A Practical Total Synthesis of Both *E*- and *Z*-Isomers of Optically Pure (*S*)-14-Methylhexadec-8-enal (Trogodermal)

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Abstract: The total synthesis of both *E*- and *Z*-isomers of optically pure (*S*)-14-methylhexadec-8-enal (trogodermal) is described. Key steps involved Corey–Fuchs reaction, zipper isomerization, and different hydrogenation conditions for *cis*- and *trans*-isomers.

Key words: sex pheromone, trogodermal, (*R*)-citronellol, Corey–Fuchs reaction, zipper isomerization

Beetles that belong to *Trogoderma* genus create havoc in rice storage. It certainly requires a nonpesticidal management strategy to protect the stored grain, which is possible only with the application of insect pheromones. As early as 1969, Rodin et al. isolated (–)-(*Z*)-14-methylhexadec-8-en-l-ol (**2**) and (–)-methyl (*E*)-14-methylhexadec-8-enoate (**5**) as the sex pheromone of the female dermestid beetle (*Trogoderma inclusum*) by extracting whole insect bodies.[1] In 1976, Cross et al.[1c] isolated the genuine sex pheromone systems of *Trogoderma inclusum*, *Trogoderma variabile*, and *Trogoderma glabrum*. They identified it as (*Z*)-14-methylhexadec-8-enal (**1**) in both *T. inclusum* and *T. variabile*, but the corresponding *E*-isomer in *T. glabrum*. However, both isomers were found in *T. granarium* in a *Z*/*E* ratio of 92:8. Although the two pheromone[2–4] aldehydes **1** and **3** (Figure 1) as well as their enantiomers have been synthesized by other research groups, which include those of Mori[2] and R. Rossi,[3] they remain of interest in terms of an affordable synthesis considering their application in the management of storage pests.

As a part of our ongoing work on the synthesis of pheromones,[5] herein we report the synthesis of trogodermals **1** and **3** using reactions such as the Corey–Fuchs reaction and zipper isomerization from the readily available starting material citronellol. Our retrosynthetic analysis is outlined in Scheme 1. It is envisioned that the two trogodermals **1** and **3** can be synthesized by coupling the corresponding alkyne fragment **6** and respective bromo compound **7A**. The alkyne fragment can be obtained from readily available starting material (*R*)-citronellol (**8**), whereas the bromo compound can be obtained from heptane-1,7-diol (**7**).

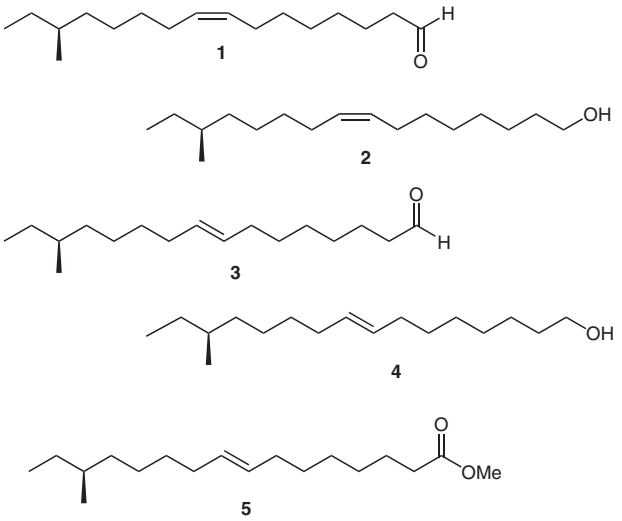
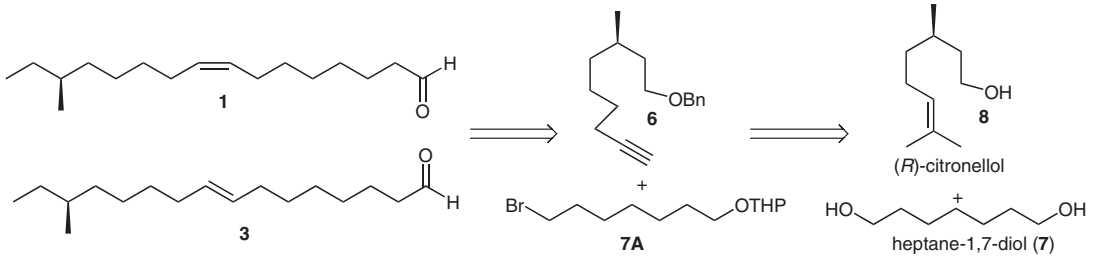


Figure 1 *Trogoderma* pheromone components



Scheme 1 Retrosynthetic analysis of (*S*,*Z*)- and (*S*,*E*)-trogodermals

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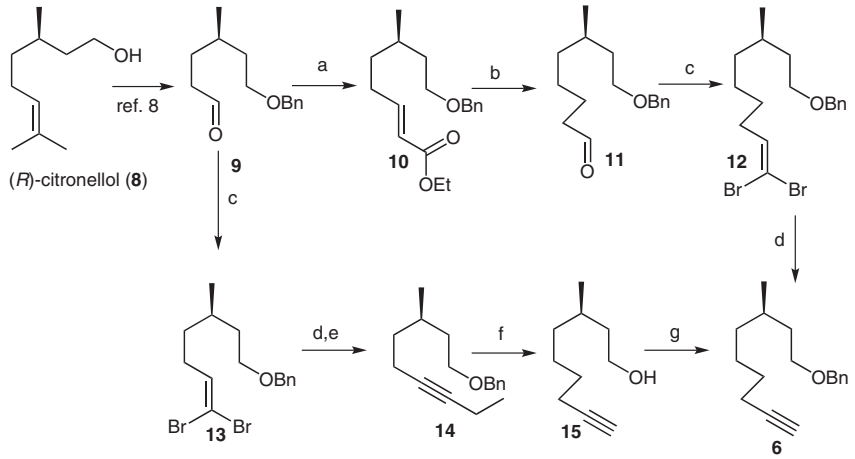


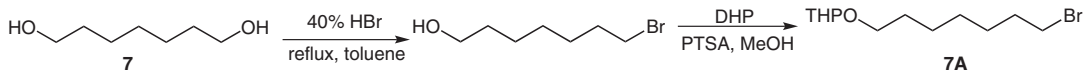
Scheme 2 *Reagents and conditions:* (a) $Ph_3P{=}CHCO_2Et$, CH_2Cl_2, 0–25 °C, 2 h, 80%; (b) 1. $LiAlH_4$, THF, 73%; 2. IBX, DMSO–CH_2Cl_2 (1:3), 1 h, 90%; (c) CBr_4, Ph_3P, CH_2Cl_2, 12 h, 90%; (d) BuLi, THF, 0 °C, 90%; (e) EtI, THF, –78 °C, 80%; (f) 1. Na, liq NH_3, THF, –33 °C, 15 min, 94%; 2. $NaNH_2$, Li 1,3-diaminopropane, 65 °C, 6 h, 68%; (g) NaH, BnBr, THF, 90%.

Accordingly, alkyne fragment **6** is derived from aldehyde **9**,[8] which is prepared from (*R*)-citronellol (**8**). Aldehyde **9** was treated with a C_2-Wittig salt in benzene to give α,β-unsaturated ester **10**, which upon treatment with lithium aluminum hydride in tetrahydrofuran provided the corresponding alcohol in 73% yield. The alcohol on oxidation with 2-iodoxybenzoic acid in dimethyl sulfoxide–dichloromethane (1:3) at room temperature afforded the aldehyde **11** in 90% yield. Compound **11** was subjected to Corey–Fuchs[6] reaction using triphenylphosphine and carbon tetrabromide in dichloromethane at 0 °C to obtain to dibromoalkene **12** in 90% yield. Dibromoalkene **12** was converted into alkyne **6** using butyllithium in tetrahydrofuran at 0 °C in 90% yield as described in Scheme 2.

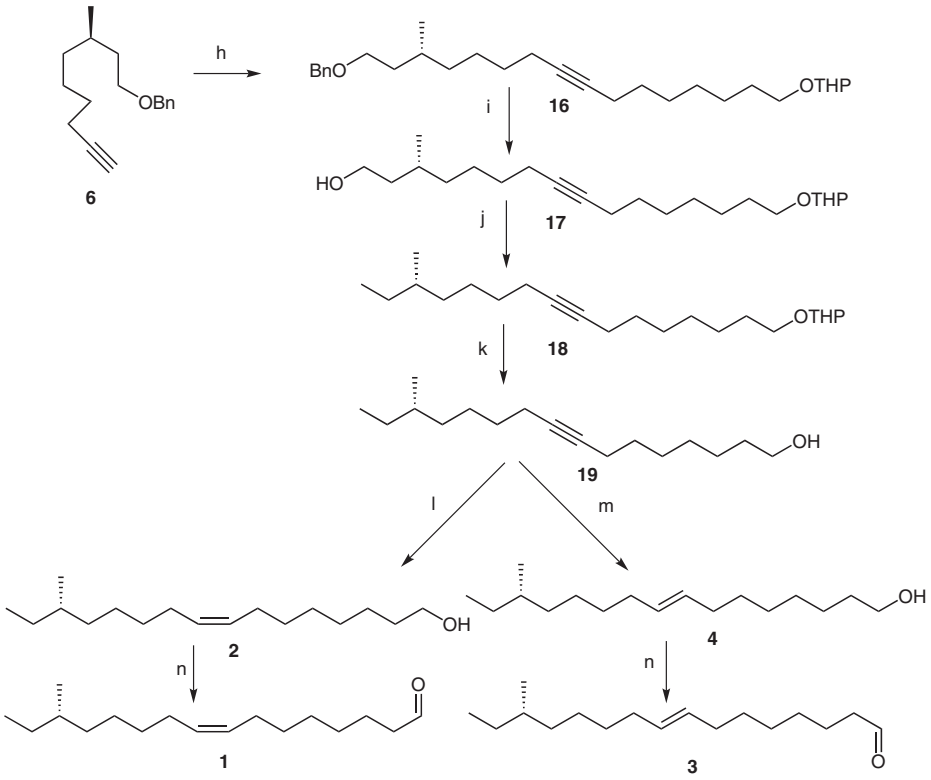
The fragment **6** was also synthesized from aldehyde **9** by subjecting it to Corey–Fuchs[6] reaction and converting it into dibromoalkene **13** in 90% yield. Compound **13** was converted into alkyne **14** in 80% yield (Scheme 2) using butyllithium in tetrahydrofuran at 0 °C followed by reaction with iodoethane in tetrahydrofuran at –78 °C. Alkyne **14** was subjected to zipper isomerization[7] under different reaction conditions (*t*-BuOK, 1,3-diaminopropane, 80 °C, 6 h; *t*-BuOK, Li, 1,3-diaminopropane, r.t., 20 h; $NaNH_2$, NaH, or NaH, THF in 1,3-diaminopropane, 60 °C, 6 h). However, in every case the reaction was unsuccessful, but after deprotection of the benzyl group the reaction gave alkyne **15** in 68% yield. Upon protection with the benzyl group, using benzyl bromide and sodium hydride in tetrahydrofuran, compound **15** yielded the required alkyne **6** as described in Scheme 2.

For the preparation of trogodermals **1** and **3**, compound **6** was converted into the corresponding alkynyllithium using lithium in liquid ammonia and then coupled with bromo compound **7A** (for the synthesis of **7A** see Scheme 3) to produce alkyne **16** in 85% yield (Scheme 4). Deprotection of the benzyl group with sodium in liquid ammonia at –33 °C produced alcohol **17** in 94% yield, which upon tosylation with tosyl chloride and triethylamine in dichloromethane followed by reduction with lithium aluminum hydride afforded the alkyne **18** in 95% yield. The alkyne **18** was treated with 4-toluenesulfonic acid in methanol to give primary alcohol **19** in 90% yield. Catalytic partial hydrogenation of alcohol **19** with Lindlar's catalyst[7g] containing quinoline gave the *Z*-isomer of trogodermol **2** in 94% yield, which on further oxidation with 2-iodoxybenzoic acid in dimethyl sulfoxide–dichloromethane (1:3) provided (*Z*)-trogodermal **1** in 87% yield. Similarly, *trans* reduction of alcohol **19** with sodium in liquid ammonia at –33 °C afforded the *E*-isomer of trogodermol **4** in 94% yield, which on further oxidation with 2-iodoxybenzoic acid in dimethyl sulfoxide–dichloromethane (1:3) afforded (*E*)-trogodermal **3** in 87% yield (Scheme 4). The spectral data of the thus synthesized compounds **1** and **3** are in agreement with the reported products.[1–4]

In summary, a practical total synthesis of both *E*- and *Z*-isomers of optically pure (*S*)-14-methylhexadec-8-enal (trogodermal) is successfully accomplished in 21.6% overall yield from (*R*)-8-(benzyloxy)-6-methyloctanal, which can be easily prepared from (*R*)-citronellol, a commercially available compound. The key steps involve the Corey–Fuchs reaction and zipper isomerization.



Scheme 3



Scheme 4 *Reagents and conditions:* (h) Li, liq NH_3, **7A**, HMPA, THF, –78 °C, 85%; (i) Na, liq NH_3, THF, –33 °C, 15 min, 94%; (j) 1. TsCl, Et_3N, CH_2Cl_2, 0 °C to r.t., 6 h, 95%; 2. $LiAlH_4$, THF, 0 °C to r.t., 4 h, 95%; (k) PTSA, MeOH, 1 h, 90%; (l) $Pd/BaSO_4$, H_2, quinoline, EtOH, 6 h, 94%; (m) Na, liq NH_3, THF, –33 °C, 12 h, 94%; (n) IBX, DMSO–CH_2Cl_2 (1:3), 90%.

All reactions were carried out under an inert atmosphere unless mentioned following standard syringe septa techniques. Solvents were dried and purified by conventional methods prior to use. The progress of all the reactions was monitored by TLC using glass plates precoated with silica gel-60 F_{254} to a thickness of 0.5 mm (Merck). Column chromatography was performed on silica gel (60–120 mesh) and neutral alumina using Et_2O, EtOAc, petroleum ether (PE), and hexane as the eluents. Optical rotation values were measured with a Perkin-Elmer P241 polarimeter and Jasco DIP-360 digital polarimeter at 25 °C and IR spectra were recorded with a Perkin-Elmer FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with Bruker Avance 300 MHz spectrometer using TMS as an internal standard in $CDCl_3$. Mass spectra were recorded on Micro mass VG-7070H for EI and VG Autospec M for FAB-MS.

Ethyl (*R*,*E*)-8-(Benzyloxy)-6-methyloct-2-enoate (10)

Ethyl (triphenylphosphoranylidene)acetate (7.7 g, 22.11 mmol) was added to a stirred soln of **9** (4.0 g, 18.43 mmol) in CH_2Cl_2 (38 mL) at 0 °C; the mixture was stirred for 2 h at r.t. The solvent was removed in vacuo, and the residue was purified by column chromatography (silica gel, EtOAc–PE, 1:9; R_f = 0.6) to afford pure **10** (4.2 g, 80%) as a colorless liquid; $[\alpha]_D^{25}$ +2.9 (*c* 1.0, $CHCl_3$).

IR (KBr): 3432, 2925, 2856, 1719, 1200, 1101, 738, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.17–7.36 (m, 5 H), 6.84–6.97 (m, 1 H), 5.76 (td, *J* = 1.5, 15.6 Hz, 1 H), 4.45 (s, 2 H), 4.15 (q, *J* = 7.1 Hz, 2 H), 3.45 (dt, *J* = 14.7, 2.4 Hz, 2 H), 2.20 (m, 2 H), 1.33–1.71 (m, 5 H), 1.28 (t, *J* = 7.1 Hz, 3 H), 0.89 (d, *J* = 6.42 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7, 149.3, 138.4, 128.3, 127.6, 127.5, 72.8, 68.4, 60.0, 36.4, 35.1, 29.6, 29.4, 19.2, 14.2.

MS (ESI): *m*/*z* = 313 $[M + Na]^+$.

(*R*)-8-(Benzyloxy)-6-methyloctanal (11)

To a stirred suspension of $LiAlH_4$ (1.1 g, 28.96 mmol) in anhyd THF (10 mL) at 0 °C, a soln of α,β-unsaturated ester **10** (4.2 g, 14.48 mmol) in anhyd THF (20 mL) was added dropwise. Then the mixture was refluxed for 4 h and cooled to 0 °C, diluted with Et_2O, and quenched by dropwise addition of sat. aq Na_2SO_4. The solid material was filtered and washed thoroughly with hot EtOAc several times. The combined organic layers were dried (anhyd Na_2SO_4). The solvent was removed in vacuo and the crude alcohol was used directly without purification. To a stirred soln of 2-iodoxybenzoic acid (4.1 g, 14.7 mmol) in DMSO (5 mL) was added a soln of alcohol (2.64 g, 10.57 mmol) in CH_2Cl_2 (15 mL) at r.t. and the mixture was stirred for 1 h. When the reaction was complete (TLC monitoring), H_2O (10 mL) was added to the mixture, the precipitated solid was filtered off, and the filtrate was diluted with H_2O (50 mL) and extracted with Et_2O (4 × 50 mL). The combined organic layers were washed with aq $NaHCO_3$, H_2O, and brine, and dried (Na_2SO_4). The solvent was removed and the residue was purified by column chromatography (silica gel, EtOAc–PE, 1:9; R_f = 0.7) to afford pure **11** (2.313 g, 90%) as a viscous liquid; $[\alpha]_D^{25}$ +1.3 (*c* 1.0, $CHCl_3$).

IR (KBr): 2927, 2859, 1712, 1454, 1365, 1219, 1106, 1072, 772 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.70 (t, *J* = 1.70 Hz, 1 H), 7.25–7.32 (m, 5 H), 4.45 (s, 2 H), 3.44 (dt, *J* = 6.6, 1.1 Hz, 2 H), 2.36 (dt, *J* = 7.1, 1.7 Hz, 2 H), 1.52–1.68 (m, 4 H), 1.23–1.45 (m, 4 H), 1.07–1.19 (m, 1 H), 0.87 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.2, 138.5, 128.2, 127.5, 127.4, 72.83, 68.4, 43.8, 36.71, 36.66, 29.64, 26.47, 22.27, 19.55.

MS (ESI): *m*/*z* = 271 $[M + Na]^+$.

(*R*)-[(9,9-Dibromo-3-methylnon-8-enyloxy)methyl]benzene (12)

To a soln of aldehyde **11** (2.3 g, 9.32 mmol) in CH_2Cl_2 (30 mL) were added CBr_4 (7.7 g, 23.3 mmol) and Ph_3P (9.7 g, 37.28 mmol), and the mixture was stirred at r.t. for 12 h. The mixture was concentrated under reduced pressure to leave a crude oil. Purification by chroma-

tography (silica gel, EtOAc–PE, 1:9; R_f = 0.8) afforded **12** (3.3 g, 90%) as a magenta-colored liquid; $[\alpha]_D^{25}$ +1.7 (*c* 1.0, $CHCl_3$).

IR (KBr): 3449, 2925, 2855, 1455, 1101, 772 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.18–7.34 (m, 5 H), 6.34 (t, *J* = 7.36 Hz, 1 H), 4.45 (s, 2 H), 3.40–3.50 (m, 2 H), 2.03–2.13 (m, 2 H), 1.54–1.69 (m, 2 H), 1.21–1.46 (m, 7 H), 0.87 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.6, 138.4, 128.2, 127.4, 127.3, 96.2, 72.9, 68.4, 68.3, 36.8, 33.0, 29.8, 28.4, 28.4, 26.5, 25.7, 19.8.

(*R*)-[(3-Methylnon-8-ynyloxy)methyl]benzene (6)

To soln of dibromo compound **12** (3.3 g, 8.34 mmol) in anhyd THF (24 mL), 1.6 M BuLi in THF (1.2 mL, 12.5 mmol) was added at –78 °C over 0.5 h; the mixture was stirred for 2 h. The mixture was quenched with sat. $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with sat. NaCl (10 mL) and H_2O (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, EtOAc–PE, 1:9, R_f = 0.85) to afford pure **6** (1.79 g, 90%) as a colorless liquid; $[\alpha]_D^{25}$ +0.3 (*c* 1.00, $CHCl_3$).

IR (KBr): 3305, 2928, 2858, 1456, 1365, 1101, 737 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.18–7.34 (m, 5 H), 4.45 (s, 2 H), 3.40–3.50 (m, 2 H), 2.12–2.19 (dt, *J* = 6.8, 1.9 Hz, 1 H), 1.82 (s, 1 H), 1.55–1.67 (m, 2 H), 1.07–1.53 (m, 8 H), 0.88 (d, *J* = 6.83 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.6, 128.2, 127.5, 127.4, 72.8, 68.5, 68.2, 36.7, 36.4, 29.7, 29.3, 28.6, 26.0, 19.6, 18.3.

MS (ESI): *m*/*z* = 267 $[M + Na]^+$.

(*R*)-[(7,7-Dibromo-3-methylhept-6-enyloxy)methyl]benzene (13)

To a soln of aldehyde **9** (1.0 g, 4.60 mmol) in CH_2Cl_2 (50 mL) were added CBr_4 (3.8 g, 11.5 mmol) and Ph_3P (4.8 g, 18.4 mmol) and the mixture was stirred at r.t. for 1 h. The mixture was concentrated under reduced pressure to leave a crude oil. Purification by chromatography (silica gel, EtOAc–PE, 1:9, R_f = 0.7) afforded **13** (1.6 g, 90%) as a magenta-colored liquid.

IR (KBr): 3449, 3029, 2925, 2855, 1455, 1101, 772 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.18–7.34 (m, 5 H), 6.34 (t, *J* = 7.36 Hz, 1 H), 4.45 (s, 2 H), 3.40–3.50 (m, 2 H), 2.03–2.13 (m, 2 H), 1.54–1.69 (m, 2 H), 1.21–1.46 (m, 3 H), 0.87 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.6, 138.4, 128.2, 127.4, 96.2, 72.9, 68.4, 36.8, 33.0, 29.0, 28.19, 19.8.

(*R*)-[(3-Methylnon-6-ynyloxy)methyl]benzene (14)

To a soln of dibromo compound **13** (1.6 g, 4.14 mmol) in anhyd THF (15 mL), 1.6 M BuLi in THF (10 mL, 10.31 mmol) was added at –78 °C. Then slowly EtI (0.4 mL, 2.5 mmol) was added at –78 °C and the mixture was stirred for 2 h. The mixture was quenched with sat. $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were washed with sat. NaCl (10 mL) and H_2O (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, EtOAc–PE, 1:9, R_f = 0.75) to afford pure **14** (0.80 g, 80%) as a colorless liquid.

IR (KBr): 2926, 2858, 1722, 1455, 1366, 1273, 1103, 737 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.33 (m, 5 H), 4.47 (s, 2 H), 3.48 (dt, *J* = 6.7, 1.5 Hz, 2 H), 2.06–2.18 (m, 4 H), 1.36–1.79 (m, 2 H), 1.21–1.35 (m, 3 H), 1.10 (t, *J* = 7.3 Hz, 2 H), 0.94–1.0 (m, 1 H), 0.89 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 129.4, 128.2, 127.5, 127.3, 72.8, 68.4, 36.3, 29.6, 19.4, 19.1, 16.3, 14.2, 12.3.

MS (ESI): *m*/*z* = 267 $[M + Na]^+$.

(*R*)-3-Methylnon-8-yn-1-ol (15)

To a soln of Na (0.50 g, 19.8 mmol) in liquid NH_3 (25 mL) was added compound **14** (0.8 g, 3.31 mmol) in anhyd THF (8 mL) at –33 °C. The mixture was stirred for 15 min and quenched with solid NH_4Cl (1.5 g). NH_3 was allowed to evaporate and Et_2O was added to the residual mixture and it was filtered through a pad of celite. The filtrate was dried (anhyd Na_2SO_4). The solvent was removed in vacuo to give a residue (0.473 g, 94%) that was used for the next reaction without purification. Li wire (0.63 g, 90 mmol) was added to 1,3-diaminopropane (4 mL) in a 100-mL two-necked pear-shaped flask. The soln was heated at 80 °C for 2 h until the blue color had discharged and the white lithium salt was evident. The mixture was cooled to r.t., and $NaNH_2$ (0.58 g, 64.8 mmol) was added in one portion. The resulting yellow soln was stirred for 15 min. A soln of the internal alkyne (0.47 g, 3.0 mmol) in 1,3-diaminopropane (5 mL) was added dropwise, and the blood-red soln was heated at 65 °C for 6 h. The resulting brown soln was cooled to r.t. and then in an ice bath and quenched with sat. aq NH_4Cl. The resulting mixture was poured into H_2O (10 mL) and acidified with concd HCl (10 mL). This mixture was then extracted with $CHCl_3$. Evaporation of the $CHCl_3$, addition of benzene (10 mL), and subsequent evaporation afforded a tan solid that was adsorbed onto silica gel and added to the top of a chromatography column. Flash chromatography (10% EtOAc–hexanes) gave **15** (0.32 g, 68%) as colorless oil; R_f = 0.2 (EtOAc–PE, 1:9).

IR (KBr): 3305, 2931, 2860, 2117, 1727, 1462, 1433, 1378, 1056, 629 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.61–3.73 (m, 2 H), 2.19 (dt, *J* = 6.7, 1.2 Hz, 2 H), 2.02–2.08 (br, 1 H), 1.94 (t, *J* = 2.5 Hz, 1 H), 1.12–1.65 (m, 9 H), 0.90 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 84.6, 68.13, 61.1, 39.8, 36.5, 29.3, 28.6, 26.0, 19.5, 18.3.

MS (EI): *m*/*z* = 155 $[M + H]^+$.

2-[(*R*)-16-(Benzyloxy)-14-methylhexadec-8-ynyloxy]tetrahydro-2*H*-pyran (16)

Into a suitable flask fitted with an NH_3 condenser at –40 °C, NH_3 (45 mL) was collected and to this was added a catalytic amount of $Fe_2(NO_3)_3$ (20 mg, 0.17 mmol) followed by Li (0.33 g, 47.14 mmol) over a period of 20 min. The contents were stirred for 30 min to form $LiNH_2$. Then (*R*)-[(3-methylnon-8-ynyloxy)methyl]benzene (**6**, 1.0 g, 4.09 mmol) was added in THF (8 mL) followed by HMPA (3 mL) as co-solvent. The contents were stirred for 2 h and then compound **7A** (1.2 gm) in THF (5 mL) was added. The mixture was stirred for 6 h and quenched with NH_4Cl (1 g). The mixture was warmed to r.t. for evaporation of NH_3. The residue was dissolved in Et_2O (20 mL) and sat. NH_4Cl soln (10 mL) was added. The organic layer was separated and washed with brine (10 mL). The organic layer was concentrated under reduced pressure and the residue was subjected to column chromatography to give **16** (1.53 g, 85%) as a colorless liquid; R_f = 0.6 (EtOAc–PE, 1:9); $[\alpha]_D^{25}$ +0.3 (*c* 0.6, $CHCl_3$).

IR (KBr): 3305, 3030, 2930, 2858, 1638, 1456, 1364, 1103, 1029, 908, 737, 631 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.22–7.37 (m, 5 H), 4.57 (t, *J* = 3.39 Hz, 1 H), 4.45 (s, 2 H), 3.81–3.90 (m, 1 H), 3.67–3.76 (m, 1 H), 3.45–3.54 (m, 3 H), 3.31–3.41 (m, 1 H), 2.09–2.16 (m, 4 H), 1.22–1.87 (m, 25 H), 0.88 (d, *J* = 6.42 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.6, 128.2, 127.5, 127.4, 98.7, 80.18, 80.13, 72.8, 68.6, 67.5, 62.2, 62.9, 36.7, 36.5, 30.7, 29.7, 29.6, 29.3, 29.0, 28.9, 28.7, 26.1, 25.4, 19.6, 19.5, 18.7.

MS (ESI): *m*/*z* = 465 $[M + Na]^+$.

(3*R*)-3-Methyl-16-(tetrahydro-2*H*-pyran-2-yloxy)hexadec-8-yn-1-ol (17)

To a soln of Na (0.80 g, 34.78 mmol) in liquid NH_3 (25 mL) was added compound **16** (1.50 g, 3.40 mmol) in anhyd THF (8 mL) at

–33 °C. The mixture was stirred for 15 min and was quenched with solid NH_4Cl (5.5 g). NH_3 was allowed to evaporate and Et_2O was added to the residual mixture and this was filtered through a pad of celite. The filtrate was dried (anhyd Na_2SO_4). Removal of the solvent under vacuum and purification of the crude product by column chromatography afforded the alcohol **17** (1.14 g, 94%) as colorless oil; R_f = 0.1 (EtOAc–PE, 1:9); $[\alpha]_D^{25}$ –2.0 (*c* 0.3, $CHCl_3$).

IR (KBr): 3421, 2931, 2858, 1458, 1352, 1125, 1069, 1029, 869, 726 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.56 (t, *J* = 3.77 Hz, 1 H), 3.58–3.91 (m, 4 H), 3.44–3.54 (m, 1 H), 3.31–3.43 (m, 1 H), 2.08–2.17 (m, 4 H), 1.75–1.89 (m, *J* = 6.4 Hz, 1 H), 1.20–1.70 (m, 25 H), 0.89 (d, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 98.7, 80.2, 80.0, 67.6, 62.2, 61.0, 39.8, 36.5, 30.6, 29.6, 29.3, 29.2, 29.0, 28.9, 28.7, 26.0, 25.4, 19.6, 18.6.

MS (ESI): *m*/*z* = 375 $[M + Na]^+$.

2-[(*S*)-14-Methylhexadec-8-ynyloxy]tetrahydro-2*H*-pyran (18)
To soln of alcohol **17** (1.1 g, 3.25 mmol) in anhyd CH_2Cl_2 (15 mL), Et_3N (2.7 mL, 19.40 mmol) was added at 0 °C. Then TsCl (1.23 g, 6.5 mmol) was added over 2 h. The mixture was allowed to warm to 25 °C and stirred for 6 h. The mixture was treated with 1 M aq HCl (10 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with sat. $NaHCO_3$ (15 mL) and H_2O (15 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give a residue (1.50 g, 95%) that was used for the next reaction without purification. $LiAlH_4$ (0.22 g, 5.92 mmol) was added to THF (8 mL) at 0 °C, then tosyl compound (1.5 g) was added and the mixture was stirred at r.t. for 4 h. The reaction was quenched with ice cubes at 0 °C (100 mg), The mixture was extracted with EtOAc (3 × 30 mL) and the combined extracts were washed with H_2O (15 mL) and brine (15 mL), and dried (anhyd Na_2SO_4). The solvent was evaporated under reduced pressure and the crude was subjected to column chromatography (silica gel) to give **18** (0.94 g, 95%) as a colorless liquid; R_f = 0.5 (EtOAc–PE, 1:9); $[\alpha]_D^{25}$ +1.3 (*c* 1.0, $CHCl_3$).

IR (KBr): 3447, 2929, 2857, 1459, 1351, 1263, 1126, 1074, 1030, 974, 904, 871, 812 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.57 (t, *J* = 3.49 Hz, 1 H), 3.84–3.90 (m, 1 H), 3.69–3.77 (m, 1 H), 3.47–3.54 (m, 1 H), 3.35–3.43 (m, 1 H), 2.14 (t, *J* = 6.49 Hz, 4 H), 1.79–1.87 (m, 1 H), 1.67–1.74 (m, 1 H), 1.24–1.63 (m, 22 H), 1.07–1.19 (m, 1 H), 0.83–0.91 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 98.8, 80.2, 80.1, 67.6, 62.3, 36.0, 34.2, 30.7, 29.7, 29.4, 29.4, 29.1, 29.0, 28.7, 26.3, 26.6, 25.5, 19.6, 19.1, 18.7, 18.7, 11.3.

MS (ESI): *m*/*z* = 359 $[M + Na]^+$.

(*S*)-14-Methylhexadec-8-yn-1-ol (19)
To a stirred soln of compound **18** (0.9 g, 2.8 mmol) in MeOH (10 mL), PTSA (catalytic amount, 0.02 g) was added at 0 °C and the mixture was stirred for 1 h at r.t. The mixture was quenched with sat. aq $NaHCO_3$ soln (2 mL) and extracted with EtOAc (2 × 15 mL) The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude residue was purified by column chromatography (EtOAc–PE, 1:9; R_f = 0.3); to afford **19** (0.6 g, 90%) as a colorless liquid; $[\alpha]_D^{25}$ +1.5 (*c* 0.29, $CHCl_3$).

IR (KBr): 3339, 2929, 2856, 1459, 1376, 1334, 1056, 725 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.64 (t, *J* = 6.61 Hz, 2 H), 1.94–2.18 (m, 4 H), 1.24–1.61 (m, 19 H), 1.19–1.04 (m, 1 H), 0.82–0.89 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$) : δ = 63.0, 36.0, 35.7, 34.2, 32.6, 29.4, 29.0, 28.9, 28.7, 26.2, 25.6, 19.1, 18.7, 18.6, 11.3.

MS (ESI): *m*/*z* = 275 $[M + Na]^+$.

(*S*,*E*)-14-Methylhexadec-8-en-1-ol (4)
To freshly condensed NH_3 (15 mL) at –33 °C, compound **19** (0.3 g) in THF (8 mL) was added slowly followed by Na (0.53 g) in a portionwise manner. The mixture was stirred for 12 h and then it was quenched with NH_4Cl (1 g). The NH_3 was allowed to evaporate and sat. NH_4Cl soln was added carefully at 0 °C. The mixture was extracted with Et_2O (2 × 20 mL) and the combined extracts were washed with brine (10 mL). The soln was dried (anhyd Na_2SO_4) and concentrated under reduced pressure to give the crude product. Purification by column chromatography gave the *trans*-olefin **4** (0.284 g, 94%); R_f = 0.35 (EtOAc–PE, 1:9); $[\alpha]_D^{25}$ +5.29 (*c* 2.823, $CHCl_3$).

IR (KBr): 3339, 2956, 2925, 2855, 1460, 1376, 1219, 1055, 965, 772 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.28–5.40 (m, 2 H), 3.64 (t, *J* = 6.61 Hz, 2 H), 1.93–2.01 (m, 4 H), 1.50–1.60 (m, 2 H), 1.21–1.46 (m, 16 H), 1.04–1.18 (m, 2 H), 0.82–0.92 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 130.3, 130.1, 62.9, 36.3, 34.2, 32.6, 32.5, 29.9, 29.4, 29.4, 29.2, 29.0, 26.5, 25.6, 25.6, 19.1, 11.3.

MS (ESI): *m*/*z* = 277 $[M + Na]^+$.

Anal. Calcd for $C_{17}H_{34}O$: C, 80.24; H, 13.47. Found: C, 80.04; H, 13.01.

(*S*,*E*)-14-Methylhexadec-8-enal (3)
To an ice-cooled soln of 2-iodoxybenzoic acid (0.327 g, 1.17 mmol) in DMSO (0.55 mL, 7.55 mmol) was added a soln of alcohol **4** (0.2 g, 0.78 mmol) in anhyd CH_2Cl_2 (1.5 mL). The mixture was stirred at r.t. for 2 h and then filtered through a celite pad and washed with Et_2O. The combined organic filtrates were washed with H_2O, brine, dried (anhyd Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (silica gel, EtOAc–PE, 1:9; R_f = 0.7) to afford pure **3** (0.178 g, 90%) as a viscous liquid; $[\alpha]_D^{25}$ +5.83 (*c* 3.55, Et_2O).

IR(KBr): 2956, 2928, 2856, 2715, 1728, 1461, 1377, 967, 730 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.75 (t, *J* = 1.51 Hz, 1 H), 5.32–5.37 (m, 2 H), 2.37–2.44 (m, 2 H), 1.90–2.05 (m, 4 H), 1.57–1.70 (m, 2 H), 1.22–1.43 (br, 13 H), 1.05–1.18 (m, 1 H), 0.81–0.90 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.2, 130.3, 130.0, 129.3, 43.6, 36.5, 34.3, 32.5, 32.5, 32.1, 29.4, 28.5, 27.1, 27.0, 26.7, 26.5, 22.0, 19.1, 11.1.

Anal. Calcd for $C_{17}H_{32}O$: C, 80.88; H, 12.78. Found: C, 80.40; H, 12.27.

(*S*,*Z*)-14-Methylhexadec-8-en-1-ol (2)
Compound **19** (0.3 g) was dissolved in abs EtOH (10 mL), and Lindlar's catalyst (10 mg) was added along with quinoline (2–3 drops). The flask was hydrogenated with stirring until no more H_2 consumption was noticed. The mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was subjected to column chromatography (silica gel) to afford alcohol **2** (0.28 g, 94%); R_f = 0.35 (EtOAc–PE, 1:9); $[\alpha]_D^{25}$ +5.31 (*c* 4.57, $CHCl_3$).

IR (KBr): 3379, 2923, 2854, 1650, 1458, 1375, 1054, 966, 721 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.25–5.37 (m, 2 H), 3.61 (t, *J* = 6.4 Hz, 2 H), 1.92–2.05 (m, 4 H), 1.49–1.61 (m, 2 H), 1.22–1.40 (m, 16 H), 1.04–1.18 (m, 2 H), 0.82–0.90 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 130.3, 130.1, 29.0, 27.2, 27.1, 26.7, 26.5, 25.6, 19.1, 11.3.

MS (ESI): *m*/*z* = 277 $[M + Na]^+$.

Anal. Calcd for $C_{17}H_{34}O$: C, 80.24; H, 13.42. Found: C, 79.60; H, 13.12.

(*S*,*Z*)-14-Methylhexadec-8-enal (1)

To an ice-cooled soln of 2-iodoxybenzoic acid (0.327 g, 1.17 mmol) in DMSO (0.55 mL, 7.55 mmol) was added a soln of alcohol **3** (0.2 g, 0.7874 mmol) in anhyd CH_2Cl_2 (1.5 mL). The mixture was stirred at r.t. for 2 h and then filtered through a celite pad and washed with Et_2O. The combined organic filtrates were washed with H_2O, brine, dried (anhyd Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (silica gel, EtOAc–PE, 1:9; R_f = 0.7) to afford pure **1** (0.178 g, 90%) as a viscous liquid; $[\alpha]_D^{25}$ +6.31 (*c* 4.958, Et_2O).

IR(KBr): 2985, 2940, 2910, 2840, 2695, 1710, 1440, 1360, 723 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.75 (t, *J* = 2.0 Hz, 1 H), 5.26–5.37 (m, 2 H), 2.37–2.44 (m, 2 H), 1.92–2.05 (m, 4 H), 1.58–1.69 (m, 2 H), 1.24–1.41 (m, 13 H), 1.05–1.18 (m, 1 H), 0.81–0.91 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.8, 130.5, 130.0, 129.5, 43.8, 36.4, 34.3, 32.6, 32.4, 32.0, 29.4, 28.9, 27.2, 27.0, 26.7, 26.5, 22.0, 19.1, 11.0.

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