First Stereoselective Total Synthesis of Oplopandiol

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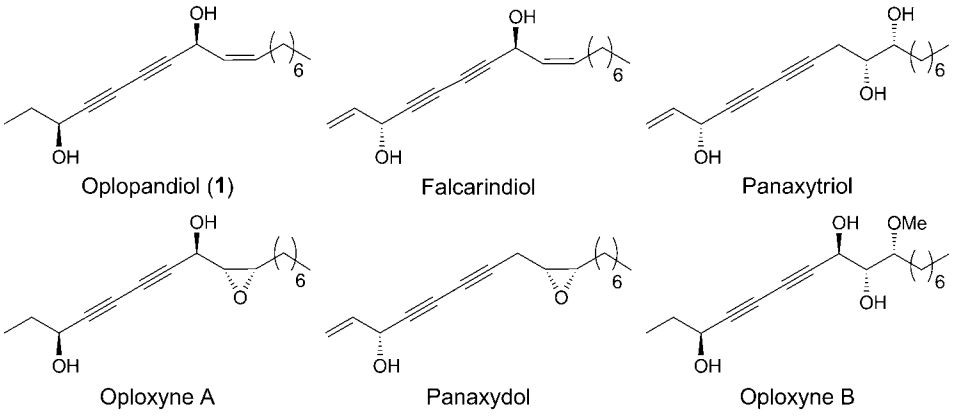
The first stereoselective synthesis of the naturally occurring conjugated diyne oplopandiol is reported. The pivotal functionalities are derived from *Cadiots–Chodkiewicz* cross-coupling reaction, *Ohira–Bestmann* alkynation, asymmetric *Noyori* reduction, and *cis*-olefination reaction

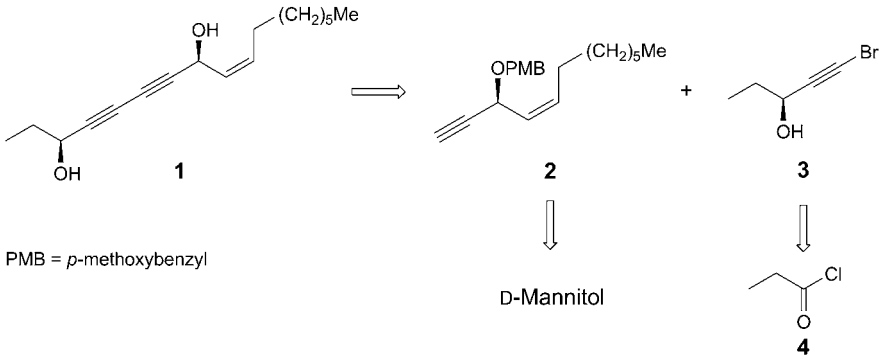
Introduction. – Several natural conjugated acetylenic compounds such as oplopandiol (**1**), falcarindiol, panaxytriol, panaxydol, and oploxynes A and B posses excellent biological activities [1] including antibacterial, antituberculosis, anticancer, antiviral, and pesticidal properties. Chinese and Koreans widely used *Oplopanax elatus* NAKAI in traditional medicine for analgesic and anti-inflammatory purposes [2][3]. *Kobaisy et al.* in 1997 first reported the isolation of oplopandiol (**1**) from *Oplopanax horridus*, a medicinal plant from North America [4]. Later, in 2010 *Yang et al.* reported the isolation of **1** and other conjugated diynes from the stem of *Oplopanax elatus* [5]. Falcarindiol, oplopandiol (**1**), and oploxynes A and B show promising anti-inflammatory activities and inhibit the formation of nitric oxide (NO) and prostaglandin E_2 (PGE_2) in lipopolysaccharide (LPS)-induced murine macrophage RAW 267.7 cells. Oplopandiol (**1**) shows IC_{50} values of 2.72 ± 0.10 and 2.9 ± 0.37 (NO and PGE_2), resp. and also exhibited moderate cytotoxic and antimycobacterial properties. The absolute configuration of **1**, *i.e.*, (3*S*,8*S*,9*Z*)-heptadec-9-ene-4,6-diyne-3,8-diol, was determined by spectroscopic methods [4–6].



In continuation of our ongoing program [7] towards the total synthesis of biologically active natural products, herein we describe the first stereoselective total synthesis of **1**. In 2000, *Xu et al.* reported the synthesis of oplopandiol acetate *via Cadiots–Chodkiewicz* cross-coupling reaction as a common key step [8].

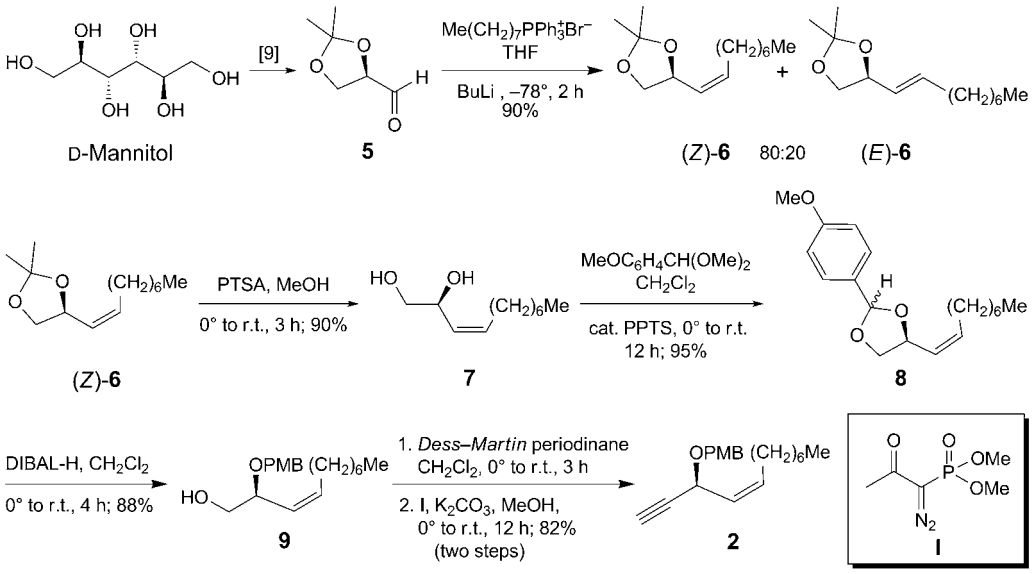
Results and Discussion. – Our synthetic approach for oplopandiol (**1**) was envisioned through the retrosynthetic strategy as depicted in *Scheme 1*. Accordingly, we proposed that **1** could be derived from coupling of the two key fragments **2** and **3** by the *Cadiot–Chodkiewicz* cross-coupling. The alkyne key fragment **2** could be obtained by *Ohira–Bestmann* alkynation, regioselective reduction of 4-methoxybenzaldehyde acetal and *cis-Wittig* olefination of D-glyceraldehyde (**5**), which could be obtained from commercially available D-mannitol. The preparation of the other key fragment **3** was planned *via* asymmetric *Noyori* reduction of a pent-1-yn-3-one derivative, which can be prepared from propionyl chloride (**4**).

Scheme 1. *Retrosynthetic Scheme for Oplopandiol* (**1**)



The synthesis of key fragment **2** started from readily available D-mannitol utilizing a chiral-pool approach. It can be easily converted into **5** by using a well-known method [9] (*Scheme 2*). *Olefination of* D-*glyceraldehyde* (**5**) *upon treatment with* $Me(CH_2)_7PPh_3^+Br^-$ *in the presence of BuLi at* $-78°$ *for 2 h afforded* (*Z*)-**6** and (*E*)-**6** in 90% combined yield with a high diastereoselectivity [10] ((*Z*)/(*E*) 80:20; ^{1}H-NMR). The less polar major (*Z*)-alkene (*Z*)-**6** was easily separated by flash column chromatography and obtained in 72% yield, and the minor (*E*)-alkene (*E*)-**6** in 18% yield. Subsequently, deprotection of the acetonide by using PTSA (*p*-toluenesulfonic acid) in MeOH at room temperature for 3 h afforded diol **7** in 90% yield. The latter was converted to the corresponding anisidine acetal **8** in 95% yield by treating with 4-methoxybenzaldehyde acetal and catalytic amounts of PPTS (pyridinium *p*-toluenesulfonate) in CH_2Cl_2 for 12 h at room temperature. Regioselective reduction of **8** by using DIBAL-H (= diisobutylaluminium hydride) in CH_2Cl_2 at room temperature for 4 h afforded primary alcohol **9** in 88% yield [11]. Next, compound **9** was treated with *Dess–Martin* periodinane in CH_2Cl_2 at room temperature for 3 h to afford an aldehyde, which, on subsequent alkyne homologation by using *Ohira–Bestmann*

Scheme 2. *Synthesis of Fragment* **2**



reagent **I** and K_2CO_3 in MeOH at room temperature for 12 h gave the required key intermediate alkyne **2** in 82% overall yield for two steps [12] (*Scheme 2*).

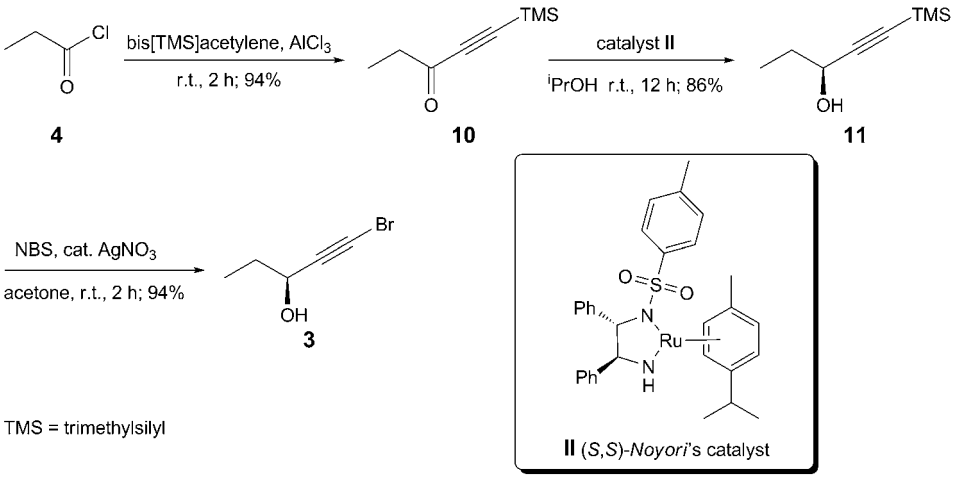
The other key fragment, bromo alkynol **3**, was synthesized from propanoyl chloride (**4**), which can be smoothly converted to alkynone **10**, in 94% yield, by the reaction with bis(trimethylsilyl)acetylene and $AlCl_3$ in dry CH_2Cl_2 at room temperature for 2 h (*Scheme 3*). Stereoselective reduction of **10** using the *Noyori* catalyst [RuCl((*S*,*S*)-TsDPEN)(*p*-cymene)] (TsDPEN = *N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine; **II**) in ^{i}PrOH at room temperature for 12 h afforded **11** with high enantioselectivity and in 86% yield [13]. Desilylation and subsequent bromination of **11** using NBS (*N*-bromosuccinimide) and catalytic amount of $AgNO_3$ in acetone at room temperature for 2 h afforded **3** in 94% yield [14] (*Scheme 3*).

Thus, compound **2** was cross-coupled with bromo alkynol **3** under *Cadiot–Chodkiewicz* conditions to afford diynol **12** in 83% yield [15] (*Scheme 4*). Examining the deprotection of the PMB (*p*-methoxybenzyl) ether by various reaction conditions such as with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) in CH_2Cl_2 and CAN (ceric ammonium nitrate ($(NH_4)_2Ce(NO_3)_6$)) in MeCN led to decomposition. Eventually, the PMB ether was easily converted to the final target molecule **1** by a single deprotection step using TFA (CF_3COOH) in CH_2Cl_2 at room temperature for 15 h **1** in 66% yield [16] (*Scheme 4*).

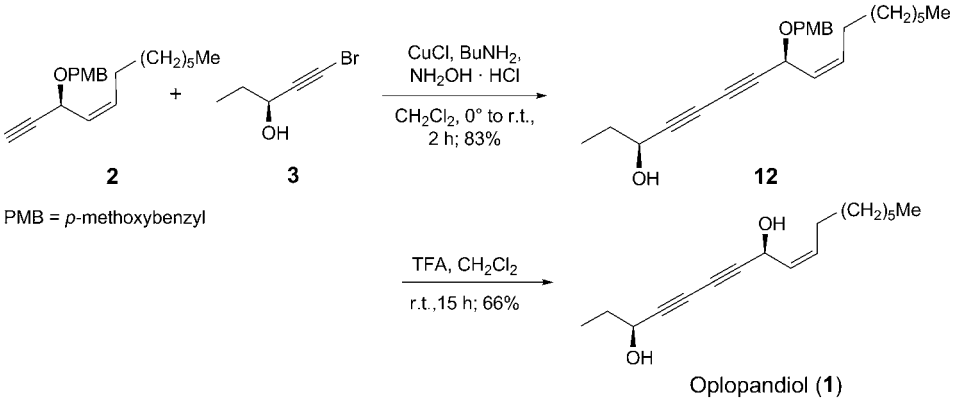
The spectroscopic data of our synthetic compound **1** were compared with the reported data of the isolated natural product and found to be identical. Optical rotation of the synthetic **1**: $[\alpha]_D^{24} = +242$ ($c = 1.3$, MeOH); [5]: $[\alpha]_D^{25} = +248$ ($c = 1.3$, MeOH).

In conclusion, we have achieved a simple, versatile, and efficient stereoselective total synthesis of oplopandiol (**1**). Our synthetic strategy involves asymmetric *Noyori* reduction, (*Z*)-olefination, and *Cadiots–Chodkiewicz* cross-coupling reactions. Further

Scheme 3. *Synthesis of Fragment* **3**



Scheme 4. Cadiot–Chodkiewicz *Cross-Coupling Reaction*



syntheses of conjugated alkyne natural products are in progress and will be disclosed in due course.

B. N. K. thanks *U. G. C.*, New Delhi, for the financial support, and Director of the Indian Institute of Chemical Technology (IICT), for his encouragement.

Experimental Part

General. All solvents and reagents were used as received from the suppliers. TLC: *Merck Kieselgel 60*, F_{254} plates with the layer thickness of 0.25 mm. Column chromatography (CC): silica gel (SiO_2; 100–200 mesh); gradient of AcOEt and hexane as mobile phase. Optical rotations: *JASCO* digital polarimeter. IR Spectra: *Perkin–Elmer RX-1* FT-IR system; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR spectra: at 300 and 500 (^1H), and 75 MHz (^{13}C); δ in ppm rel. to Me_4Si as internal standard, J in Hz. HR-MS: *ORBITRAP* high-resolution mass spectrometer; in m/z.

(4S)-2,2-Dimethyl-4-[(1Z)-non-1-en-1-yl]-1,3-dioxolane ((*Z*)-**6**). To a stirred soln. of $Me(CH_2)_7PPh_3^+Br^-$ (41.90 g, 92.3 mmol) in dry THF (150 ml) at $-78°$ under N_2 was added slowly BuLi (33.23 ml, 83.07 mmol, 2.5M), and the mixture was stirred for 30 min at the same temp. Then, a soln. of D-glyceraldehyde (6 g, 46.25 mmol) in dry THF (50 ml) was transferred *via* cannula to the mixture, which was then stirred for 2 h at $-78°$. The reaction was quenched with sat. aq. NH_4Cl (50 ml). The org. layer was separated, and the aq. layer was extracted with AcOEt (3 × 100 ml). The combined org. layers were washed with H_2O (1 × 100 ml), and brine (1 × 100 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by CC (SiO_2 (100–200 mesh); 2% AcOEt in hexane) to afford the less polar major (*Z*)-**6** (7.50 g, 72%) as a colorless oil, along with the more polar minor (*E*)-**6** (1.88 g, 18%). Colorless oil.

Data of (Z)-**6**. $[\alpha]_D^{24} = +6.0$ ($c = 3.0$, $CHCl_3$). IR (neat): 3323, 2956, 1721, 1461, 1379, 1214, 1061, 861, 867, 723. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.54 (*dt*, *J* = 10.5, 7.5, 1 H); 5.34 (*dd*, *J* = 10.5, 8.3, 1 H); 4.74 (*q*, *J* = 7.5, 1 H); 3.97 (*dd*, *J* = 8.3, 6.0, 1 H); 3.42 (*t*, *J* = 8.3, 1 H); 2.17–1.96 (*m*, 2 H); 1.40–1.19 (*m*, 16 H); 0.86 (*t*, *J* = 6.7, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 135.2; 126.8; 109.0; 71.9; 69.4; 31.7; 29.5; 29.1; 25.9; 27.7; 26.7; 25.9; 22.6; 14.0. ESI-MS: 249 ($[M + Na]^+$).

(2S,3Z)-Undec-3-ene-1,2-diol (**7**). To a stirred soln. of (*Z*)-**6**) (5 g, 22.12 mmol) in MeOH (50 ml) was added cat. PTSA and stirred for 3 h at r.t. The reaction was quenched with sat. aq. $NaHCO_3$ (20 ml), and the mixture was extracted with CH_2Cl_2 (3 × 60 ml). The combined org. extracts were washed with H_2O (1 × 60 ml) and brine (1 × 60 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by CC (SiO_2 (100–200 mesh); 25% AcOEt in hexane) to afford **7** (3.7 g, 90%). Colorless oil. $[\alpha]_D^{24} = +3.5$ ($c = 6.0$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 5.57 (*dt*, *J* = 11.0, 7.7, 1 H); 5.35 (*dd*, *J* = 11.0, 8.8, 1 H); 4.54 (*td*, *J* = 8.8, 3.3, 1 H); 3.55 (*dd*, *J* = 11.0, 3.3, 1 H); 3.47 (*dd*, *J* = 11.0, 7.7, 1 H); 3.0 (br. *s*, OH, 1 H); 2.18–2.03 (*m*, 2 H); 1.43–1.14 (*m*, 10 H); 0.88 (*t*, *J* = 6.6, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 134.0; 128.0; 68.7; 66.3; 31.9; 29.7; 29.32; 29.27; 28.0; 22.7; 14.2. ESI-MS: 186 (M^+).

(4S)-2-(4-Methoxyphenyl)-4-[(1Z)-non-1-en-1-yl]-1,3-dioxolane (**8**). To a stirred soln. of **7** (3.70 g, 19.9 mmol) and dist. *p*-methoxybenzaldehyde acetal (3.7 ml, 21.8 mmol) in dry CH_2Cl_2 (50 ml) was added PPTS (0.225 g, 0.99 mmol) at 0° under N_2. Then, the mixture was stirred for 12 h at r.t. The reaction was quenched with Et_3N (0.2 ml), and the mixture was concentrated under reduced pressure. The residue was purified by CC (SiO_2 (100–200 mesh); 2% AcOEt in hexane) to yield **8** (5.74 g, 95%). Colorless oil. $[\alpha]_D^{24} = -3.7$ ($c = 3.2$, $CHCl_3$). IR (neat): 3446, 2922, 2852, 1613, 1513, 1247, 1037, 830, 724. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.40–7.30 (*m*, 2 H); 6.84 (*d*, *J* = 8.6, 2 H); 5.87 (*s*, 0.5 H); 5.75 (*s*, 0.5 H); 5.62 (*dt*, *J* = 10.9, 7.3, 1 H); 5.49 (*dd*, *J* = 10.9, 8.4, 1 H); 4.94–4.82 (*m*, 1 H); 4.23 (*dd*, *J* = 7.9, 6.4, 0.5 H); 4.06 (*t*, *J* = 7.1, 0.5 H); 3.8 (*s*, 3 H); 3.64–3.51 (*m*, 1 H); 2.25–1.99 (*m*, 2 H); 1.54–1.20 (*m*, 10 H); 0.85 (*t*, *J* = 6.7, 3 H); ^{13}C-NMR (75 MHz, $CDCl_3$): 160.3; 160.2; 135.31; 135.28; 130.4; 129.9; 128.0; 127.7; 126.8; 126.7; 113.6; 104.1; 103.4; 73.1; 72.1; 70.8; 70.0; 55.2; 31.7; 29.5; 29.1; 27.8; 27.7; 22.6; 14.0. ESI-MS: 327 ($[M + Na]^+$). HR-ESI-MS: 327.1950 ($[M + Na]^+$, $C_{19}H_{28}NaO_3^+$; calc. 327.1936).

(2S,3Z)-2-[(4-Methoxybenzyl)oxy]undec-3-en-1-ol (**9**). To a stirred soln. of **8** (4 g, 13.15 mmol) in dry CH_2Cl_2 (60 ml) at 0° under N_2 was added slowly DIBAL-H (12.33 ml, 1.6M in toluene, 19.73 mmol) dropwise, the mixture was and stirred for 15 min at the same temp. and then for 4 h at r.t. The reaction was quenched with sat. sodium potassium tartrate soln. (10 ml), and the mixture was stirred for 2 h at r.t. The org. layer was separated, and the aq. layer was extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were washed with H_2O (1 × 20 ml), and brine (1 × 20 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by flash CC (SiO_2 (100–200 mesh); 10% AcOEt in hexane) to afford **9** (3.54 g, 88%). Colorless oil. $[\alpha]_D^{24} = +25.0$ ($c = 2.5$, $CHCl_3$). IR (neat): 3446, 2952, 2854, 1612, 1513, 1462, 1247, 1037, 822, 756. ^{1}H-NMR: (300 MHz, $CDCl_3$): 7.25–7.16 (*m*, 2 H); 6.87–6.78 (*m*, 2 H); 5.68 (*dt*, *J* = 10.5, 7.5, 1 H); 5.27 (*dd*, *J* = 10.5, 9.0, 1 H); 4.52 (*t*, *J* = 11.3, 1 H); 4.26 (*d*, *J* = 10.5, 2 H); 3.78 (*s*, 3 H); 3.56–3.26 (*m*, 2 H); 2.32 (br. *s*, OH, 1 H); 2.12–1.96 (*m*, 2 H); 1.44–1.19 (*m*, 10 H); 0.87 (*t*, *J* = 6.7, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 159.1; 136.1; 130.3; 129.4; 126.5; 113.7; 75.0; 69.8; 65.1; 55.1; 31.7; 29.6; 29.2; 29.1; 27.9; 22.5; 14.0. ESI-MS: 329 ($[M + Na]^+$). HR-ESI-MS: 329.2105 ($[M + Na]^+$, $C_{19}H_{30}NaO_3^+$; calc. 329.2092).

1-{[(3S,4Z)-Dodec-4-en-1-yn-3-yloxy]methyl}-4-methoxybenzene (**2**). To a stirred soln. of **9** (3 g, 9.80 mmol) in dry CH_2Cl_2 (40 ml) at 0° under N_2 was added *Dess–Martin* periodinane (5.1 g,

11.79 mmol), and then the resulting mixture was stirred for 3 h at r.t. The reaction was quenched with aq. $Na_2S_2O_3$ (5 ml). The org. layer was separated, and the aq. layer was extracted with CH_2Cl_2 (3 × 40 ml). The combined org. extracts were washed with H_2O (1 × 40 ml), and brine (1 × 40 ml), dried (Na_2SO_4), filtered, and concentrated to afford a crude aldehyde as colorless oil, which was used in the next step without purification. To the resulting crude aldehyde, dissolved in dry MeOH (12 ml), *Ohira–Bestmann* reagent **I** (2.35 g, 12.2 mmol) and K_2CO_3 (2.7 g, 19.6 mmol) were added, and the mixture was stirred at r.t. for 10 h under N_2. The solvent was evaporated in *vacuo*, the residue was diluted with H_2O and extracted with $CHCl_3$ (3 × 30 ml). The combined org. layers were washed H_2O (1 × 30 ml), and brine (1 × 30 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by flash CC (SiO_2 (100–200 mesh); 12% AcOEt in hexane) to afford **2** (2.04 g, 82%). Colorless oil. $[\alpha]_D^{24} = -2.0$ (c = 1.0, $CHCl_3$). IR (neat): 3432, 2922, 2852, 1733, 1513, 1463, 1249, 1038, 756. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.28–7.20 (*m*, 2 H); 6.85–6.79 (*m*, 2 H); 5.60–5.45 (*m*, 2 H); 4.74 (*dd*, *J* = 7.4, 1.8, 1 H); 4.58 (*d*, *J* = 11.5, 1 H); 4.47 (*d*, *J* = 11.5, 1 H); 3.78 (*s*, 3 H); 2.41 (*d*, *J* = 2.0, 1 H); 2.0 (*q*, *J* = 6.7, 2 H); 1.42–1.16 (*m*, 10 H); 0.88 (*t*, *J* = 6.7, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 159.3; 134.6; 129.7; 129.3; 126.8; 113.8; 82.3; 73.6; 69.4; 63.4; 55.2; 31.8; 29.23; 29.16; 29.1; 27.7; 22.6; 14.1. ESI-MS: 323 ([M + Na]$^+$). HR-ESI-MS: 323.2001 ([M + Na]$^+$, $C_{20}H_{28}NaO_2^+$; calc. 323.1987).

1-(Trimethylsilyl)pent-1-yn-3-one (**10**). To a stirred soln. of bis(trimethylsilyl)acetylene (3.0 g, 17.64 mmol)) and propanoyl chloride (4; 1.67 ml, 17.64 mmol) in dry CH_2Cl_2 (60 ml) at 0° under N_2, a soln. of $AlCl_3$ (2.34 g, 17.64 mmol) in dry CH_2Cl_2 (30 ml) was added *via* cannula, and the mixture, was then stirred for 2 h at r.t. After completion of the reaction, the mixture was cooled to 0°, and then reaction was quenched with 1N HCl (20 ml). The org. layer was separated, and the aq. layer was extracted with CH_2Cl_2 (3 × 30 ml). The combined org. extracts were washed with H_2O (1 × 30 ml), and brine (1 × 30 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by CC (SiO_2 (100–200 mesh); 5% AcOEt in hexane) to afford **10** (2.5 g, 94%). Yellow oil. IR (neat): 2964, 2904, 2150, 1733, 1679, 1459, 1411, 1346, 1253, 1195, 1130, 1051, 962, 850, 761. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.56 (*q*, *J* = 7.5, 2 H); 1.13 (*t*, *J* = 7.5, 3 H); 0.23 (*s*, 9 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 186.9; 102.1; 96.5; 38.5; 7.9; −0.6. ESI-MS: 154 (M^+).

(3S)-1-(Trimethylsilyl)pent-1-yn-3-ol (**11**). To a dried two-neck round bottom flask containing dichloro(*p*-cymene)ruthenium(II) dimer (43 mg, 0.07 mmol), (+)-(1*S*,2*S*)-*N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine (51 mg, 0.140 mmol), and KOH (56.25 mg, 1.0 mmol) were added, followed by addition of 3 ml of dry CH_2Cl_2. After stirring for 5 min, the color of the orange soln. turned to purple. Then, 2.25 ml of H_2O and 2 ml of CH_2Cl_2 were added to the mixture. The CH_2Cl_2 layer was separated and washed again with 2 ml of H_2O. The CH_2Cl_2 layer was dried (CaH_2), filtered, and evaporated to afford [(*S*,*S*)-TsDPEN)Ru(*p*-cymene)]Cl_2 (**II**) as dark purple crystals. Catalyst **II** (70 mg, 0.11 mmol) was dissolved in 15 ml of degassed ^{i}PrOH at r.t. under N_2. To this soln. was added a soln. of **9** (4 g, 25.9 mmol), dissolved in ^{i}PrOH (5 ml), during 1 h using a syringe pump. The mixture was allowed stirred for an additional 12 h, and the solvent was evaporated under reduced pressure. The residue was purified by CC (SiO_2 (100–200 mesh); 10% AcOEt in hexane) to afford **11** (3.5 g, 86%). Colorless oil. $[\alpha]_D^{24} = -5.9$ (c = 2.0, $CHCl_3$). IR (neat): 3338, 2964, 2173, 1736, 1464, 1409, 1336, 1251, 1118, 1016, 968, 846, 759. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.20 (*t*, *J* = 6.9, 1 H); 2.34 (br. *s*, OH, 1 H); 1.72–1.60 (*m*, 2 H); 1.02–0.92 (*m*, 3 H); 0.14 (*s*, 9 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 107.0; 89.2; 63.9; 30.7; 9.5; −0.01. ESI-MS: 156 (M^+).

(3S)-1-Bromopent-1-yn-3-ol (**3**). To a stirred soln. of **11** (204 mg, 1.32 mmol) in acetone (3 ml), NBS (353 mg, 1.98 mmol) and $AgNO_3$ (45 mg, 0.26 mmol) were added. The mixture was stirred for 2 h at r.t., cooled to 0°, with cold H_2O, and extracted with Et_2O (3 × 10 ml). The combined org. extracts were washed with H_2O (1 × 10 ml) and brine (1 × 10 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by CC (SiO_2; 100–200 mesh); 5% AcOEt in hexane) to afford **3** (200 mg, 94%). Colorless oil. $[\alpha]_D^{24} = -9.3$ (c = 0.5, $CHCl_3$). IR (neat): 3338, 2964, 2173, 1736, 1464, 1409, 1336, 1251, 1118, 1016, 968, 846, 759. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.32 (*t*, *J* = 6.6, 1 H); 1.78–1.72 (*m*, 2 H); 1.02 (*t*, *J* = 6.6, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 80.9; 64.4; 44.8; 30.6; 9.3. ESI-MS: 163 (M^+).

(3S,8S,9Z)-8-[(4-Methoxybenzyl)oxy]heptadec-9-ene-4,6-diyn-3-ol (**12**). To a stirred soln. of **2** (50 mg, 0.16 mmol) in MeOH (3 ml), CuCl (1.2 mg, 0.012 mmol), $NH_2OH \cdot HCl$ (11 mg, 0.16 mmol),

and $BuNH_2$ (2 ml) were added at r.t. A soln. of **3** (32.4 mg, 0.19 mmol) in CH_2Cl_2 was added dropwise to the mixture at 0° during 1 h using a syringe pump, and the mixture was stirred at 0°. The reaction was quenched by H_2O, extracted with CH_2Cl_2 (3×10 ml). The combined org. extracts were washed with H_2O (1×10 ml) and brine (1×10 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by CC (SiO_2 (100–200 mesh); 10% AcOEt in hexane) to afford **12** (50 mg, 83%). Colorless oil. $[\alpha]_D^{24} = +2.8$ ($c = 1.0$, $CHCl_3$). IR (neat): 3443, 2952, 2854, 1612, 1513, 1461, 1247, 1037, 822, 754. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.33–7.23 (*m*, 2 H); 6.91–6.84 (*m*, 2 H); 5.63 (*dt*, $J = 10.5$, 7.5, 1 H); 5.51 (*dd*, $J = 10.5$, 8.3, 1 H); 4.88 (*d*, $J = 8.3$, 1 H); 4.63 (*d*, $J = 12.0$, 1 H); 4.48 (*d*, $J = 12.0$, 1 H); 4.38 (*t*, $J = 6.0$, 1 H); 3.8 (*s*, 3 H); 2.03–1.93 (*m*, 2 H); 1.81–1.70 (*m*, 2 H); 1.65 (br. *s*, OH, 1 H); 1.39–1.19 (*m*, 10 H); 1.02 (*t*, $J = 7.5$, 3 H); 0.88 (*t*, $J = 6.7$, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 159.3; 135.1; 129.8; 129.3; 125.9; 113.8; 80.1; 77.9; 69.7: 69.6; 69.0; 64.0; 63.9; 55.2; 31.7; 30.6; 29.1; 29.0; 27.7; 22.6; 14.1; 9.3. ESI-MS: 405 ($[M + Na]^+$). HR-ESI-MS: 405.2420 ($[M + Na]^+$, $C_{25}H_{34}NaO_3^+$; calc. 405.2405).

Oplopandiol (=*(3S,8S,9Z)-Heptadec-9-ene-4,6-diyne-3,8-diol*; **1**). To a stirred soln. of **12** (40 mg, 0.105 mmol) in CH_2Cl_2 (10 ml), TFA (0.015 ml, 0.2 mmol) was added at 0°, and then the mixture was stirred for 15 h at r.t. The soln. was concentrated under reduced pressure, and the resulting residue was purified by CC (SiO_2 (100–200 mesh); 20% AcOEt/hexane) to afford **1** (18 mg, 66%). Colorless oil. $[\alpha]_D^{24} = +242$ ($c = 1.3$, MeOH). IR (neat): 3354, 2925, 2856, 1716, 1652, 1459, 1015, 959, 769. ^{1}H-NMR ($CDCl_3$, 500 MHz): 5.60 (*dtd*, $J = 10.8$, 7.9, 0.9, 1 H); 5.52 (*ddt*, $J = 10.8$, 8.5, 0.9, 1 H); 5.2 (*d*, $J = 8.5$, 1 H); 4.38 (*t*, $J = 5.9$, 1 H); 2.11 (*dq*, $J = 7.9$, 0.9, 2 H); 1.90–1.80 (br. *s*, OH, 1 H); 1.79–1.71 (*m*, 2 H); 1.44–1.35 (*m*, 2 H); 1.33–1.22 (*m*, 8 H); 1.01 (*t*, $J = 7.9$, 3 H); 0.85 (*t*, $J = 6.9$, 3 H); ^{13}C-NMR (75 MHz, $CDCl_3$): 134.6; 127.7; 80.7; 79.2; 68.9; 68.8; 64.0; 58.6; 31.8; 30.6; 29.3; 29.14; 29.09; 27.7; 22.6; 14.1; 9.3. ESI-MS: 285 ($[M + Na]^+$). HR-ESI-MS: 263.2009 ($[M + H]^+$, $C_{17}H_{27}O_2^+$; calc. 263.2011)

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