Tetrahedron 65 (2009) 3536–3544

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Stereoselective synthesis of 10,14-dimethyloctadec-1-ene, 5,9-dimethyloctadecane, and 5,9-dimethylheptadecane, the sex pheromones of female apple leafminer

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ARTICLE INFO

Article history:
Received 29 May 2008
Received in revised form 6 January 2009
Accepted 14 January 2009
Available online 31 January 2009

Keywords:
Apple leafminer pheromone
Chiral auxiliary
Evans alkylation
TosMIC alkylation and reduction

ABSTRACT

The stereoselective synthesis of (10*R*,14*R*)-10,14-dimethyloctadec-1-ene (**1**), (5*R*,9*R*)-5,9-dimethyloctadecane (**2**), and (5*R*,9*R*)-5,9-dimethylheptadecane (**3**) the sex pheromone components of female apple leafminer was accomplished by reductive elimination tosyl and isonitrile groups of dialkylated tosylmethyl isonitrile. The key steps involved were dialkylation of TosMIC with 1-iodo 2-methyl alkanes, which were derived from Evan's alkylation of chiral auxiliary and subsequent reduction.

1. Introduction

The apple leafminer (*Lyonetia prunifoliella*) is a pest on apple orchards in Eastern North America. In 1997 Gries et al. identified three methyl branched hydrocarbons, 10,14-dimethyloctadec-1-ene (**1**), 5,9-dimethyloctadecane (**2**), and 5,9-dimethylheptadecane (**3**) as its synergistic female produced sex pheromone components.[1] Structural assignment of **1**, **2**, and **3** was carried out by comparing natural products with the corresponding synthetic hydrocarbons obtained as stereoisomeric mixtures. In field trapping experiments, **1**, **2**, and **3** individually were unattractive to males, but as ternary mixture attracted numerous male moths. The importance of **1** in the pheromone communication of *L. prunifoliella* was revealed by the fact that no attraction of males to the pheromone lure was observed without **1**[1] in the pheromone blend.

In 1999, Mori et al. synthesized all of the possible stereoisomers of **1**, **2**, and **3** by starting from the enantiomers of citronellal and methyl 3-hydroxy-2-methyl propanoate.[2] In 2000, Mori et al. developed a route to synthesize (2*R*,6*S*)-*syn*-2,6-dimethyl heptane-1,7-diol monotetrahydropyranyl ether starting from commercially available enantiomers of methyl 3-hydroxy-2-methylpropanoate or (*R*)-3-*tert*-butoxycarbonyl-2-methylpropanoic acid and methyl phenyl sulfone.[3,4]

In 2005, Feringa[5] et al. reported a method based on the Cu–phosphoramidite catalyzed asymmetric conjugate addition of dialkylzinc reagents to cyclic substrates.

The present synthetic approach to achieve target molecules **1**, **2**, and **3** is based on TosMIC alkylation and reduction. It is envisaged that all the three components could be synthesized from readily available chiral starting material, D-phenylalanine **4**. For connecting the respective alkyl chains, the TosMIC alkylation methodology is selectively utilized for carbon insertion. A convenient reduction of the dialkylated TosMICs using Li/liq. NH_3, a methodology[6] developed by our group gave the corresponding pheromones in adequate yield. The retrosynthetic analysis is outlined in Scheme 1. The female apple leafminer pheromone components could be obtained in a three-step sequence from their respective tosylmethyl isocyanide intermediates derived from the respective 2-methyl alkanols. It is envisioned that the 2-methyl alkanols could be obtained from the reductive cleavage of Evan's alkylation products of (*R*)-3-(1-oxopropyl)-4-(phenylmethyl)oxazolidine-2-thione, the **7**, which was in turn obtained from commercially available D-phenylalanine **4**.

2. Results and discussion

The key starting material, **7** was obtained from commercially available D-phenylalanine in three steps.[7] The selective Evans alkylation[8] of **7** with bromobutane followed by reductive cleavage with DIBAL-H[9] and subsequent reduction has resulted (*R*)-2-methyl

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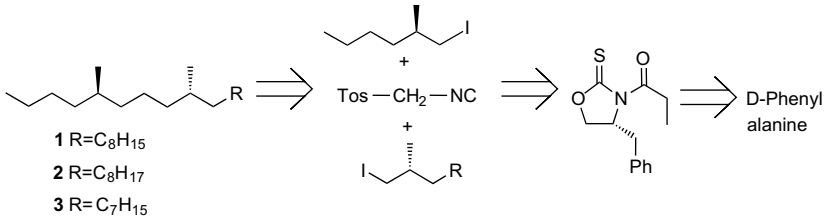
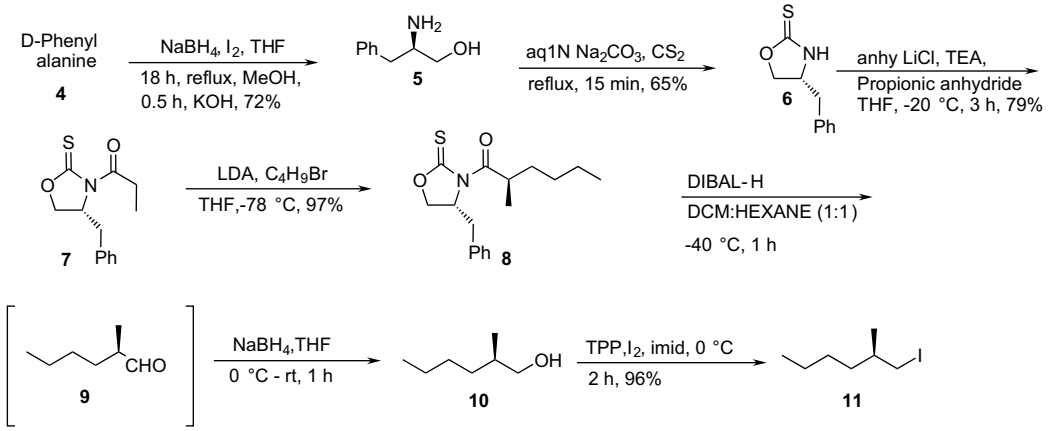
0040-4020/$ – see front matter © 2009 Published by Elsevier Ltd.
doi:10.1016/j.tet.2009.01.093



Scheme 1. Retrosynthesis of apple leafminer pheromones.

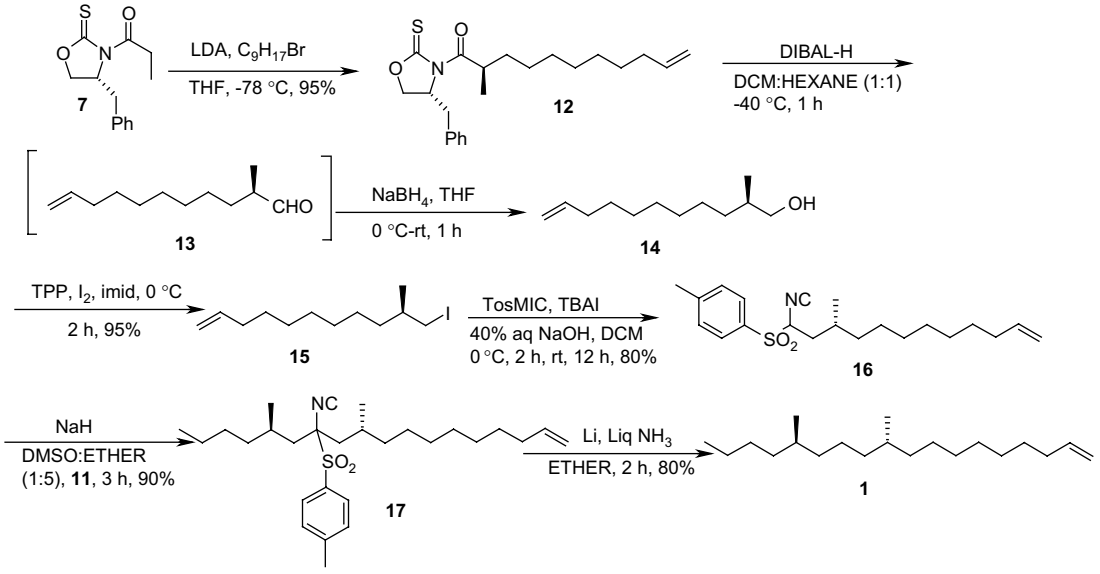


Scheme 2.

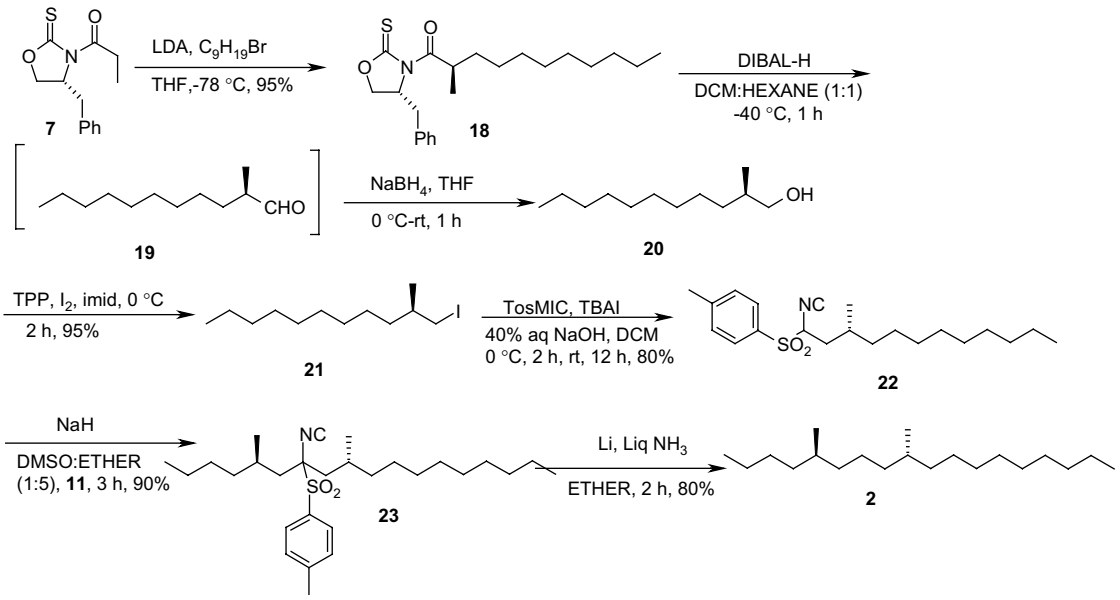
hexanol **10**. 2-Methyl hexanol **10** in presence of TPP, imidazole, iodine in ether, acetonitrile (3:1)[10] gave the required (*R*)-2-methylhexyl iodide **11** as depicted in Scheme 2. The asymmetric alkylation of chiral imide enolates has been well reported and the reduction of the alkylated imides conveniently produced the required alkanols.[16]

The Evans alkylation[8] of **7** with 9-bromonon-1-ene, followed by reductive cleavage with DIBAL-H[9] and subsequent reduction gave the (*R*)-2-methyl-undec-10-en-1-ol **14**. The alcohol **14** in the presence of TPP, imidazole, iodine in ether, acetonitrile (3:1)[10] provided the required 11-iodo-10-methyl-undec-1-ene (**14**). The alkyl halide **15** on treatment with TosMIC (tosylmethyl isocyanide) in 40% aqueous NaOH and CH_2Cl_2 in the presence of phase transfer catalyst afforded monoalkylated TosMIC **16** in 80% yield.[11] The monoalkylated TosMIC **16** on treatment with sodium hydride and the 2-methylhexyl iodide **11** afforded the dialkylated TosMIC **17** in 90% yield.[11] The ethereal solution of the dialkylated TosMIC was treated with lithium in liquid ammonia for 2 h to afford (10*R*,14*R*)-10,14-dimethyloctadec-1-ene **1** in 80% yield (Scheme 3).[6,11]

The Evans alkylation[8] of **7** with bromononane, followed by reductive cleavage with DIBAL-H[9] and reduction of corresponding aldehyde yielded the (*R*)-2-methyl-undecan-1-ol **20**. The alcohol **20**



Scheme 3.



Scheme 4.

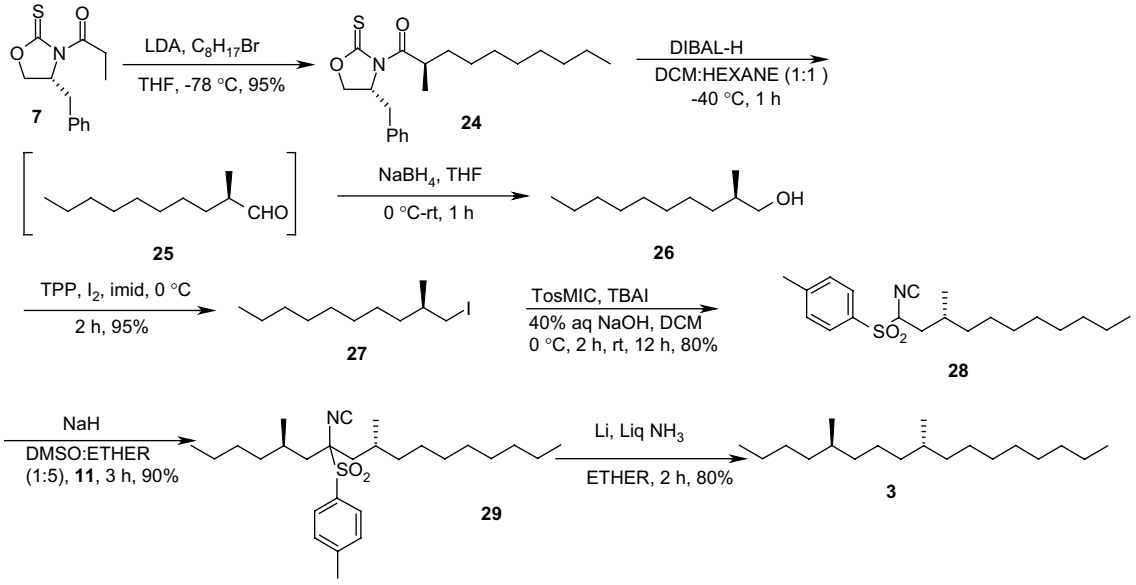
in the presence of TPP, imidazole, iodine in ether, acetonitrile (3:1)[10] gave the required (*R*)-1-Iodo-2-methyl-undecane **21**. The alkyl halide **21** on treatment with TosMIC, in 40% aqueous NaOH and CH_2Cl_2 in the presence of phase transfer catalyst afforded monoalkylated TosMIC in 80% yield.[11] The monoalkylated TosMIC **22** on treatment with sodium hydride and the (*R*)-2-methylhexyl iodide **11** afforded the dialkylated TosMIC **23** in 90% yield.[11] The ethereal solution of the dialkylated TosMIC was treated with lithium in liquid ammonia for 2 h to afford (5*R*,9*R*)-5,9-dimethyloctadecane **2** in 80% yield (Scheme 4).[6,11]

The Evans alkylation[8] of **7** with bromooctane, followed by reductive cleavage with DIBAL-H[9] and reduction gave the (*R*)-2-methyl decan-1-ol **26**. The alcohol **26** in the presence of TPP, imidazole, iodine in ether, acetonitrile (3:1)[10] gave the required (*R*)-1-iodo-2-methyl-decane **27**. The alkyl halide **27** on treatment with TosMIC, in 40% aqueous NaOH and CH_2Cl_2 in the presence of phase transfer catalyst afforded monoalkylated TosMIC **28** in 80% yield.[11] The monoalkylated TosMIC **28** on treatment with sodium hydride and the 2-methylhexyl iodide **11** afforded the dialkylated TosMIC **29** in 90% yield.[11] The ethereal solution of the dialkylated TosMIC was treated with lithium in liquid ammonia for 2 h to afford (5*R*,9*R*)-5,9-dimethylheptadecane **3** in 80% yield (Scheme 5).[6,11]

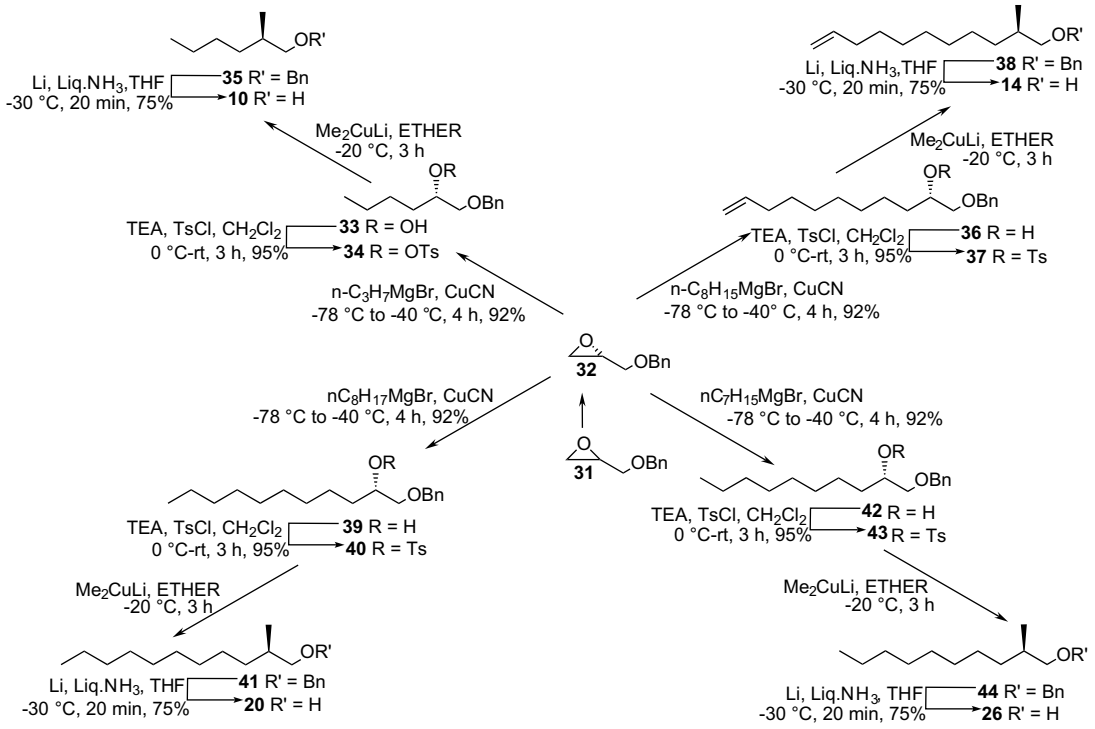
The spectroscopic (^{1}H NMR, ^{13}C NMR, IR, mass), physical data (specific rotation), and elemental analysis of all pheromone components **1**, **2**, and **3** were in good agreement with those reported.[3]

An alternative strategy, devised for the synthesis of respective (*R*)-2-methyl alcohols is delineated in Scheme 6.

The synthetic strategy is initiated with the commercially available (±)-benzyl glycidyl ether **31**. The Jacobsen resolution of compound of (±)-benzyl glycidyl ether **31** using (*R*,*R*)-(salen)Co(II) precatalyst, AcOH and H_2O (0.51 equiv) for 22 h resulted in (*S*)-benzyl glycidyl ether **32**.[12] Regioselective opening of epoxide **32** with respective alkyl magnesium bromide (formed by the addition of alkyl bromide to Mg in THF) in the presence of CuCN[13] gave the



Scheme 5.



Scheme 6.

respective (*S*)-1-benzyloxy alkanols **33**, **36**, **39**, and **42**. The chiral (*S*)-1-benzyloxy alkanol upon tosylation followed by Gilman reaction with Me_2CuLi resulted in the benzyl deprotected respective (*R*)-2-methyl alkanols,[14] which on debenzylation[15] using lithium and liquid ammonia provided the required alcohols **10**, **14**, **20**, and **26** (Scheme 6). The optically active tosylates reacted smoothly with lithium dimethylcuprate(I) reagent with inversion of stereochemistry at the electrophilic carbon atom.[17]

The spectroscopic (^{1}H NMR, ^{13}C NMR, IR, mass), physical data (specific rotation), and elemental analysis of all alcohols **10**, **14**, **20**, and **26** were in good agreement with those alcohols synthesized from **7**.

3. Conclusion

In summary, the stereoselective synthesis of (10*R*,14*R*)-10,14-dimethyloctadec-1-ene (**1**), (5*R*,9*R*)-5,9-dimethyloctadecane (**2**), and (5*R*,9*R*)-5,9-dimethylheptadecane (**3**) is successfully accomplished from **7**, which can be easily prepared from D-phenylalanine. The key step in the synthesis is the dialkylation of TosMIC with respective alkyl halides and subsequent reduction of dialkylated tosylmethyl isocyanide.

4. Experimental

4.1. General

All reactions were carried out under 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 thin-layer chromatography (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) using diethyl ether, ethyl acetate, pentane, 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. ^{1}H and ^{13}C NMR spectra were recorded with Varian Gemini 200 MHz, Bruker Avance 300 MHz, Varian Unity 400 MHz or Varian Inova 500 MHz spectrometer using tetramethylsilane as an internal standard in $CDCl_3$. Mass spectra were recorded on Micro mass VG-7070H for EI and VG Autospec M for FABMS. Elemental analysis data were recorded on Vario EL, Elementar.

4.2. 4-Benzyl-3-(*R*-2-methyl-1-oxohexyl)-1,3-oxazolidine-2-thione 8

To a stirred solution of LDA (14.59 mmol, generated from 9.12 mL of 1.6 M *n*-BuLi in hexane and 2.08 mL diisopropylamine) in THF (10 mL) was added lithium chloride (1.85 g, 43.7 mmol) at −78 °C. The resulting suspension was warmed to 0 °C briefly and then was cooled to −78 °C. An ice-cooled solution of (+)-**7** (1.9 g, 7.66 mmol) in THF (10 mL, followed by a 4-mL rinse) was added via cannula. The mixture was stirred at −78 °C for 1 h, at 0 °C for 15 min and at 20 °C for 5 min. The mixture was cooled to 0 °C and bromobutane (3.96 mL, 36.4 mmol) was added neat to the reaction via cannula. After being stirred for 12 h at 0 °C, the reaction mixture was treated with saturated ammonium chloride solution (30 mL) and the resulting mixture was extracted with ethyl acetate (4×50 mL). The combined organic extracts were dried over sodium sulfate and concentrated in vacuo. Purification of the residue by flash column chromatography afforded **8** (2.26 g, 97%). R_f=0.7 (SiO_2, 30% EtOAc in hexane); $[\alpha]_D^{25}$ −4.22 (*c* 1.20, $CHCl_3$); IR (neat): ν 3027, 2959, 2929, 2868, 1605, 1454, 1147 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.29–7.14 (m, 5H), 4.42–3.97 (m, 3H), 3.15–2.95 (m, 2H), 2.61 (dd, 1H, *J*=8.59, 8.59 Hz), 1.77–1.27 (m, 9H), 0.96 (t, 3H, *J*=7.03 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.8, 137.8, 129.2, 128.4,

126.4, 73.0, 67.7, 41.6, 31.6, 31.4, 21.7, 13.5; MASS (ESI-MS): m/z 306 $[M+H]^+$. Elemental analysis calcd for $C_{17}H_{23}NO_2S$ (305.44): C 66.85, H 7.59, N 4.59, S 10.50; found C 66.82, H 7.56, N 4.55, S 10.46%.

4.3. (*R*)-2-Methyl-1-hexanol 10

A solution of DIBAL-H (20 wt % solution in toluene) in THF (10 mL) was injected dropwise into a yellow solution of **8** (2 g, 6.54 mmol) in dry *n*-hexane (12.5 mL), dry dichloromethane (12.5 mL) at −50 °C to −20 °C with stirring under nitrogen until the original yellow color of the reaction medium vanished. The colorless mixture was washed with aqueous Na_2CO_3, water and brine, and then dried. After the solvent evaporation, the crude aldehyde **9** was used in the next step without purification.

Reduction of aldehyde: to a solution of above aldehyde **9**, in THF was added $NaBH_4$ (0.17 g, 4.71 mmol) and the mixture was stirred at room temperature for 1 h and then treated with 10% HCl solution to destroy excess $NaBH_4$. The acidic solution was extracted with CH_2Cl_2 and washed with brine solution. The CH_2Cl_2 solution was dried and evaporated in vacuo to give the alcohol **10** as colorless oil (0.49 g, 65%). R_f=0.3 (SiO_2, 20% EtOAc in hexane); $[\alpha]_D^{25}$ +0.56 (*c* 1.21, $CHCl_3$); [lit.[18] $[\alpha]_D^{25}$ +14.5 (*c* 2.25, MeOH)]; IR (neat): ν 3395, 2972, 2928, 1379, 1315, 1163 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.46–3.30 (m, 2H), 2.88 (s, 1H), 1.64–1.02 (m, 7H), 0.92–0.88 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 68.0, 35.5, 32.7, 29.0, 22.8, 16.4, 13.8; MASS (ESI-MS): m/z 116 $[M]^+$. Elemental analysis calcd for $C_7H_{16}O$ (116): C 72.35, H 13.88; found: C 72.34, H 13.86%.

4.4. (*R*)-2-Methyl-1-iodo-hexane 11

To a stirred solution of alcohol **10** (0.14 g, 1.25 mmol) in a mixture of 9 mL dry ether and 3 mL dry acetonitrile were added TPP (0.65 g, 2.5 mmol), imidazole (0.17 g, 2.5 mmol), and iodine (0.47 g, 1.87 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 1 h. Solid was filtered and washed with ether. The filtrate extracted with ether. The combined ether extract was washed with 10% aqueous sodium thiosulphate solution, water, brine, and dried over Na_2SO_4. Concentration under reduced pressure and purification by silica gel column chromatography afforded iodide **11** (0.27 g, 96% yield) as a liquid. R_f=0.2 (SiO_2, 20% EtOAc in hexane); IR (neat): ν 2922, 2852, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.28–3.12 (m, 2H), 1.53–1.08 (m, 7H), 0.96 (d, 3H, J=6.79 Hz), 0.91–0.82 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.1, 34.7, 29.1, 22.6, 20.5, 17.8, 13.9; MASS (ESI-MS): m/z 227 $[M+H]^+$.

4.5. 4-Benzyl-3-(*R*-2-methyl-1-oxo undecenyl)-1,3-oxazolidine-2-thione 12

Compound **12** (2.68 g, 95%) was prepared from **7** (1.88 g, 7.57 mmol) using LDA (14.42 mmol, generated from 9.01 mL of 1.6 M *n*-BuLi in hexane and 2.05 mL diisopropylamine), lithium chloride (1.83 g, 43.7 mmol), bromononene (7.39 g, 36.07 mmol) following the same procedure as described for the synthesis of **8**. Compound **12** was pale yellow oil. R_f=0.7 (SiO_2, 30% EtOAc in hexane); $[\alpha]_D^{25}$ −4.47 (*c* 1.0, $CHCl_3$); IR (neat): ν 3026, 2926, 2853, 1605, 1455, 1147 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.27–7.14 (m, 5H), 5.82–5.68 (m, 1H), 4.98–4.88 (m, 2H), 4.39–4.29 (m, 1H), 4.24–4.18 (m, 1H), 4.04–3.98 (m, 1H), 3.10 (dd, 1H, J=4.53, 4.53 Hz), 3.02–2.94 (m, 2H), 2.64–2.57 (m, 2H), 2.06–2.0 (m, 2H), 1.75–1.65 (m, 2H), 1.43–1.26 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.9, 139.0, 137.7, 129.2, 128.5, 126.5, 114.3, 73.1, 67.7, 41.6, 33.7, 31.9, 29.3, 28.9, 28.8, 28.6, 14.2; MASS (ESI-MS): m/z 396 $[M+23]^+$. Elemental analysis calcd for $C_{22}H_{31}NO_2S$ (373.55): C 70.74, H 8.36, N 3.75, S 8.58; found: C 70.72, H 8.36, N 3.70, S 8.54%.

4.6. (*R*)-2-Methyl-undec-10-en-1-ol 14

Compound **14** (0.63 g, 65%) was prepared from **12** (2 g, 5.35 mmol) using DIBAL-H (10 mL) (20 wt % solution in toluene) and $NaBH_4$ (0.14 g, 3.85 mmol) following the same procedure as described for the synthesis of **10**. Compound **14** was colorless oil. R_f=0.3 (SiO_2, 20% EtOAc in hexane); $[\alpha]_D^{25}$ +2.97 (*c* 1.32, $CHCl_3$); IR (neat): ν 3451, 2925, 2928, 1638, 1379, 1315, 1163 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.82–5.68 (m, 1H), 4.98–4.88 (m, 2H), 3.52–3.32 (m, 2H), 2.64–2.57 (m, 2H), 1.75–1.65 (m, 2H), 1.43–1.03 (m, 11H), 0.89 (t, 3H, J=6.79 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.0, 114.2, 68.2, 35.7, 33.1, 31.8, 29.9, 29.5, 29.2, 26.9, 22.6, 16.5; MASS (ESI-MS): m/z 167 $[M-17]^+$. Elemental analysis calcd for $C_{12}H_{24}O$ (184.32): C 78.20, H 13.12; found: C 78.22, H 13.10%.

4.7. (*R*)-11-Iodo-10-methyl-undec-1-ene 15

Compound **15** (0.15 g, 95%) was prepared from **14** (0.10 g, 0.54 mmol) using TPP (0.28 g, 1.08 mmol), imidazole (0.07 g, 1.08 mmol), and iodine (0.20 g, 0.81 mmol) following the same procedure as described for the synthesis of **11**. Compound **15** was colorless oily liquid. R_f=0.2 (SiO_2, 20% EtOAc in hexane); IR (neat): ν 2922, 2852, 1638, 759 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 5.6–5.8 (m, 1H), 4.8–4.9 (m, 2H), 3.25–3.09 (m, 2H), 1.98–2.0 (m, 2H), 1.55–1.08 (m, 13H), 0.98 (t, 3H, J=6.78 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138, 114.2, 36.4, 34.7, 31.8, 29.6, 29.5, 26.8, 22.6, 20.5, 17.8; MASS (ESI-MS): m/z 317 $[M+23]^+$.

4.8. (*R*)-1-(1-Isocyano-3-methyl-dodec-11-ene-1-sulfonyl)-4-methyl-benzene 16

A mixture of tosylmethyl isocyanide (TosMIC, 0.19 g, 1.01 mmol), 1-iodo-2-methyl-undecene **15** (0.20 g, 0.67 mol), tetrabutylammonium iodide (0.0753 g, 0.20 mmol), 40% aqueous NaOH (8.72 mL), and dichloromethane (8.72 mL) was stirred for 2 h at 0 °C and then at room temperature for 12 h. The reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was washed with water, brine, and dried (Na_2SO_4). Removal of the solvent under reduced pressure followed by column purification gave a colorless liquid **16** (0.19 g, 80% yield). R_f=0.2 (SiO_2, 20% Et_2O in pentane); IR (neat): ν 2133, 1596, 665 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, 2H, J=8.08 Hz), 7.42 (d, 2H, J=8.08 Hz), 5.82–5.68 (m, 1H), 4.98–4.88 (m, 2H), 2.51 (s, 3H), 2.05–1.98 (m, 4H), 1.86–1.75 (m, 2H), 1.72–1.15 (m, 15H); MASS (EIMS): m/z 365 $[M+H]^+$. Elemental analysis calcd for $C_{21}H_{33}NO_2S$ (363.54): C 69.38, H 9.15, N 3.85, S 8.82; found: C 69.32, H 9.14, N 3.83, S 8.78%.

4.9. 1-((5*R*,9*R*)-7-Isocyano-5,9-dimethyl-octadec-17-ene-7-sulfonyl)-4-methylbenzene 17

A solution of **16** (0.10 g, 0.27 mmol) in DMSO/ether (1:5, 6 mL) was added dropwise, to a stirred suspension of prewashed sodium hydride (0.01 g, 0.83 mmol) in ether (2 mL) during 5 min at room temperature under nitrogen atmosphere. The 1-iodo-2-methyl-hexane **11** (0.06 g, 0.27 mmol) in ether (2 mL) was added to the reaction mixture and stirring was continued for an additional 3 h. The reaction mixture was poured into cold water (5 mL) and extracted with ether. The organic extract was washed with water, brine, and dried (Na_2SO_4). Solvent was removed at room temperature to afford **17** (0.11 g) in 90% yield as a pale yellow oily liquid. R_f=0.1 (SiO_2, 20% Et_2O in pentane); IR (neat): ν 2145, 1633, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.84 (d, 2H, J=8.01 Hz), 7.40 (d, 2H, J=8.01 Hz), 5.82–5.68 (m, 1H), 4.98–4.88 (m, 2H), 2.5 (s, 3H), 2.06–1.86 (m, 6H), 1.75–1.04 (m, 23H), 0.93 (t, 6H, J=6.79 Hz); MASS (EIMS): m/z 449 $[M+1]^+$. Elemental analysis calcd for

$C_{27}H_{45}NO_2S$ (447.72): C 72.43, H 10.13, N 3.13, S 7.16; found: C 72.42, H 10.10, N 3.10, S 7.13%.

4.10. (10*R*,14*R*)-10,14-Dimethyloctadec-1-ene 1

To liq. NH_3 (50 mL) at −33 °C, was added lithium (0.01 g, 1.63 mmol), followed by dialkylated TosMIC **17** (0.075 g, 0.16 mmol) in ether (5 mL), ethanol (0.12 mL). After 2 h, ammonia was allowed to evaporate by bringing the reaction mixture to room temperature. Then water was added and extracted with ether. The organic layer was washed with water, dried (Na_2SO_4), concentrated, and purification by column chromatography afforded pheromone **1** (0.03 g, 80%) as a colorless oil. R_f=compound is eluted in pentane; $[\alpha]_D^{25}$ −1.72 (*c* 1.3, $CHCl_3$); [lit.[2] $[\alpha]_D^{25}$ −1.70 (*c* 1.27, $CHCl_3$)] IR (neat): ν 2925, 1638 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.82 (ddt, 1H, *J*=6.37, 10.35, 17.52 Hz), 4.90–4.99 (m, 2H), 2.04 (m, 2H), 1.03–1.43 (m, 26H), 0.89 (t, 3H, *J*=6.37 Hz), 0.843 (d, 3H, *J*=6.37 Hz), 0.840 (d, 3H, *J*=6.37 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.9, 114.2, 37.4, 36.8, 33.8, 32.7, 32.7, 30.0, 29.5, 29.3, 29.2, 29.0, 27.1, 24.5, 23.0, 19.7, 14.2; MASS: 279 $[M-H]^+$. Elemental analysis calcd for $C_{20}H_{40}$ (280.53): C 85.63, H 14.37; found: C 85.02, H 13.92%.

4.11. 4-Benzyl-3-(*R*-2-methyl-1-oxo undecyl)-1,3-oxazolidine-2-thione 18

Compound **18** (2.71 g, 95%) was prepared from **7** (1.89 g, 7.61 mmol) using LDA (14.50 mmol, generated from 9.06 mL of 1.6 M *n*-BuLi in hexane and 2.06 mL diisopropylamine), lithium chloride (1.84 g, 43.52 mmol), bromononane (7.51 g, 36.2 mmol) following the same procedure as described for the synthesis of **8**. Compound **18** was a pale yellow oil. R_f=0.7 (SiO_2, 30% EtOAc in hexane); $[\alpha]_D^{25}$ −4.43 (*c* 1.05, $CHCl_3$); IR (neat): ν 3027, 2925, 2854, 1605, 1454, 1148 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.27–7.14 (m, 5H), 4.39–4.29 (m, 1H), 4.23–4.17 (m, 1H), 4.02–3.97 (m, 1H), 3.09 (dd, 1H, *J*=5.28, 5.28 Hz), 3.04–2.89 (m, 2H), 2.64–2.56 (m, 2H), 1.74–1.65 (m, 2H), 1.42–1.28 (m, 15H), 0.88 (t, 3H, *J*=5.28 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.5, 137.7, 129.1, 128.3, 126.3, 72.93, 67.6, 41.7, 31.8, 29.5, 29.4, 29.3, 29.1, 28.7, 22.6, 14.1; MASS (ESI-MS): *m*/*z* 376 $[M+H]^+$. Elemental analysis calcd for $C_{22}H_{33}NO_2S$ (375.57): C 70.36, H 8.86, N 3.73, S 8.54; found: C 70.34, H 8.56, N 3.70, S 8.52%.

4.12. (*R*)-2-Methyl-undecan-1-ol 20

Compound **20** (0.64 g, 65%) was prepared from **18** (2 g, 5.32 mmol) using DIBAL-H (10 mL) (20 wt % solution in toluene) and $NaBH_4$ (0.14 g, 3.83 mmol) following the same procedure as described for the synthesis of **10**. Compound **20** was colorless oil. R_f=0.3 (SiO_2, 20% EtOAc in hexane); $[\alpha]_D^{25}$ +4.8 (*c* 0.34, $CHCl_3$). IR (neat): ν 3395, 2972, 2928, 1379, 1315, 1163 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.52–3.32 (m, 2H), 1.75–1.03 (m, 17H), 0.92–0.85 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 68.3, 35.7, 33.1, 31.8, 29.9, 29.5, 29.2, 26.9, 22.6, 16.5, 14.0; MASS (ESI-MS): *m*/*z* 226 $[M+39]^+$. Elemental analysis calcd for $C_{12}H_{26}O$ (186.33): C 77.35, H 14.06; found: C 77.32, H 14.03%.

4.13. (*R*)-1-Iodo-2-methyl-undecane 21

Compound **21** (0.16 g, 95%) was prepared from **20** (0.10 g, 0.54 mmol) using TPP (0.31 g, 1.18 mmol), imidazole (0.08 g, 1.18 mmol), and iodine (0.22 g, 0.88 mmol) following the same procedure as described for the synthesis of **11**. Compound **21** was colorless liquid. R_f=0.2 (SiO_2, 20% EtOAc in hexane); IR (neat): ν 2928, 2856, 760 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.25–3.09 (m, 2H), 1.55–1.08 (m, 17H), 0.99 (d, 3H, *J*=5.87 Hz), 0.90 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.4, 34.7, 31.8, 29.6, 29.5, 29.2, 26.8, 22.6, 20.5, 17.8, 14.0; MASS (ESI-MS): *m*/*z* 295 $[M-1]^+$.

4.14. (*R*)-1-(1-Isocyano-3-methyl-dodecane-1-sulfonyl)-4-methyl-benzene 22

Compound **22** (0.11 g, 80%) was prepared from **21** (0.11 g, 0.38 mmol), tosylmethyl isocyanide (TosMIC, 0.11 g, 0.57 mmol), tetrabutylammonium iodide (0.042 g, 0.11 mmol), 40% aqueous NaOH (8.72 mL), and dichloromethane (8.72 mL) following the same procedure as described for the synthesis of **16**. Compound **22** was colorless liquid. R_f=0.2 (SiO_2, 20% Et_2O in pentane); IR (neat): ν 2133, 1600 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.84 (d, 2H, *J*=8.08 Hz), 7.40 (d, 2H, *J*=8.08 Hz), 4.33 (dd, 1H, *J*=3.67, 3.67 Hz), 2.51 (s, 3H), 2.08–1.98 (m, 2H), 1.72–1.15 (m, 20H), 0.87 (t, 3H, *J*=6.61 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.3, 14.1, 18.6, 20.3, 21.7, 22.5, 26.6, 27.4, 29.0, 32.4, 72.7, 120.2, 130.0, 138.0, 146.5, 164.7; MASS (EIMS): *m*/*z* 363 $[M]^+$. Elemental analysis calcd for $C_{21}H_{35}NO_2S$ (365.24): C 69.99, H 9.65, N 3.83, S 8.77; found: C 69.92, H 9.61, N 3.81, S 8.75%.

4.15. 1-((5*R*,9*R*)-7-Isocyano-5,9-dimethyl-octadecane-7-sulfonyl)-4-methyl-benzene 23

Compound **23** (0.10 g, 90%) was prepared from **22** (0.09 g, 0.25 mmol) in DMSO/ether (1:5, 6 mL), prewashed sodium hydride (0.018 g, 0.75 mmol) in ether (5 mL), 1-iodo-2-methyl-hexane **11** (0.05 g, 0.25 mmol) in ether (5 mL) following the same procedure as described for the synthesis of **17**. Compound **23** was pale yellow oily liquid. R_f=0.1 (SiO_2, 20% EtOAc in pentane); IR (neat): ν 2130, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, 2H, *J*=8.30 Hz), 7.40 (d, 2H, *J*=8.30 Hz), 2.5 (s, 3H), 2.06–1.86 (m, 4H), 1.64–1.04 (m, 30H), 0.88 (t, 6H, *J*=6.79 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 146.2, 138.1, 131.2, 129.7, 125.4, 120.2, 119.1, 80.0, 46.2, 37.1, 32.6, 31.8, 31.3, 30.3, 29.7, 29.1, 23.4, 22.6, 21.7, 14.0, 11.3; MASS (EIMS): *m*/*z* 451 $[M]^+$. Elemental analysis calcd for $C_{27}H_{47}NO_2S$ (449.73): C 72.11, H 10.53, N 3.11, S 7.13; found: C 72.08, H 10.51, N 3.09, S 7.12%.

4.16. (5*R*,9*R*)-5,9-Dimethyloctadecane 2

Compound **2** (0.03 g, 80%) was prepared from dialkylated TosMIC **23** (0.06 g, 0.14 mmol) using lithium (0.01 g, 1.48 mmol), in ether (5 mL), ethanol (0.12 mL) following the same procedure as described for the synthesis of **1**. Compound **2** was colorless oil. R_f=compound is eluted in pentane; $[\alpha]_D^{25}$ −1.88 (*c* 0.965, Hexane) [lit.[3] $[\alpha]_D^{25}$ *c* −1.88 (*c* 2.56, hexane)]; IR (neat): ν 2925 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.03–1.43 (m, 30H), 0.88–0.89 (t, 6H, *J*=6.37 Hz), 0.843 (d, 3H, *J*=6.37 Hz), 0.840 (d, 3H, *J*=6.37 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 37.4, 37.2, 36.8, 32.75, 32.74, 32.72, 31.9, 30.0, 29.7, 29.6, 29.3, 29.3, 27.1, 24.5, 22.7, 19.7, 14.2, 14.1. MASS: 283 $[M+H]^+$. Elemental analysis calcd for $C_{20}H_{42}$ (282.55): C 85.02, H 14.98; found: C 84.68, H 14.59%.

4.17. 4-Benzyl-3-(*R*-2-methyl-1-oxo decyl)-1,3-oxazolidine-2-thione 24

Compound **24** (2.61 g, 95%) was prepared from **7** (1.89 g, 7.61 mmol) using LDA (14.49 mmol, generated from 9.06 mL of 1.6 M *n*-BuLi in hexane and 2.06 mL diisopropylamine), lithium chloride (1.84 g, 43.52 mmol), bromooctane (7.0 g, 36.2 mmol) following the same procedure as described for the synthesis of **8**. Compound **24** was a pale yellow oil. R_f=0.7 (SiO_2, 30% EtOAc in hexane); $[\alpha]_D^{25}$ −4.01 (*c* 1.08, $CHCl_3$); IR (neat): ν 3027, 2925, 2854, 1605, 1454, 1147 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.28–7.14 (m, 5H), 4.39–4.29 (m, 1H), 4.21 (t, 1H, *J*=8.30 Hz), 4.01 (t, 1H, *J*=6.79 Hz), 3.10 (dd, 1H, *J*=5.28, 4.53 Hz), 2.97 (ddd, 2H, *J*=3.02, 3.02, 3.02 Hz), 2.64–2.56 (m, 1H), 1.74–1.65 (m, 2H), 1.47–1.16 (m, 14H), 0.89 (t, 3H, *J*=6.79 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.9, 137.8, 129.2, 128.4, 126.4, 73.0, 67.7, 41.6, 31.9, 31.7, 29.4, 29.1, 29.0,

28.6, 22.6, 14.0; MASS (ESI-MS): m/z 359 $[M-2]^+$. Elemental analysis calcd for $C_{21}H_{31}NO_2S$ (361.54): C 69.76, H 8.64, N 3.87, S 8.87; found: C 69.72, H 8.64, N 3.83, S 8.85%.

4.18. (*R*)-2-Methyl-decan-1-ol 26

Compound **26** (0.61 g, 65%) was prepared from **24** (2 g, 5.53 mmol) using DIBAL-H (10 mL) (20 wt % solution in toluene) and $NaBH_4$ (0.15 g, 3.98 mmol) following the same procedure as described for the synthesis of **10**. Compound **26** was colorless oil. R_f=0.3 (SiO_2, 20% EtOAc in hexane); $[\alpha]_D^{25}$ +1.82 (c 2.32, $CHCl_3$); [lit.[19] (*S*)-2-methyl-decan-1-ol $[\alpha]_D^{25}$ −9.8 (neat)]; IR (neat): ν 3395, 2972, 2928, 1379, 1315, 1163 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.46–3.31 (m, 2H), 1.65–0.92 (m, 15H), 0.90–0.79 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 68.2, 35.6, 33.1, 31.8, 29.9, 29.5, 29.2, 26.9, 22.6, 16.5, 13.9; MASS (ESI-MS): m/z 195 $[M+23]^+$. Elemental analysis calcd for $C_{11}H_{24}O$ (172.31): C 76.68, H 14.04; found: C 76.66, H 14.02%.

4.19. (*R*)-1-Iodo-2-methyl-decane 27

Compound **27** (0.20 g, 95%) was prepared from **26** (0.12 g, 0.71 mmol) using TPP (0.37 g, 1.43 mmol), imidazole (0.09 g, 1.43 mmol), and iodine (0.27 g, 1.07 mmol) following the same procedure as described for the synthesis of **11**. Compound **27** was colorless liquid. R_f=0.2 (SiO_2, 20% EtOAc in hexane); IR (neat): ν 2922, 2852, 760 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.24–3.08 (m, 2H), 1.48–1.1 (m, 15H), 0.98 (d, 3H, J=5.87 Hz), 0.92–0.85 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 36.3, 34.6, 31.7, 29.6, 29.4, 29.2, 26.8, 22.5, 20.5, 17.8, 14.04; MASS (ESI-MS): m/z 283 $[M+H]^+$.

4.20. (*R*)-1-(1-Isocyano-3-methyl-undecane-1-sulfonyl)-4-methyl-benzene 28

Compound **28** (0.12 g, 80%) was prepared from **27** (0.12 g, 0.43 mmol), tosylmethyl isocyanide (TosMIC, 0.12 g, 0.64 mmol), tetrabutylammonium iodide (0.047 g, 0.12 mmol), 40% aqueous NaOH (8.72 mL), and dichloromethane (8.72 mL) following the same procedure as described for the synthesis of **16**. Compound **28** was colorless liquid. R_f=0.2 (SiO_2, 20% Et_2O in pentane); IR (neat): ν 2140, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, 2H, J=8.30 Hz), 7.42 (d, 2H, J=7.55 Hz), 4.37 (dd, 1H, J=3.77, 6.79 Hz), 2.51 (s, 3H), 2.08–1.98 (m, 2H), 1.72–1.15 (m, 18H), 0.87 (t, 3H, J=6.04 Hz); MASS (EIMS): m/z 350 $[M+1]^+$. Elemental analysis calcd for $C_{20}H_{31}NO_2S$ (351.22): C 68.33, H 9.46, N 3.98, S 9.12; found: C 68.29, H 9.44, N 3.89, S 9.10%.

4.21. 1-((5*R*,9*R*)-7-Isocyano-5,9-dimethyl-heptadecane-7-sulfonyl)-4-methyl-benzene 29

Compound **29** (0.11 g, 90%) was prepared from **28** (0.10 g, 0.28 mmol) in DMSO/ether (1:5, 6 mL), prewashed sodium hydride (0.0068 g, 0.28 mmol) in ether (5 mL), 1-iodo-2-methyl-hexane **11** (0.06 g, 0.28 mmol) in ether (5 mL) following the same procedure as described for the synthesis of **17**. Compound **29** was pale yellow oily liquid. R_f=0.1 (SiO_2, 20% Et_2O in pentane); IR (neat): ν 2119, 1631, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.84 (d, 2H, J=8.12 Hz), 7.39 (d, 2H, J=8.12 Hz), 2.5 (s, 3H), 2.06–1.86 (m, 4H), 1.64–1.04 (m, 28H), 0.88 (t, 6H, J=6.79 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.1, 146.2, 138.1, 131.2, 129.7, 125.4, 120.2, 119.1, 79.8, 46.2, 37.1, 32.6, 31.8, 31.3, 30.3, 29.70, 29.1, 23.4, 22.6, 21.7, 14.0, 11.3; MASS (EIMS): m/z 436 $[M]^+$. Elemental analysis calcd for $C_{26}H_{45}NO_2S$ (435.71): C 71.67, H 10.41, N 3.21, S 7.36; found: C 71.63, H 10.38, N 3.18, S 7.34%.

4.22. (5*R*,9*R*)-5,9-Dimethylheptadecane 3

Compound **3** (0.03 g, 80%) was prepared from dialkylated TosMIC **29** (0.07 g, 0.15 mmol) using lithium (0.010 g, 1.56 mmol), in ether (5 mL), ethanol (0.12 mL) following the same procedure as described for the synthesis of **1**. Compound **3** was colorless oil. R_f=compound is eluted in pentane; $[\alpha]_D^{25}$ −2.02 (c 2.4, Hexane) [lit.[3] $[\alpha]_D^{25}$ −2.02 (c 2.60, hexane)]; IR (neat): ν 2980 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.03–1.43 (m, 28H), 0.88–0.89 (t, 6H, J=6.37 Hz), 0.843 (d, 3H, J=6.37 Hz), 0.840 (d, 3H, J=6.37 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 37.4, 37.2, 36.8, 32.7, 31.9, 30.0, 29.7, 29.3, 29.3, 27.1, 23.1, 24.5, 22.7, 19.7, 14.2, 14.1; MASS (EIMS): 268 $[M^+]^+$. Elemental analysis calcd for $C_{19}H_{40}$ (268.52): C 84.99, H 15.01; found: C 85.00, H 14.09%.

4.23. (*S*)-1-Benzyloxy-hexan-2-ol 33

To the magnesium (3.51 g, 146.34 mmol) in dry THF (60 mL) at room temperature was sequentially added 1,2-dibromoethane (three drops) and 1-bromopropane (20.99 g, 170.73 mmol) dropwise. After allowing the reaction mixture to stir for 0.5 h CuCN (218 mg, 5 mol %) was added. Then the mixture was cooled to −78 °C and epoxide **32** (8.0 g, 48.78 mmol) in THF (10 mL) was added and warmed the mixture to −40 °C and stirred for 4 h. Then the reaction mixture was quenched with saturated NH_4Cl solution (50 mL) and extracted with EtOAc (3×30 mL). Combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification by silica gel column chromatography afforded **33** (9.33 g, 92%) as colorless liquid. R_f=0.45 (SiO_2, 30% EtOAc in hexane); $[\alpha]_D^{25}$ 6.4 (c 1.09, $CHCl_3$); IR (neat): ν 3386, 2932, 2871, 1460 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.32–7.23 (m, 5H), 4.5 (s, 2H), 3.73 (br s, 1H), 3.42 (dd, 1H, J=3.02, 9.06 Hz), 3.25 (t, 1H, J=8.30 Hz), 2.52 (d, 1H, J=2.26 Hz), 1.44–1.24 (m, 6H), 0.89 (t, 3H, J=6.79 Hz); ^{13}C NMR (300 MHz, $CDCl_3$): δ 138.1, 128.4, 127.7, 74.8, 73.2, 70.3, 32.9, 27.7, 22.7, 14.0; MASS (ESI-MS): m/z 226 $[M+18]^+$. Elemental analysis calcd for $C_{13}H_{20}O_2$ (208.30): C 74.96, H 9.68; found: C 74.94, H 9.66%.

4.24. (*S*)-1-Benzyloxymethyl-pentyl 4-methylbenzenesulfonate 34

To the solution of alcohol **33** (7.53 g, 36.2 mmol) in dry CH_2Cl_2 (30.0 mL), triethylamine (50.42 mL, 362 mmol), DMAP (0.44 g, 3.62 mmol) was added at 0 °C. Then added tosyl chloride (7.59 g, 39.82 mmol) was added over a period of 2 h. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was treated with aqueous 1 N HCl (10 mL) and extracted with CH_2Cl_2 (3×30 mL). The organic layer was washed with saturated $NaHCO_3$ (15 mL) and water (15 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Flash chromatography of the crude afforded mono tosylate **34** (12.45 g, 95%) as colorless gummy liquid. R_f=0.6 (SiO_2, 30% EtOAc in hexane); IR (neat): ν 2957, 2869, 1598, 1454 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, 2H, J=8.30 Hz), 7.3–7.16 (m, 7H), 4.60 (s, 1H), 4.38 (dd, 2H, J=12.08, 5.28 Hz), 3.52–3.42 (m, 2H), 2.41 (s, 3H), 1.68–1.62 (m, 2H), 1.35–1.1 (m, 4H), 0.84 (t, 3H, J=6.79 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.0, 137.5, 134.1, 129.2, 127.9, 127.4, 127.27, 127.2, 81.6, 72.8, 70.5, 30.9, 26.5, 21.9, 21.1, 13.4; MASS (ESI-MS): m/z 385 $[M+23]^+$.

4.25. (*R*)-(2-Methyl-hexyloxymethyl)-benzene 35

To a solution of Me_2CuLi, prepared from CuI (18.71 g, 98.24 mmol) and MeLi (4.32 g, 196.49 mmol, 1.0 M in ether) in ether (100 mL) at −30 °C was added an ethereal solution of tosylate **34** (5.93 g, 16.37 mmol) and the reaction mixture was slowly

warmed to 0 °C. After 3 h of stirring, the mixture was quenched with saturated NH_4Cl: aqueous NH_3 (9:1) and extracted with ether. Following solvent removal, the crude product was purified by column chromatography to give **35** (3.04 g, 90%) as a colorless oil. R_f=0.6 (SiO_2, 20% EtOAc in hexane); IR (neat): ν 1460, 1367 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.34–7.21 (m, 5H), 4.53 (s, 2H), 3.75–3.58 (m, 2H), 1.92–1.68 (m, 2H), 1.58–1.16 (m, 7H), 0.92 (t, 3H, J=6.79 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.9, 128.4, 127.8, 75.8, 72.9, 36.2, 34.2, 31.4, 22.0, 14.0; MASS (ESI-MS): m/z 245 $[M+39]^+$. Elemental analysis calcd for $C_{14}H_{22}O$ (206.32): C 81.50, H 10.75; found: C 81.46, H 10.70%.

4.26. (*R*)-2-Methyl-1-hexanol 10

To a solution of lithium (0.62 g, 88.69 mmol) in liquid NH_3 (25 mL) was added compound **35** (3.6 g, 17.73 mmol) in dry THF (8 mL). The mixture was stirred for 20 min and was quenched with solid NH_4Cl (5.5 g). Ammonia was allowed to evaporate and ether was added to the residual mixture and filtered through a pad of Celite. The filtrate was dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure and purification by column chromatography of the crude product afforded the alcohol **10** (1.54 g, 75%) as colorless oil. R_f=0.3 (SiO_2, 20% EtOAc in hexane).

Compound **10** prepared here from **35** was identical in all respects with the one prepared from **8**.

4.27. (*S*)-1-Benzyloxy-undec-10-en-2-ol 36

Compound **36** (9.03 g, 92%) was prepared from magnesium (2.28 g, 99.48 mmol), 1,2-dibromoethane (three drops), 8-bromo-1-octene (12.60 g, 66.32 mmol), CuCN (148 mg, 5 mol %), and epoxide **32** (5.43 g, 33.16 mmol), following the same procedure as described for the synthesis of **33**. Compound **36** was colorless oil. R_f=0.45 (SiO_2, 30% EtOAc in hexane); $[\alpha]_D^{25}$ +2.30 (*c* 1.2, $CHCl_3$); IR (neat): ν 3386, 2932, 2871, 1638, 1460 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–7.15 (m, 5H), 5.81–5.67 (m, 1H), 4.98–4.84 (m, 2H), 4.47 (s, 2H), 3.75 (br s, 1H), 3.52–3.22 (m, 2H), 2.98–2.78 (m, 1H), 2.06–1.96 (m, 2H), 1.59–1.19 (m, 12H); MASS (ESI-MS): m/z 299 $[M+23]^+$. Elemental analysis calcd for $C_{18}H_{28}O_2$ (276.41): C 78.21, H 10.21; found: C 78.18, H 10.19%.

4.28. (*S*)-1-Benzyloxymethyl-dec-9-enyl 4-methylbenzenesulfonate 37

Compound **37** (10.36 g, 95%) was prepared from alcohol **36** (7.0 g, 25.36 mmol), triethylamine (35.31 mL, 253 mmol), DMAP (0.30 g, 2.53 mmol), tosyl chloride (5.31 g, 27.89 mmol) following the same procedure as described for the synthesis of **34**. Compound **37** was colorless gummy liquid. R_f=0.6 (SiO_2, 30% EtOAc in hexane); IR (neat): ν 2957, 2869, 1598, 1638, 1454 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.75–7.72 (m, 2H), 7.34–7.16 (m, 7H), 5.81–5.67 (m, 1H), 4.98–4.84 (m, 2H), 4.63–4.53 (m, 1H), 4.39 (dd, 2H, J=12.08, 5.28 Hz), 3.52–3.42 (m, 2H), 2.41 (s, 3H), 2.06–1.96 (m, 2H), 1.71–1.54 (m, 2H), 1.36–1.06 (m, 10H); MASS (ESI-MS): m/z 453 $[M+23]^+$.

4.29. (*R*)-(2-Methyl-undec-10-enyloxymethyl)-benzene 38

Compound **38** (1.43 g, 90%) was prepared from tosylate **37** (2.5 g, 5.81 mmol) using a solution of Me_2CuLi, prepared from CuI (6.64 g, 34.87 mmol) and MeLi (1.53 g, 69.74 mmol, 1.0 M in ether) in ether (50 mL) following the same procedure as described for the synthesis of **35**. Compound **38** was colorless oil. R_f=0.6 (SiO_2, 20% EtOAc in hexane); IR (neat): ν 1638, 1460, 1367 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.56–7.19 (m, 5H), 5.81–5.67 (m, 1H), 4.98–4.84 (m, 2H), 4.55 (s, 2H), 4.2–4.07 (m, 2H), 2.06–1.96 (m, 2H), 1.98–1.65 (m, 2H), 1.64–1.13 (m, 13H); MASS (ESI-MS): m/z 297 $[M+23]^+$. Elemental analysis calcd for $C_{19}H_{30}O_2$ (274.44): C 83.15, H 11.02; found: C 83.13, H 10.99%.

4.30. (*R*)-2-Methyl-undec-10-en-1-ol 14

Compound **14** (1.50 g, 75%) was prepared from **38** (3.0 g, 10.93 mmol) using lithium (0.38 g, 54.65 mmol) in liquid NH_3 (25 mL) following the same procedure as described for the synthesis of **10**. Compound **14** was colorless oil. R_f=0.3 (SiO_2, 20% EtOAc in hexane).

Compound **14** prepared here from **38** was identical in all respects with the one prepared from **12**.

4.31. (*S*)-1-Benzyloxy-undecan-2-ol 39

Compound **39** (12.47 g, 92%) was prepared from magnesium (3.51 g, 146.34 mmol), 1,2-dibromoethane (three drops), bromooctane (32.97 g, 170.73 mmol), CuCN (218 mg, 5 mol %), and epoxide **32** (8.0 g, 48.78 mmol), following the same procedure as described for the synthesis of **33**. Compound **39** was colorless oil. R_f=0.45 (SiO_2, 30% EtOAc in hexane); $[\alpha]_D^{25}$ +3.5 (*c* 1.38, $CHCl_3$); IR (neat): ν 3386, 2932, 2871, 1460 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.35–7.13 (m, 5H), 4.47 (s, 2H), 3.70 (br s, 1H), 3.42–3.2 (m, 2H), 2.88 (br s, 1H), 1.63–1.03 (m, 16H), 0.88 (t, 3H, J=6.62 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.1, 128.3, 127.6, 74.8, 73.2, 70.3, 33.3, 31.9, 29.7, 29.6, 29.3, 29.1, 25.6, 22.7, 14.1; MASS (ESI-MS): m/z 301 $[M+23]^+$. Elemental analysis calcd for $C_{18}H_{30}O_2$ (278.43): C 77.65, H 10.86; found: C 77.63, H 10.85%.

4.32. (*S*)-1-Benzyloxymethyl-decyl 4-methylbenzenesulfonate 40

Compound **40** (10.33 g, 95%) was prepared from alcohol **39** (7.0 g, 25.17 mmol), triethylamine (35.06 mL, 251 mmol), DMAP (0.30 g, 3.62 mmol), tosyl chloride (5.28 g, 27.69 mmol) following the same procedure as described for the synthesis of **34**. Compound **40** was colorless gummy liquid. R_f=0.6 (SiO_2, 30% EtOAc in hexane); IR (neat): ν 2957, 2869, 1598, 1454 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.71 (d, 2H, J=8.30 Hz), 7.29–7.09 (m, 7H), 4.61–4.51 (m, 1H), 4.35 (dd, 2H, J=12.08, 5.28 Hz), 3.50–3.40 (m, 2H), 2.43–2.31 (m, 3H), 1.68–1.55 (m, 2H), 1.36–1.07 (m, 16H), 0.87 (t, 3H, J=6.79 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.0, 137.5, 134.1, 129.2, 127.9, 127.4, 127.27, 127.2. 81.6, 72.8, 70.5, 30.9, 26.5, 21.9, 21.1, 13.4; MASS (ESI-MS): m/z 455 $[M+23]^+$.

4.33. (*R*)-(2-Methyl-undecyloxymethyl)-benzene 41

Compound **41** (4.46 g, 90%) was prepared from tosylate **40** (7.75 g, 17.95 mmol) using a solution of Me_2CuLi, prepared from CuI (20.51 g, 107.71 mmol) and MeLi (4.73 g, 215.42 mmol, 1.0 M in ether) in ether (100 mL) following the same procedure as described for the synthesis of **35**. Compound **41** was colorless oil. R_f=0.6 (SiO_2, 20% EtOAc in hexane); IR (neat): ν 1460, 1367 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.38–7.20 (m, 5H), 4.52 (s, 2H), 3.75–3.55 (m, 2H), 1.87–1.67 (m, 2H), 1.61–1.08 (m, 17H), 0.87 (t, 3H, J=6.61 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.8, 128.3, 127.5, 75.7, 72.8, 36.4, 34.0, 31.7, 29.4, 29.2, 28.7, 22.6, 14.0; MASS (ESI-MS): m/z 299 $[M+23]^+$. Elemental analysis calcd for $C_{19}H_{32}O$ (276.46): C 82.55, H 11.67; found: C 82.53, H 11.64%.

4.34. (*R*)-2-Methyl-undecan-1-ol 20

Compound **20** (2.58 g, 75% yield) was prepared from **41** (5.12 g, 18.55 mmol) using lithium (0.64 g, 92.76 mmol) in liquid NH_3 (25 mL) following the same procedure as described for the

synthesis of **10**. Compound **20** was colorless oil. R_f=0.3 (SiO_2, 20% EtOAc in hexane).

Compound **20** prepared here from **41** was identical in all respects with the one prepared from **18**.

4.35. (*S*)-1-Benzyloxy-decan-2-ol 42

Compound **42** (11.84 g, 92%) was prepared from magnesium (3.51 g, 146.34 mmol), 1,2-dibromoethane (three drops), bromoheptane (30.57 g, 170.73 mmol), CuCN (218 mg, 5 mol %), and epoxide **32** (8.0 g, 48.78 mmol), following the same procedure as described for the synthesis of **33**. Compound **42** was colorless oil. R_f=0.45 (SiO_2, 30% EtOAc in hexane); $[\alpha]_D^{25}$ +4.3 (*c* 1.34, $CHCl_3$); IR (neat): ν 3386, 2932, 2871, 1460 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–7.15 (m, 5H), 4.47 (s, 2H), 3.70 (br s, 1H), 3.52–3.22 (m, 2H), 2.98–2.78 (m, 1H), 1.59–1.19 (m, 14H), 0.87 (t, 3H, *J*=6.79 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.8, 127.9, 127.2, 74.4, 72.8, 69.9, 32.9, 31.5, 29.3, 29.2, 28.9, 28.7, 25.2, 22.3, 13.7; MASS (ESI-MS): *m*/*z* 287 $[M+23]^+$. Elemental analysis calcd for $C_{17}H_{28}O_2$ (264.40): C 77.22, H 10.67; found: C 77.19, H 10.64%.

4.36. (*S*)-1-Benzyloxymethyl-nonyl 4-methylbenzenesulfonate 43

Compound **43** (11.19 g, 95%) was prepared from alcohol **42** (7.44 g, 28.19 mmol), triethylamine (39.26 mL, 281 mmol), DMAP (0.34 g, 2.81 mmol), tosyl chloride (5.91 g, 31.01 mmol) following the same procedure as described for the synthesis of **34**. Compound **43** was colorless gummy liquid. R_f=0.6 (SiO_2, 30% EtOAc in hexane); IR (neat): ν 2957, 2869, 1598, 1454 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, 2H, *J*=8.30 Hz), 7.34–7.16 (m, 7H), 4.63–4.53 (m, 1H), 4.37 (dd, 2H, *J*=12.08, 5.28 Hz), 3.52–3.42 (m, 2H), 2.4 (s, 3H), 1.71–1.54 (m, 2H), 1.36–1.06 (m, 12H), 0.88 (t, 3H, *J*=6.42 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.8, 137.4, 134.1, 129.1, 127.8, 127.3, 127.1, 81.4, 72.7, 70.5, 31.3, 31.1, 28.8, 28.7, 28.6, 24.2, 22.1, 21.0, 13.6; MASS (ESI-MS): *m*/*z* 441 $[M+23]^+$.

4.37. (*R*)-(2-Methyl-decyloxymethyl)-benzene 44

Compound **44** (3.46 g, 90%) was prepared from tosylate **43** (2.5 g, 5.81 mmol) using a solution of Me_2CuLi, prepared from CuI (16.74 g, 87.9 mmol) and MeLi (3.86 g, 175.8 mmol, 1.0 M in ether) in ether (100 mL) following the same procedure as described for the synthesis of **35**. Compound **44** was colorless oil. R_f=0.6 (SiO_2, 20% EtOAc in hexane); IR (neat): ν 1460, 1367 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.56–7.19 (m, 5H), 4.55 (s, 2H), 3.77–3.58 (m, 2H), 1.98–1.65 (m, 2H), 1.64–1.13 (m, 15H), 0.89 (t, 3H, *J*=6.52 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.8, 128.3, 127.5, 75.7, 72.8, 36.4, 34.0, 31.7, 29.3, 29.1, 28.7, 22.5, 14.0; MASS (ESI-MS): *m*/*z* 280 $[M+18]^+$. Elemental analysis calcd for $C_{18}H_{30}O$ (262.43): C 82.38, H 11.52; found: C 82.34, H 11.40%.

4.38. (*R*)-2-Methyl-decan-1-ol 26

Compound **26** (2.13 g, 75%) was prepared from **44** (4.35 g, 16.57 mmol) using lithium (0.58 g, 82.87 mmol) in liquid NH_3 (25 mL) following the same procedure as described for the synthesis of **10**. Compound **26** was colorless oil. R_f=0.3 (SiO_2, 20% EtOAc in hexane).

Compound **26** prepared here from **44** was identical in all respects with the one prepared from **24**.

Acknowledgements

K.U.G. and N.T. thank CSIR, New Delhi for the award of fellowships.

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