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Stereoselective total synthesis of microcarpalide☆

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Abstract—A stereoselective total synthesis of microcarpalide using ring-closing metathesis (RCM) as a key step is reported. L-Ascorbic acid was used as a chiral pool material for the construction of the olefinic alcohol and an asymmetric aldol reaction provided the chiral precursor for the synthesis of olefinic acid.

1. Introduction

Medium ring compounds[1] are important in organic chemistry, as they are contained in an ever growing number of natural products. Microcarpalide **1**, a 10-membered lactone was isolated and characterized by Hemscheidt et al.[2] from the bark of the tropical tree *Ficus microcarpa* L. Microcarpalide was found to disrupt actin microfilaments. Moreover, it displayed a weak cytotoxicity to mammalian cells. Owing to its biological activity, a few total syntheses have appeared.[3] In continuation of our interest on the synthesis of natural lactones,[4] we herein, report the stereoselective synthesis of microcarpalide **1** (Fig. 1).

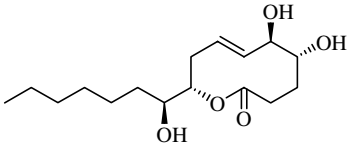

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Figure 1.

The synthetic strategy for microcarpalide **1** (Scheme 1) was designed to explore two pivotal tactical issues. First, we envisioned a convergent disconnection of the microcarpalide by exploiting esterification and ring-closing metathesis. Second, we designed each of the fragments **3** and **4** to contain two stereogenic carbon atoms and bear a terminal alkene group suitable for RCM macrocyclization. Fragment **3** could be prepared from L-ascorbic acid, whereas fragment **4** was prepared from 1,4-butanediol using Evan's aldol reaction as the key step.

2. Results and discussions

Accordingly, 3,4-*O*-isopropylidene-L-threitol[5] **7** derived from L-ascorbic acid was treated with *p*-TsCl and Et_3N in CH_2Cl_2 at room temperature (Scheme 2) to furnish monotosylate **8** as the major product, which on treatment with K_2CO_3 in MeOH gave epoxide **5**. The regioselective opening of the epoxide with *n*-pentylmagnesium bromide in the presence of cuprous iodide in dry THF provided compound **9**. The secondary alcohol in **9** was protected using BnBr and NaH in THF to furnish **10**, which on acetonide hydrolysis with 60% aq AcOH afforded diol **11**. Tosylation of **11** with *p*-TsCl and Et_3N in CH_2Cl_2 gave **12** as the major product, which on treatment with K_2CO_3 in MeOH gave epoxide **13**. The regioselective opening of this epoxide ring with vinylmagnesium bromide, in the presence of cuprous iodide in dry THF, gave the desired alcohol **3** with *S*,*S*-absolute configuration, thus releasing the free hydroxy required for the coupling reaction with fragment **4**.

The acidic segment **4** was prepared from commercially available 1,4-butanediol. Accordingly, treatment of 1,4-butanediol with BnBr in the presence of NaH gave **14** (Scheme 2), which on oxidation under Swern conditions furnished aldehyde **15**. To introduce the two adjacent stereocenters with the required absolute (*R*)-configuration in a *threo* fashion, aldehyde **15** was subjected to the Evans

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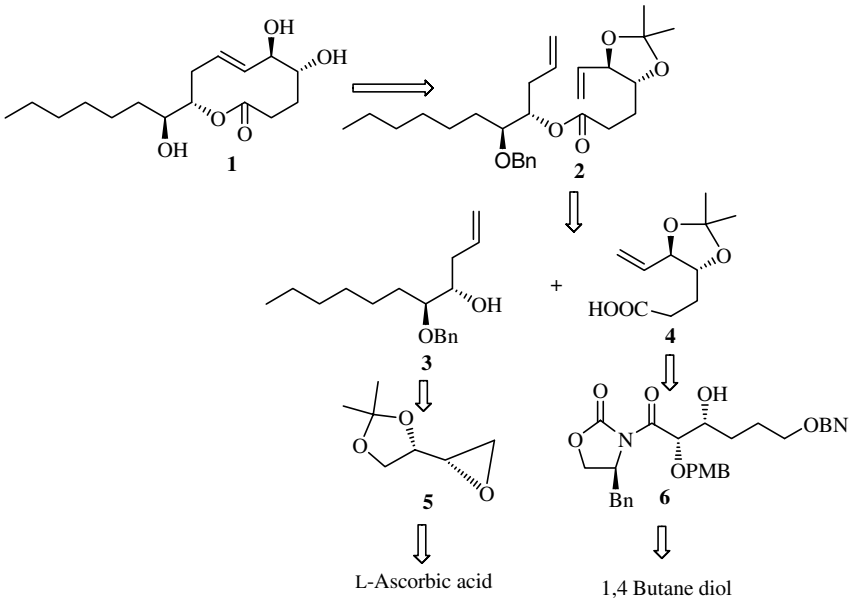
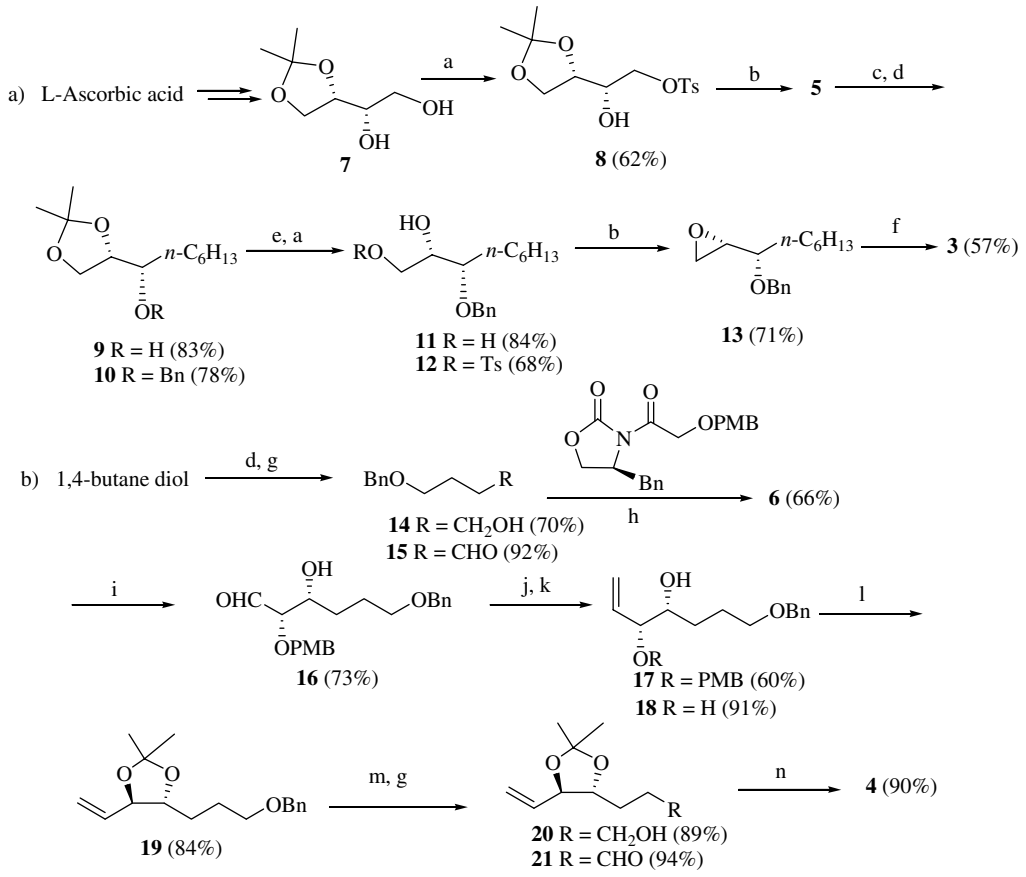


Scheme 1.

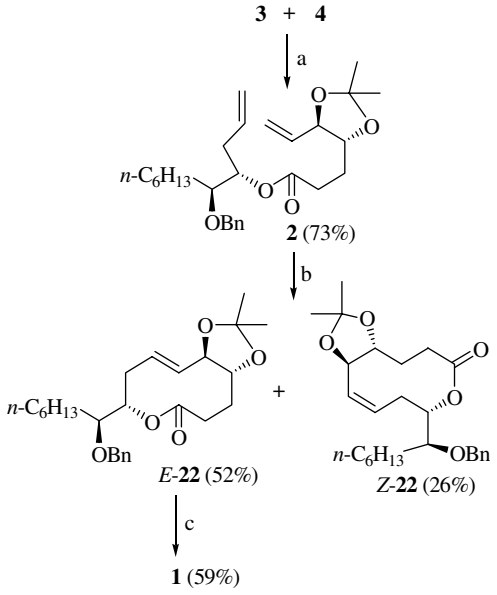


Scheme 2. Reagents and conditions: (a) *p*-TsCl, Et_3N, CH_2Cl_2, rt, 12 h; (b) K_2CO_3, MeOH, rt, 1 h; (c) *n*-$C_5H_{11}MgBr$, CuI, THF, −30 °C, 1 h; (d) BnBr, NaH, rt, 3 h; (e) 60% aq AcOH, rt, 12 h; (f) vinylmagnesium bromide, CuI, THF, −30 °C, 1 h; (g) $(COCl)_2$, DMSO, Et_3N, −78 °C, 3 h; (h) Bu_2BOTf, *N*-ethyldiisopropyl amine, CH_2Cl_2, 0 °C −78 °C, 5 h; (i) DIBAL-H, CH_2Cl_2, −78 °C, 2 h; (j) Ph_3PCH_3I, *n*-BuLi, 0 °C, 3 h; (k) $ZrCl_4$, CH_3CN, 1 h; (l) 2,2-DMP, PTSA (cat.), DMSO, rt, 5 h; (m) DDQ, CH_2Cl_2/H_2O (19:1), reflux, 3 h; (n) $NaClO_2$, 30% H_2O_2, *t*-BuOH, rt, 6 h.

aldol reaction.[6] The oxazolidinone auxiliary was treated with dibutylboron triflate in the presence of *N*-ethyldiisopropyl amine at −78 to 0 °C in CH_2Cl_2, followed by aldehyde **15**, to furnish aldol product **6**, which on reduction

with DIBAL-H in dry CH_2Cl_2 at −78 °C gave aldehyde **16**. Aldehyde **16** was immediately homologated with (methylene)triphenyl phosphorane in THF at −20 °C to provide **17**. Deprotection of the PMB group in **17** using 20 mol % of $ZrCl_4$ in acetonitrile gave diol **18**, which was treated with 2,2-dimethoxypropane (DMP) and *p*-toluenesulfonic acid (PTSA) (cat.) in dry DMSO at room temperature for 5 h to furnish **19**. Oxidative deprotection of the benzyl group in **19** using DDQ in aq CH_2Cl_2 (1:19) at reflux furnished alcohol **20**, which upon oxidation under Swern conditions gave aldehyde **21**. Further, oxidation of **21** using $NaClO_2$ and 30% H_2O_2 in *t*-BuOH/H_2O (2:1) gave acid **4**.

The union of the two advanced fragments **3** and **4** was successfully carried out using Yamaguchi's[7] protocol (2,4,6-trichlorobenzoyl chloride, Et_3N, THF, DMAP, toluene) to give the coupling product **2** in 73% yield. A highly diluted solution of diene **2** in anhydrous CH_2Cl_2 was heated at reflux for 48 h in the presence of Grubbs' catalyst **I**[8] and resulted in an efficient closure to afford the 10-membered lactone **22** as a mixture of two geometric isomers in a 67:33 *E*:*Z*-ratio. The desired *trans*-oxecin (*E*)-**22** was separated by column chromatography from the *cis*-analogue (*Z*)-**22**. Treatment of (*E*)-**22** with titanium tetrachloride in CH_2Cl_2 at 0 °C resulted in the simultaneous removal of all protecting groups, affording a single product **1**, whose spectral data matched perfectly with that reported for the natural compound **1**[2] (Scheme 3).



Scheme 3. Reagents and conditions: (a) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, DMAP, toluene, rt, 24 h; (b) Grubb's catalyst I, CH_2Cl_2, reflux, 48 h; (c) $TiCl_4$, CH_2Cl_2, 0 °C, 1 h.

3. Conclusion

A new stereoselective total synthesis of microcarpalide **1** has been accomplished. The formation of the required 10-membered lactone was achieved by means of ring-closing metathesis (RCM) of a suitable diene ester, which was assembled by coupling the two advanced fragments **3** and **4**. Fragment **3** has been synthesized by a chiral pool approach from L-ascorbic acid, while fragment **4** from 1,4-butanediol. The required C_7 backbone of **4** has been constructed from the C_4-starting synthon using Evans aldol reaction as a key step, which allowed the introduction of the two asymmetric centers with the final absolute (*R*)-configuration. Completion of the total synthesis used a Yamaguchi-mediated coupling between partners **3** and **4**, followed by RCM using Grubbs' catalyst **I**, providing the desired 10-membered macrocyclic framework with good stereoselectivity (67:33 *E*–*Z*) and in excellent yield. Finally, cleavage of the protecting groups afforded a single product whose spectroscopic properties were identical to those of the natural compound **1**.

4. Experimental

4.1. General

All moisture sensitive reactions were performed under a nitrogen atmosphere using flame-dried glasswares. Solvents were dried over standard drying agents and freshly distilled prior to use. NMR spectra were recorded on Varian Gemini FT-200 MHz, Unity-400 MHz (21 °C) and Inova-500 MHz (30 °C) spectrometers, with 7–10 mM solutions in appropriate solvents using TMS as the internal standard. ^{13}C NMR spectra were recorded with complete proton decoupling. Optical rotations were measured with a JASCO DIP-370 instrument, and $[\alpha]_D$-values are in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were taken with a Perkin–Elmer 1310 spectrometer. Mass spectra were recorded on CEC-21-11013 or Finnigan Mat 1210 double focusing mass spectrometers operating at a direct inlet system, and FAB MS were measured using VG AUTOSPEC mass spectrometers at 5 or 7 K resolution, using perfluorokerosene as an internal reference. Nomenclature mentioned in Section 3 was adopted from ACD/Name Version 1.0β, Advanced Chemistry Development Inc., Toronto, Canada. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 40 °C in vacuo.

4.1.1. (2*S*,3*S*)-2-Hydroxy-3,4-isopropylidenedioxy-1-(*p*-toluenesulfonyloxy)-butane (8). To a cooled (0 °C) solution of diol **7** (15.00 g, 92.60 mmol) and Et_3N (38.60 mL, 2.77 mol) in CH_2Cl_2 (150 mL), *p*-TsCl (19.40 g, 101.8 mmol) was added portionwise and stirred at room temperature for 8 h. The solvent was evaporated and the obtained residue was purified by column chromatography (Silica gel 60–120 mesh, EtOAc/hexane, 1:4) to afford (2*S*,3*S*)-2-hydroxy-3,4-isopropylidenedioxy-1-(*p*-toluenesulfonyloxy)-butane **8** (18.10 g) in 62% yield as a yellow syrup. $[\alpha]_D = -8.6$ (*c* 1.5, $CHCl_3$); IR (neat): 580, 820, 1090, 1170, 2950, 3420 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.29, 1.35 (2s, 6H, –CH_3), 2.44 (s, 3H, Ar–CH_3), 3.66–3.86 (m, 2H, H-4a′), 3.92–4.17 (m, 4H, H-1, 2, 3), 7.32, 7.78 (2d, 4H, $J = 7.80$ Hz, Ar–H).

4.1.2. (2*S*,3*S*)-1,2-Epoxy-3,4-isopropylidenedioxy-butane 5. A solution of compound **8** (18.00 g, 56.96 mmol) in

MeOH (100 mL) was treated with K_2CO_3 (19.60 g, 142.40 mmol) and stirred for 1 h at room temperature. The reaction mixture was further treated with aqueous NH_4Cl solution (20 mL). MeOH was evaporated at 25 °C under reduced pressure, and the residue was extracted with solvent ether (3 × 100 mL). The organic layer was washed with water (1 × 75 mL), brine (1 × 75 mL), dried over Na_2SO_4, and evaporated. The obtained residue was purified by column chromatography (Silica gel 60–120 mesh, EtOAc/hexane, 1:4) to afford **5** (5.98 g) in 73% yield as a colorless liquid. IR (neat): 1180, 1750, 2830, 2900 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.35, 1.40 (2s, 6H, $-CH_3$), 2.62 (dd, 1H, $J = 2.30$, 6.60 Hz, H-1), 2.74 (t, 1H, $J = 5.20$ Hz, H-1′), 2.92–3.00 (m, 1H, H-2), 3.79 (dd, 1H, $J = 0.47$, 7.10 Hz, H-4), 3.91–4.11 (m, 2H, H-4′, 3).

4.1.3. 1-[2,2-Dimethyl-(4*S*)-1,3-dioxolan-4-yl]-(1*S*)-heptan-1-ol 9. A suspension of magnesium (1 g, 41.66 mmol) in THF (10 mL) was treated with *n*-pentyl bromide (6.29 g, 41.66 mmol) in THF (10 mL) over 1 h. The resulting mixture was stirred for 30 min and copper(I) iodide (0.52 g, 2.77 mmol) was added and the mixture cooled to −30 °C. A solution of **5** (2 g, 13.88 mmol) in dry THF (10 mL) was then added dropwise. After the addition was complete, the mixture was stirred for 3 h and then quenched by pouring it into cold saturated aqueous NH_4Cl solution (30 mL). The solution was extracted with ether (30 mL) and the organic layers combined, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography (Silica gel 60–120 mesh, EtOAc/hexane, 1:4) to afford **9** (2.5 g) in 83% yield as a colorless liquid. $[\alpha]_D = +3.3$ (*c* 0.6, $CHCl_3$); IR (neat): 1070, 1455, 1603, 2858, 2931, 3060, 3445 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 0.91 (t, 3H, $J = 4.76$ Hz, $-CH_2CH_3$), 1.26–1.32 (m, 8H), 1.34 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.42–1.46 (m, 2H), 2.05 (br s, 1H, –OH), 3.45–3.49 (m, 1H, H-3), 3.71 (dd, 1H, $J = 7.20$, 6.70 Hz, H-1′), 3.91–4.02 (m, 2H, H-1, 2); FAB MS (*m*/*z*, %): 217 (M^++1, 32), 181 (94), 151 (26), 127 (100), 91 (44).

4.1.4. 4-[1-Benzyloxy-(1*S*)-heptyl]-2,2-dimethyl-(4*S*)-1,3-dioxolane 10. To a cooled (0 °C) suspension of NaH (0.511 g, 21.29 mmol, 60% w/w dispersion in paraffin oil) in THF (10 mL), a solution of **9** (1.82 g, 10.64 mmol) in THF (10 mL) was added dropwise. After 15 min, BnBr (1.20 g, 10.64 mmol) was added dropwise at 0 °C and stirred for 4 h at room temperature. Saturated aqueous NH_4Cl solution (10 mL) was added dropwise at 0 °C and extracted with ether (50 mL). The organic layer was separated and washed with water (25 mL), brine (25 mL), dried over Na_2SO_4, and evaporated. The obtained residue was purified by column chromatography (Silica gel 60–120 mesh, EtOAc/hexane, 1:5) to give **10** (2.5 g) in 78% yield as a light yellow liquid. $[\alpha]_D = -18.8$ (*c* 1.3, $CHCl_3$); IR (neat): 856, 1070, 1455, 1700, 2860, 2931, 3060, 3400 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, $J = 4.76$ Hz, $-CH_2CH_3$), 1.26–1.32 (m, 10H), 1.38 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 3.39 (m, 1H, H-3), 3.62 (dd, 1H, $J = 7.20$, 6.70 Hz, H-1′), 3.96 (dd, 1H, $J = 7.20$, 6.70 Hz, H-1), 4.18 (dd, 1H, $J = 6.71$, 4.32 Hz, H-2), 4.61 (d, 1H, $J = 11.7$ Hz, $-OCH_2Ph$), 4.76 (d, 1H, $J = 11.7$ Hz, $-OCH_2Ph$), 7.22–7.38 (m, 5H, Ar–H); FAB MS (*m*/*z*, %): 306 (M^+, 6), 305 (M^+-1, 9), 199 (4), 157 (2), 101 (12), 91 (100). Analysis calcd for $C_{19}H_{30}O_3$ (306): C, 74.47; H, 9.87. Found: C, 74.45; H, 9.85.

4.1.5. 3-Benzyloxy-(2*S*,3*S*)-nonane-1,2-diol 11. A mixture of compound **10** (2.2 g, 8.27 mmol) in 60% aq AcOH (20 mL) was stirred at room temperature for 12 h. The reaction mixture was neutralized with solid $NaHCO_3$ (pH 7) and extracted with EtOAc (3 × 30 mL). The combined organic layers were evaporated, and the obtained residue was purified by filtration through a small pad of silica gel with a 1:1 EtOAc/hexane solvent system to afford diol **11** (1.6 g) in 84% yield as a pale yellow syrup. $[\alpha]_D = +42.5$ (*c* 0.6, $CHCl_3$); IR (neat): 856, 1070, 1450, 1610, 2855, 2931, 3060, 3462 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, $J = 4.76$ Hz, $-CH_2CH_3$), 1.26–1.38 (m, 10H), 3.39 (m, 1H, H-3), 3.62 (dd, 1H, $J = 7.10$, 6.70 Hz, H-1′), 3.82–3.89 (m, 2H, H-1, 2), 4.72 (s, 2H), 7.22–7.38 (m, 5H, Ar–H); FAB MS (*m*/*z*, %): 267 (M^++1, 16), 181 (4), 159 (8), 107 (12), 91 (100).

4.1.6. 3-Benzyloxy-2-(4-methylphenylsulfonyloxy)-(2*S*,3*S*)-nonyl4-methyl-1-benzenesulfonate 12. To a cooled (0 °C) solution of diol **11** (1.4 g, 5.26 mmol) and Et_3N (1.47 mL, 10.52 mol) in CH_2Cl_2 (20 mL), *p*-TsCl (1.1 g, 5.78 mmol) was added portionwise and stirred at room temperature for 8 h. The solvent was evaporated, and the obtained residue was purified by column chromatography (Silica gel 60–120 mesh, EtOAc/hexane, 1:9) to give benzyloxy-2-hydroxy-(2*S*,3*S*)-nonyl4-methyl-1-benzenesulfonate **12** (1.5 g) in 68% yield as a yellow syrup. $[\alpha]_D = -4.7$ (*c* 0.75, $CHCl_3$); IR (neat): 580, 820, 1090, 1120, 1610, 2855, 2950, 3060, 3420 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, $J = 4.76$ Hz, $-CH_2CH_3$), 1.26–1.42 (m, 10H), 2.44 (s, 3H, Ar–CH_3), 3.39 (m, 1H, H-3), 3.62 (dd, 1H, $J = 7.22$, 6.72 Hz, H-1′), 3.94–3.96 (dd, 1H, $J = 7.20$, 6.70 Hz, H-1), 4.18 (dd, 1H, $J = 6.71$, 8.30 Hz, H-2), 4.61 (d, 1H, $J = 11.7$ Hz, $-OCH_2Ph$), 4.76 (d, 1H, $J = 11.7$ Hz, $-OCH_2Ph$), 7.22–7.42 (m, 7H, Ar–H), 7.78 (d, 2H, $J = 7.80$ Hz, Ar–H); FAB MS (*m*/*z*, %): 421 (M^++1, 3), 391 (9), 154 (22), 91 (100).

4.1.7. 1-Benzyloxy-1-[(2*S*)-oxiran-2-yl]-(1*S*)-heptane 13. A solution of compound **12** (1.2 g, 2.85 mmol) in MeOH (10 mL) was treated with K_2CO_3 (0.78 g, 5.71 mmol) and stirred for 1 h at room temperature. The reaction mixture was worked up as described for **5** and purified by column chromatography (Silica gel 60–120 mesh, EtOAc/hexane, 1:9) to afford **13** (0.5 g) in 71% yield as a colorless liquid. $[\alpha]_D = -13.43$ (*c* 0.8, $CHCl_3$); IR (neat): 820, 1090, 1180, 1170, 1750, 2830, 2900 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, $J = 4.76$ Hz, $-CH_2CH_3$), 1.26–1.44 (m, 10H), 2.38–2.42 (m, 1H, H-2), 2.70–2.74 (m, 1H, H-1), 2.81–2.84 (m, 1H, H-1′), 2.96 (m, 1H, H-3), 4.59 (d, 1H, $J = 11.7$ Hz, $-OCH_2Ph$), 4.76 (d, 1H, $J = 11.7$ Hz, $-OCH_2Ph$), 7.22–7.36 (m, 5H, Ar–H); FAB MS (*m*/*z*, %): 249 (M^++1, 32), 181 (9), 154 (26), 127 (10), 91 (100).

4.1.8. 1-[1-Benzyloxy-(1*S*)-heptyl]-(1*S*)-3-butenyl alcohol 3. A suspension of magnesium (0.11 g, 4.83 mmol) in THF (5 mL) was treated with vinyl bromide (0.51 g, 4.83 mmol) in THF (5 mL), which was added dropwise.

The resulting mixture was stirred for 30 min, and copper(I) iodide (0.06 g, 0.32 mmol) was then added and the mixture cooled to −30 °C. A solution of **13** (0.4 g, 1.61 mmol) in dry THF (5 mL) was then added dropwise. After 3 h, the reaction mixture was worked up as described for **9** and purified by column chromatography (Silica gel 60–120 mesh, EtOAc/hexane, 1:4) to give **3** (0.25 g) in 57% yield as a colorless liquid. $[\alpha]_D = +17.8$ (*c* 1.5, $CHCl_3$); IR (neat): 820, 1090, 1180, 1170, 1750, 2830, 2900 cm^{-1}; ^1H NMR (300 MHz): δ 0.90 (t, 3H, $J = 6.7$, H-11), 1.22–1.81 (m, 10H, H-6 to H-10), 2.15–2.45 (m, 3H, OH and H-3), 3.34 (q, 1H, $J = 5.5$, H-5), 3.56–3.72 (m, 1H, H-4), 4.52 (d, 1H, $J = 11.3$, $-OCH_2Ph$), 4.67 (d, 1H, $J = 11.3$, $-OCH_2Ph$), 5.04–5.16 (dd, 2H, $J = 17.6$, 7.0 Hz, H-1, 1′), 5.87–5.92 (m, 1H, H-2), 7.24–7.40 (m, 5H, Ar–H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 13.9, 22.5, 25.2, 29.5, 30.2, 32.7, 38.1, 72.1, 72.4, 81.5, 117.1, 127.7, 127.8, 128.4, 135.0, 138.5; FAB MS (*m*/*z*, %): 277 (M^++1, 12), 181 (6), 154 (8), 127 (10), 107 (9), 91 (100). Analysis calcd for $C_{18}H_{28}O_2$ (276): C, 78.21; H, 10.71. Found: C, 78.19; H, 10.69.

4.1.9. 4-Benzyloxy-butane-1-ol 14. To a stirred solution of 1,4-butanediol (5 g, 55.55 mmol) in dry THF (30 mL), NaH (2.66 g, 111.11 mmol, 60% suspension) was added in portions with constant stirring at 0 °C. After 10 min, BnBr (9.5 g, 55.55 mmol) was added through a syringe and stirred at room temperature for 3 h. The excess of NaH was quenched by slow and careful addition of MeOH (5 mL), diluted with water (10 mL), and extracted into ether (2 × 20 mL). The combined ether extracts were washed with brine solution (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure, and the residue was purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane; 1:4) to afford **14** (7 g) in 70% yield as a colorless syrup. IR (neat): 1024, 1240, 1455, 1612, 2939, 3440 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.26–1.34 (m, 4H), 3.68 (t, 2H, $J = 6.4$ Hz), 3.74 (t, 2H, $J = 6.2$ Hz), 4.56 (s, 2H), 7.16–7.28 (m, 5H, Ar–H); EIMS (*m*/*z*): 181 (M^++1, 18), 131 (44), 117 (28), 69 (32).

4.1.10. 4-Benzyloxybutanal 15. To a stirred solution of oxalyl chloride (5 mL, 41.66 mmol) in dry CH_2Cl_2 (10 mL), DMSO (5.91 mL, 83.33 mmol) was added at −78 °C and stirred at the same temperature for 30 min. A solution of **14** (5 g, 27.77 mmol) in dry CH_2Cl_2 (20 mL) was added at −78 °C to the reaction mixture and stirred for 2.5 h at the same temperature. Et_3N (23.28 mL, 166.66 mmol) was added at 0 °C and stirred for an additional 30 min. The reaction mixture was diluted with water (30 mL) and extracted with dichloromethane (2 × 50 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), and concentrated to give **15** (4.5 g) in 92% yield as a pale yellow syrup. IR (neat): 1024, 1247, 1463, 1705, 2859, 2933 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.26–1.42 (m, 2H), 2.67 (t, 2H, $J = 4.7$ Hz, H-2, 2′), 3.58 (t, 2H, $J = 6.2$ Hz), 4.58 (s, 2H), 7.19–7.32 (m, 5H), 9.8 (s, 1H, –CHO).

4.1.11. 1-[4-Benzyl-2-oxo-(4*S*)-1,3-oxazolan-3-yl]-6-benzyloxy-3-hydroxy-2-(4-methoxybenzyloxy)-(2*S*,3*R*)-hexan-1-one 6. To a solution of the chiral auxiliary (5 g, 14.08 mmol) in CH_2Cl_2 (20 mL) at −78 °C, *N*-ethyldiisopropyl amine (2.95 mL, 16.90 mmol) and dibutylboron triflate (15.49 mL, 15.49 mmol, 1 M solution in toluene) were added and stirred for 1 h at −78 °C, then at 0 °C for 45 min and recooled to −78 °C. A solution of aldehyde **15** (3.25 g, 18.30 mmol) in CH_2Cl_2 (10 mL) was added in one portion and stirred at −78 °C for 1 h, followed by 1 h at −45 °C. The reaction mixture was treated with MeOH (30 mL) and 0.5 M pH 7 phosphate buffer (10 mL). After 1 h, 30% aqueous H_2O_2 (5 mL) was added and stirred for 30 min at 0 °C, then at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with water (20 mL), brine (10 mL), dried over Na_2SO_4, concentrated under reduced pressure, and the residue was purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane, 1:2) to give **6** (5 g) in 66% yield as a gummy syrup. $[\alpha]_D = +27.3$ (*c* 0.75, $CHCl_3$); IR (neat): 1172, 1245, 1513, 2859, 2931, 3064, 3446 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.37–1.39 (m, 1H), 1.68–1.72 (m, 3H), 2.82 (dd, 1H, $J = 4.7$, 6.2 Hz), 3.34 (dd, 1H, $J = 4.7$, 6.3 Hz), 3.45 (t, 2H, $J = 6.1$ Hz), 3.63 (d, 2H, $J = 5.7$ Hz), 3.81 (s, 3H), 4.18–4.24 (m, 2H) 4.46 (s, 2H), 4.61–4.65 (m, 3H), 6.86 (d, 2H, $J = 8.2$ Hz, Ar–H), 7.18 −7.42 (m, 12H, Ar–H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 25.9, 30.8, 35.0, 37.7, 41.5, 53.7, 55.2, 55.6, 66.9, 69.6, 70.0, 72.3, 72.7, 72.8, 79.1, 113.9, 127.2, 127.4, 127.5, 128.3, 128.9, 129.2, 129.3, 129.7, 130.1, 135.1, 135.9, 138.5, 153.3, 159.6, 170.8; FAB MS (*m*/*z*, %): 534 (M^++1, 6), 391 (45), 307 (18), 154 (92), 121 (100). Analysis calcd for $C_{31}H_{35}NO_7$ (533): C, 69.78; H, 6.61. Found: C, 69.74; H, 6.58.

4.1.12. 6-Benzyloxy-3-hydroxy-2-(4-methoxybenzyloxy)-(2*S*,3*R*)-hexanal 16. To a stirred solution of **6** (4.5 g, 8.44 mmol) in dry CH_2Cl_2 (40 mL), DIBAL-H (4.22 mL, 8.44 mmol, 2 M solution in toluene) was added at −78 °C and stirred at the same temperature for 1 h. Methanol (15 mL) was added to the reaction mixture at 0 °C and stirred for an additional 10 min. Saturated aq solution of sodium potassium tartarate (15 mL) was added and stirred for 10 min. Methanol was evaporated, the residue diluted with water (10 mL), and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), concentrated, and the residue purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane, 1:4) to afford **16** (2.2 g) in 73% yield as a gummy syrup. IR (neat): 1510, 1586, 1705, 2062, 2906, 3390 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.38–1.68 (m, 4H), 3.38–3.54 (m, 4H), 3.78 (s, 3H), 4.27 (d, 1H, $J = 11.3$ Hz, $-OCH_2Ph$), 4.42 (s, 2H, $-OCH_2Ph$), 4.54 (d, 1H, $J = 11.3$ Hz, $-OCH_2Ph$), 6.84 (d, 2H, $J = 8.2$ Hz, Ar–H), 7.19 −7.37 (m, 7H, Ar–H), 9.7 (s, 1H, –CHO).

4.1.13. 1-(3-Benzyloxypropyl)-2-(4-methoxybenzyloxy)-(1*R*,2*R*)-3-butenyl alcohol 17. To a solution of (methyl)triphenylphosphonium iodide (4.51 g, 11.17 mmol) in dry THF (50 mL), *n*-BuLi (6.98 mL, 11.17 mmol, 1.6 M solution in *n*-hexane) was added at −20 °C and stirred for 30 min. A solution of **16** (2 g, 5.58 mmol) in THF (10 mL) was added dropwise and stirred for 5 h at room temperature. Saturated aqueous NH_4Cl solution (15 mL) was added and extracted with EtOAc (3 × 50 mL). The organic layer was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4), evaporated, and the obtained residue purified by column chromatography

(Silica gel 60–120 mesh, EtOAc/hexane, 1:4) to furnish **17** (1.2 g) in 60% yield as a pale yellow liquid. $[\alpha]_D = +9.7$ (*c* 0.8, $CHCl_3$); IR (neat): 1155, 1240, 1515, 2865, 2931, 3064, 3446 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.38–1.68 (m, 4H), 3.38–3.52 (m, 4H), 3.79 (s, 3H), 4.26 (d, 1H, $J = 11.3$ Hz, $-OCH_2Ph$), 4.42 (s, 2H, $-OCH_2Ph$), 4.52 (d, 1H, $J = 11.3$ Hz, $-OCH_2Ph$), 5.34 (dd, 2H, $J = 4.6$, 10.2 Hz), 5.71–5.74 (m, 1H), 6.84 (d, 2H, $J = 8.2$ Hz, Ar–H), 7.18 −7.37 (m, 7H, Ar–H); FAB MS (*m*/*z*, %): 355 ($M^+ - 1$, 6), 326 (4), 281 (16), 147 (41), 73 (100).

4.1.14. 7-Benzyloxy-(3*R*,4*R*)-1-heptene-3,4-diol 18. To a stirred solution of **17** (1 g, 2.08 mmol) in dry acetonitrile, $ZrCl_4$ (0.130 g, 0.561 mmol) was added and stirred at room temperature for 1 h. The solvent was removed under reduced pressure and the residue treated with EtOAc (20 mL). It was then washed with water (15 mL), brine (15 mL), dried over Na_2SO_4, and evaporated under reduced pressure. The residue purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane, 1:2) to furnish **18** (0.6 g) in 91% yield as a colorless syrup. $[\alpha]_D = +5.2$ (*c* 0.5, $CHCl_3$); IR (neat): 1255, 1450, 1605, 2596, 3034, 3580 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.38–1.68 (m, 4H), 3.38–3.52 (m, 4H), 4.24 (d, 1H, $J = 11.3$ Hz, $-OCH_2Ph$), 4.51 (d, 1H, $J = 11.3$ Hz, $-OCH_2Ph$), 5.34 (dd, 2H, $J = 4.6$, 10.2 Hz), 5.72 (m, 1H), 7.17–7.39 (m, 5H, Ar–H); FAB MS (*m*/*z*, %): 237 (M^++1, 6), 181 (28), 157 (24), 121 (100).

4.1.15. 3-[2,2-Dimethyl-5-vinyl-(4*R*,5*R*)-1,3-dioxolan-4-yl]-1-benzyloxy-propane 19. To a solution of **18** (0.5 g, 2.11 mmol) and 2,2-dimethoxypropane (0.44 g, 4.22 mmol) in dry DMSO (20 mL), PTSA (0.05 mg) was added and stirred for 5 h at room temperature. The reaction mixture was treated with saturated aqueous $NaHCO_3$ solution (20 mL) and extracted with 30% EtOAc in a hexane solvent system (3×75 mL). The organic layer was washed with water (50 mL), brine (50 mL), dried over Na_2SO_4, evaporated, and the residue purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane, 1:4) to afford **19** (0.5 g) in 84% yield as a gummy syrup. $[\alpha]_D = -27.2$ (*c* 0.5, $CHCl_3$); IR (neat): 873, 1057, 1239, 1376, 2937, 2986 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.40 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.45–1.49 (m, 2H), 1.77–1.84 (m, 2H), 3.44–3.56 (m, 3H), 4.18 (dd, 1H, $J = 8.1$, 7.3 Hz), 4.44 (s, 2H, $-OCH_2Ph$), 5.27–5.36 (ddd, 2H, $J = 1.1$, 1.5, 10.2 Hz), 5.72–5.77 (m, 1H), 7.18–7.35 (m, 5H, Ar–H); FAB MS (*m*/*z*, %): 277 (M^++1, 8), 184 (24), 121 (100), 91 (52). Analysis calcd for $C_{17}H_{24}O_3$ (276): C, 73.88; H, 8.75. Found: C, 73.84; H, 8.71.

4.1.16. 3-[2,2-Dimethyl-5-vinyl-(4*R*,5*R*)-1,3-dioxolan-4-yl]-1-propanol 20. To a stirred solution of **19** (0.5 g, 1.81 mmol) in CH_2Cl_2 (5 mL), DDQ (1.64 g, 7.24 mmol) was added and stirred at reflux for 4 h. Saturated aq $NaHCO_3$ solution (10 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with water (15 mL), brine (10 mL), dried over Na_2SO_4, and concentrated. The crude residue was purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane, 1:4) to afford **20** (0.3 g) in 89% yield as a colorless syrup. $[\alpha]_D = -8.6$ (*c* 1.6, $CHCl_3$); IR (neat): 878, 1055, 1235, 1378, 2935, 2986, 3402 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.39 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.44–1.49 (m, 2H), 1.77–1.86 (m, 2H), 3.48–3.64 (m, 3H), 4.12 (dd, 1H, $J = 8.1$, 7.3 Hz), 5.28–5.38 (ddd, 2H, $J = 1.1$, 1.5, 10.2 Hz), 5.72–5.77 (m, 1H); FAB MS (*m*/*z*, %): 187 (M^++1, 4), 171 (24), 98 (100), 97 (69).

4.1.17. 3-[2,2-Dimethyl-5-vinyl-(4*R*,5*R*)-1,3-dioxolan-4-yl]-propanal 21. To a stirred solution of oxalyl chloride (0.29 mL, 2.41 mmol) in dry CH_2Cl_2 (10 mL), DMSO (0.34 mL, 4.83 mmol) was added at −78 °C and stirred at the same temperature for 30 min. A solution of **20** (0.3 g, 1.61 mmol) in dichloromethane (5 mL) was added at −78 °C and stirred for 3 h at the same temperature. The reaction mixture was cooled to 0 °C, treated with Et_3N (1.35 mL, 9.67 mmol) and stirred for 15 min. The reaction mixture was then worked up as described for **15** to afford **21** (0.28 g) in 94% yield as a pale yellow syrup. IR (neat): 1170, 1458, 1705, 2855, 2935 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.39 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.77–1.86 (m, 2H), 2.67 (t, 2H, $J = 4.7$ Hz), 3.62–3.65 (m, 1H), 3.98 (dd, 1H, $J = 8.1$, 7.3 Hz), 5.27–5.36 (ddd, 2H, $J = 1.1$, 1.5, 10.2 Hz), 5.72–5.77 (m, 1H), 9.7 (s, 1H, –CHO).

4.1.18. 3-[2,2-Dimethyl-5-vinyl-(4*R*,5*R*)-1,3-dioxolan-4-yl]-propanoic acid 4. To a stirred solution of **21** (0.28 g, 1.52 mmol) in *tert*-butanol/water (7:3, 10 mL), sodium chlorite (0.20 g, 2.28 mmol), and H_2O_2 (1 mL, 7.60 mmol, 30% aq soln) were added and stirred at room temperature for 10 h. The reaction mixture was concentrated, the residue dissolved in ethyl acetate (10 mL), washed with water (5 mL) and brine (5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane, 1:3) to afford **4** (0.27 g) in 90% yield as a pale yellow syrup. $[\alpha]_D = +25.6$ (*c* 0.8, $CHCl_3$); IR (neat): 1165, 1220, 1427, 1607, 1714, 2878, 2987, 3085 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.39 (s, 6H, $2CH_3$), 1.77–1.96 (m, 2H), 2.44–2.58 (m, 2H, H-2, 2′), 3.61–3.66 (m, 1H, H-4), 3.98 (dd, 1H, $J = 7.3$, 8.1 Hz, H-5), 5.27–5.36 (ddd, 2H, $J = 1.1$, 1.5, 10.2 Hz, H-7, 7′), 5.72–5.77 (m, 1H, H-6); FAB MS (*m*/*z*, %): 200 (M^+, 4), 185 (64), 167 (4), 144 (5), 98 (93). Analysis calcd for $C_{10}H_{16}O_4$ (200): C, 59.98; H, 8.05. Found: C, 59.94; H, 8.01.

4.1.19. 1-[1-Benzyloxy-(1*S*)-heptyl]-(1*S*)-3-butenyl 3-[2,2-dimethyl-5-vinyl-(4*R*,5*R*)-1,3-dioxolan-4-yl]propanoate 2. To a stirred solution of **4** (0.12 g, 0.60 mmol) in dry THF (5 mL), was added Et_3N (0.16 mL, 1.20 mmol) at room temperature and stirred for 30 min. A solution of 2,4,6-trichlorobenzoyl chloride (0.148 mL, 0.60 mmol) in dry THF (2 mL) was added to the reaction mixture and stirred for 5 h at room temperature. The solvent was evaporated, residue diluted with toluene (20 mL) and treated with DMAP (0.146 g, 1.20 mmol) and **3** (0.156 g, 0.60 mmol). After 14 h, toluene was evaporated; the crude residue was purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane, 1:3) to afford **2** (0.2 g) in 73% yield as a colorless syrup. $[\alpha]_D = -1.9$ (*c* 4.2, $CHCl_3$); IR (neat): 1150, 1255, 1350, 1455, 1605, 1710, 2590, 3035 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H, $J = 6.5$ Hz, $3 \times$ H-7″), 1.26 (br m, 8H, H-3″ to H-6″), 1.39 (s, 3H, Me_2C), 1.41

(s, 3H, Me_2C), 1.44–1.62 (m, 2H, 2 × H-2″), 1.72–1.96 (m, 2H, 2 × H-3), 2.23–2.54 (m, 4H, 2 × H-2 and 2 × H-2′), 3.42 (dt, 1H, $J = 7.1$, 4.5 Hz, H-1″), 3.64 (dt, 1H, $J = 8.1$, 3.9 Hz, H-4), 3.97 (dd, 1H, $J = 8.1$, 7.2 Hz, H-5), 4.60 (s, 2H, CH_2Ph), 4.97–5.18 (m, 3H, H-1′ and 2 × H-4′), 5.25 (ddd, 1H, $J = 10.2$, 1.5, 0.8 Hz, H-7), 5.38 (ddd, 1H, $J = 17.1$, 1.5, 0.9 Hz, H-7), 5.63–5.79 (m, 2H, H-3′, 6), 7.23–7.40 (m, 5H, Ar–H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 14.0, 22.5, 25.5, 26.8, 27.2, 29.3, 29.9, 30.7, 31.6, 34.3, 72.3, 73.5, 79.0, 82.4, 108.7, 117.5, 118.9, 127.6, 127.8, 128.3, 134.1, 135.1, 138.5, 172.6. FAB MS (*m*/*z*, %): 458 (M^+, 0.4%), 443 (0.8), 361 (0.8), 294 (11), 275 (3.5), 259 (5.6), 223 (3.8), 205 (11), 183 (6.8), 143 (9.7), 125 (70), 98 (35), 91 (100), 83 (10), 69 (9.2), 55 (9.0), 43 (12). Analysis calcd for $C_{28}H_{42}O_5$ (458): C 73.3, H 9.2. Found: C 73.1, H 9.1.

4.1.20. (5*R*,6*R*,7*E*,10*S*)- and (5*R*,6*R*,7*Z*,10*S*)-10-[(1*S*)-1-Benzyloxyheptyl]-5,6-isopropylidenedioxy-3,4,5,6,9,10-hexahydro-2*H*-oxecin-2-one, *E*-22 and *Z*-22. Ester **2** (0.150 g, 0.327 mmol) was dissolved in freshly distilled degassed anhydrous CH_2Cl_2 (230 mL), treated with Grubbs' catalyst **I** (0.048 g, 0.0589 mmol) and heated at reflux for 2 days under an Ar flow until TLC (hexane/EtOAc; 80:0) showed complete disappearance of the starting material. Most of the solvent was then distilled off and the concentrated solution left to stir at room temperature for 2 h under air bubbling, in order to decompose the catalyst. The reaction mixture was evaporated to dryness to give a brown residue, which was purified by column chromatography (Silica gel, 60–120 mesh, EtOAc/hexane, 3:97 to 20:80) to allow the separation of the desired *trans*-stereoisomer (*E*)-**22** (75 mg) from *cis* derivative (*Z*)-**22** (35 mg) (combined 78% yield).

4.1.20.1. *trans*-(5*R*,6*R*,7*E*,10*S*)-2. $[\alpha]_D = -37.9$ (*c* 3.0, $CHCl_3$); IR (neat): 1155, 1255, 1330, 1450, 1602, 1715, 2590 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, 3H, $J = 6.5$, 3 × H-7′), 1.27 (br envelope, 8H, H-3′ to H-6′), 1.41 (s, 6H, 2 × Me_2C), 1.51–1.65 (m, 2H, 2 × H-2′), 1.87–2.71 (m, 6H, 2 × H-3, H-4 and H-9), 3.47 (m, 1H, H-1′), 3.61 (m, 1H, H-5), 3.89 (t, 1H, $J = 9.2$ Hz, H-6), 4.56 (d, 1H, $J = 11.6$ Hz, CH_2Ph), 4.62 (d, 1H, $J = 11.6$, CH_2Ph), 4.92 (m, 1H, H-10), 5.29 (dd, 1H, $J = 15.6$, 9.2 Hz, H-7), 5.72 (ddd, 1H, $J = 15.6$, 11.0, 4.7 Hz, H-8), 7.29–7.40 (m, 5H, Ar–H). ^{13}C NMR: 14.0, 22.5, 25.4, 25.6, 26.9, 27.1, 29.4, 29.7, 31.7, 34.2, 72.5, 73.4, 79.8, 80.4, 84.4, 108.8, 127.8, 127.9, 128.4, 129.2, 130.3, 138.2, 171.8. FAB MS (*m*/*z*, %): 430 (M^+, 0.22), 415 (0.33), 373 (0.60), 328 (1.1), 298 (0.71), 237 (3.3), 220 (1.8), 205 (4.3), 203 (7.0), 179 (1.8), 123 (6.2), 113 (14), 91 (100), 85 (23), 79 (6.2). Analysis calcd for $C_{26}H_{38}O_5$ (430): C 72.5, H 8.9. Found: C 72.3, H 8.71.

4.1.20.2. *cis*-(5*R*,6*R*,7*Z*,10*S*)-22. $[\alpha]_D = +4.5$ (*c* 1.6, $CHCl_3$); IR (neat): 1155, 1255, 1330, 1450, 1602, 1715, 2590 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.89 (t, 3H, $J = 6.5$ Hz, 3 × H-7′), 1.27 (br envelope, 8H, H-3′ to H-6′), 1.40 (s, 3H, Me_2C), 1.42 (s, 3H, Me_2C), 1.50–1.77 (m, 2H, 2 × H-2′), 2.01–2.77 (m, 6H, 2 × H-3, H-4 and H-9), 3.49 (m, 1H, H-1′), 3.66 (ddd, 1H, $J = 10.2$, 9.5, 2.3 Hz, H-5), 4.52 (dd, 1H, $J = 9.5$, 8.0 Hz, H-6), 4.58 (d, 1H, $J = 11.6$ Hz, CH_2Ph), 4.66 (d, 1H, $J = 11.6$ Hz, CH_2Ph), 5.10 (ddd, 1H, $J = 11.8$, 4.4, 2.2 Hz, H-10), 5.50 (t, 1H, $J = 10.3$ Hz, H-7), 5.74 (dt, 1H, $J = 0.3$, 7.0 Hz, H-8), 7.28–7.44 (m, 5H, Ar–H). ^{13}C NMR: 14.0, 22.5, 25.4, 26.8, 27.0, 29.3, 29.6, 30.5, 31.7, 32.1, 72.6, 72.8, 77.1, 79.7, 81.5, 107.6, 127.7, 128.4, 130.3, 130.9, 138.0, 176.6. FAB MS (*m*/*z*, %): 430 (M^+, 0.69%), 415 (2.3), 373 (0.30), 328 (1.1), 298 (0.60), 265 (1.7), 237 (3.0), 220 (1.7), 205 (3.9), 203 (6.3), 123 (5.1), 113 (13), 91 (100), 85 (16), 79 (6.6).

4.1.21. (5*R*,6*R*,7*E*,10*S*)-5,6-Dihydroxy-10-[(1*S*)-1-hydroxyheptyl]-3,4,5,6,9,10-hexahydro-2*H*-oxecin-2-one, microcarpalide, 1. Titanium tetrachloride (0.044 g, 0.232 mmol) in anhydrous CH_2Cl_2 (1 mL) was slowly added dropwise over 10 min to a stirred solution of *trans* derivative *E*-**22** (0.050 g, 0.116 mmol) in dry CH_2Cl_2 (2.5 mL) and cooled to 0 °C. After 1.5 h, the ochre-yellow cloudy mixture was poured into water (5 mL), diluted with CH_2Cl_2 (4 mL), and treated with satd $NaHCO_3$ (8 mL), brine (5 mL), and EtOAc (15 mL) in a separating funnel. After settling, the upper milky layer was discarded, whereas the clear lower phase was separated, dried over Na_2SO_4, filtered, and concentrated under reduced pressure; silica gel chromatography of the crude residue using ethyl acetate as eluent, afforded **1** as a beige oil (0.020 g) in 59% yield. $[\alpha]_D = -23.6$ (*c* 1.0, MeOH) (lit., −22.0). NMR analysis clearly showed the presence of two slowly interconverting conformers in a 76:24 ratio (in CD_3CN), which is identical to the value described in the literature for the natural compound in the same solvent. IR (neat): 1150, 1255, 1350, 1450, 1602, 1710, 2590, 3035 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (t, 3H, $J = 6.8$ Hz, 3 × H-7′), 1.26–1.38 (br envelope, 8H, H-3′ to H-6′), 1.41–1.47 (br m, 2H, 2 × H-2′), 1.80 (br dddd, 1H, H-4), 2.02 (br ddd, 1H, H-4 minor conformer), 2.11–2.23 (br m, 3H, H-3, H-4 and H-9), 2.27–2.34 (br m, 1H, H-9), 2.36 (ddd, 1H, $J = 5.2$, 2.7, 1.1 Hz, H-9 minor), 2.47–2.58 (m, 1H, H-3), 3.28 (br dt, 1H, H-5 minor), 3.54–3.60 (br m, 1H, H-1′), 3.64 (dt, 1H, $J = 3.1$, 9.1 Hz, H-6 minor), 3.80 (br m, 1H, H-5), 4.13 (br m, 1H, H-6), 4.63 (ddd, 1H, $J = 8.4$, 4.5, 2.7 Hz, H-10 minor), 4.84 (ddd, 1H, $J = 11.3$, 4.9, 3.3 Hz, H-10), 5.08 (dd, 1H, $J = 15.7$, 9.4 Hz, H-7 minor), 5.53 (dddd, 1H, $J = 15.8$, 10.3, 5.3, 2.2 Hz, H-8), 5.69 (m, 1H, H-8 minor), 5.73 (dd, 1H, $J = 15.8$, 2.5 Hz, H-7). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 14.4 (*C*-7), 23.3 (*C*-6), 26.1 (*C*-3), 26.5 (*C*-4), 29.3 (*C*-3), 30.0 (*C*-4), 32.2 (*C*-9, minor conformer), 32.3 (*C*-5, minor), 32.6 (*C*-5), 33.9 (*C*-2, minor), 34.3 (*C*-2), 35.9 (*C*-3, minor), 36.7 (*C*-9), 72.5 (*C*-6), 72.9 (*C*-1), 73.5 (*C*-5), 73.8 (*C*-1, minor), 76.4 (*C*-10, minor), 77.0 (*C*-5, minor), 79.5 (*C*-6, minor), 79.7 (*C*-10), 126.7 (*C*-8), 130.0 (*C*-8, minor), 133.8 (*C*-7, minor), 134.6 (*C*-7), 173.5 (*C*-2, minor), 176.4 (*C*-2); FAB MS (*m*/*z*, %): 301 (M^++1, 1.4), 283 (0.55), 265 (0.78), 198 (6.2), 180 (55), 141 (10), 129 (30), 113 (13), 110 (16), 95 (39), 84 (100), 73 (44), 70 (80), 55 (64).

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