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Total Synthesis of Microcarpalide†

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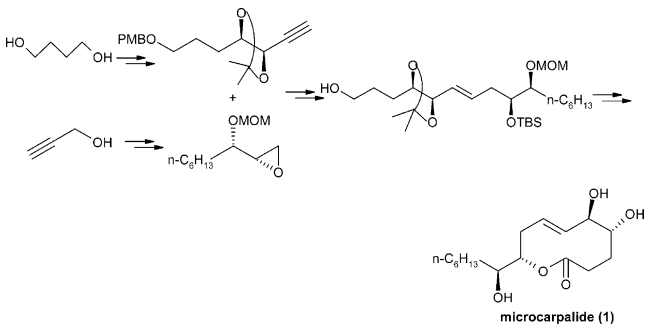
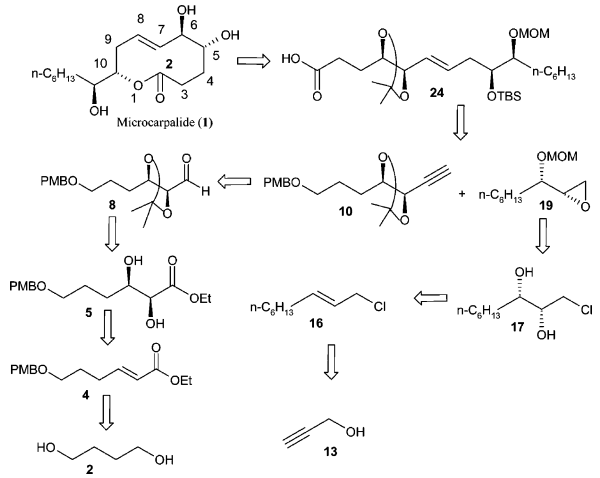


An efficient, convergent approach for the total synthesis of microcarpalide (**1**) is described. The synthetic strategy features the Sharpless asymmetric dihydroxylation, regioselective epoxide opening with various nucleophiles such as a lithium acetylide and cuprates derived from the vinyl stannane and the vinyl iodide for the construction of a C7−C8 *trans*-double bond and Yamaguchi macrolactonization as the key steps.

Microcarpalide, a new alkyl-substituted nonenolide, was isolated by Hemscheidt and co-workers in 2001 from fermentation broths of an unidentified endophytic fungus growing on the bark of *Ficus microcarpa* L.[1] This compound acts as a strong microfilament disrupting agent and displayed a weak cytotoxicity to mammalian cells, thus making it an attractive tool for studying cell motility and metastasis and a potential lead structure to develop new anticancer drugs.

So far five total syntheses of microcarpalide have been reported in the literature.[2] Most of the approaches described are based on ring-closing metathesis for the key macrocyclization to construct the olefin with selectivities between 2:1 to 10:1 in favor of the desired (*E*)-isomer. Moreover the stereogenic centers were mainly derived from chiral pool starting materials such as tartaric acid,[2a,c] (*R*)-glycidol,[2a] D-mannose,[2b] malic acid,[2d] etc. As a part of our research program aimed at developing enantioselective synthesis of naturally occurring lactones[3] and amino alcohols,[4] we became interested in developing a general route capable of providing not only the target molecule **1** but also its congeners with desired stereo- and enantioselectivities for studies on the relationship between structure and pharmacological activity. Herein we report our successful endeavors toward the total synthesis of **1** utilizing the Sharpless asymmetric dihydroxylation as the source of chirality from the commercially available starting materials 1,4-butane diol and propargyl alcohol.

SCHEME 1. Retrosynthetic Analysis for Microcarpalide (1)



The retrosynthetic analysis is based on a convergent approach as outlined in Scheme 1. We envisioned that the ring closing could be effected via Yamaguchi macrolactonisation of **24**, which in turn would be obtained by Yamaguchi coupling of epoxide **19** with acetylene **10**. The acetylene **10** would be obtained through a Corey−Fuchs protocol from the aldehyde **8**, which in turn could be obtained from the diol **5**. In this strategy, the stereogenic centers of both fragments were obtained through Sharpless asymmetric dihydroxylation of olefins **4** and **16**, which in turn could be obtained from the commercially available starting materials 1,4-butane diol **2** and propargyl alcohol **13**.

Synthesis of Fragment 10 (Scheme 2). The synthesis of acetylene component **10** started from commercially

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† Dedicated to Professor Dr. Richard R. Schmidt on the occasion of his 70th birthday.

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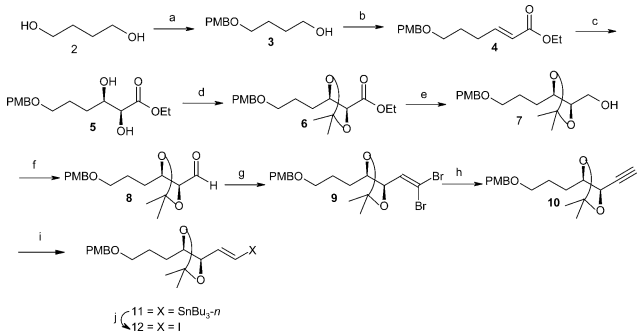
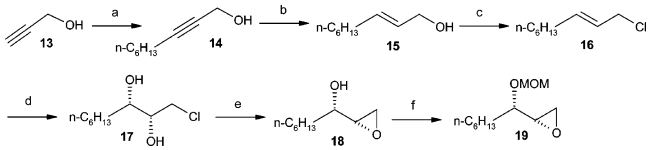
SCHEME 2[a]



[a] Reagents and conditions: (a) *p*-$CH_3OC_6H_4CH_2Br$, NaH, dry DMF, cat. TBAI, 0 °C to rt, 1 h, 90%; (b) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 to −60 °C; (ii) $Ph_3P{=}CHCO_2Et$, benzene, reflux, 6 h, 89%; (c) $(DHQD)_2PHAL$, K_2CO_3, $K_3Fe(CN)_6$, $MeSO_2NH_2$, OsO_4 (0.1 M in toluene), *t*-BuOH/H_2O (1:1), 0 °C, 24 h, 96%; (d) *p*-TSA, 2,2-DMP, CH_2Cl_2, 95%; (e) DIBAL-H, CH_2Cl_2, 0 °C to rt, 2 h, 96%; (f) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 to −60 °C, 94%; (g) CBr_4, PPh_3, CH_2Cl_2, −78 °C, 2 h, 98%; (h) *n*-BuLi, THF, −78 °C, 1 h, 92%; (i) $(n\text{-}Bu)_3SnH$, AIBN, C_6H_6, reflux, 4 h, 99%; (j) I_2, CH_2Cl_2, 30 min, 96%.

available 1,4-butane diol. Thus selective mono hydroxyl protection of **2** with *p*-methoxybenzyl bromide in the presence of NaH gave **3** in 90% yield. Compound **3** was oxidized to the corresponding aldehyde under Swern conditions[5] and subsequently treated with (ethoxycarbonylmethylene)triphenylphosphorane in benzene under reflux conditions to furnish the *trans*-olefin **4**[6] in 89% yield. The olefin **4** was treated with osmium tetroxide and potassium ferricyanide as co-oxidant in the presence of $(DHQD)_2PHAL$ ligand under AD conditions[7] to give the diol **5** in 96% yield with 97% ee.[8] Treatment of diol **5** with 2,2-dimethoxypropane in the presence of catalytic amount of *p*-TSA gave compound **6**, which on subsequent reduction using DIBAL-H provided the alcohol **7** in excellent yield. Subsequent homologation to the acetylene **10** was carried out by Corey−Fuchs protocol[9] in a three-step sequence involving Swern oxidation, dibromomethylenation of the aldehyde, and dehalogenation. Thus compound **7** was oxidized to the aldehyde **8** using standard Swern conditions followed by dibromomethylenation with CBr_4 and PPh_3 in CH_2Cl_2 at −78 °C to furnish the dibromo olefin **9** in essentially quantitative yield. Treatment of **9** with an excess of *n*-BuLi in THF at −78 °C provided the acetylene **10** in 92% yield, which was readily converted into (*E*)-vinyl stannane **11** by reaction with tri-*n*-butyltin hydride and AIBN in refluxing benzene.[10] Tributyltin was then replaced with iodide by using I_2 in CH_2Cl_2[11] to afford the corresponding iodo compound **12** in excellent yield.

SCHEME 3[a]



[a] Reagents and conditions: (a) Li, liq NH_3, $Fe(NO_3)_3$, *n*-$C_6H_{13}Br$, THF, −78 °C, 95%; (b) $LiAlH_4$, THF, reflux, 96%; (c) *N*-chlorosuccinimide, PPh_3, CH_2Cl_2, 0 °C to rt, 3 h, 89%; (d) $(DHQ)_2PHAL$, K_2CO_3, $K_3Fe(CN)_6$, $MeSO_2NH_2$, OsO_4 (0.1 M in toluene), *t*-BuOH/H_2O (1:1), 0 °C, 24 h, 91%; (e) NaOH, THF, 2 h, 0 °C to rt, 90%; (f) MOMCl, *i*-Pr_2EtN, CH_2Cl_2, 0 °C to rt, 6 h, 98%.

Synthesis of Fragment 19 (Scheme 3). The synthesis of epoxy component **19** commenced from propargyl alcohol **13**. Thus, alkylation of **13** with *n*-hexyl bromide in THF gave the propargylic alcohol **14** in 95% yield, which was further converted into (*E*)-allylic alcohol **15** in 96% yield by $LiAlH_4$ reduction[12] and then to the chloride **16** in 89% yield. The allylic chloride **16** was treated with osmium tetroxide in the presence of $(DHQ)_2PHAL$ ligand under AD conditions to afford the diol **17** in 91% yield and 95% ee.[13] To minimize the epoxide formation, the reaction was carried out under "buffered" conditions[14] (with 3 equiv of $NaHCO_3$). Treatment of diol **17** with 2 equiv of NaOH in THF at 0 °C afforded the epoxide **18** in good yield. The protection of the free hydroxy group of **18** with MOMCl in CH_2Cl_2 in the presence of diisopropylethylamine gave the epoxy compound **19** in excellent yield.

Coupling of Epoxide 19 with Different Nucleophiles (Scheme 4). Having completed the synthesis of both fragments **10** and **19**, we needed to couple two fragments by regioselective epoxide opening and carry out subsequent macrolactonization. To this end, we studied the opening of epoxide with different nucleophiles such as **10**, **11**, and **12**. Thus, vinyl stannane **11** was treated with *n*-BuLi in THF at −78 °C for 1 h and further treated with CuCN followed by addition of epoxide **19** to form the coupling product **20** in 51% yield.[15] In the same way compound **12** was transformed into the corresponding cuprate by sequential treatment with *n*-BuLi and CuCN followed by addition of epoxide to give compound **20** in 78% yield. In both these reactions 2−3 equiv of cuprate was utilized. Though the compound **20** was obtained with requisite *trans*-geometry of the double

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(8) For the measurement of enantiomeric excess, the diol **5** was converted into its dibenzoate. The enantiomeric purity of the dibenzoate was estimated to be 97% by chiral HPLC analysis using Lichocart 250-4 (4 mm i.d. × 25 cm) HPLC Cartridge (R.R.-Whelk-01), 1% *i*PrOH in hexane, 1 mL/min.

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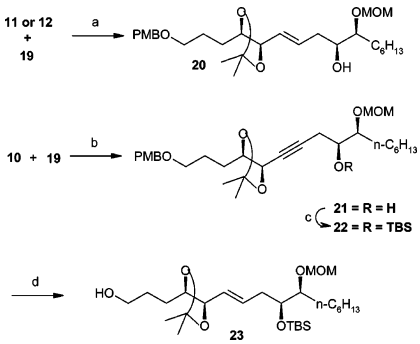
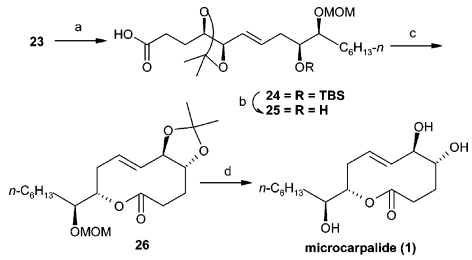
SCHEME 4[a]



[a] Reagents and conditions: (a) For **11**: *n*-BuLi/**11**, −78 °C for 1 h, −50 °C for 1.5 h, then CuCN, −78 °C, 1.5 h, then epoxide **19**, 51%; for **12**: *n*-BuLi/**12**, −78 °C, CuCN, THF, 5 h, 78%; (b) *n*-BuLi, THF, −78 to −20 °C, 30 min, then $BF_3{\cdot}Et_2O$, −78 °C, 10 min, then **19**, 30 min, 89%; (c) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 30 min, 98%; (d) Na/liq NH_3, THF, −40 °C, 89%.

SCHEME 5[a]



[a] Reagents and conditions: (a) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 to −60 °C, 95%; (ii) $NaClO_2$, DMSO, H_2O, NaH_2PO_4, rt, 1.5 h, 86%; (b) TBAF, THF, rt, overnight; (c) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, then DMAP, benzene, 86% from **24**; (d) $BF_3{\cdot}Et_2O$, $(CH_2SH)_2$, CH_2Cl_2, 1 h, 88%.

bond, the drawback of this reaction was in employing 2−3 equiv of substrates **11** or **12** with respect to the epoxide. The epoxide opening reaction did not work with the use of 1−1.5 equiv of cuprates even in the presence of $BF_3{\cdot}Et_2O$. Initially we tried Yamaguchi coupling of the epoxide **19** with acetylide generated directly from the debromination of dibromoalkene **9** in the presence of $BF_3{\cdot}Et_2O$ and *n*-BuLi; however, the reaction was not very clean, affording only a mixture of compounds that could not be separated. This may be attributed to the use of excess of *n*-BuLi in the debromination reaction. To circumvent these problems, the acetylide **10** (1.5 equiv) was finally coupled with epoxide **19** (1 equiv) via Yamaguchi method[16] in the presence of $BF_3{\cdot}Et_2O$ at −78 °C to afford **21** in 89% yield. The free hydroxy group of **21** was protected with TBSCl to furnish compound **22**. Reduction of the alkyne under Birch conditions using Na/liq NH_3[17] proceeded smoothly with the required *E*-geometry of the C7=C8 double bond and concomitant removal of the PMB group affording **23** in good yield. Thus the *E*-selective construction of C7=C8 double bond in the synthesis of target molecule **1** is a significant improvement over all reported syntheses.

Synthesis of Microcarpalide 1 (Scheme 5). Oxidation of primary alcohol in **23** to the corresponding aldehyde using Swern conditions and further oxidation using $NaClO_2$ in DMSO under buffer conditions[18] afforded the acid **24**. The TBS group in **24** was removed with TBAF to give the seco acid **25** for lactonization. Macrolactonization of **25** under Yamaguchi conditions[19] provided the macrocyclic lactone **26** in quantitative yield, which on subsequent cleavage of the protective groups[2a] afforded the target molecule **1** in 88% yield. The physical and spectroscopic data of **1** were identical with those reported.[1,2a]

In conclusion, a convergent and efficient total synthesis of microcarpalide **1**, with high enantioselectivities has been developed in which all the stereocenters were established by Sharpless asymmetric dihydroxylation. Notable features of this approach include Corey−Fuchs protocol to synthesize the acetylene fragment, various nucleophiles used in the regioselective epoxide opening to establish the C7−C8 *trans*-olefin geometry exclusively and Yamaguchi protocol in the macrocyclization step. The synthetic strategy described for **1** might be easily amenable for the preparation of either enantiomer and its double-bond isomer simply by partial hydrogenation using Lindlar's catalyst. Further application of this methodology to the syntheses of other biologically active compounds for the studies of structure activity relationship is currently underway in our laboratory.

Experimental Section

2,3-Dihydroxy-6-(4-methoxybenzyloxy)-hexanoic Acid Ethyl Ester (5). To a mixture of $K_3Fe(CN)_6$ (18.45 g, 56.0 mmol), K_2CO_3 (7.74 g, 56.0 mmol) and $(DHQD)_2PHAL$ (145 mg, 1 mol %), in *t*-BuOH−H_2O (1:1, 100 mL) cooled at 0 °C was added OsO_4 (0.79 mL, 0.1 M solution in toluene, 0.4 mol %) followed by methanesulfonamide (1.78 g, 18.71 mmol). After being stirred for 5 min at 0 °C, the olefin **4** (5.20 g, 18.68 mmol) was added in one portion. The reaction mixture was stirred at 0 °C for 24 h and then quenched with solid sodium sulfite (25 g). The stirring was continued for an additional 45 min, and then the solution was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with 10% KOH and brine, dried (Na_2SO_4), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (3:2) as eluent gave the diol **5** (5.63 g, 96%) as a colorless syrupy liquid. $[\alpha]^{25}_D$ +6.7 (*c* 1.6, $CHCl_3$). IR (neat): ν_{max} 3440, 2938, 2864, 1736, 1612, 1513, 1248, 1130, 1032 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, 2H, J = 10.1 Hz); 6.88 (d, 2H, J = 10.1 Hz), 4.44 (s, 2H), 4.26 (q, 2H, J = 5.0 Hz), 4.06 (m, 1H), 3.91(d, 1H, J = 5.3 Hz), 3.80 (s, 3H), 3.49 (t, 2H, J = 6.1 Hz), 2.82 (br s, 2H), 1.73 (m, 4H), 1.30 (t, 3H, J = 6.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.2, 158.8, 130.1, 128.9, 113.4, 73.4, 72.1, 69.5, 61.2, 54.8, 42.5, 30.0, 25.6, 13.7. Anal. Calcd for $C_{16}H_{24}O_6$ (312.36): C, 61.52; H, 7.74. Found: C, 61.78; H, 7.82.

Tributyl-(2-{5-[3-(4-methoxybenzyloxy)-propyl]-2,2-dimethyl-[1,3]dioxolan-4-yl}-vinyl)-stannane (11). To a stirred solution of **10** (0.500 g, 1.64 mmol) in benzene (25 mL) were added *n*-Bu_3SnH (0.65 mL, 2.45 mmol) and AIBN (catalytic) at room temperature under N_2. The reaction mixture was gently refluxed with stirring for 4 h. The solvent was removed and the residue was purified by silica gel column chromatography using petroleum ether/EtOAc (9:1) as eluent to give **11** (968 mg, 99%) as a yellowish oil. $[\alpha]^{25}_D$ +8.4 (*c* 0.9, $CHCl_3$). IR ($CHCl_3$): ν_{max} 3004, 2957, 2928, 2853, 1612, 1513, 1464, 1378, 1247, 1173, 1036 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.25 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 6.36 (d, J = 19.0 Hz, 1H), 5.95 (dd, J

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= 19.0, 5.1 Hz, 1H), 4.44 (s, 2H), 3.98 (t, J = 7.3 Hz, 1H), 3.81 (s, 3H), 3.73−3.79 (m, 1H), 3.48 (t, J = 5.9 Hz, 2H), 1.61−1.69 (m, 4H), 1.42−1.48 (m, 8H), 1.41 (s, 3H), 1.38 (s, 3H), 1.26−1.31 (m, 10H), 0.88−0.93 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0, 144.8, 134.1, 130.6, 129.1, 113.6, 108.3, 85.3, 80.2, 80.4, 72.4, 69.7, 55.1, 29.1, 29.0, 28.5, 27.3, 27.1, 26.9, 26.1, 13.6, 11.1, 10.6, 10.1, 9.4, 8.8. Anal. Calcd for $C_{30}H_{52}O_4Sn$ (595.43): C, 60.51; H, 8.80; Sn, 19.94. Found: C, 60.73; H, 8.64; Sn, 20.12.

4-(2-Iodovinyl)-5-[3-(4-methoxybenzyloxy)-propyl]-2,2-dimethyl-[1,3]dioxolane (12). To a cooled (0 °C), stirred solution of **11** (250 mg, 0.42 mmol) in CH_2Cl_2 (15 mL) was added iodine (213 mg, 0.84 mmol). After 10 min at 0 °C, the reaction mixture was diluted with CH_2Cl_2 and washed with saturated $Na_2S_2O_3$ and 10% KF solutions, and brine. The organic layer was dried (Na_2SO_4), filtered, and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (9.5:0.5) as eluent gave **12** (174 mg, 96%) as a yellowish oil. $[\alpha]^{25}_D$ +7.6 (c 1.1, $CHCl_3$). IR ($CHCl_3$): ν_{max} 2946, 2932, 2856, 1612, 1513, 1465, 1372, 1174, 1092, 947 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.29 (d, J = 8.6 Hz, 2H), 6.53 (d, J = 8.7 Hz, 2H), 6.29 (m, 2H), 4.44 (s, 2H), 3.94−4.01 (m, 1H), 3.81 (s, 3H), 3.63−3.76 (m, 1H), 3.47 (t, J = 5.8 Hz, 2H), 1.61−1.78 (m, 4H), 1.40 (s, 3H), 1.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.4, 147.6, 129.5, 128.6, 114.0, 101.7, 86.5, 81.6, 75.8, 74.3, 70.1, 56.2, 28.8, 26.2, 25.5. Anal. Calcd for $C_{18}H_{25}IO_4$ (432.29): C, 50.01; H, 5.83, I, 29.36. Found: C, 50.42; H, 5.75, I, 30.01.

2-(1-Methoxymethoxyheptyl)-oxirane (19). A solution of hydroxy epoxide **18** (2.1 g, 13.27 mmol) and DIPEA (6.8 mL, 39.30 mmol) in dry CH_2Cl_2 (50 mL) was treated under argon with MOM chloride (1.27 g, 1.2 mL, 15.77 mmol) at 0 °C and the reaction mixture was stirred for 6 h at room temperature. The reaction was quenched by addition of water and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was washed with brine, dried (Na_2SO_4), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (9:1) as eluent gave **19** (2.63 g, 98%) as a colorless oil. $[\alpha]^{25}_D$ +4.2 (c 1.1, $CHCl_3$). IR (neat): ν_{max} 2943, 2859, 1615, 1518, 1244, 1132, 1030 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.71 (s, 2H), 3.75−3.80 (q, J = 10.9 Hz, 1H), 3.64−3.71 (m, 2H), 3.57 (dd, J = 10.9, 5.8 Hz, 1H), 3.42 (s, 3H), 1.53−1.63 (m, 2H), 1.29−1.36 (m, 8H), 0.89 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.9, 22.4, 25.2, 29.2, 30.7, 31.6, 45.9, 55.8, 72.7, 79.2, 96.8. Anal. Calcd for $C_{11}H_{22}O_3$ (202.29): C, 65.31; H, 10.96. Found: C, 65.64; H, 11.01.

1-{5-[3-(4-Methoxybenzyloxy)-propyl]-2,2-dimethyl-[1,3]-dioxolan-4-yl}-5-methoxymethoxy-undec-1-yn-4-ol (21). To a solution of acetylene **10** (0.8 g, 2.63 mmol) in THF (20 mL) was added n-BuLi (1.6 M solution in hexane) (1.8 mL, 2.88 mmol) at −78 °C and the reaction mixture was stirred for 10 min. Then, $BF_3{\cdot}Et_2O$ (2.89 mmol, 0.36 mL) was added to the reaction mixture and stirring was continued for 10 min at −78 °C. Finally a solution of epoxide **19** (354 mg, 1.75 mmol) in THF (2 mL) was added, and after stirring for 30 min at −78 °C, the reaction was quenched by adding aqueous ammonium chloride. After the two layers were separated, the aqueous layer was extracted with EtOAc (3 × 20 mL) and the combined organic layer was washed with brine, dried (Na_2SO_4), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (8:2) as eluent gave compound **21** (789 mg, 89%) as a yellowish liquid. $[\alpha]^{25}_D$ +10.3 (c 1.24, $CHCl_3$). IR ($CHCl_3$): ν_{max} 3414, 3019, 2933, 2860, 2400, 1612, 1513, 1465, 1372, 1216, 1097, 757 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.2 Hz, 2H), 4.65 (s, 2H), 4.44 (s, 2H), 4.23 (d, J = 7.8 Hz, 1H), 3.96 (dt, J = 7.8, 4.6 Hz, 1H), 3.78 (s, 3H), 3.77 (dt, J = 5.5, 1.9 Hz, 1H), 3.64 (dt, J = 6.0, 1.9 Hz, 1H), 3.47−3.50 (m, 2H), 3.41 (s, 3H), 2.72 (br s, 1H), 2.44−2.49 (m, 1H), 2.39 (ddd, J = 15.1, 7.8, 1.4 Hz, 1H), 1.63−1.80 (m, 6H), 1.44 (s, 3H), 1.39 (s, 3H), 1.26−1.31 (m, 8H), 0.89 (t, J = 6.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 131.5, 130.6, 129.11, 113.72, 113.54, 109.3, 96.8, 83.6, 81.4, 80.7, 78.8, 72.4, 71.6, 70.1, 69.6, 55.7, 55.1, 31.6, 30.7, 29.29, 28.97, 27.0, 26.2, 25.90, 25.24, 24.0, 22.5, 13.9. Anal. Calcd for $C_{29}H_{46}O_7$ (506.67): C, 68.74; H, 9.15. Found: C, 68.81; H, 9.24.

Microcarpalide (1). A stirred solution of compound **26** (40 mg, 0.104 mmol) in CH_2Cl_2 (5 mL) was cooled to 0 °C and treated with $BF_3{\cdot}Et_2O$ (13 μL, 0.104 mmol), and ethanedithiol (38 μL, 0.45 mmol). The resulting mixture was stirred at 0 °C for 1 h and then quenched with aqueous $NaHCO_3$, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. Silica gel column chromatography of the crude product using EtOAc as eluent gave microcarpalide **1** as a yellow syrupy liquid (28 mg, 88%) and a 3.2:1 (as judged by ^{1}H NMR spectra) mixture of conformers. $[\alpha]^{25}_D$ −23.4 (c 0.9, MeOH); [lit.[1,2a] −22.0 (c 0.67, MeOH)]. IR (neat): 3370, 2922, 2863, 1711, 1430, 1226, 1153, 1067. ^{1}H NMR (500 MHz, CD_3CN): δ 5.69 (dd, J = 15.5, 2.5 Hz, 1H), 5.50 (dddd, J = 15.6, 9.9, 5.1, 2.1 Hz, 1H), 4.81 (ddd, J = 11.1, 4.8, 3.3 Hz, 1H), 4.11 (br, 1H), 3.78 (br, 1H), 3.54 (br m, 1H), 3.08 (br d, 1H), 2.85 (br m, 2H), 2.47−2.50 (m, 1H), 2.15−2.25 (m, 2H), 1.98−2.14 (m, 2H), 1.77−1.93 (m, 1H), 1.38−1.44 (m, 2H), 1.29−1.36 (m, 8H). 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, CD_3CN, observed as a mixture of two conformers): δ 176.3, 174.1, 134.5, 126.6, 79.7, 73.5, 72.8, 72.3, 36.7, 34.2, 32.5, 29.9, 26.4, 26.1, 23.3, 14.4.

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Supporting Information Available: The spectroscopic data and full experimental procedure for compounds **3**, **4**, **6**, **7**, **9**, **10**, **14**−**18**, **20**, **22**−**24, 26**, and ^{1}H and ^{13}C NMR spectra of compounds **4**, **5**, **9**−**11**, **17**−**19**, **21**, **22**, **26**, and microcarpalide **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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