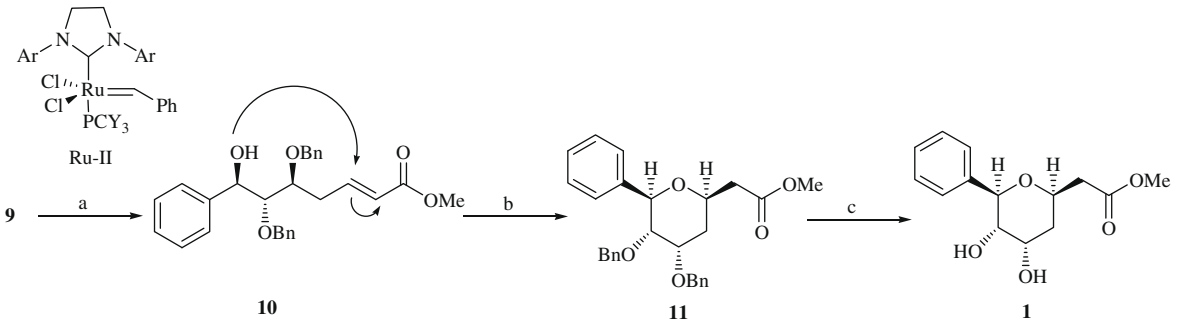
All reagents were purchased from Aldrich. IR spectra were recorded on a Perkin–Elmer RX-1 FT-IR system. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on Bruker Avance-300 MHz spectrometer. Optical rotations were measured with Horiba-SEPA-300 digital polarimeter. Mass spectra were recorded on a Q STAR mass spectrometer (Applied Biosystems, USA).

4.1.1. (*S*)-1-((*R*)-1,4-Dioxaspiro[4.5]decan-2-yl)but-3-en-1-ol 3

Allyl bromide (4.96 mL, 58.82 mmol) in THF (50 mL) was added to mixture of **2** (5.0 g, 29.41 mmol), Zn dust (3.73 g, 58.82 mmol), and a saturated aqueous solution of NH_4Cl (15 mL) dropwise over a period of 30 min with vigorous stirring at 10 °C. The mixture was stirred for 4 h at ambient temperature until the aldehyde was totally consumed as evidenced by TLC analysis. The mixture was filtered, and the precipitate was thoroughly washed with $CHCl_3$. The aqueous layer was separated and treated with 5% HCl to dissolve the suspended turbid material. The clear solution was extracted with $CHCl_3$. The combined organic layer was washed successively with 10% $NaHCO_3$, water, and brine. After solvent removal under reduced pressure, the residue was purified by column chromatography (EtOAc–hexane, 1:9) to give **3** as a colorless oil (5.61 g, 91%). $[\alpha]_D^{25} = +10.0$ (*c* 1, $CHCl_3$), lit[7] ($[\alpha]_D^{25} = +10.5$); IR (neat, cm^{-1}): ν_{max} 3456, 3076, 2936, 2860, 1641, 1446, 1367, 1280, 1231, 1162, 1101, 1043, 926, 846, 773; ^1H NMR (300 MHz, $CDCl_3$): δ 1.40–1.69 (m, 10H), 1.85 (br s, 1H), 2.10–2.38 (m, 2H), 3.66–3.81 (m, 1H), 3.83–4.11 (m, 3H), 5.07–5.26 (m, 2H), 5.73–5.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7, 23.9, 25.1, 34.8, 36.2, 37.6, 64.8, 70.4, 77.7, 109.6, 118.3, 134.1; EI-MS: m/z = 235 $[M+Na]^+$.

4.1.2. (*R*)-2-((*S*)-1-(Benzyloxy)but-3-enyl)-1,4-dioxaspiro[4.5]decane 4

A solution of **3** (3.0 g, 14.15 mmol) in dry THF (20 mL) was added dropwise to a stirred suspension of NaH (0.68 g, 28.3 mmol) in dry THF (10 mL) at 0 °C under nitrogen atmosphere. After stirring at room temperature for 15 min, benzyl bromide (1.64 mL, 14.15 mmol) was added and the reaction mixture was stirred for



Scheme 2. Reagents and conditions: (a) methyl acrylate, Grubbs's II (5 mol %), DCM, 40 °C, 4 h, 91%; (b) NaH, THF, −20 °C, 1 h, 90%; (c) H_2/Pd–C, EtOAc, 4 h, 98%.

1 h, quenched with saturated aq NH_4Cl at 0 °C, and extracted with ether (2 × 50 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by column chromatography (EtOAc–hexane, 5:95). The benzyl-protected product **4** was obtained as a yellow oil (3.97 g, 93%). $[\alpha]_D^{25} = +27.0$ (*c* 1, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3452, 3069, 3030, 2936, 2860, 1640, 1450, 1365, 1279, 1162, 1103, 1038, 925, 846, 738, 698; ^1H NMR (300 MHz, $CDCl_3$): δ 1.38–1.43 (m, 2H), 1.54–1.63 (m, 8H), 2.27–2.46 (m, 2H), 3.52 (q, *J* = 5.66, 10.66 Hz, 1H), 3.78–3.86 (m, 1H), 3.95–4.05 (m, 2H), 4.61 (q, *J* = 11.52, 23..42 Hz, 2H), 5.05–5.14 (m, 2H), 5.79–5.93 (m, 1H), 7.12–7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8, 24.1, 25.2, 34.9, 35.7, 36.4, 66.2, 72.5, 76.8, 79.0, 109.6, 117.5, 127.6 (×2), 127.9 (×2), 128.3, 134.3, 138.5; EI-MS: *m*/*z* = 325 $[M+Na]^+$.

4.1.3. (2*R*,3*S*)-3-(Benzyloxy)hex-5-ene-1,2-diol 5

Compound **4** (3.0 g, 9.93 mmol) was dissolved in 90% aq CF_3COOH (20 mL) at 0 °C and the mixture was stirred at the same temperature for 2 h. The reaction mixture was then extracted with CH_2Cl_2 (3 × 50 mL). The collected organic layers were combined, washed with 10% $NaHCO_3$ (3 × 50 mL), water, and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc–hexane, 3:7) to obtain **5** (1.764 g, 80%) as a syrup. $[\alpha]_D^{25} = +34.0$ (*c* 1, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3445, 3076, 2936, 2860, 1641, 1446, 1367, 1280, 1162, 1099, 1042, 923, 845, 768; ^1H NMR (500 MHz, $CDCl_3$): δ 1.47 (br s, 1H), 2.06 (br s, 1H), 2.32–2.51 (m, 2H), 3.56 (q, *J* = 5.8, 11.7 Hz, 1H), 3.64–3.60 (m, 2H), 3.68–3.74 (m, 1H), 4.56 (dd, *J* = 11.71, 6.50 Hz, 2H), 5.06–5.14 (m, 2H), 5.79–5.87 (m, 1H), 7.24–7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.0, 63.4, 72.4, 72.5, 80.4, 117.7, 127.8 (×3), 128.5 (×2), 134.2, 138.3; EI-MS: *m*/*z* = 245 $[M+Na]^+$. HRMS (EI): *m*/*z* calcd for $C_{13}H_{18}O_3Na$: 245.1153; found 245.1148.

4.1.4. (2*R*,3*S*)-3-(Benzyloxy)-1-(*tert*-butyldimethylsilyloxy)hex-5-en-2-ol 6

To an ice cold solution of **5** (1.5 g, 6.756 mmol) in CH_2Cl_2 (35 mL), imidazole (0.61 g, 10.134 mmol) was added followed by TBDMSCl (1.02 g, 6.756 mmol) and the reactants were stirred for 4 h at room temperature. The reaction mixture was then treated with 20 mL of saturated aqueous NH_4Cl solution and extracted with CH_2Cl_2 (2 × 30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc–hexane, 15:85) to afford **6** (1.86 g, 82%) as a liquid. $[\alpha]_D^{25} = +26.0$ (*c* 1, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3466, 3071, 3031, 2930, 2859, 1640, 1464, 1392, 1254, 1212, 1097, 1004, 912, 838, 777, 740, 697; ^1H NMR (300 MHz, $CDCl_3$): δ 0.06 (s, 6H), 0.90 (s, 9H), 2.28 (d, *J* = 4.2 Hz 1H), 2.33–2.51 (m, 2H), 3.47 (q, *J* = 6.0, 10.6 Hz, 1H), 3.58–3.66 (m, 2H), 3.69–3.75 (m, 1H), 4.46–4.67 (m, 2H), 5.05–5.15 (m, 2H), 5.81–5.95 (m, 1H), 7.20–7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.4 (×2), 18.2, 25.8 (×3), 34.7, 63.7, 72.1, 72.4, 78.7, 117.2, 127.6, 127.8 (×2), 128.3 (×2), 134.7, 138.4; EI-MS: *m*/*z* = 337 $[M+1]^+$. HRMS (EI): *m*/*z* calcd for $C_{19}H_{32}O_3NaSi$: 359.2018; found 359.2033.

4.1.5. (2*R*,3*S*)-2,3-Bis(benzyloxy)hex-5-en-1-ol 8

To a stirred solution of the compound **6** (1.5 g, 4.46 mmol) in dry THF (10 mL), sodium hydride (0.214 g, 8.92 mmol), benzyl bromide(0.52 mL, 4.46 mmol), and TBAI (catalytic amount) were added at 0 °C and stirred at room temperature for 6 h. After completion of the reaction, THF was evaporated, and the residue was extracted with $CHCl_3$ (2 × 30 mL). The chloroform extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude **7**. This was dissolved in dry THF, cooled to 0 °C, and TBAF (7.4 mL, 7.4 mmol, 1 M in THF) was added slowly. The reaction mixture was stirred for 1 h at room temperature. After completion of the reaction, the reaction mixture was quenched with water and THF was evaporated. The residue was extracted with $CHCl_3$ (2 × 25 mL). The combined extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc–hexane, 1:9) to afford **8** (1.18 g, 85% from two steps) as a yellow liquid. $[\alpha]_D^{25} = +9.5$ (*c* 1, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3434, 3067, 3031, 2875, 1718, 1640, 1454, 1395, 1274, 1209, 1096, 915, 741, 698; ^1H NMR (300 MHz, $CDCl_3$): δ 2.06 (br s, 1H), 2.28–2.49 (m, 2H), 3.45 (q, *J* = 4.5, 10.5 Hz, 1H), 3.64 (q, *J* = 6.0, 11.3 Hz, 1H), 3.67–3.74 (m, 2H), 4.53–4.64 (m, 4H), 5.04–5.10 (m, 2H), 5.75–5.89 (m, 1H), 7.20–7.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.2, 61.1, 72.0, 72.4, 78.6, 80.0, 117.5, 127.6, 127.7, 127.8 (×2), 127.84(×2), 128.3 (×2), 128.4 (×2), 134.3, 137.98, 138.03; EI-MS: *m*/*z* = 335 $[M+Na]^+$. HRMS (EI): *m*/*z* calcd for $C_{20}H_{24}O_3Na$: 335.1623; found 335.1610.

4.1.6. (1*R*,2*R*,3*S*)-2,3-Bis(benzyloxy)-1-phenylhex-5-en-1-ol 9

At first, DMSO (0.91 mL, 12.84 mmol) was added to a stirred solution of oxalyl chloride (0.542 mL, 6.42 mmol) in dry CH_2Cl_2 (20 mL) at −78 °C, and stirred for 30 min. Compound **8** (1.0 g, 3.21 mmol) in dry CH_2Cl_2 (10 mL), was then added to the reaction mixture at −78 °C and stirred for 2 h at the same temperature. Next, DIPEA (2.21 mL, 12.84 mmol) was added at −78 °C and the reaction mixture was allowed to warm to room temperature for 30 min. The reaction mixture was then diluted with water (20 mL) and extracted with $CHCl_3$ (2 × 25 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to afford crude aldehyde as a yellow syrup. The crude aldehyde was dissolved in dry ether (20 mL) and was cooled to −78 °C. To this, phenyl magnesium bromide (5.60 mL of 2 M solution in diethyl ether, 22.4 mmol) was added slowly and the reaction mixture was stirred at the same temperature for 3 h. After completion of the reaction, the reaction mixture was treated with saturated aqueous NH_4Cl solution (20 mL) and extracted with CH_2Cl_2 (2 × 30 mL). The combined extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc–hexane, 1:9) to afford **9** (0.633 g, 59%) as a yellow liquid. $[\alpha]_D^{25} = +40.0$ (*c* 1, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3459, 3064, 3030, 2919, 1639, 1494, 1452, 1394, 1208, 1093, 913, 742, 698; ^1H NMR (300 MHz, $CDCl_3$): δ 2.37 (m, 2H), 3.09 (d, *J* = 6.0 Hz, 1H), 3.52 (q, *J* = 5.2, 10.5 Hz, 1H), 3.61–3.70 (m, 1H), 4.20–4.62 (m, 4H), 4.87 (dd, *J* = 3.8, 6.0 Hz, 1H), 5.00–5.12 (m, 2H), 5.74–5.92 (m, 1H), 7.10–7.38 (m,15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 43.9, 72.3 (×2), 73.9, 78.6, 83.6, 117.5, 126.4 (×3), 127.4(×2), 127.8(×2), 128.1(×3), 128.3(×2), 128.4(×3), 134.7, 137.9, 141.3, 141.7; EI-MS: *m*/*z* = 411 $[M+Na]^+$. HRMS (EI): *m*/*z* calcd for $C_{26}H_{28}O_3Na$: 411.1936; found 411.1949.

4.1.7. (5*S*,6*R*,7*R*,*E*)-Methyl 5,6-bis(benzyloxy)-7-hydroxy-7-phenylhept-2-enoate 10

Grubbs's second generation catalyst (0.05 g, 5 mol %) was placed in a two-necked flask equipped with nitrogen inlet, a magnetic stirring bar, and a rubber septum. A solution of **9** (0.3 g, 0.773 mmol) and methyl acrylate (0.21 mL, 2.32 mmol) in CH_2Cl_2 (20 mL) was introduced at 40 °C and the resultant pink solution was stirred for 6 h. When TLC analysis indicated complete consumption of **9**, the reaction mixture was exposed to air and concentrated. The crude product was purified by column chromatography on silica gel (EtOAc–hexane, 3:22) to give α,β-unsaturated ester **10** (0.314 g, 91%) as a pale yellow liquid. $[\alpha]_D^{25} = +11.0$ (*c* 1, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3466, 3061, 3030, 2920, 1721, 1654, 1450, 1395, 1322, 1270, 1209, 1168, 1092, 746, 699; ^1H NMR (400 MHz, $CDCl_3$): δ 2.48–2.54 (m,2H), 2.98

(br s, 1H), 3.55 (q, J = 5.8, 10.9 Hz, 1H), 3.62–3.67 (m, 1H), 3.72 (s, 3H), 4.25–4.50 (m, 4H), 4.82 (br s, 1H), 5.80 (d, J = 14.7 Hz, 1H), 6.86–6.94 (m, 1H), 7.15–7.38 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 33.4, 51.5, 70.4, 72.3, 72.4, 74.2, 83.8, 123.2, 126.3, 126.7, 127.1, 127.6, 127.7, 127.8, 127.9, 128.0, 128.12, 128.26, 128.32, 128.38, 128.5(×3), 131.0, 137.5, 145.5, 145.9, 166.0; EI-MS: m/z = 469 $[M+Na]^+$. HRMS (EI): m/z calcd for $C_{28}H_{30}O_5Na$: 469.1990; found 469.2010.

4.1.8. Methyl 2-((2*R*,4*S*,5*S*,6*R*)-4,5-bis(benzyloxy)-6-phenyltetrahydro-2*H*-pyran-2-yl)acetate 11

Sodium hydride (60% dispersion in mineral oil, 15 mg) was added to a solution of compound **10** (0.25 g, 0.56 mmol) in 15 mL dry THF at −20 °C. The reaction mixture was allowed to reach room temperature while stirring, and then stirred at room temperature for 1 h. The reaction mixture was then cooled in ice and quenched with 2 mL saturated NH_4Cl solution. The solvent was evaporated under reduced pressure, after which the residue was extracted with EtOAc (2 × 15 mL) and dried with anhydrous Na_2SO_4. After evaporation of ethyl acetate, the residue was chromatographed over silica gel (EtOAc–hexane, 15:85) yielding **11** (0.375 g, 90%) as a colorless oil. $[\alpha]_D^{25} = +28.5$ (c 1, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3450, 3031, 2922, 2854,1737, 1636, 1452, 1266, 1169, 1077, 748, 697; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.44–1.56 (m, 1H), 2.07–2.17 (m, 1H), 2.39 (dd, J = 6.6, 15.3 Hz, 1H), 2.57 (dd, J = 6.5, 15.3 Hz, 1H), 3.21 (dd, J = 2.6, 9.4 Hz, 1H), 3.65 (s, 3H), 3.89–3.95 (m, 1H), 3.96–4.06 (m, 2H), 4.32–4.44 (m, 1H), 4.67–4.76 (m, 2H), 4.80 (d, J = 9.7, Hz, 1H), 6.81–6.92 (m, 2H), 7.06–7.18 (m, 2H), 7.19–7.33 (m, 9H), 7.35–7.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.2, 40.5, 51.6, 68.5, 71.4 (×2), 71.5, 76.6, 80.6, 127.4, 127.5, 127.6 (×3), 127.7, 127.8 (×2), 128.0 (×2), 128.1 (×2), 128.3 (×2), 128.5, 137.9, 138.6, 140.3, 171.4; EI-MS: m/z = 469 $[M+Na]^+$. HRMS (EI): m/z calcd for $C_{28}H_{30}O_5Na$: 469.1990; found 469.1999.

4.1.9. Methyl 2-((2*R*,4*S*,5*S*,6*R*)-4,5-dihydroxy-6-phenyltetrahydro-2*H*-pyran-2-yl)acetate 1

A solution of **11** (0.12 g, 0.269 mmol) in ethyl acetate (10 mL) was stirred with 20 mg of 10% Pd/C under a hydrogen atmosphere for 4 h. The reaction mixture was filtered and the filtrate was concentrated. The crude product was purified on silica gel column chromatography (EtOAc–hexane, 3:9) to obtain **1** as a white solid (70 mg, 98%). Mp: 90 °C (lit.[5] mp. 92 °C); $[\alpha]_D^{25} = -28.0$ (c 0.5, $CHCl_3$), lit.[5] $[\alpha]_D^{25} = -27.2$ (c 0.3, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3432, 2922, 2853, 1733, 1441, 1344, 1286, 1170, 1078, 918, 859, 757, 700, 515; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.74 (ddd, J = 2.2, 3.0, 13.6 Hz, 1H), 2.10 (ddd, J = 2.2, 3.0, 13.6 Hz, 1H), 2.44 (dd, J = 6.0, 15.1 Hz, 1H), 2.60 (dd, J = 6.9, 15.1 Hz, 1H), 3.48 (dd, J = 3.0, 9.8, Hz, 1H), 3.65 (s, 3H), 4.20–4.23 (m,1H), 4.33–4.44 (m, 1H), 4.53 (d, J = 9.8, Hz, 1H), 7.28–7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 37.1, 40.3, 51.6, 67.0, 68.4, 72.6, 77.7, 127.3, 128.2, 128.4, 139.2, 171.2; EI-MS: m/z = 289 $[M+Na]^+$. HRMS (EI): m/z calcd for $C_{14}H_{18}O_5Na$: 289.1051; found 289.1062.

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