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Formal total synthesis of (+)-didemniserinolipid B

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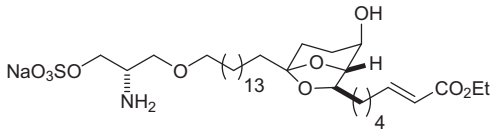
ABSTRACT

The formal total synthesis of (+)-didemniserinolipid B, a marine tunicate possessing a 6,8-dioxabicyclo[3.2.1]octane framework, was accomplished starting from L-(+)-tartaric acid. The key transformations in the synthesis include the elaboration of a γ-hydroxy-amide readily obtained by desymmetrization of tartaric acid bis-amide via the controlled addition of a Grignard reagent followed by stereoselective reduction of the resulting ketone.

1. Introduction

Didemniserinolipid B **1**, is a 6,8-dioxabicyclo[3.2.1]octane framework containing natural product isolated from the marine tunicate belonging to the genus *Didemnum* sp. reported by Gonzalez et al.[1] Contrary to simple insect pheromones, which possess similar bicylic skeletal framework with simple alkyl substituents, didemniserinolipids comprise an extended alkyl chains, containing a 2-aminopropane 1,3-diol ether, and an α,β-unsaturated ester. Due to the bio-activity of related didemniserinolipids as inhibitors of HIV-1 integrase,[2] the synthesis of didemniserinolipids has attracted the attention of synthetic chemists. Ley et al. reported the early synthesis and structural revision of didemniserinolipid B,[3a] while Burke et al. disclosed the synthesis of **1** employing their ketalization/ring closing metathesis strategy.[3b,c] Ramana and Induvadana reported a formal synthesis of didemniserinolipid B involving a Pd-mediated alkynediol cycloisomerization.[3d] Recently, we have accomplished a formal total synthesis of (−)-didemniserinolipid B, from L-(+)-tartaric acid.[4] Herein, we report an easy and efficient stereoselective formal total synthesis of (+)-**1**, starting from the same chiral pool precursor L-(+)-tartaric acid, thus enabling the enantiodivergent syntheses of both antipodes of **1** from a common chiral source.



(+)-didemniserinolipid B **1**

2. Results and discussion

Our approach for the synthesis of (+)-**1** is based on the elaboration of bicyclic acetal **3** via the known ester **2** as shown in Scheme 1. The synthesis of the bicyclic acetal **3** was planned by intramolecular ketalization of the trihydroxy ketone **4**. Extension of aldehyde **5** followed by hydrogenation was envisioned for the synthesis of ketone **4**. γ-Hydroxy amide **6**, derived from the bis-amide **7**, was chosen as the appropriate precursor for the synthesis of aldehyde **5**.

The synthetic sequence started with the addition of 5-benzyloxypentylmagnesium bromide to bis-dimethylamide **7** derived from tartaric acid resulting in the ketoamide **8** in 82% yield.[5] The stereoselective reduction of the ketone in **8** with $NaBH_4$ in the presence of $CeCl_3{\cdot}7H_2O$ afforded a mixture of diastereomeric alcohols (dr ~ 9:1 by NMR,[6] with **6** being the major isomer) in 91% yield. The hydroxy amide **6** was transformed into the rearranged hydroxy ester **9** by employing a methodology developed by us previously for an analogous compound.[5h] Thus, treating the hydroxy amide **6** with an excess of 2,2-dimethoxypropane and *p*-toluenesulfonic acid in refluxing benzene followed by column purification resulted in pure α-hydroxy ester **9** in 81% yield. Mitsunobu inversion of the secondary alcohol in **9** furnished the epimeric alcohol **10** in 91% yield. Silver oxide mediated protection of the hydroxy group in **10** as the benzyl ether, followed by reduction of the ester with $NaBH_4$ produced the primary alcohol **11** in 89% yield. Oxidation of **11** with IBX gave aldehyde **5**, which upon reaction with the phosphonate **12**[7] resulted in a 3:1 *E*/*Z* mixture of the α,β-unsaturated ketone **13** in 82% yield over two steps.[8] Hydrogenation of the olefin in **13** furnished the saturated ketone **4** in 87% yield. Reaction of ketone **4** with $FeCl_3$ affected the deprotection[9] of the acetonide with concomitant intramolecular ketalization furnishing the bicyclic acetal **3** in 93% yield (31% overall yield over 10 steps from **7**). Conversion of the bicylic acetal **3** into didemniserinolipid B **1**, via ester **2** has already been described.[3c,d,4] Hence the present sequence constitutes a formal total synthesis of (+)-didemniserinolipid B (Scheme 2).

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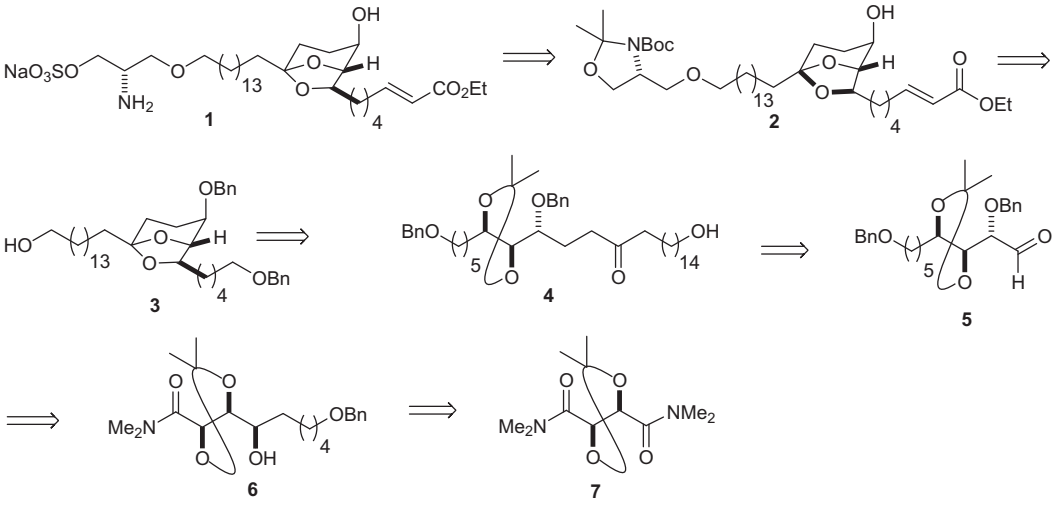
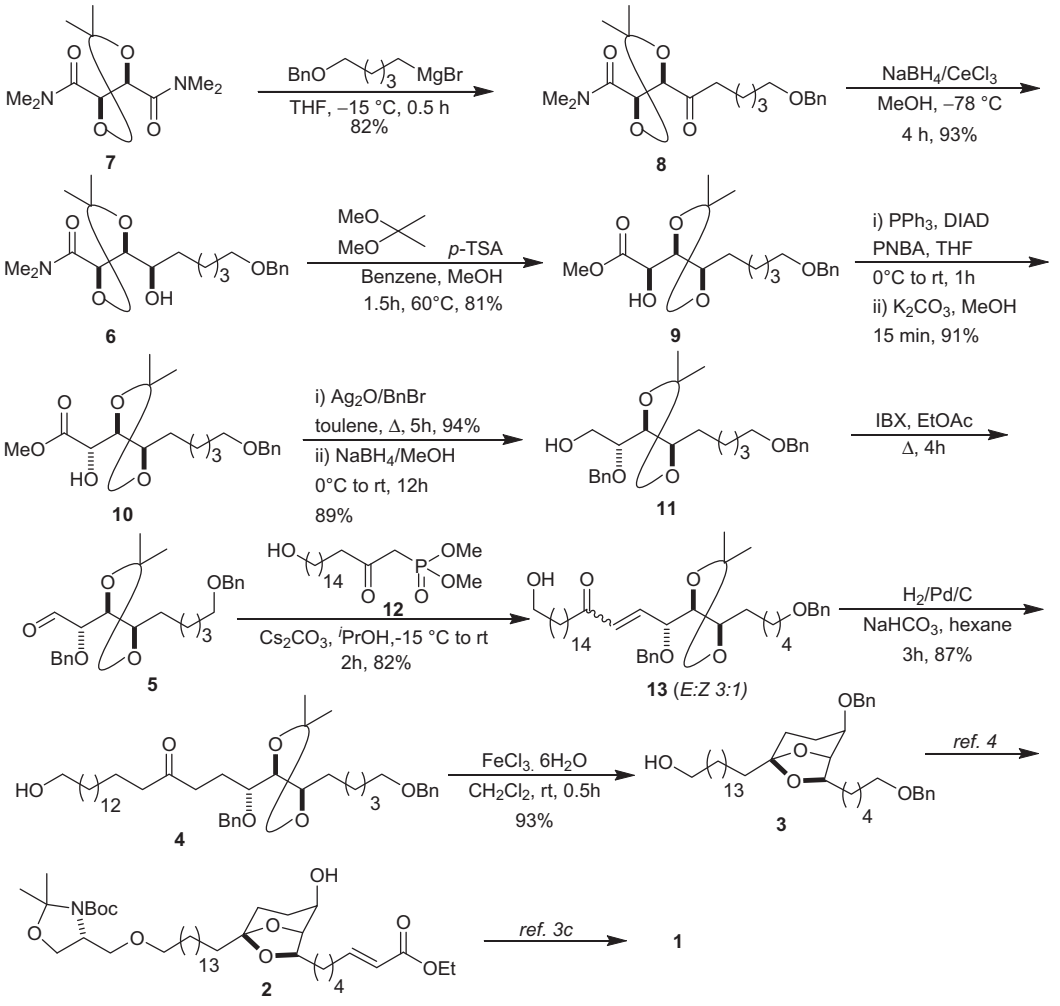


Scheme 1. Retrosynthesis for didemniserinolipid B.



Scheme 2. Formal total synthesis of didemniserinolipid B.

3. Conclusion

In conclusion, a concise approach for the formal total synthesis of (+)-didemniserinolipid B has been accomplished. The key reactions in the synthetic sequence include the formation of the 6,8-dioxabicyclo[3.2.1]octane framework by elaboration of a γ-hydroxy amide obtained by desymmetrization of the tartaric acid bis-amide. The synthetic sequence depicted herein, in

combination with our earlier approach[4] for the other enantiomer provides amenable strategies for the synthesis of a number of analogs in both enantiomeric forms.

4. Experimental

4.1. General procedures

Column chromatography was performed on silica gel, Acme grade 100–200 mesh. TLC plates were visualized either with UV, in an iodine chamber, or with phosphomolybdic acid spray, unless noted otherwise. Unless stated otherwise, all reagents were purchased from commercial sources and used without additional purification. THF was freshly distilled over Na-benzophenone ketyl. Melting points were uncorrected. Unless stated otherwise, all the reactions were performed under inert atmosphere. Unless stated otherwise, all the NMR spectra were recorded in $CDCl_3$.

4.2. Preparation of (4*R*,5*R*)-5-(6-(benzyloxy)hexanoyl)-*N*,*N*,2,2-tetramethyl-1,3-dioxolane-4-carboxamide 8

In a two necked 100 mL, round bottomed flask equipped with a magnetic stirrer bar, rubber septum, and argon inlet was placed **7** (1.6 g, 6.6 mmol). This was dissolved in 10 mL of THF and was cooled to −10 °C to −15 °C. A freshly prepared THF solution of 5-benzyloxy-pentylmagnesium bromide (20 mL of 0.5 M solution in THF, 10 mmol) was added at such a rate that the internal temperature does not rise above −10 °C. The progress of the reaction was monitored by TLC and after the reaction was complete (~0.5 h), it was cautiously quenched by the addition of a saturated solution of NH_4Cl (5 mL). It was then poured into water (10 mL) and extracted with ethyl acetate (2 × 20 mL). The combined EtOAc extracts were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of the solvent and silica gel column chromatography of the resulting residue with petroleum ether/EtOAc (3:2) as eluent yielded **8** (2.05 g, 86%) as a colorless oil. $[\alpha]_D$ = +10.1 (*c* 3.8, $CHCl_3$); IR (neat) 3030, 2938, 1715, 1656, 1260 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.15 (m, 5H), 5.11 (d, *J* = 5.8 Hz, 1H), 4.77 (d, *J* = 5.8 Hz, 1H), 4.47 (s, 2H), 3.44 (t, *J* = 6.5 Hz, 2H), 3.11 (s, 3H), 2.96 (s, 3H), 2.78–2.45 (m, 2H), 1.95–1.51 (m, 5H), 1.48–1.15 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.3, 168.2, 138.6, 128.4, 127.6, 127.5, 112.1, 82.3, 75.2, 73.1, 70.4, 39.6, 37.3, 36.3, 29.8, 26.6, 26.3, 26.0, 23.1; HRMS for $C_{21}H_{31}NO_5$+Na calcd 400.2100; found 400.2108.

4.3. Preparation of 6

To a stirred solution of **8** (1 g, 2.75 mmol) in methanol (10 mL) was added $CeCl_3 \cdot 7H_2O$ (1.23 g, 3.31 mmol) and stirred for 1 h at room temperature. Then the reaction mixture was cooled to −78 °C and $NaBH_4$ (0.13 g, 3.31 mmol) was added portion wise over a period of 0.5 h and stirred at the same temperature. It was then cautiously quenched by the addition of water (20 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and concentrated. Silica gel column chromatography of the resulting residue with petroleum ether/EtOAc (2:3) as eluent gave alcohol **6** (0.93 g, 93%) as a colorless oil. $[\alpha]_D$ = −12.8 (*c* 1.6, $CHCl_3$); IR (neat) 3446, 2987, 1651, 1373, 1069, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.15 (m, 5H), 4.74–4.50 (m, 2H), 4.49 (s, 2H), 3.58 (br s, 1H), 3.46 (t, *J* = 6.6 Hz, 2H), 3.13 (s, 3H), 2.96 (s, 3H), 2.08 (d, *J* = 8.6 Hz, 1H, exchangable with D_2O), 1.65–1.15 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 138.6, 128.3, 127.6, 127.4, 110.2, 80.1, 74.1, 72.7, 70.3, 69.9, 37.0, 35.6, 34.7, 29.6, 26.7, 26.1, 26.0, 25.6; HRMS for $C_{21}H_{33}NO_5$+Na calcd 402.2256; found 402.2243.

4.4. Preparation of (*R*)-methyl 2-((4*R*,5*R*)-5-(5-(benzyloxy)-pentyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-hydroxyacetate 9

To a stirred solution of **6** (0.6 g, 1.58 mmol) in benzene (6 mL) was added *p*-toluenesulfonic acid (0.33 g, 1.74 mmol) at room temperature. It was then heated to 60 °C and kept at the same temperature for 30 min. The reaction mixture was cooled to room temperature, after which 2,2-dimethoxy propane (0.78 mL, 6.33 mmol) and methanol (0.78 mL) were introduced. The reaction mixture was then stirred for 1 h at 60 °C, cooled to room temperature and solid K_2CO_3 (0.24 g) was added. The reaction mixture was filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (2 × 10 mL). Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (7:3) as eluent gave the hydroxy ester **9** (0.48 g, 82%) as a colorless oil. $[\alpha]_D$ = +14.3 (*c* 1.5, $CHCl_3$); IR (neat) 3446, 2988, 2863, 1748, 1456, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.05 (m, 5H), 4.52 (s, 2H), 4.24–4.01 (m, 2H), 3.98–3.86 (m, 1H), 3.86 (s, 3H), 3.49 (t, *J* = 6.3 Hz, 2H), 3.03 (br s, 1H), 1.97–1.15 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 138.6, 128.3, 127.6, 127.5, 109.3, 81.4, 76.4, 72.8, 70.2, 68.8, 52.8, 32.5, 29.6, 27.4, 26.5, 26.3, 25.8; HRMS for $C_{20}H_{30}O_6$+Na calcd 389.1940; found 389.1936.

4.5. Preparation of 10

To a solution of **9** (0.36 g, 1 mmol) in dry THF (6 mL), were added triphenyl phosphine (0.79 g, 3 mmol), and *p*-nitrobenzoic acid (0.5 g, 3 mmol) under an argon atmosphere and stirred for 10 min at room temperature. The reaction mixture was cooled to 0 °C and DIAD (0.6 mL, 3 mmol) was introduced into the reaction mixture over a period of 15 min. It was then warmed to room temperature and stirred at room temperature for 1 h. After the reaction was complete (TLC), most of the solvent was removed under reduced pressure and the crude ester thus obtained was purified by column chromatography with petroleum ether/ether (9:1) as eluent to yield the corresponding *p*-nitrobenzoate ester (0.45 g) which was subjected to the next step immediately.

To a methanol (5 mL) solution of *p*-nitrobenzoate ester (0.45 g, 1 mmol) obtained above was added K_2CO_3 (0.21 g, 1.5 mmol) and stirred for 15 min at 0 °C. After the reaction was complete (TLC), the reaction mixture was poured into ice-cold water (5 mL) and extracted with ethyl acetate (2 × 15 mL). The combined organic layers were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and silica gel column chromatography of the crude residue with petroleum ether/EtOAc (7:3) as eluent yielded **10** (0.34 g, 91%) as a colorless oil. $[\alpha]_D$ = +27.9 (*c* 2.0, $CHCl_3$); IR (neat) 3447, 2938, 2862, 1747, 1456, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.15 (m, 5H), 4.52 (s, 2H), 4.34 (br s, 1H), 4.19–4.05 (m, 1H), 3.98–3.84 (m, 1H), 3.82 (s, 3H), 3.48 (t, *J* = 6.3 Hz, 2H), 3.00 (d, *J* = 4.5 Hz, 1H), 1.77–1.15 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 138.6, 128.3, 127.6, 127.5, 109.1, 82.0, 76.6, 72.8, 70.7, 70.2, 52.6, 33.3, 29.6, 27.4, 26.8, 26.2, 25.7; HRMS for $C_{20}H_{30}O_6$+Na calcd 389.1940; found 389.1938.

4.6. Preparation of (*R*)-2-(benzyloxy)-2-((4*S*,5*R*)-5-(5-(benzyloxy)-pentyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol 11

To a stirred solution of the hydroxy ester **10** (0.35 g, 0.96 mmol) in toluene (6 mL) was added Ag_2O (0.55 g, 2.4 mmol) under an argon atmosphere at room temperature and stirred for 1 h at the same temperature. Benzyl bromide (0.18 mL, 1.44 mmol) was then introduced into the reaction mixture, stirred at room temperature for 1 h and then for a further 3 h at reflux. It was then cooled to room temperature, filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (2 × 10 mL). Evaporation of

solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (4:1) as eluent yielded the corresponding benzyloxy ester (0.41 g, 94%) as a colorless oil. $[\alpha]_D = -11.9$ (*c* 1.2, $CHCl_3$); IR (neat) 3032, 2936, 2860, 1749, 1370, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.12 (m, 10H), 4.74 (d, *J* = 11.8 Hz, 1H), 4.52 (s, 2H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.07 (d, *J* = 4.6 Hz, 1H), 3.94 (t, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 3.48 (t, *J* = 6.3 Hz, 2H), 1.77–1.15 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 138.6, 136.9, 128.4, 128.3, 128.1, 128.0, 127.6, 127.5, 109.3, 80.7, 78.8, 78.2, 72.9, 72.8, 70.3, 52.1, 33.6, 29.6, 27.5, 26.8, 26.2, 25.8; HRMS for $C_{27}H_{36}O_6$+Na calcd 479.2410; found 479.2409.

In a single necked round bottomed flask equipped with a magnetic stirrer bar and guard tube was placed a solution of the benzyloxy ester (0.4 g, 0.88 mmol) in 5 mL of MeOH. Next, $NaBH_4$ (0.17 g, 4.4 mmol) was then introduced in to the reaction mixture portionwise at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight at the same temperature. Most of the methanol was evaporated off; water (10 mL) was added and extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (7:3) as eluent gave alcohol **11** (0.33 g, 88%) as a colorless oil. $[\alpha]_D = -3.7$ (*c* 1.9, $CHCl_3$); IR (neat) 3447, 3031, 2935, 1456, 1251, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.12 (m, 10H), 4.62 and 4.53 (ABq, *J* = 11.6 Hz, 2H), 4.44 (s, 2H), 3.78 (ddd, *J* = 15.8, 12.0, 4.4 Hz, 2H), 3.74–3.63 (m, 2H), 3.51–3.42 (m, 1H), 3.40 (t, *J* = 6.6 Hz, 2H), 2.0 (br s, 1H), 1.75–1.42 (m, 5H), 1.32 (d, *J* = 12.1 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 137.7, 128.5, 128.3, 128.0, 127.6, 127.5, 108.8, 80.4, 80.0, 79.9, 72.8, 72.4, 70.3, 61.8, 34.1, 29.7, 27.3, 27.0, 26.2, 26.1; HRMS for $C_{26}H_{36}O_5$+Na calcd 451.2460; found 451.2469.

4.7. Preparation of (*R*,*E*)-1-(benzyloxy)-1-((4*S*,5*R*)-5-(5-(benzyloxy)pentyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-19-hydroxynonadec-2-en-4-one 13

To a stirred solution of alcohol **11** (0.1 g, 0.23 mmol) in EtOAc (4 mL) was added IBX (0.2 g, 0.69 mmol) at room temperature and refluxed for 4 h. The reaction mixture was then filtered through a short pad of Celite and the Celite pad was washed with ether (2 × 10 mL). The organic layer was washed with saturated $NaHCO_3$ solution (5 mL), brine (5 mL), and dried over Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (7:3) as eluent afforded aldehyde **5** (0.08 g), which was used for the next step immediately.

To a pre-cooled suspension of Cs_2CO_3 (0.3 g, 0.92 mmol) in ^{i}PrOH (2 mL) was added the solid phosphonate **12**[3c] (0.17 g, 0.46 mmol) at 15 °C and was slowly warmed to room temperature, stirred for 20 min at the same temperature. It was then cooled to −15 °C, and a solution of the aldehyde **5** (0.08 g, 0.23 mmol) in ^{i}PrOH (2 mL) was added at the same temperature. The reaction mixture was slowly allowed to return to room temperature and stirred for 1.5 h at room temperature. It was then quenched with saturated NH_4Cl solution (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (7:3) as eluent furnished **13** (0.13 g, 82%) as a colorless oil. $[\alpha]_D = -6.4$ (*c* 3.3, $CHCl_3$); IR (neat) 3446, 2986, 2854, 1694, 1682, 1455, 1072 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.15 (m, 10H), 6.75 (dd, *J* = 16.1, 6.3 Hz, 1H), 6.27 (d, *J* = 16.2 Hz, 1H), 4.63 (d, *J* = 11.9 Hz, 1H), 4.49 (s, 2H), 4.42 (d, *J* = 11.9 Hz, 1H), 3.98 (t, *J* = 6.1 Hz, 1H), 3.87–3.79 (m, 1H), 3.74–3.66 (m, 1H), 3.62 (t, *J* = 6.6 Hz, 2H), 3.45 (t, *J* = 6.6 Hz, 2H), 2.57 (t, *J* = 7.4 Hz, 2H), 2.46 (m, 1H), 1.69–1.50 (m, 10H), 1.49–1.23 (m, 30H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 200.4, 143.1, 142.2, 138.7, 138.61, 138.12, 137.4, 132.0, 130.0, 128.4, 128.3, 128.2, 128.1, 127.93, 127.90, 127.61, 127.55, 127.43, 127.40, 109.1, 108.8, 82.6, 82.1, 79.3, 79.2, 74.4, 72.8, 71.73, 71.66, 70.37, 70.26, 63.0, 44.2, 40.3, 34.0, 32.8, 29.59, 29.56, 29.53, 29.44, 29.39, 29.24, 29.16, 27.4, 26.9, 26.2, 25.9, 25.7, 24.1, 23.8; HRMS for $C_{43}H_{66}O_6$+Na calcd 701.4757; found 701.4747.

4.8. Preparation of (*R*,)-1-(benzyloxy)-1-((4*R*,5*R*)-5-(5-(benzyloxy)pentyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-19-hydroxynonadecan-4-one 4

To a solution of **13** (56 mg, 0.08 mmol) in hexane (2 mL) was added solid $NaHCO_3$ (30 mg) and palladium on activated charcoal (20 mg). The reaction mixture was stirred for 2 h under a hydrogen atmosphere, after which it was filtered through a short pad of Celite and the Celite pad was washed with ether (10 mL). Evaporation of the solvent followed by silica gel column chromatography of the residue with petroleum ether/EtOAc (4:1) as eluent afforded **4** (49 mg, 87%) as a colorless oil. $[\alpha]_D = +14.1$ (*c* 1.5, $CHCl_3$); IR (neat) 3422, 2927, 1718, 1369, 1071 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.15 (m, 10H), 4.56 and 4.53 (ABq, *J* = 11.7 Hz, 2H), 4.49 (s, 2H), 3.88 (td, *J* = 7.7, 3.0 Hz, 1H), 3.74–3.59 (m, 3H), 3.58–3.49 (m, 1H), 3.44 (t, *J* = 5.8 Hz, 2H), 2.59–2.44 (m, 2H), 2.32 (td, *J* = 7.4, 3.4 Hz, 2H), 2.19–1.75 (m, 2H), 1.73–1.48 (m, 8H), 1.44–1.15 (m, 32H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.1, 138.7, 138.2, 128.63, 128.58, 128.3, 128.0, 127.9, 127.7, 108.5, 82.0, 79.6, 78.7, 73.1, 72.4, 70.6, 63.3, 43.2, 37.8, 34.7, 33.1, 29.9 (5C), 29.7 (4C), 29.5 (4C), 29.3 (3C), 27.6, 27.3, 26.5, 26.4, 26.0, 24.6, 24.1; HRMS for $C_{43}H_{68}O_6$+Na calcd 703.4914; found 703.4904.

4.9. Preparation of 15-((1*R*,2*R*,5*S*,7*R*)-2-(benzyloxy)-7-(5-(benzyloxy)pentyl)-6,8-dioxa-bicyclo[3.2.1]octan-5-yl)-pentadecan-1-ol 3

To a stirred solution of **4** (10 mg, 0.015 mmol) in CH_2Cl_2 (1.5 mL) was added $FeCl_3{\cdot}6H_2O$ (10 mg, 0.04 mmol) at room temperature under an argon atmosphere. The progress of the reaction was monitored by TLC and after the reaction was complete (~0.5 h), it was filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (5 mL). The organic layer was washed with saturated solution of $NaHCO_3$ (2 mL) followed by brine (3 mL) and dried over Na_2SO_4. Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether/ether (4:1) as eluent yielded **3** (8 mg, 94%) as a colorless oil. $[\alpha]_D = +23.5$ (*c* 0.5, $CHCl_3$); Lit[4] $[\alpha]_D = -21.2$ (*c* 3, $CHCl_3$); IR (neat) 3373, 2927, 2854, 1543, 1027 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.15 (m, 10H), 4.62 and 4.59 (ABq, 12.9 Hz, 2H), 4.49 (s, 2H), 4.17 (br s, 1H), 3.90–3.73 (m, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.46 (t, *J* = 6.6 Hz, 2H), 3.29 (br s, 1H), 2.37 (t, *J* = 5.1 Hz, 1H), 1.99–1.15 (m, 40H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.5, 128.42, 128.37, 127.68, 127.63, 127.51, 109.4, 80.1, 77.8, 72.9, 72.3, 70.4 (2C), 63.1, 37.4, 35.3, 32.8, 30.8, 29.8, 29.67, 29.62, 29.5, 26.1, 25.8, 25.5, 22.8, 22.0; HRMS for $C_{40}H_{62}O_5$+Na calcd 645.4495; found 645.4481.

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