Accepted Manuscript

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PII: S0040-4020(16)30767-0

DOI: 10.1016/j.tet.2016.08.009

Reference: TET 27990

To appear in: *Tetrahedron*

Received Date: 1 June 2016

Revised Date: 27 July 2016

Accepted Date: 3 August 2016

Please cite this article as: Gangadhar P, Sathish Reddy A, Srihari P, A facile approach for the total synthesis of neurotrophic diyne tetraol petrosiol A and petrosiol E, *Tetrahedron* (2016), doi: 10.1016/j.tet.2016.08.009.

Graphical Abstract

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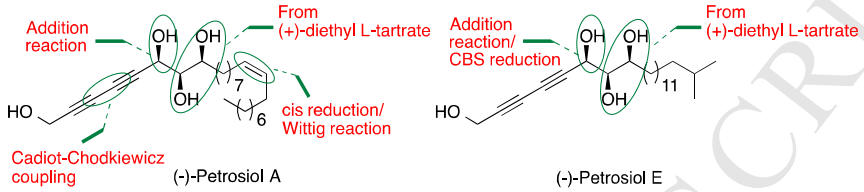

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A facile approach for the total synthesis of neurotrophic diyne tetraol petrosiol A and petrosiol E

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
polyacetylene
neurotrophic
Cadiot Chodkiewicz
Swern oxidation
CBS reduction

ABSTRACT

The first total synthesis of neurotrophic diacetylenic tetraol, petrosiol A and stereoselective total synthesis of petrosiol E was accomplished. The total synthesis involves Cadiot-Chodkiewicz coupling reaction as the key step for petrosiol A. The diastereorich chiral alcohol (third chiral center) was synthesized from CBS mediated stereoselective ketone reduction reaction for petrosiol E. Of the three chiral centers, the two chiral centers are originated from (+)-diethyl L-tartrate and the third chiral center was generated by an addition reaction of lithium trimethylsilylacetylide leading to two diastereomers which were used for the synthesis of both the natural products and their diastereomer C6-*epi*-petrosiol A and C6-*epi*-petrosiol E respectively.

1. Introduction

Polyacetylene containing molecules continue to attract significant attention due to their impressive biological properties such as anti-inflammatory, antimicrobial, antitumor, antiviral, cytotoxic, neurotrophic and phytotoxic properties.[1] For example panaxydol[2] **1** displayed antiproliferative effects against malignant cells and panaxytriol[3] **2** displayed inhibitory activity against MK-1 cells with IC_{50} 8.5 ng/mL. Very often the scarce availability of natural products becomes the bottleneck for investigating their further biological properties, and this challenge can be easily overcome by their total synthesis. For example, our recent attempt for the total synthesis of diacetylene natural products oploxyne A (**3**) and B (**4**) not only lead to the accessibility of the materials but also ended up with structural revision of the natural product oploxyne B.[4] Also, on further investigation these molecules were found to display cytotoxicity against neuroblastoma and prostate cancer cell lines. In continuation to our studies on the total synthesis of natural products and their analogues for CNS activities,[5] we have recently accomplished the first total synthesis of petrosiol D **5**,[6] which was isolated from an extract of the Okinawan sponge *Petrosia strongylata* along with four other acetylene metabolites petrosiol A-C (**6-8**) (Figure 1) and petrosiol E **9** by Ojika et al.[7] In biological aspects, these compounds induced nerve growth factor (NGF)-like neuronal differentiation of PC12 cells and in terms of cytotoxicity, the IC_{50} value of petrosiol A was found to be 5.4 μM in the MTT assay and 0.22 μM for A431(human epidermoid) cell line.[7] So far there have been only two synthetic contributions for petrosiols.

The first contribution was from our own group[6] wherein we have accomplished the total synthesis of petrosiol D in a linear fashion and the second contribution was from Yoguo Du *et al.* wherein they have accomplished the total synthesis of (-)-petrosiol E following a chiron approach starting from D-xylose.[8] Herein, we describe the total synthesis of petrosiol A, petrosiol E and their diastereomers starting from the readily available material (+)-Diethyl L-tartrate.

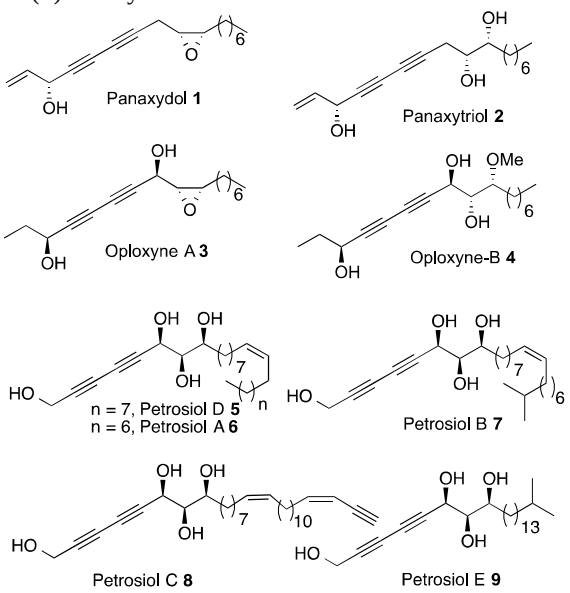

Figure 1: Diacetylene polyol compounds

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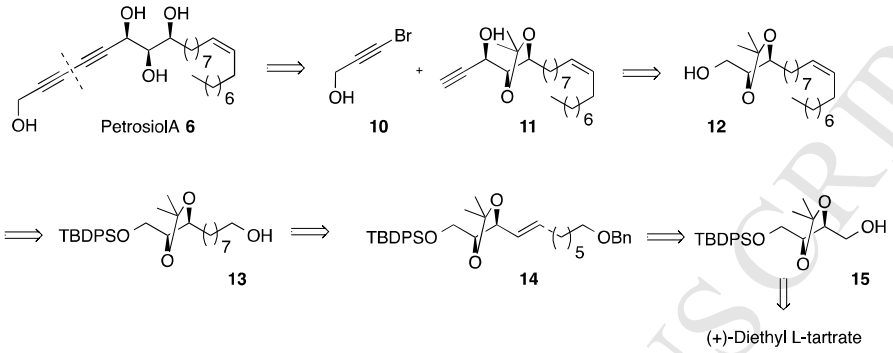
2. Results and discussion

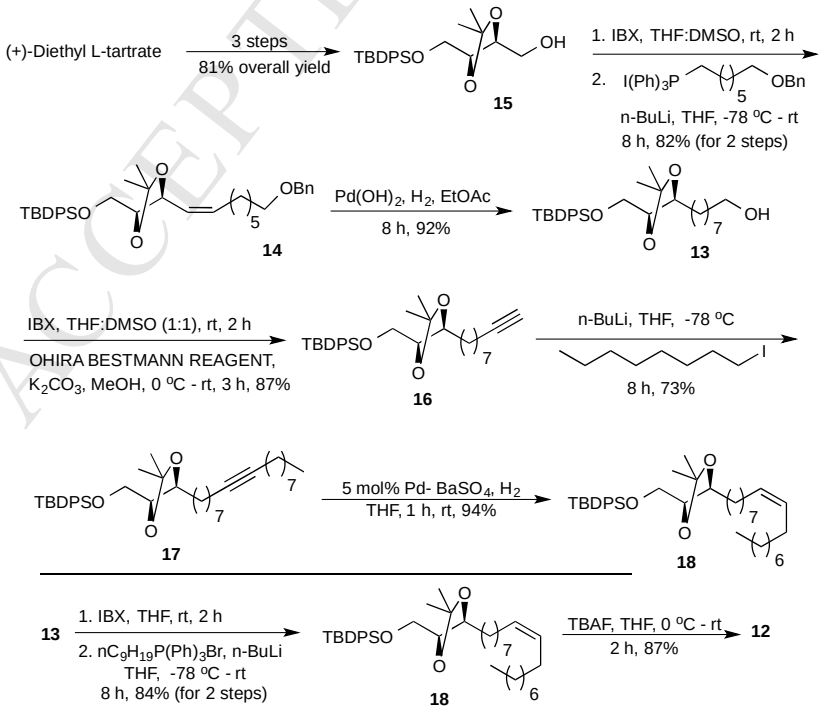
Our retrosynthetic analysis for petrosiol A is depicted in scheme 1. Accordingly, we envisaged the target compound **6** to be synthesized by Cadiot-Chodkiewicz coupling reaction of 3-bromo-2-propyne-1-ol **10** with substituted alkyne **11** followed by acetonide deprotection. The intermediate **11** can be synthesized from alcohol **12** in three steps i.e., oxidation of primary alcohol to aldehyde, an addition reaction with lithium trimethylsilylacetylide followed by trimethylsilyl deprotection. The alcohol **12** in turn can be synthesized from **13** through 5-step sequence i.e., oxidation, Ohira Bestmann reaction, coupling of acetylene with n-iodo octane, Lindlars reduction of triple bond to *cis* double bond and finally TBDPS deprotection or in 3-step sequence i.e., oxidation, 9-carbon Wittig reaction and TBDPS deprotection. Compound **13** can be synthesized from **14** through one pot benzyl deprotection and olefin reduction. Compound **14** in turn can be obtained from known intermediate **15** by an oxidation reaction followed by a 7-carbon Wittig reaction. Compound **15** can be easily accessible from commercially available inexpensive (+)-diethyl L-tartrate.



Scheme 1: Retrosynthesis for petrosiol A

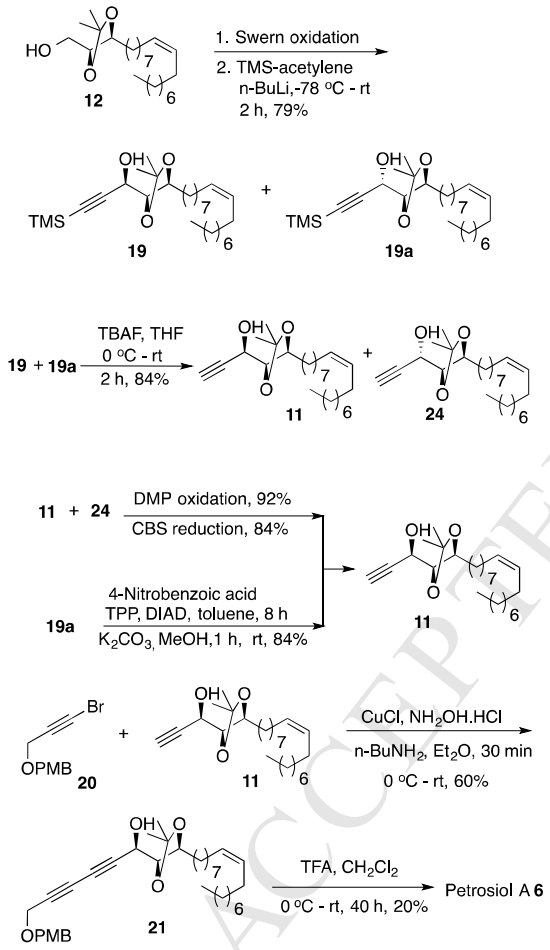
2.1 Synthesis of petrosiol A 6

The synthesis began with the oxidation of the readily available alcohol **15** (synthesized from (+)-diethyl L-tartrate in three steps with an overall yield of 81%)[6,9] employing iodoxybenzoic acid (IBX)[10] to yield the aldehyde which was subjected to a Wittig reaction with 7-(benzyl)oxy-1-heptyl-(triphenyl)phosphonium iodide and n-BuLi to provide the corresponding olefin **14**. One pot debenzylation and double bond saturation was easily achieved with $Pd(OH)_2$ under hydrogen atmosphere to yield the alcohol **13** in 92% yield (Scheme 2). The resulting primary alcohol was further oxidized with IBX to yield aldehyde and was subjected to Ohira-Bestmann reaction to get the terminal acetylene **16**. Coupling of **16** with n-iodo octane afforded disubstituted acetylene **17**. Lindlar's reduction of alkyne **17** afforded *cis* olefin **18** exclusively. Alternatively, **18** was also synthesized in 2-step sequence from **13** through an oxidation reaction (IBX oxidation) followed by the Wittig reaction with (1-nonyl)triphenylphosphonium bromide in presence of n-BuLi to give *cis*-Wittig product **18** exclusively.[11] The compound **18** upon exposure to TBAF furnished desilylated alcohol **12**.



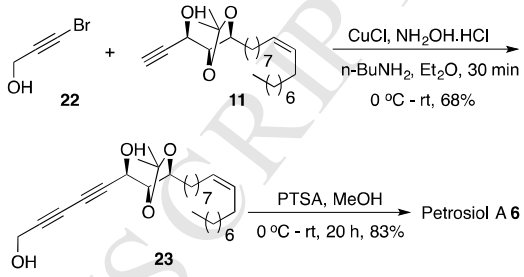
Scheme 2: Synthesis of intermediate **12**.

After constructing the right hand portion of the molecule, we proceeded further for the total synthesis of the molecule. Towards this, the alcohol **12** was oxidized under Swern conditions[12] to yield the corresponding aldehyde and then subjected to an addition reaction with lithium trimethylsilylacetylide to yield the mixture of diastereomers **19** and **19a** without useful level of stereoselectivity (1:1).[13] To obtain diastereorich hydroxy compound, the mixture of **11** and **24** obtained after desilylation of **19** and **19a** with TBAF was oxidized to ketone under Dess-Martin conditions and then subjected to the stereoselective ketone reduction[15] with Corey-Bakshi-Shibata (CBS) catalyst to yield the desired alcohol **19** albeit with poor diastereoselectivity 40% de. Yet this non-selectivity was not an issue as the undesired diastereomer **19a** can be easily converted to the desired compound **11** through a Mitsunobu inversion[14] reaction to improve the overall yield for selected target. Presently, we decided to proceed further with both the diastereomers independently to synthesize the target molecule petrosiol A (Scheme 3,4) and also its diastereomer 6-*epi* petrosiol A (Scheme 5).



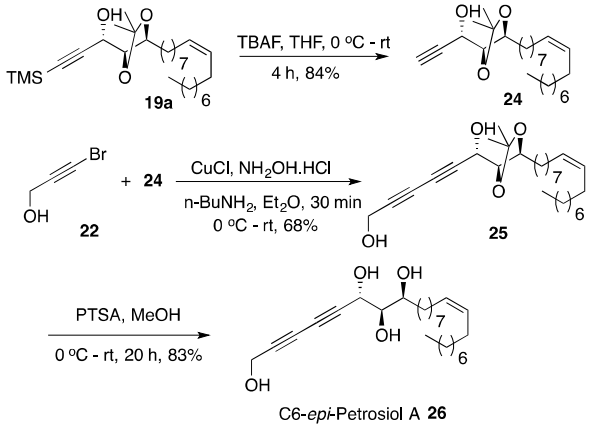
Scheme 3: Synthesis of petrosiol A (**6**) from **20** and **11**.

The geometry of the resulting chiral center for **19** was confirmed relatively after one step ahead based on its conversion to the similarly known intermediate **11** obtained after TMS deprotection.[6] Also, the diastereomer **19** was converted to the final target molecule (vide infra) thus reconfirming the geometry of the chiral center generated. To proceed further, the TMS deprotection in **19** was achieved with TBAF to provide the corresponding propargyl alcohol **11** in 84% yield.[6] Our initial attempts to couple **11** with brominated PMB protected propargyl alcohol **20** under Cadiot-Chodkiewicz conditions[16] provided compound **21** in 60% yield. The spectral properties of **21** was compared with the similar compound synthesized earlier having one extra methylene group in the long chain.[6] Though our attempts for one pot deprotection of PMB group and acetonide moiety with TFA was successful and resulted in petrosiol A, the yield was very poor (20%). Thus, as an alternate, we employed 3-bromoprop-2-yn-1-ol **22** directly to couple with monosubstituted alkyne **11** under Cadiot-Chodkiewicz coupling reaction conditions to furnish the precursor **23**. Compound **23** upon exposure to PTSA in methanol furnished the target compound petrosiol A **6** neatly in 83% yield (Scheme 4). The spectral properties of the synthetic petrosiol A were comparable with that of the reported data for the isolated natural product.[7]



Scheme 4: Synthesis of petrosiol A (**6**) employing **22** and **11**.

After successfully accomplishing the total synthesis of natural product from **19**, the other diastereomer **19a** was also utilized further to synthesize 6-*epi*-petrosiol A **26** following similar set of reactions as used for the synthesis of petrosiol A. Thus, **19a** was treated with TBAF to get the free terminal alkyne **24** and was coupled with **22** under Cadiot-Chodkiewicz coupling reaction condition to furnish precursor **25**, which upon exposure to PTSA methanol provided C6-*epi*-petrosiol A **26** (Scheme 5).

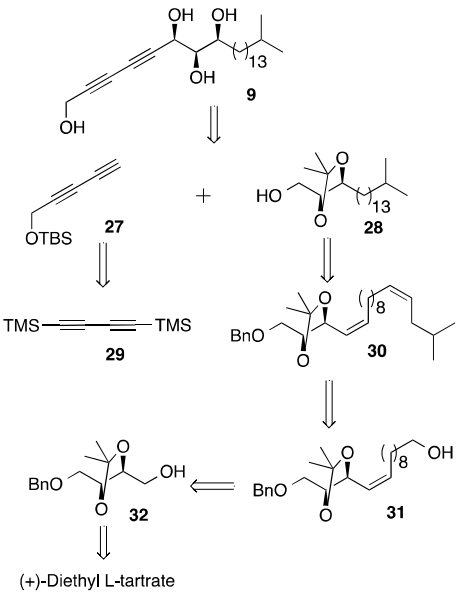


Scheme 5: Synthesis of 6-*epi*-petrosiol A **26**.

2.2 Synthesis of petrosiol E

With the successful accomplishment of first total synthesis of petrosiol A, we turned our attention to another natural product petrosiol E **9**. Once again, we relied on addition reaction of acetylene moiety onto aldehyde to generate mixture of diastereomers towards accessing the natural product along with its diastereomer. Retrosynthetically, petrosiol E **9** was envisaged to be obtained by the addition reaction of terminal acetylene **27** onto the aldehyde (obtained from oxidation of the alcohol **28**) followed by TBS deprotection. While the alcohol **28** can be obtained from the corresponding di-unsaturated benzyl ether **30** through one pot di-olefin reduction and benzyl deprotection, the diacetylene TBS ether **27** can be obtained from commercially

available dialkyne **29**. The compound **30** can be synthesized from **31** through oxidation followed by a Wittig reaction and **31** in turn can be prepared from the common intermediate **32** which is easily accessible from commercially available (+)-diethyl L-tartrate.

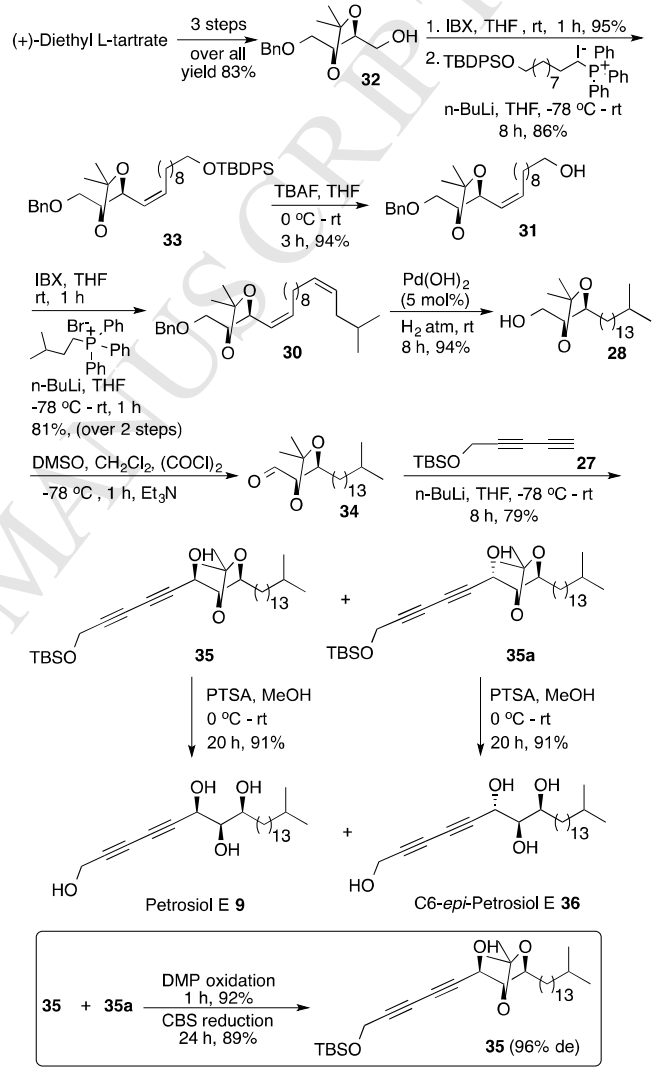


Scheme 6: Retrosynthesis of petrosiol E **9**.

The synthesis starts from known benzyl alcohol **32** easily synthesized from (+)-diethyl L-tartrate in three steps following literature procedures.[17] The alcohol **32** was oxidized with iodoxybenzoic acid (IBX) and then subjected to a Wittig reaction with (10-((*tert*-butyldiphenylsilyl)oxy)decyl)triphenylphosphonium iodide in presence of n-BuLi as the base to yield **33** in 86% yield. TBS deprotection of silyl ether **33** was easily achieved with TBAF to furnish alcohol **31**, which was further subjected to an oxidation reaction with IBX followed by the Wittig reaction with (3-methylbutyl)(triphenyl)phosphonium bromide in presence of n-BuLi afforded the di-unsaturated benzyl ether **30**. The compound **30** on exposure to $Pd(OH)_2$ under hydrogen atmosphere afforded fully saturated and debenzylated alcohol **28**. Compound **28** on oxidation under Swern conditions afforded aldehyde **34**, which was treated with lithium acetylide (obtained by in situ treatment of **27** with n-BuLi) to get the mixture of diastereomeric alcohols (1:1) **35** and **35a** that were separable by silica gel column chromatography (230-400 mesh). The compound **27** was synthesized from bis(trimethylsilyl)butadiyne **29** following known protocol.[18] The diastereo rich chiral compound **35** can be obtained by oxidation of mixture of **35** and **35a** to the corresponding ketone and stereoselective reduction of ketone functionality following Corey's protocol with (*R*)-CBS catalyst (Scheme 7). The two diastereomers were independently utilized further to synthesize the natural product and also its C6-epimer respectively. Thus, compound **35** upon global deprotection by exposing to PTSA in MeOH at 0 ^{o}C afforded natural product petrosiol E. The spectral properties were identical with the data of the isolated natural product.[7] Similarly, the diastereomer **35a** upon exposure to PTSA afforded C6-*epi*-petrosiol E **36**.

3. Conclusion

In conclusion, we have accomplished the total synthesis of the natural products petrosiol A and petrosiol E and also their diastereomers 6-*epi* petrosiol A and 6-*epi* petrosiol E in a simple fashion starting from the readily available raw material (+)-Diethyl L-tartrate. The synthesis of petrosiol A was achieved in 11 steps with an overall yield of 9.04% from the known alcohol **15**. And the synthesis of petrosiol E was achieved in 11 steps with an overall yield of 29.40% from known intermediate **32**. Although CBS catalysis reduction reaction has been successful for petrosiol E to get the third chiral center in the stereoselective manner, the similar attempt for petrosiol A was unsuccessful. The utilization of alkyne addition reaction onto aldehyde enabled us to access both the natural products and their diastereomers. The synthesis of other members and analogues for these compounds for further biological evaluation are currently being investigated in our laboratory.



Scheme 7: Total synthesis of petrosiol E **9** and its C6-epimer **36**.

4. Experimental section

^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or $CDCl_3$+CD_3OD mixture as solvent on 300 MHz or 500 MHz spectrometer at ambient temperature. The coupling constant *J* is given in Hz. The chemical shifts are reported in ppm on scale downfield from TMS as internal standard and signal patterns are indicated as follows: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, q = quartet, qd = quartet of doublet, m = multiplet, br = broad. FTIR spectra were recorded on KBr disc and reported in wave number (cm^{-1}). For

low (MS) and High (HRMS) resolution, *m/z* ratios are reported as values in atomic mass units. Mass analysis was done in ESI mode. Optical rotations were measured on Anton Paar digital polarimeter and the values given are specific rotations. All reagents were reagent grade and used without further purification unless specified otherwise. Solvents for reactions were distilled prior to use: THF, toluene and diethyl ether were distilled from Na and benzophenone ketyl; MeOH from Mg and I_2; CH_2Cl_2 from CaH_2. All air- or moisture-sensitive reactions were conducted under a nitrogen or argon atmosphere in flame-dried or oven-dried glassware with magnetic stirring. Reactions were monitored by thin-layer chromatography carried out on silica plates (silica gel 60 F254, Merck) using UV-light, iodine and anisaldehyde for visualization. Column chromatography was carried out using silica gel (60-120 mesh or 100- 200 mesh) packed in glass columns. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use.

4.1. (7((4*S*,5*S*)-5-((*E*)-8-(Benzyloxy)oct-1-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)(*tert*-butyl)diphenylsilane (14)

To the mono protected alcohol **15** (10.0 g, 25 mmol) dissolved in a solvent mixture THF:DMSO (1:1, 140 mL), was added at once 2-iodoxybenzoic acid (IBX) (10.5 g, 37 mmol) and stirred for 2 h at room temperature. The reaction mixture was diluted with ice cold water (300 mL) and extracted with CH_2Cl_2 (5x100 mL). Combined organic layers were washed with saturated $NaHCO_3$ (250 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure yielded the crude aldehyde (10.0 g, 25.1 mmol), which was directly used for next step without further purification. 7-(Benzyl)oxy-n-heptyl(triphenyl)phosphonium iodide (22.38 g, 37.6 mmol) was dissolved in dry THF (150 mL) and cooled to -78 ^oC. To this n-BuLi (20.4 mL, 32.6 mmol, 1.6 M) was added drop wise and stirred for 3 h at the same temperature. During this time reaction color was changed from colorless to brick red. To this, the crude aldehyde dissolved in anhydrous THF (50 mL) was added drop wise and stirred for overnight after allowing the reaction mixture to warm to room temperature. The reaction mixture was quenched with saturated ammonium chloride (40 mL) at 0 ^oC. The reaction mixture was extracted with ethyl acetate (5x40 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified through silica gel (60-120 mesh) column chromatography to afford compound **14** as colorless liquid (12.01 g, 20.50 mmol, 82% over two steps). R_f = 0.75 (20% EtOAc-Hexane). $[\alpha]^{25}_D$= +6.87 (*c*, 1.5, $CHCl_3$). IR ν_{max}: 2931, 2857, 1719, 1428, 1370, 1030, 822, 606, 702 cm^{-1}. ^{1}HNMR (500 MHz, $CDCl_3$): δ 7.72-7.66 (m, 4H), 7.43-7.32 (m, 11H), 5.66-5.61 (m, 1H), 5.39-5.35 (m, 1H), 4.88 (t, *J* = 8.8 Hz, 1H), 4.49 (s, 2H), 3.83 (dd, *J* =11.4, 3.0 Hz, 1H), 3.72-3.70 (m, 1H), 3.65 (dd, *J* = 11.4, 3.5 Hz, 1H), 3.43 (t, *J* = 6.7 Hz, 2H), 2.24-2.15 (m, 1H), 2.10-1.98 (m, 1H), 1.63-1.55 (m, 2H), 1.50-1.42 (m, 1H), 1.46 (s, 3H), 1.44 (s, 3H), 1.36-1.23 (m, 5H), 1.06 (s, 2H), 1.05 (s, 7H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.67, 136.13, 135.68, 135.60, 133.36, 133.16, 129.65, 129.60, 128.31, 127.62, 127.59, 127.44, 126.37, 108.83, 81.71, 72.84, 70.45, 62.24, 29.74, 29.61, 29.33, 29.18, 27.83, 27.33, 27.02, 26.78, 26.11, 19.23 ppm. MS(ESI): *m/z* 605 $[M+NH_4]^+$. HRMS(ESI) *m/z* calculated for $C_{37}H_{50}O_4NaSi$ 609.33706, found 609.33588.

4.2. 8-((4*S*,5*S*)-5-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)octan-1-ol (13)

To the compound **14** (3.0 g, 5.11 mmol) dissolved in HPLC grade EtOAC (7 mL) was added $Pd(OH)_2$ (75 mg) and the reaction was stirred under H_2 atmosphere for 8 h. The reaction mixture was filtered over celite and concentrated under reduced pressure. The crude product was purified through silica gel (60-120 mesh) column chromatography to afford compound **13** as colorless liquid (2.34 g, 4.70 mmol, 92%). R_f = 0.3 (25% EtOAc-Hexane). $[\alpha]^{25}_D$= -9.33 (*c* 0.6, $CHCl_3$). IR ν_{max}: 3447, 3070, 2984, 2930, 2857, 1590, 1465, 1372, 1109, 822, 703, 607, 505 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.65 (m, 4H), 7.46-7.34 (m, 6H), 3.98-3.92 (m, 1H), 3.76-3.69 (m, 3H), 3.63 (t, *J* = 6.6 Hz, 2H), 1.67-1.52 (m, 4H), 1.40 (s, 3H), 1.37 (s, 3H), 1.36-1.25 (m, 10H), 1.05 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.61, 135.54, 135.49, 129.70, 129.67, 127.83, 127.68, 108.34, 81.10, 78.51, 66.30, 64.21, 63.06, 33.44, 32.78, 29.69, 29.53, 29.48, 29.44, 29.39, 27.42, 26.98, 26.80, 26.60, 25.71, 25.54, 19.21 ppm. HRMS(ESI) *m/z* calculated for $C_{30}H_{46}O_4NaSi$ 521.30576, found 521.30603.

4.3. *tert*-Butyl(((4*S*,5*S*)-2,2-dimethyl-5-(non-8-yn-1-yl)-1,3-dioxolan-4-yl)methoxy)diphenylsilane (16)

To the alcohol **(13)** (1.0 g, 2.0 mmol) dissolved in a solvent mixture THF:DMSO (1:1, 20 mL) was added at once IBX (0.84 g, 3.0 mmol) and the mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with ice-cold water (10 mL) and extracted with CH_2Cl_2 (5x15 mL). Combined organic layers were washed with saturated $NaHCO_3$ (15 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to yield the crude aldehyde (1.0 g, 2.01 mmol) which was directly used for next step without further purification.

The solution of crude aldehyde (1.0 g, 2.01 mmol) in dry methanol (10 mL) was treated with K_2CO_3 (0.41 g, 3.0 mmol). To this mixture was added Ohira-Bestmann reagent i.e., dimethyl-(1-diazo-2-oxopropyl)phosphonate (0.46 g, 2.4 mmol) at room temperature. After 12 h, the reaction mixture was concentrated under reduced pressure and the residue was dissolved in Et_2O, washed sequentially with water (15 mL) and saturated aqueous NaCl (17 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Silica gel column chromatography (60-120 mesh) afforded the alkyne **16** (0.85 g, 87%) as a pale yellow liquid. R_f = 0.5 (10:90 ethyl acetate/hexanes); $[\alpha]^{25}_D$ = -6.96 (*c* 1.0, $CHCl_3$). IR ν_{max}: 3304, 2928, 2858, 1733, 1462, 1430, 1374, 1249, 1220, 1102, 1078, 859, 815, 750, 700 cm^{-1}. ^{1}H NMR(500 MHz, $CDCl_3$): δ 7.71-7.64 (m, 4H), 7.45-7.34 (m, 6H), 3.95 (dt, *J* = 4.2, 7.6Hz 1H), 3.76-3.69 (m, 3H), 2.18 (dt, *J* = 2.5, 7.0 Hz, 2H), 1.93 (t, *J* = 2.5 Hz, 1H), 1.61-1.64 (m, 2H), 1.40 (s, 3H), 1.37 (s, 3H), 1.33-1.25 (m, 10H), 1.06 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.60, 133.23, 133.19, 129.71, 129.68, 127.66, 108.34, 84.69, 81.09, 78.49, 68.08, 64.21, 33.36, 29.67, 29.55, 28.96, 28.67, 28.44, 27.41, 26.99, 26.80, 26.02, 19.21, 18.36 ppm. MS(ESI): *m/z* 515 $[M+Na]^+$.

4.4. *tert*-Butyl(((4S,5S)-5-(heptadec-8-yn-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)diphenylsilane (17)

Under nitrogen atomosphere, a solution of n-BuLi (1.6M in hexane, 1.2 mL, 2.0 mmol) was added to a THF solution (10 mL) of alkyne **16** (500 mg, 1.0 mmol) at -20 °C, and the mixture was stirred for 30 min. Then solution of n-iodo octane (360 mg, 1.5 mmol) was added to the solution, and the mixture was warmed to 0 °C and stirred for 8 h. Then the reaction was quenched by adding aqueous saturated NH_4Cl (5 mL) solution and the aqueous solution was extracted with ether (10 mL×4). The organic layer was washed with brine (20 mL), and dried over $MgSO_4$. After removal of the solvent, compound **17** (448 mg, 73%) was

obtained by 60-120 silica gel column chromatography. R_f = 0.6 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = – 6.24 (*c* 0.52, $CHCl_3$). IR ν_{max}: 3062, 2927, 2857, 1461, 1432, 1373, 1250, 1104, 1081, 859, 816, 740, 701 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.70-7.65 (m, 4H), 7.45-7.36 (m, 6H), 3.95 (dt, *J* = 4.3, 7.3 Hz, 1H), 3.76-3.69 (m, 3H), 2.16-2.11 (m, 4H), 1.60-1.43 (m, 2H), 1.40 (s, 3H), 1.37 (s, 3H), 1.33-1.24 (m, 21H), 1.06 (s, 9H), 0.88 (t, *J* = 6.7 Hz, 3H) ppm.^{13}C NMR (75 MHz, $CDCl_3$): δ 135.61, 133.25, 133.19, 129.71, 129.68, 127.66, 108.35, 81.12, 80.26, 80.15, 78.50, 77.19, 64.21, 33.39, 31.83, 29.64, 29.17, 29.21, 29.64, 29.12, 29.06, 28.87, 28.83, 27.42, 26.99, 26.80, 26.07, 22.65, 19.21, 18.75, 14.09 ppm. MS(ESI): *m/z* 628 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{39}H_{60}O_3SiNa$627.4204, found 627.4209.

4.5. *tert*-Butyl(((*4S,5S*)-5-((*Z*)-heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)diphenylsilane (18)

Dry ethyl acetate (3 mL) was added to a 25 mL Round bottomed flask with Pd-$BaSO_4$ (0.050 g). At room temperature the mixture was saturated with H_2. Under a stream of N_2, a solution of **17** (0.3 g, 0.49 mmol) in dry ethyl acetate (2 mL) and quinoline (0.1 mL) were added. After exchanging the N_2 with H_2, the reaction mixture was stirred for 1 h at rt. The mixture was filtered and evaporated to afford the crude residue. Purification by column chromatography (5% ethyl acetate:hexane) afforded **18** as a colorless liquid (0.28 g, 94%).

4.6. (*Z*)-*tert*-Butyl((5-(heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)diphenylsilane (18)

To the compound **13** (5.0 g, 10.04 mmol) dissolved in a solvent mixture THF: DMSO (1:1, 60 mL) was added IBX (4.21 g, 15.06 mmol) in one portion and stirred for 2 h at room temperature. The reaction mixture was diluted with ice-cold water (50 mL) and extracted with CH_2Cl_2 (5x40 mL). Combined organic layers were washed with saturated $NaHCO_3$ (60 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to yield the crude aldehyde (5.0 g) which was directly used further without purification.

n-BuLi (9.4 mL, 15.1 mmol) was added to a solution of (1-nonyl)triphenylphosphonium bromide (7.5 g, 16.1 mmol) in dry THF (80 mL) at -78 ^oC and stirred for 1 h at same temperature. During this time, the reaction color was changed from colorless to red. To this solution, the above crude aldehyde (5.0 g, 10.08 mmol, dissolved in 40 mL THF) was added drop wise at-78 ^oC and stirred for overnight at room temperature. The reaction mixture was quenched with aq. saturated ammonium chloride solution (30 mL) at 0 ^oC. The reaction mixture was extracted with ethyl acetate (5x30 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified through silica gel (60-120 mesh) column chromatography to afford compound **18** as a colorless liquid (5.1 g, 8.73 mmol, 84% over 2 steps). R_f = 0.6 (5% EtOAc-Hexane). $[\alpha]^{25}_D$= – 3.86 (*c* 0.78, $CHCl_3$). IR ν_{max}: 2928, 2857, 1464,1377,1219, 1111, 823,773, 704 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.70-7.65 (m, 4H), 7.45-7.36 (m, 6H), 5.37-5.34 (m, 2H), 3.39 (dt, *J* = 4.3, 7.5 Hz, 1H), 3.76-3.70 (m, 3H), 2.04-1.98 (m, 4H), 1.37 (s, 3H), 1.40 (s, 3H), 1.36-1.22 (m, 25H), 1.06 (s, 9H), 0.88 (t, *J* = 6.7 Hz, 3H) ppm.^{13}C NMR (75 MHz, $CDCl_3$): δ 135.60, 133.23, 133.18, 129.91, 129.79, 129.71, 129.68, 127.66, 108.33, 81.12, 78.49, 64.19, 33.40, 31.88,29.76, 29.71, 29.51, 29.44, 29.31, 29.27, 27.42, 27.21, 26.98, 26.79, 26.09, 22.66, 19.20, 14.10 ppm. MS(ESI): *m/z* 629 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{39}H_{62}O_3SiNa$ 629.4360, found 629.4377.

4.7 (*Z*)-(5-(Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (12)

Compound **18** (4.0 g, 6.60 mmol) was dissolved in dry THF (35 mL) and cooled to 0 ^oC. To this n-tetrabutylammonium fluoride (9.9 mL, 9.9 mmol, 1.0 M) was added dropwise and stirred for 2 h. The reaction was quenched with saturated aqueous ammonium chloride solution (15 mL) at 0 ^oC. The reaction mixture was extracted with ethyl acetate (3x30 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified through silica gel (60-120 mesh) column chromatography, to afford compound **12** as pale yellow liquid (2.1 g, 0.005 mmol, 87%). R_f = 0.4 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = 0.72 (*c* 0.36, $CHCl_3$). IR ν_{max}: 3449, 2925, 2854, 1740, 1461, 1374, 1257, 1168, 1047, 855, 800, 872 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.36-5.33 (m, 2H), 3.88 (dt, *J* = 4.2, 7.9 Hz, 1H), 3.80 (dd, *J* = 3.0, 11.9 Hz, 1H), 3.75-3.71 (m, 1H), 3.59 (dd, *J* = 4.4, 11.9 Hz, 1H), 2.04-1.98 (m, 4H), 1.42 (s, 3H), 1.40 (s, 3H), 1.36-1.22 (m, 24H), 0.88 (t, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.03, 129.86, 108.64, 81.65, 77.38, 62.16, 33.18, 31.99, 29.86, 29.82, 29.78, 29.61, 29.49, 29.41, 29.30, 27.46, 27.30, 27.27, 27.11, 26.08, 22.77, 14.21ppm. MS(ESI): *m/z* 391 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{23}H_{45}O_3$ 369.3363, found 369.3358.

4.8 (*R*),(*S*) -1-((4*S*,5*S*)-5-((*Z*)-Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(trimethylsilyl)prop-2-yn-1-ol (19)

A solution of oxalyl chloride (0.7 mL, 8.0 mmol) in dry CH_2Cl_2 (6 mL) was cooled to –78 ^oC under an atmosphere of argon. A solution of DMSO (1.2 mL, 16 mmol) in CH_2Cl_2 (5 mL) was added at a rate such that the reaction temperature remained below –65 ^oC. After stirring for 5 min, a solution of **12** (1.50 g, 4.0 mmol) in CH_2Cl_2 (15 mL) was added slowly, and the resulting mixture was stirred for 15 min. Triethyl amine (3.4 mL, 24 mmol) was added slowly and after stirring the reaction for additional 10 min. at –78 ^oC, the cooling bath was removed and the reaction was allowed to warm to room temperature for 45 min. Upon reaching room temperature, water (35 mL) was added and stirring was continued for additional 15 min. The reaction mixture was transferred to a separatory funnel, washed successively with, saturated $NaHCO_3$ solution (30 mL), and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford an oil (aldehyde), which was directly used for next step without further purification.

A solution of n-BuLi in hexane (1.6 M, 4.6 mL, 7.3 mmol) was added dropwise to a stirred and cooled solution of trimethylsilyl acetylene (1.14 mL, 8.1 mmol) in dry THF (10 mL) at -70 ^oC under argon. After the addition, the stirred mixture was allowed to warm to-10 ^oC to ensure the formation of LiCCTMS. It was then cooled again to -78^oC and to this was added a solution of aldehyde (1.50 g, 4.09 mmol) obtained from **12** in dry THF (20 mL) dropwise. The mixture was stirred for 1 h at same temperature, and then left to stand overnight with gradual warming to room temperature. The mixture was then diluted with ice and aq. NH_4Cl solution, and extracted with ethyl acetate (4x20 mL). The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo and separated by using silica gel (100-200 mesh) to give **19** as a yellow liquid along with **19a**. (**19**:**19a** (1:1)), 1.5 g, 79%).

19: R_f = 0.5 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = -7.17 (*c* 0.21, $CHCl_3$). IR ν_{max}: 3447, 2955, 2924, 2853, 1711, 1461, 1376, 1248, 1186, 1080, 968, 845, 761 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.36-5.32 (m, 2H), 4.34 (d, *J* = 6.5, 1H), 3.92 (dt, *J* =

3.3, 7.9 Hz, 1H), 3.72 (t, *J* = 6.8, 1H), 2.04-1.98 (m, 4H), 1.79-1.70 (m, 1H), 1.63-1.54 (m, 1H), 1.43 (s, 3H), 1.40 (s, 3H), 1.35-1.23 (m, 23H), 0.88 (t, *J* = 6.7 Hz, 3H), 0.18 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 129.92, 129.77, 109.28, 102.45, 83.31, 78.13, 64.43, 34.01, 31.88, 29.74, 29.67, 29.48, 29.26, 27.54, 27.19, 27.10, 26.04, 22.66, 14.10, -0.30 ppm. MS(ESI): *m/z* 487 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{28}H_{53}O_3SiH$ 465.3758, found 465.3793.

(*S*)-1-((4*S*,5*S*)-5-((*Z*)-Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(trimethylsilyl)prop-2-yn-1-ol (19a)

R_f = 0.5 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = -5.29 (*c* 0.17, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 5.36-5.31 (m, 2H), 4.08 (dt, *J* = 3.3, 8.2 Hz, 1H), 3.78 (dd, *J* = 3.0, 8.0 Hz, 1H), 2.37 (bs, 1H), 2.04-1.98 (m, 4H), 1.79-1.71 (m, 1H), 1.63-1.55 (m, 2H), 1.43 (s, 3H), 1.41 (s, 3H), 1.35-1.24 (m, 22H), 0.88 (t, *J* = 6.5 Hz, 3H), 0.18 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 129.93, 129.78, 108.83, 101.90, 92.30, 82.26, 76.81, 62.25, 34.06, 31.89, 29.75, 29.73, 29.51, 29.48, 29.31, 29.26, 27.54, 27.20, 26.86, 26.06, 22.67, 14.10, -0.30.

4.9. (*R*)-1-((4*S*,5*S*)-5-((*Z*)-Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-ol (11)

To the solution of compound **19** (0.07 g, 0.15 mmol) dissolved in dry THF (5 mL) at 0 °C was added n-tetrabutylammonium fluoride (0.22 mL, 0.22 mmol, 1.0 M) dropwise and stirred for 2 h. The reaction was quenched with saturated aqueous ammonium chloride solution (5 mL) at 0 °C. The reaction mixture was extracted with ethyl acetate (3x7 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified through silica gel (60-120 mesh) column chromatography, to afford compound **11** as colorless liquid (49 mg, 0.12 mmol, 84%). R_f = 0.4 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = -8.7 (*c* 0.32, $CHCl_3$). IR ν_{max}: 3446, 3309, 2987, 2925, 2854, 1633, 1461, 1375, 1246, 1218, 1167, 1055, 870, 720, 659. ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 5.37-5.31 (m, 2H), 4.36-4.30 (m, 1H), 3.96 (dt, *J* = 3.7, 7.5 Hz, 1H), 3.75 (dd, *J* = 4.5, 7.5 Hz, 1H), 2.52 (d, *J* = 2.2 Hz, 1H), 2.48 (d, *J* = 6.7 Hz, 1H), 2.06-1.93 (m, 4H), 1.69-1.50 (m, 3H), 1.43 (s, 3H),1.41 (s, 3H), 1.37-1.21 (m, 24H), 0.88 (t, *J* = 7.5 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 129.92, 129.75, 109.41, 83.23,81.54, 77.52, 74.33, 62.54, 33.53, 31.85, 29.69(2C), 29.64, 29.47, 29.34(2C), 29.26, 29.17, 27.52, 27.16, 25.89, 22.63, 14.08 ppm.MS(ESI): *m/z* 415 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{24}H_{46}O_3Na$ 415.3183, found 415.3196.

4.10 (*R*)-1-((4*S*,5*S*)-5-((*Z*)-Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-ol (11) from 19a

To a solution of compound **19a** (50 mg, 0.1 mmol) in toluene (3 mL) was added Ph_3P (56 mg, 0.2 mmol) and 4-nitrobenzoic acid (16.7 mg, 0.1 mmol). The solution was cooled to 0 °C and then diisopropyl azodicarboxylate DIAD (0.04 mL, 0.2 mmol) was added. The solution was warmed to rt over 90 min and stirred for over night. The mixture was concentrated in vacuum to reveal the crude product, which was used for the next step without further purification. IR ν_{max}: 3451, 2925, 2854, 2182, 1737, 1640, 1608, 1532, 1492, 1462, 1374, 760, 719, 541 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 8.32-8.24 (m, 4H), 5.76 (d, 1H, *J* = 7.4 Hz), 5.40-5.34 (m, 2H), 4.12 (dt, *J* = 3.3, 8.2 Hz, 1H), 3.99-3.94 (m, 1H), 2.06-1.94 (m, 4H), 1.70-1.57 (m, 2H), 1.42 (s, 3H), 1.40 (s, 3H), 1.37-1.22 (m, 25H), 0.88 (t, 3H, *J* = 6.5 Hz) ppm. HRMS calculated for $C_{35}H_{55}NaNO_6Si$ 636.3691, found 636.3727. To the solution of crude ester obtained above (67 mg, 0.1 mmol) in MeOH (4 mL) was added K_2CO_3 (22 mg, 0.16 mmol) and the mixture was stirred for 1 h. The solvents were evaporated under vacuum. The crude product was purified using silica gel (60-120) column chromatography to afford colorless liquid (35 mg, 0.09 mmol, 84%). The analytical data of this compound was found to be identical with compound (**11**).

4.11. (*R*)-1-((4*S*,5*S*)-5-((*Z*)-Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)-6-((4-methoxybenzyl)oxy)hexa-2,4-diyn-1-oldiyn-1-ol (21)

CuCl (1 mg) was added to a 30% n-butylamine solution (3 mL) to get a blue colored solution. After the addition of few crystals of hydroxylamine hydrochloride, blue color was disappeared. Then the alkyne **11** (10 mg, 0.025 mmol) in 5 mL diethyl ether was added at once and immediately cooled to 0 °C. Then the bromo alkyne **20** (5.8 mg, 0.022 mmol) was added at once and stirred for 60 min. During the reaction it was necessary to add hydroxylamine hydrochloride crystals (to maintain lower oxidation state of copper) in appropriate intervals. The reaction mixture was extracted with diethyl ether (5x15 mL). Combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified through silica gel (60-120 mesh) column chromatography to afford compound **21** (8.6 mg, 60%). R_f = 0.3 (10% EtOAc-Hexane). $[\alpha]^{25}_D$= -1.00 (*c* 0.3, $CHCl_3$). IR ν_{max}: 3423, 2924, 2853, 1737, 1612, 1513, 1461, 1348, 1249, 1075, 1037, 820, 578 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 7.29-7.24 (m, 2H), 6.91-6.86 (m, 2H), 5.36-5.32 (m, 2H), 4.53 (s, 2H), 4.42 (d, *J* = 4.5 Hz, 1H), 4.20 (s, 2H), 3.39 (dt, *J*= 3.8, 7.8 Hz, 1H), 3.81 (s, 3H), 3.75 (dd, *J* = 4.5, 7.7 Hz, 1H), 2.05-1.93 (m, 4H), 1.70-1.56 (m, 2H), 1.44 (s, 3H), 1.42(s, 3H), 1.40-1.18 (m, 25H), 0.88 (t, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 159.48, 129.94, 129.84, 129.78, 128.95, 113.87, 109.59, 83.02, 77.55, 76.49, 76.38, 71.38, 70.25, 70.12, 63.06, 57.04, 55.26, 33.49, 31.89, 29.75, 29.69, 29.55, 29.51, 29.40, 29.30, 29.22, 27.56, 27.20, 27.18, 26.98, 25.90, 22.67, 14.11 ppm. MS(ESI): 589 $[M+Na]^+$. HRMS *m/z* calculated for $C_{36}H_{54}NaO_5$ 589.3863, found 589.3896.

4.12 (*R*)-1-((4*S*,5*S*)-5-((*Z*)-Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)but-2-yne-1,4-diol (23)

CuCl (1 mg) was added to a 30% n-butylamine solution (3 mL). Then the color was changed to blue. After the addition of few crystals of hydroxylamine hydrochloride, blue color was disappeared. Then the alkyne **11** (20 mg, 0.05 mmol) in 5 mL diethyl ether was added at once and immediately cooled to 0 °C. To this the brominated propargyl alcohol **22** (6.1 mg, 0.045 mmol) was added at once and stirred for 30 min. During the reaction it was necessary to add hydroxylamine hydrochloride crystals (to maintain lower oxidation state of copper) in appropriate intervals. The reaction mixture was extracted with diethyl ether (5x15 mL). Combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified through silica gel (60-120 mesh) column chromatography to afford compound **23** (15.4 mg, 0.03 mmol, 68%). R_f = 0.3 (30% EtOAc-Hexane). $[\alpha]^{25}_D$= -3.41 (*c* 0.09, $CHCl_3$). IR ν_{max}: 3421, 2925, 2854, 1741, 1462, 1376, 1219, 1041, 772 cm^{-1}. ^{1}HNMR (300 MHz, $CDCl_3$): *δ* 5.39-5.32 (m, 2H), 4.52 (s, 2H), 4.41 (d, *J* = 3.4 Hz, 1H), 4.20 (s, 2H), 3.99-3.89 (m, 1H), 3.81 (s, 3H), 3.75 (dd, *J* = 7.7, 4.5 Hz, 1H), 2.05-1.93 (m, 4H), 1.73-1.50 (m, 2H), 1.44 (s, 3H), 1.41 (s, 3H), 1.40-1.20 (m, 24H), 0.88 (t, *J* = 7.0 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 129.99, 129.79, 109.59, 83.02, 82.43, 78.06, 77.56, 63.11, 60.39, 51.41, 33.48, 31.89, 30.92, 29.75, 29.69, 29.65, 29.51, 29.43, 29.37, 29.31, 29.22, 29.10, 29.07, 27.55, 27.21, 27.19, 26.99, 25.85, 22.66, 14.11. MS(ESI): *m/z* 470 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{28}H_{46}NaO_4$ 469.3288, found 469.3298.

4.13. Petrosiol A (6)

To a solution of the **23** (8 mg, 0.017 mmol) in MeOH (3 mL), catalytic *p*-toluenesulfonic acid (PTSA) (2 mg,) was added at 0 ^{o}C and the reaction mixture was stirred at rt for 20 h. The reaction mixture was quenched by the addition of solid $NaHCO_3$ (5 mg, mmol) and the solvent was evaporated. The crude residue was purified by column chromatography (70:30) petroleum ether/EtOAc) to obtain petrosiol A (6 mg, 0.014 mmol, 83%) as a colourless liquid. R_f = 0.3 (50% EtOAc/petroleum ether). $[\alpha]^{25}_{D}$ = -4.53 (*c* 0.34, MeOH); Lit.[7] $[\alpha]^{25}_{D}$ = -2.9 (*c* 0.16, MeOH). IR ν_{max}: 3385, 2924, 2853, 1647, 1460, 1261, 1029, 722 cm^{-1}. ^{1}HNMR (300 MHz, $CDCl_3$+CD_3OD 4:1): δ 5.41-5.29 (m, 2H), 4.46 (d, *J* = 7.1 Hz, 1H), 4.26 (s, 2H), 3.83-3.73 (m, 1H), 3.81 (s, 3H), 3.43 (dd, *J* = 2.0, 7.3 Hz, 1H), 2.08-1.96 (m, 4H), 1.64-1.49 (m, 1H), 1.43-1.23 (m, 24H), 0.89 (t, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$+CD_3OD) 4:1): δ 130.47, 130.42, 78.67, 76.91, 71.63, 70.43, 69.25, 64.85, 50.83, 34.58, 32.55, 30.42, 30.38, 30.30, 30.20, 30.14, 29.95, 29.77, 27.77, 26.43, 23.28, 14.38. MS(ESI): *m/z* 429 $[M+Na]^+$. HRMS (ESI) *m/z* calculated for $C_{25}H_{42}NaO_4$ 429.2975, found 429.2989.

4.14. (*S*)-1-((4*S*,5*S*)-5-((*Z*)-Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-ol (24)

Compound **19a** (0.07 g, 0.15 mmol) was dissolved in dry THF (5 mL) and cooled to 0 ^{o}C. To this n-tetrabutylammonium fluoride (0.22 mL, 0.22 mmol, 1.0 M) was added dropwise and stirred for 2 h. The reaction was quenched with saturated aqueous ammonium chloride solution (5 mL) at 0 ^{o}C. The reaction mixture was extracted with ethyl acetate (3x7 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified through silica gel (60-120 mesh) column chromatography, to afford compound **24** as colorless liquid (49 mg, 0.12 mmol, 84%). R_f = 0.4 (10% EtOAc-Hexane). $[\alpha]^{25}_{D}$ = -5.56 (*c* 0.72, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.36-5.33 (m, 2H), 4.52-4.59 (m, 1H), 4.08 (dt, *J* = 3.6, 8.2 Hz, 1H), 3.79 (dd, *J* = 3.8, 7.7 Hz, 1H), 2.53 (d, *J* = 2.2 Hz, 1H), 2.32 (bs, 1H), 2.04-1.97 (m, 4H), 1.76-1.68 (m, 1H), 1.64-1.55 (m, 1H), 1.43 (s, 6H), 1.36-1.24 (m, 24H), 0.88 (t, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 129.94, 129.79, 109.09, 82.35, 80.87, 77.38, 75.15, 62.32, 34.03, 32.59, 32.57, 31.89, 29.75, 29.68, 29.64, 29.51, 29.31, 29.21, 29.06, 27.55, 27.26, 27.18, 26.91, 25.98, 22.67, 14.10.

4.15. (*S*)-1-((4*S*,5*S*)-5-((*Z*)-Hex-2-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)hexa-2,4-diyne-1,6-diol (25)

Similar procedure was adopted as used for the preparation of compound **18** starting from alkyne **24** (20 mg, 0.05 mmol) and brominated propargyl alcohol **22** (6.1 mg, 0.045 mmol) to yield compound **25** as a pale yellow liquid (15.4 mg, 0.03 mmol, 68%). R_f = 0.3 (30% EtOAc-Hexane). $[\alpha]^{25}_{D}$ = -6.74 (*c* 0.36, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.41-5.31 (m, 2H), 4.55 (d, *J* = 2.4, 1H), 4.35 (s, 2H), 4.04 (dt, *J* = 3.9, 7.7 Hz, 1H), 3.79 (dd, *J* = 3.7, 7.9 Hz, 1H), 2.09-1.92 (m, 4H), 1.75-1.54 (m, 4H), 1.43 (s, 6H), 1.38-1.22 (m, 30H), 0.88 (t, *J* = 5.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 129.96, 129.78, 109.38, 82.51, 77.90, 77.50, 76.48, 70.83, 69.42, 63.10, 51.28, 33.75, 32.58, 31.87, 29.74, 29.66, 29.62, 29.54, 29.48, 29.38, 29.29, 29.21, 29.16, 29.07, 27.54, 27.19, 26.88, 25.90, 22.65, 14.08.

4.16. C6-*epi*-PetrosiolA (26)

To a solution of the compound **25** (6 mg, 0.013 mmol) in MeOH (3 mL), catalytic PTSA (2 mg) was added at 0 ^{o}C and the reaction mixture was stirred at rt for 20 h. The reaction mixture was quenched by the addition of solid $NaHCO_3$ (5 mg) and the solvent was evaporated. The crude residue was purified by column chromatography (70:30) petroleum ether/EtOAc) to obtain **26** (4.5 mg, 0.011 mmol, 83%) as a yellow liquid. R_f = 0.3 (50% EtOAc/petroleum ether). $[\alpha]^{25}_{D}$ = -9.41 (*c* 0.07, MEOH). ^{1}HNMR (500MHz, $CDCl_3$): δ 5.41-5.31 (m, 2H), 4.60 (bs, 1H), 4.35 (s, 2H), 4.05 (bs, 1H), 3.78 (bs, 1H), 3.55 (bs, 1H), 2.07-1.97 (m, 4H), 1.41-1.20 (m, 25H), 0.88 (t, *J* = 6.9 Hz, 3H) ppm.^{13}C NMR (125 MHz, $CDCl_3$): δ 129.98, 129.78, 77.56, 74.21, 71.59, 66.02, 51.41, 31.90, 31.82, 29.69, 29.52, 29.47, 29.44, 29.31, 29.22, 27.22, 27.19, 25.42, 22.68, 22.64, 14.11.

4.17. (((*Z*)-4-((4*S*,5*S*)-5-((Benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-en-1-yl)oxy)(*tert*-butyl)diphenylsilane (33)

To the mono protected alcohol **32** (10.0 g, 39.6 mmol) dissolved in a solvent mixture THF:DMSO (1:1, 140 mL), was added IBX (16.6 g, 59.5 mmol) and stirred for 2 h at room temperature. The reaction mixture was diluted with ice-cold water (300 mL) and extracted with CH_2Cl_2 (5x100 mL). Combined organic layers were washed with saturated $NaHCO_3$ (250 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to yield the crude aldehyde (10.0 g, 40 mmol) which was directly used for next step without further purification. (10-((*tert*-Butyldiphenylsilyl)oxy)decyl)triphenylphosphonium iodide (47.04 g, 60 mmol) was dissolved in dry THF (150 mL) and cooled to -78 ^{o}C. To this *n*-BuLi (22.4 mL, 56 mmol, 2.5 M) was added drop wise and stirred for 3 h at the same temperature. During this time reaction color was changed from colorless to brick red. To this, the crude aldehyde dissolved in anhydrous THF (50 mL) was added drop wise and stirred for over night after allowing the reaction mixture to warm to room temperature. The reaction mixture was quenched with saturated ammonium chloride (40 mL) at 0 ^{o}C. The reaction mixture was extracted with ethyl acetate (5x40 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified through silica gel (60-120 mesh) column chromatography to afford compound **33** as yellow liquid (22.1 g, 35.19 mmol, 86% over two steps). R_f = 0.7 (10% EtOAc-Hexane). $[\alpha]^{25}_{D}$ = +2.79 (*c* 1.7, $CHCl_3$). IR ν_{max}: 2925, 2856, 1461, 1430, 1373, 1219, 1099, 1024, 914, 747 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78-7.68 (m, 4H), 7.48 - 7.28 (m, 11H), 5.74-5.66 (m, 1H), 5.46-5.39 (m, 1H), 4.73-4.66 (m, 1H), 4.62 (s, 2H), 3.94-3.87 (m, 1H), 3.73-3.53 (m, 4H), 2.21-1.99 (m, 2H), 1.65-1.56 (m, 1H), 1.48 (s, 6H), 1.41-1.24 (m, 14H), 1.09 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.94, 136.38, 135.50, 134.74, 134.10, 129.52, 129.40, 128.25, 127.61, 127.53, 127.50, 126.03, 109.12, 80.38, 73.50, 73.39, 69.14, 63.94, 32.53, 29.64, 29.55, 29.49, 29.37, 29.31, 29.18, 27.70, 27.13, 26.93, 26.83, 26.52, 25.73, 19.17 ppm. MS(ESI): *m/z* 651 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{40}H_{56}NaO_4Si$ 651.3840, found 651.3871.

4.18. (*Z*)-4-((4*S*,5*S*)-5-((Benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-en-1-ol (31)

Compound **33** (6.0 g, 9.5 mmol) was dissolved in dry THF (35 mL) and cooled to 0 ^{o}C. To this n-tetrabutylammonium fluoride (14.3 mL, 14.3 mmol, 1.0 M) was added dropwise and stirred for 2 h. The reaction was quenched with saturated aqueous ammonium chloride solution (15 mL) at 0 ^{o}C. The reaction mixture was extracted with ethyl acetate (3x30 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified through silica gel (60-120 mesh) column chromatography, to afford compound **31** as pale yellow liquid (3.49 g, 8.9 mmol, 94%). R_f = 0.6 (20% EtOAc-Hexane). $[\alpha]^{25}_{D}$ = 5.37 (*c* 1.2, $CHCl_3$). IR ν_{max}: 3431, 2984, 2924, 2855, 1725, 1657, 1456, 1372, 1247, 1221, 1165, 1075, 861, 742 cm^{-1}. ^{1}H

NMR (500 MHz, $CDCl_3$): δ 7.36-7.27 (m, 5H), 5.71-5.62 (m, 1H), 5.42-5.35 (m, 1H), 4.66 - 4.60 (m, 1H), 4.59 (s, 2H), 3.86 (dt, 1H, J = 2.9, 5.3 Hz), 3.65 - 3.52 (m, 4H), 2.15-1.95 (m, 2H), 1.59-1.50 (m, 1H), 1.44 (s, 6H), 1.37-1.22 (m, 12H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.91, 136.34, 128.22, 127.51, 125.99, 109.09, 80.34, 73.46, 73.35, 69.11, 62.83, 32.67, 29.48, 29.42, 29.29, 29.09, 27.63, 27.08, 26.90, 25.65 ppm. MS(ESI): *m/z* 413 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{24}H_{39}O_4$ 391.2843, found 391.2866.

4.19. (*4S,5S*)-4-((Benzyloxy)methyl)-2,2-dimethyl-5-((*1Z,4Z*)-7-methylocta-1,4-dien-1-yl)-1,3-dioxolane (30)

To the alcohol **31** (5.0 g, 12.8 mmol) dissolved in a solvent mixture THF:DMSO (1:1, 60 mL), was added at once IBX (5.38 g, 19.2 mmol) and stirred for 2 h at room temperature. The reaction mixture was diluted with ice cold water (70 mL) and extracted with CH_2Cl_2 (5x50 mL). Combined organic layers were washed with saturated $NaHCO_3$ (120 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure yielded the crude aldehyde (5.0 g, 12.8 mmol) which was directly used for further step without purification. (3-methyl)butyl triphenyl phosphonium bromide (15.9 g, 38.6 mmol) was dissolved in dry THF (90 mL) and cooled to -78 ^{o}C. To this n-BuLi (13.9 mL, 34.7mmol, 2.5 M) was added drop wise and stirred for 1 h at the same temperature. During this time reaction color was changed from colorless to brick red. To this, the crude aldehyde dissolved in anhydrous THF (30 mL) was added drop wise and stirred for overnight after allowing the reaction mixture to warm to room temperature. The reaction mixture was quenched with saturated ammonium chloride 30 mL) at 0 ^{o}C. The reaction mixture was extracted with ethyl acetate (5x30 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified through silica gel (60-120 mesh) column chromatography to afford compound **(30)** as colorless liquid (4.5 g, 10.2 mmol, 81% over two steps). R_f = 0.75 (20% EtOAc-Hexane). $[\alpha]^{25}_D$ = +4.98 (*c*,1.08, $CHCl_3$). IR ν_{max}: 2925, 2857, 1733, 1457, 1372, 1219, 1165, 1080, 1027, 914, 862, 745, 698 cm^{-1}. ^{1}HNMR (300 MHz, $CDCl_3$): δ 7.35 - 7.26 (m, 5H), 5.70 - 5.63 (m, 1H), 5.42 - 5.33 (m, 3H), 4.66 - 4.61 (m, 1H), 4.59 (s, 2H), 3.86 (dt, J =5.4, 3.0 Hz, 1H), 3.62 - 3.58 (m, 1H), 3.56 - 3.52 (m, 1H), 2.15 - 2.07 (m, 1H), 2.05 - 1.97 (m, 3H), 1.93 - 1.89 (m, 2H), 1.63 - 1.55 (m, 1H), 1.44 (s, 6H), 1.36-1.19 (m, 16H), 0.89 (d, 6H, J = 6.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.93, 136.31, 130.45, 128.44, 128.22, 127.51, 126.04, 109.07, 80.36, 73.47, 73.36, 69.13, 36.29, 29.66, 29.52, 29.40, 29.36, 29.23, 29.14, 28.60, 27.66, 27.21, 27.11, 26.91, 22.32 ppm. MS(ESI): *m/z* 465 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{29}H_{46}NaO_3$ 465.3339, found 465.3374.

4.20. ((*4S,5S*)-2,2-Dimethyl-5-(4-methylpentyl)-1,3-dioxolan-4-yl)methanol (28)

To the compound **30** (3.0 g, 6.78 mmol) dissolved in HPLC grade ethyl acetate (7 mL) was added $Pd(OH)_2$ (75 mg) and the reaction was stirred under H_2 atmosphere for 8 h. The reaction mixture was filtered over celite and concentrated under reduced pressure. The crude product was purified through silica gel (60-120 mesh) column chromatography to afford compound **28** as colorless liquid (2.27 g, 6.30 mmol, 94%). R_f = 0.3 (25% EtOAc-Hexane). $[\alpha]^{25}_D$= -12.36 (*c* 0.6, $CHCl_3$). IR ν_{max}: 3453, 2928, 2854, 1737, 1460, 1373, 1248, 1219, 1167, 1096, 1045, 902, 854, 804, 754, 671 cm^{-1}. ^{1}HNMR (500 MHz, $CDCl_3$): δ 3.87 (dt, J = 4.2 , 7.9 Hz, 1H), 3.79 (dd, J = 2.8, 11.9 Hz, 1H), 3.75-3.71 (m, 1H), 3.59 (dd, J = 2.8, 11.9 Hz, 1H), 1.62- 1.44 (m, 2H), 1.42 (s, 3H), 1.41 (s, 3H), 1.36 - 1.21 (m, 21H), 0.86 (d, J = 6.7 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 108.53, 81.47, 76.86, 62.06, 39.05, 33.09, 29.93, 29.67, 29.64, 29.55, 29.49, 27.95, 27.40, 27.38, 27.03, 25.97, 22.65 ppm. MS(ESI): *m/z* 379 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{22}H_{45}O_3$ 357.3363, found 357.3352.

4.21. Penta-2,4-diyn-1-ol

In an oven-dried round-bottom flask was taken 50 mL dry THF and 0.98 g (5.08 mmol) 1,4-bis(trimethylsilyl)butadiyne. The solution was cooled to –10 ºC and allowed to stir for 10 min, after which 4.29 mL MeLi·LiBr (1.5 M in ether, 6.44 mmol, 1.26 equiv.) was added dropwise. The solution turned golden in color, and was allowed to stir at –10 ºC for an additional 15 min. The cold bath was then removed, and the solution was allowed to warm to room temperature and stirred for 1 h. The solution was then recooled to 0 ºC, and to this a suspension of 0.26 g (8.72 mmol, 1.72 equiv.) paraformaldehyde in 10 mL dry THF was added slowly, which caused the mixture to become cloudy. The mixture was then warmed to room temperature and was allowed to stir for an additional 8 h. The resultant mixture was washed sequentially with saturated NH_4Cl solution, saturated $NaHCO_3$ solution, and brine. The aqueous washings were combined and extracted with ether. The combined organics were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resultant oily residue was purified through silica gel (60-120 mesh) column chromatography to afford corresponding formylated product as a pale golden oil (0.35 g, 4.32 mmol, 85%). R_f = 0.3 (20 % EtOAc-Hexane). ^{1}H NMR (500 MHz $CDCl_3$): δ 4.32 (d, J = 0.7 Hz, 2H), 2.15 (t, J = 0.9 Hz, 1H); ^{13}C NMR (75 MHz $CDCl_3$) δ 74.33, 69.90, 68.44, 67.30, 51.16. IR ν_{max}: 3286, 2919, 2861, 2063, 1629, 848, 713 cm^{-1}.

4.22. *tert*-Butyldimethyl(penta-2,4-diyn-1-yl)silane (27)

Imidazole (0.51 g, 7.5 mmol) was added to a solution of penta-2,4-diyn-1-ol (0.20 g, 2.5 mmol) in CH_2Cl_2 (5 mL) at 0 ºC. The solution was stirred for 15 min to dissolve the imidazole, before adding ^{t}BuPh$_2$SiCl (0.56 g, 3.75 mmol) at 0 ºC. The reaction mixture was allowed to warm to rt. After 1 h, the reaction mixture was diluted with water (2 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 x5 mL) and dried over ($MgSO_4$). Removal of the solvent under reduced pressure afforded a yellow oil. The resultant yellow oil was purified by silica gel (60-120 mesh) column chromatography to afford *tert*-butyldimethyl(penta-2,4-diyn-1-yl) silane as a pale yellow oil (0.44 g, 2.4 m mol 99%); R_f = 0.8 (10 % EtOAc-Hexane). ^{1}H NMR (500 MHz ($CDCl_3$): δ 4.36 (d, J = 1.1 Hz, 2H), 2.15 (t, J = 1.1 Hz, 1H), 0.91 (s, 9H), 0.12 (s, 6H). ^{13}C NMR (75 MHz) ($CDCl_3$): δ 75.05, 69.01, 67.77, 67.65, 51.89, -5.23. IR ν_{max}: 3302, 2941, 2894, 1464, 1368, 777, 720 cm^{-1}.

4.23. (*R)/(S)*-6-((*tert*-Butyldimethylsilyl)oxy)-1-((*4S,5S*)-2,2-dimethyl-5-(4-methylpentyl)-1,3-dioxolan-4-yl)hexa-2,4-diyn-1-ol (35, 35a)

A solution of oxalyl chloride (0.02 mL, 0.28 mmol) in dry CH_2Cl_2 (2 mL) was cooled to –78 ^{o}C under an atmosphere of argon. A solution of DMSO (0.039 mL, 0.56 mmol) in CH_2Cl_2 (2 mL) was added at a rate such that the reaction temperature remained below –65 ^{o}C. After stirring for 5 min, a solution of alcohol **28** (50 mg, 0.14 mmol) in CH_2Cl_2 (15 mL) was added slowly, and the resulting mixture was stirred for 15 min. Triethylamine (0.11 mL, 0.84 mmol) was added slowly and after stirring the reaction for additional 10 min. at –78 ^{o}C, the cooling bath was removed and the reaction was allowed to warm to room temperature for 45 min. Upon reaching room temperature, water (5 mL) was added and stirring was continued for an additional 15 min. The reaction mixture was transferred to a separatory funnel, washed successively with, saturated $NaHCO_3$ solution (30 mL),

and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford the oil **34** (aldehyde), which was directly used for next step without further purification.

A solution of n-BuLi in hexane (1.6 M, 0.15 mL, 0.23 mmol) was added dropwise to a stirred and cooled solution of compound **27** (54 mg, 0.28 mmol) in dry THF (5 mL) at -78 ^oC under argon atmosphere. To this was added the solution of above crude aldehyde **34** (50 mg, 0.14 mmol in 3 mL THF) and the mixture was stirred for 1 h at same temperature, and then left to stand overnight with gradual warming to room temperature. The mixture was then diluted with ice-cooled and aq. NH_4Cl solution, and extracted with ethyl acetate (4x5 mL). The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuum and the products were purified by using silica gel (230 - 400 mesh) chromatography to give **35** and **35a** as a yellow liquids (77 mg, 0.14 mmol, 79%).

(*R*)-6-((*tert*-Butyldimethylsilyl)oxy)-1-((*4S,5S*)-2,2-dimethyl-5-(4-methylpentyl)-1,3-dioxolan-4-yl)hexa-2,4-diyn-1-ol (35)

35: R_f = 0.5 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = -3.37 (*c* 075, $CHCl_3$). IR ν_{max}: 3247, 2924, 2855, 1716, 1461, 1372, 1251, 1219, 1165, 1089, 837, 776, 749, 668 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 4.42 - 4.39 (m, 1H), 4.38 (s, 2H), 3.95 (dt, *J* = 3.9, 7.9 Hz, 1H), 3.74 (dd, *J*=4.8, 7.5Hz, 1H), 1.71-1.45 (m, 2H), 1.44 (s, 3H), 1.41 (s, 3H), 1.35-1.20 (m, 24H), 0.90 (s, 9H), 0.86 (d, *J* = 6.7 Hz, 6H), 0.12 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 109.54, 83.05, 78.67, 77.64, 76.24, 70.47, 68.57, 63.28, 52.01, 39.05, 33.55, 29.94, 29.69, 29.59, 29.51, 27.96, 27.55, 27.41, 26.99, 25.91, 25.72, 22.65, -5.20 ppm. MS(ESI): *m/z* 572 $[M+Na]^+$. HRMS(ESI) *m/z* calculated for $C_{33}H_{60}O_4SiNa$ 571.4153, found 571.4177.

(*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-1-((*4S,5S*)-2,2-dimethyl-5-(4-methylpentyl)-1,3-dioxolan-4-yl)hexa-2,4-diyn-1-ol (35a)

R_f = 0.5 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = -5.68 (*c* 0.64, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 4.55 (d, *J* = 2.8 Hz, 1H), 4.38 (s, 2H), 4.04 (dt, *J* = 3.8, 8.0 Hz, 1H), 3.79 (dd, *J* = 3.5, 7.9 Hz, 1H), 1.71-1.45 (m, 2H), 1.43 (s, 6H), 1.36- 1.20 (m, 24H), 0.90 (s, 9H), 0.86 (d, *J* = 6.5 Hz, 6H), 0.12 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 109.29, 82.48, 78.58, 75.69, 71.26, 68.62, 63.04, 52.02, 39.05, 33.82, 31.91, 29.94, 29.69, 29.52, 29.35, 29.26, 29.15, 29.08, 29.04, 28.94, 27.96, 27.57, 27.41, 27.19, 26.88, 25.96, 25.74, 22.65, -5.19 .

4.24. Petrosiol E (9)

To a solution of the **35** (8 mg, 0.014 mmol) in MeOH (3 mL), catalytic PTSA (2.50 mg, 0.03 mmol) was added at 0 ^oC and the reaction mixture was stirred at rt for 20 h. The reaction mixture was quenched by the addition of solid $NaHCO_3$ (2.52 mg, 0.03 mmol) and the solvent was evaporated. The crude residue was purified by column chromatography to obtain petrosiol E **9** (5.2 mg, 0.013 mmol, 91%) as a colorless liquid: R_f = 0.3 (50% EtOAc/petroleum ether); $[\alpha]^{25}_D$ = -4.16 (*c* 0.4, MeOH); Lit.[7] $[\alpha]^{25}_D$ = -1.0 (*c* 0.06, MeOH). IR ν_{max}: 3357, 2922, 2854, 1719, 1459, 1373, 1215, 1028, 752, 669 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$+CD_3OD 4:1): δ 4.46 (d, *J* = 2.1Hz, 1H), 4.27 (s, 2H), 3.80-3.72 (m, 1H), 3.44 (dd, *J* = 2.1, 6.7 Hz, 1H), 1.41-1.21 (m, 24H), 0.87 (d, *J* = 6.4 Hz, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$+CD_3OD (4:1)): δ 78.31, 77.64, 76.16, 71.29, 70.09, 68.94, 64.44, 50.61, 39.25, 34.17, 30.13, 29.87, 28.15, 27.60, 25.92, 22.73. MS(ESI): *m/z* 417 $[M+Na]^+$. HRMS (ESI) *m/z* calculated for $C_{24}H_{42}NaO_4$417.2975, found 417.2966.

4.25. C6-*epi*-Petrosiol E (36)

To a solution of the **35a** (8 mg, 0.014 mmol) in MeOH (3 mL), catalytic PTSA (2.5 mg, 0.03 mmol) was added at 0 ^oC and the reaction mixture was stirred at rt for 20 h. The reaction mixture was quenched by the addition of solid $NaHCO_3$ (2.52 mg, 0.03 mmol) and the solvent was evaporated. The crude residue was purified by column chromatography to obtain C6 epimer of petrosiol E **36** (5.2 mg, 0.013 mmol, 91%) as a colourless liquid; R_f = 0.3 (50% EtOAc/petroleum ether). $[\alpha]^{25}_D$ = 7.52 (*c* 0.073, MeOH). ^1H NMR (500 MHz, $CDCl_3$+CD_3OD (4:1)): δ 4.44 (d, *J* = 6.8 Hz, 1H), 4.25 (s, 2H), 3.83-3.76 (m, 1H), 3.40 (dd, *J* = 2.4, 6.7 Hz, 1H), 1.38-1.22 (m, 25H), 0.87 (d, *J*= 6.6 Hz, 6H) ppm. ^{13}C NMR(75 MHz, $CDCl_3$+CD_3OD) 4:1): δ 78.54, 75.43, 71.02, 64.77, 50.70, 42.61, 39.42, 33.76, 32.28, 30.29, 30.03, 29.70, 28.32, 27.77, 26.02, 23.02, 22.84 ppm.

Procedure for stereoselective reduction of ketone functionality:

4.26. (*R*)-1-((*4S,5S*)-5-((*Z*)-Heptadec-8-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-ol (11)

Dess-Martin periodinane (300 mg, 0.3 mmol) was added to the solution of alcohols **11** and **24** (139 mg, 0.35 mmol) in dichloromethane (3 mL) solution at 0 ºC. The reaction was allowed to stir at room temperature for 30 mins. After the reaction was completed as determined by TLC, the solid was removed by filtration of the reaction mixture through a pad of celite and washed twice with dichloromethane (3 mL). The filtrate was washed sequentially with aqueous sodium bicarbonate and brine and dried over $MgSO_4$. The solvent was removed under reduced pressure to afford a solid residue that was purified through silica gel (60-120 mesh) column chromatography to furnish the corresponding propargylic ketone (127 mg, 0.32 mmol, 92%) as a colourless liquid. R_f = 0.5 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = -9.40 (*c* 0.22, $CHCl_3$). IR ν_{max}: 3253, 2924, 2855, 2312, 2095, 1748, 1688, 1619, 1459, 1376, 1221, 1164, 1081, 867 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 5.40-5.32 (m, 2H), 4.14 (dt, *J* = 4.2, 7.6 Hz, 1H), 4.09 (d, *J* = 7.6 Hz, 1H), 3.43 (s, 1H), 2.05-1.97 (m, 4H), 1.80-1.64 (m, 2H), 1.49 (s, 3H), 1.46 (s, 3H), 1.37-1.23 (m, 24H), 0.88 (t, *J* = 6.5 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 186.10, 129.96, 129.75, 111.35, 85.70, 82.80, 79.55, 78.36, 33.44, 32.59, 32.55, 31.89, 29.75, 29.71, 29.65, 29.51, 29.47, 29.44, 29.34, 29.31, 29.18, 28.18, 27.29, 27.21, 27.17, 26.08, 25.61, 22.67, 14.10 ppm. MS(ESI): *m/z* 392 $[M+H]^+$.

To a magnetically stirred solution of (*R*)-(+)-2-methyl-CBS-oxazaborolidine (1 M solution in toluene, 0.10 mL, 0.10 mmol) in anhydrous THF (5 mL) was added dropwise BH_3–DMS (1 M solution in THF, 0.20 mL, 0.20 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 30 min. The generated complex was cooled to –78 °C, and then a solution of above prepared ketone (0.020 g, 0.05 mmol) in THF (2 mL) was added dropwise. The stirring was continued until the complete consumption of starting material was observed (as indicated by TLC, approximately 24 h). The reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and then diluted with water (5 mL). The resulting solution was extracted with EtOAc (4X5 mL). The combined extracts were washed with brine (7 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. Purification by column chromatography (hexane/EtOAc, 90:10) gave diastereomeric mixture (0.016 g, 84%) of **11** and **24** in 7:3 ratio. The diasteromeric ratio was easily determined from ^1H NMR analysis.

4.27. Stereoseletive synthesis of (*R*)6-((*tert*-butyldimethylsilyl)oxy)-1-((*4R,5S*)-2,2-dimethyl-5-(14-methylpentadecyl)-1,3-dioxolan-4-yl)hexa-2,4-diyn-1-ol (35)

Dess-Martin periodinane (155 mg, 0.36 mmol) was added to the mixture of alcohols **35 & 35a** (100 mg, 0.18 mmol) in CH_2Cl_2 (5 mL) at 0 ºC. The reaction was allowed to stirr at room temperature for 30 min. After the reaction was complete as determined by TLC, the solid was removed by filtration of the reaction mixture through a pad of celite and washed twice with dichloromethane (5 mL). The filtrate was washed sequentially with aqueous sodium bicarbonate and brine and dried over $MgSO_4$. The solvent was removed under reduced pressure to afford a solid residue that was purified through silica gel (60-120 mesh) column chromatography to afford the corresponding propargylic ketone (91.6 mg, 0.16 mmol, 92%) as a colorless liquid R_f = 0.6 (10% EtOAc-Hexane). $[\alpha]^{25}_D$ = -18.18 (*c*, 0.44, $CHCl_3$). IR ν_{max}: 2925, 2856, 2230, 2187, 1792, 1727, 1674, 1462, 1375, 1253, 1221, 1092, 838, 752, 711 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 4.46 (s, 2H), 4.12 (dt, *J* = 4.2, 7.4 Hz), 4.06 (d, *J* = 7.7 Hz), 1.77- 1.49 (m, 2H), 1.48 (s, 3H), 1.46 (s, 3H), 1.34-1.24 (m, 24H), 0.91 (s, 9H), 0.86 (d, *J* = 6.6 Hz), 0.13 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 185.83, 111.39, 87.89, 85.86, 79.17, 78.54, 77.19, 73.25, 67.79, 52.13, 39.05, 33.35, 29.94, 29.68, 29.53, 29.46, 27.95, 27.41, 27.29, 26.03, 25.66, 25.60, 22.64, -5.24 ppm. MS(ESI): *m/z* 569 $(M+Na)^+$.

To a magnetically stirred solution of (*R*)-(+)-2-methyl-CBS-oxazaborolidine (1 M solution in toluene, 0.073 mL, 0.073 mmol) in anhydrous THF (2 mL) was added dropwise BH_3.DMS (1 M solution in THF, 0.14 mL, 0.14 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 30 min. The generated complex was cooled to –40 °C, and then a solution of above prepared ketone (0.020 g, 0.036 mmol) in THF (2 mL) was added dropwise. The stirring was continued until there was complete consumption of starting material (indicated by TLC, approximately 24 h). The reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and then diluted with water (5 mL). The resulting solution was extracted with EtOAc (4X5 mL). The combined extracts were washed with brine (7 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. Purification by column chromatography (hexane/EtOAc, 90:10) gave diastereomeric mixture (0.017 g, 89%) of **35** and **35a** in 9.8:0.2 ratio by LCMS analysis.

Acknowledgements

PG thanks CSIR, New Delhi for financial assistance in the form of fellowship. PSH thanks CSIR-New Delhi for funding under XII Five year plan programme project ORIGIN under budget head CSC-0108.

Supplementary Material

Copies of ^1H and ^{13}C NMR are available as supplementary material.

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