A simple synthetic method for chiral 1,2-epoxides and the total synthesis of a chiral pheromone epoxide

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Received (in Cambridge, UK) 13th September 1999, Accepted 13th October 1999

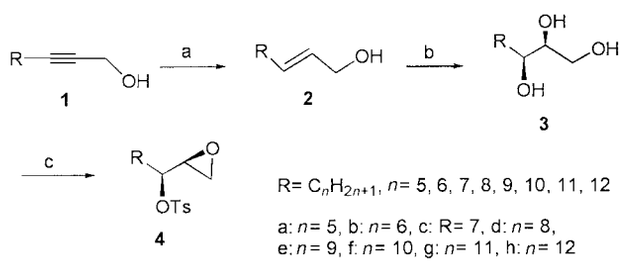
Chiral 1,2-epoxyalkan-3-ol tosyl esters **4a**–**h** were successfully synthesized from alkynols or allyl chlorides in three steps using Sharpless AD reaction as a key step in good yields. The chiral insect pheromone epoxide (6*Z*,9*S*,10*R*)-9,10-epoxyhenicos-6-ene **9** was thus smoothly synthesized from the corresponding key intermediate **4g**.

Introduction

Synthetic chemists always face a major challenge in the preparation of chiral compounds with high optical purity. The need for pure enantiomers is particularly apparent in the field of insect pheromone chemistry, since insect chemoreception can be highly stereoselective.[1–3] Optically active epoxides are an important class of natural products encountered as sex attractants of Lepidopteran pests,[4] and self-defensive substances against rice blast disease.[5] The optically active 1,2-epoxyalkan-3-ols are key intermediates in the synthesis of those insect pheromones because they can be easily converted to the corresponding optically active 2,3-epoxyalkan-1-ols through the Payne rearrangement[6] or to optically active internal epoxides *via* an alkylative rearrangement of the corresponding toluene-*p*-sulfonate (tosyl) esters.[7] In order to obtain the chiral epoxides in those synthetic approaches, until now the mostly used key reaction has been the Sharpless AE reaction on the *Z*-allylic alcohols.[7–9] Herein we report two further synthetic methods for the chiral 1,2-epoxyalkan-3-ol tosyl esters **4a**–**h** using Sharpless AD[10] as the key reaction, and the total synthesis of the insect sex pheromone (6*Z*,9*S*,10*R*)-9,10-epoxyhenicos-6-ene **9** with full experimental details.[11]

Results and discussion

Sharpless AD reaction on the starting materials **2** possessing different, long alkyl chains, prepared by reduction of the corresponding alkynols **1**[12] using $LiAlH_4$ in THF, installed the two stereogenic centers, with 95–97% enantiomeric excess (ee).[13] The resulting triols **3** were subsequently treated with NaH and Tos-Im[14] in THF to produce the key intermediates **4** in good yield (Scheme 1). To the best of our knowledge, this new synthetic approach is the shortest and the most efficient among those reported in previous literature.[7–9] Thus 1,2-epoxy-3-tosyl



Scheme 1 *Reagents, conditions and yields*: (a) $LiAlH_4$, THF, reflux; 83–94%; (b) $K_3Fe(CN)_6$, K_2CO_3, $NaHCO_3$, $MeSO_2NH_2$, $(DHQ)_2PHAL$, $K_2OsO_2(OH)_4$, $^tBuOH–H_2O$ (1:1), 0 °C; 68–89%; (c) NaH, Tos-Im, THF; 53–66%.

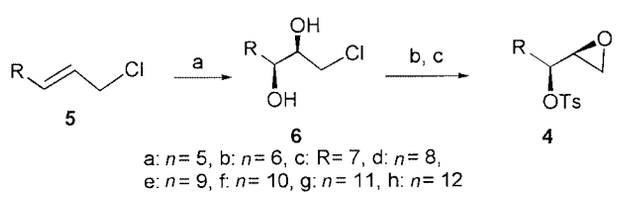
Table 1 Yields and physical properties of the obtained 1,2-epoxy-3-tosyl esters **4a**–**h**

Compound	R	Mp (*T*/°C)	$[a]_D^{20}$ (*c* 1, $CHCl_3$)	Yield (%)[a]
4a	C_5H_{11}	oil	+8.5	42
4b	C_6H_{13}	oil	+8.2	45
4c	C_7H_{15}	54–55	+8.5	47
4d	C_8H_{17}	57–58	+8.0	48
4e	C_9H_{19}	59–60	+8.7	48
4f	$C_{10}H_{21}$	72–74	+8.3	50
4g	$C_{11}H_{23}$	71–72	+8.6	54
4h	$C_{12}H_{25}$	85–86	+8.0	57

[a] Total yields in three steps.

esters (**4a**–**h**) with different alkyl chains were obtained as colorless solids or oils. Only one diastereoisomer was detected during this reaction. Their total yields in three steps, specific optical rotations and mps are summarized in Table 1. The chemical yields of **4a**–**h** slightly increased with an increase in the alkyl chain length. The specific optical rotation of the key intermediate **4g** was very close to that reported in the literature {lit.,[8] $[a]_D^{20}$ +8.3 (*c* 1, $CHCl_3$)}.

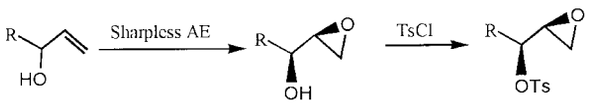
In the meantime, another alternative synthetic procedure, which is very similar to that mentioned above, also can be utilized to the preparation of **4a**–**h** using the corresponding allyl chlorides **5** as starting materials (Scheme 2). The chemical



Scheme 2 *Reagents, conditions and yields*: (a) $K_3Fe(CN)_6$, K_2CO_3, $NaHCO_3$, $MeSO_2NH_2$, $(DHQ)_2PHAL$, $K_2OsO_2(OH)_4$, $^tBuOH–H_2O$ (1:1), 0 °C; 84–88%; (b) K_2CO_3, MeOH, rt; (c) NaH, Tos-Im, THF; 50–56% (two steps).

yields and reaction conditions are shown in Scheme 2 and the obtained chiral diols **6a**–**h** with 94–97% ee[13] were directly transferred to the next reaction without purification to give epoxy tosyl esters **4** (step b, c) which have similar specific optical rotations and the same spectral data as those obtained in Scheme 1. The two synthetic routes are very convenient and useful for the synthesis of **4**, and this clearly suggests that

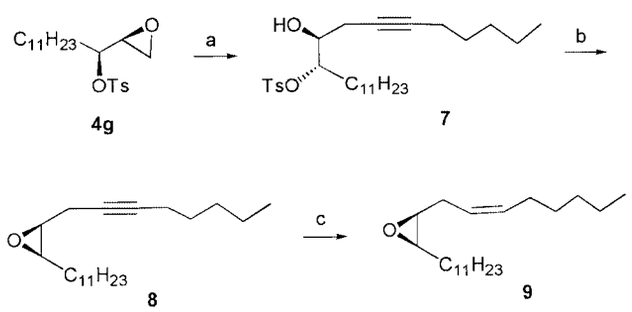
Sharpless AD is a very powerful and useful synthetic method for the construction ion of the chiral center on many substrates. Indeed, the chiral epoxides **4a**–**h** can obviously be obtained by kinetic resolution using Sharpless AE reaction (Scheme 3).



Scheme 3

However, the direct asymmetric synthesis using Sharpless AD reaction is much more effective because all the starting materials could be transferred to the desired chiral compounds.

The synthesis of the sex pheromone of *Phragmatobia fuliginosa* is depicted in Scheme 4. The epoxide **4g** was opened by



Scheme 4 *Reagents, conditions and yield*: (a) Hept-1-yne, *n*-BuLi, $BF_3{\cdot}OEt_2$, THF, −78 °C; 70%; (b) K_2CO_3, CH_3OH, rt, 60%; (c) Pd–$CaCO_3$, H_2; 80%.

1-lithioheptyne in the presence of $BF_3{\cdot}Et_2O$ to afford compound **7**. Treatment of **7** with K_2CO_3 in methanol gave another epoxide **8** in good yield. Catalytic hydrogenation of **8** over Lindlar catalyst easily gave the target compound (6*Z*,9*S*,10*R*)-9,10-epoxyhenicos-6-ene **9** in moderate yield. The specific optical rotation of our synthetic compound **9** is very close to those values reported in the literature {**9:** $[\alpha]_D^{20}$ +8.7 (*c* 0.97, $CHCl_3$); lit.,[15] $[\alpha]_D^{20}$ +9.4 (*c* 0.55, $CHCl_3$)}. Its ^1H NMR spectral data are completely consistent with those reported in the literature.[15,16]

In conclusion, we have developed two efficient and convenient procedures for the stereocontrolled synthesis of the chiral 1,2-epoxy-3-tosyl esters **4a**–**h** from which the important chiral pheromone epoxide **9** has been successfully synthesized. This new synthetic approach using Sharpless AD reaction will certainly open a new and effective synthetic route to the preparation of those highly stereoselective chemoreception insect pheromones. In order to disclose the relationship between structure and biological activity, syntheses of their pheromone analogs are in progress.

Experimental

Mps were obtained with a Yanagimoto micro-melting-point apparatus and are uncorrected. Optical rotations were determined for solutions in $CHCl_3$ or MeOH at 20 °C by using a Perkin-Elmer-241 MC digital polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. ^1H NMR spectra were determined for solutions in $CDCl_3$ with tetramethylsilane (TMS) as internal standard on a Bruker AMX-300 spectrometer; *J*-values are in Hz. IR spectra were determined by a Perkin-Elmer 983 spectrometer. Mass spectra were recorded with an HP-5989 instrument. High-resolution mass spectra were recorded on a Finnigan MA+ instrument. All solid compounds reported in this paper gave satisfactory CHN microanalyses with an Italian Carlo-Erba 1106 analyzer. Petroleum spirit refers to the fraction with distillation range 60–70 °C. Hydroquinine phthalazine-1,4-diyl diether $(DHQ)_2PHAL$ was purchased from Aldrich.

Typical reaction procedure for the preparation of *E*-allylic alcohols

(*E*)-Tetradec-2-en-1-ol 2g. To a stirred solution of tetradec-2-yn-1-ol **1g** (7.56 g, 36 mmol) in dry THF (100 ml) was added $LiAlH_4$ (3.14 g, 82.6 mmol) slowly at 0 °C under nitrogen atmosphere. After stirring for 20 min, the mixture was heated under reflux for 6 h. The reaction was quenched by adding water at 0 °C. The mixture was filtered, and extracted with diethyl ether. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by distillation under reduced pressure to afford **2g** as a colorless liquid (7.47 g, 98%); bp 104 °C/1 mmHg; IR (neat) *ν* 3324, 2920, 1597, 1466 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.89 (3H, t, *J* 6.6, CH_3), 1.20–1.40 (18H, m, CH_2), 1.95–2.10 (2H, m, CH_2), 2.20–2.30 (1H, br s, OH), 4.1 (2H, d, *J* 5.0, CH_2), 5.46–5.70 (2H, m, CH=CH); MS (EI) *m*/*z* 212 (M^+) [Calc. for $C_{14}H_{28}O$ (212.3715): C, 79.18; H, 13.29. Found: C, 79.12; H, 13.22%].

Compounds **2a**–**f** and **2h** were prepared in the same manner to that described above.

(*E*)-Oct-2-en-1-ol 2a. A colorless liquid (3.83 g, 83%); bp 88 °C/1 mmHg; IR (neat) *ν* 3324, 2923, 1669, 1466 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.89 (3H, t, *J* 6.3, CH_3), 1.20–1.40 (6H, m, CH_2), 1.96–2.08 (2H, m, CH_2), 1.80–1.90 (1H, br s, OH), 4.0 (2H, d, *J* 4.9, CH_2), 5.43–5.60 (2H, m, CH=CH); MS (EI) *m*/*z* 128 (M^+) [Calc. for $C_8H_{16}O$ (128.2120): C, 74.94; H, 12.58. Found: C, 74.86; H, 12.60%].

(*E*)-Non-2-en-1-ol 2b. A colorless liquid (4.78, g 93%); bp 90 °C/1 mmHg; IR (neat) *ν* 3323, 2924, 1704, 1468 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.89 (3H, t, *J* 6.5, CH_3), 1.20–1.42 (8H, m, CH_2), 1.98–2.10 (2H, m, CH_2), 2.60–2.70 (1H, br s, OH), 4.08 (2H, d, *J* 4.9, CH_2), 5.40–5.60 (2H, m, CH=CH); MS (EI) *m*/*z* 142 (M^+) [Calc. for $C_9H_{18}O$ (142.2386): C, 76.00; H, 12.76. Found: C, 75.87; H, 12.92%].

(*E*)-Dec-2-en-1-ol 2c. A colorless liquid (5.28 g, 94%); bp 94 °C/1 mmHg; IR (neat) *ν* 3326, 2925, 1667, 1463 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.85 (3H, t, *J* 6.7, CH_3), 1.20–1.48 (10H, m, CH_2), 1.95–2.05 (2H, m, CH_2), 2.40–2.80 (1H, br s, OH), 4.05 (2H, d, *J* 4.1, CH_2), 5.45–5.70 (2H, m, CH=CH); MS (EI) *m*/*z* 156 (M^+) [Calc. for $C_{10}H_{20}O$ (156.2652): C, 76.86; H, 12.90. Found: C, 76.90; H, 12.70%].

(*E*)-Undec-2-en-1-ol 2d. A colorless liquid (5.93 g, 92%); bp 98 °C/1 mmHg; IR (neat) *ν* 3330, 2924, 2853, 1669, 1462 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.85 (3H, t, *J* 6.1, CH_3), 1.20–1.40 (12H, m, CH_2), 1.95–2.05 (2H, m, CH_2), 2.40–2.80 (1H, br s, OH), 4.0 (2H, d, *J* 4.8, CH_2), 5.45–5.70 (2H, m, CH=CH); MS (EI) *m*/*z* 170 (M^+) [Calc. for $C_{11}H_{22}O$ (170.2918): C, 77.58; H, 13.02. Found: C, 77.54; H, 13.06%].

(*E*)-Dodec-2-en-1-ol 2e. A colorless liquid (6.16 g, 93%); bp 100 °C/1 mmHg; IR (neat) *ν* 3326, 2922, 2852, 1597, 1466 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.85 (3H, t, *J* 6.7, CH_3), 1.20–1.48 (14H, m, CH_2), 1.60–1.80 (1H, br s, OH), 1.98–2.10 (2H, m, CH_2), 4.05 (2H, d, *J* 5.05, CH_2), 5.45–5.70 (2H, m, CH=CH); MS (EI) *m*/*z* 184 (M^+) [Calc. for $C_{12}H_{24}O$ (184.3184): C, 78.20; H, 13.12. Found: C, 78.12; H, 13.17%].

(*E*)-Tridec-2-en-1-ol 2f. A colorless liquid (6.42 g, 90%); bp 104 °C/1 mmHg; IR (neat) *ν* 3328, 2924, 2854, 1597, 1466 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.88 (3H, t, *J* 6.6, CH_3), 1.20–1.40 (16H, m, CH_2), 2.05–2.12 (2H, m, CH_2), 2.40–2.80 (1H, br s, OH), 4.10 (2H, d, *J* 5.0, CH_2), 5.45–5.70 (2H, m, CH=CH); MS (EI) *m*/*z* 198 (M^+) [Calc. for $C_{13}H_{26}O$ (198.3449): C, 78.72; H, 13.21. Found: C, 78.54; H, 13.17%].

(*E*)-Pentadec-2-en-1-ol 2h. A colorless liquid (7.32 g, 90%); bp 140 °C/1 mmHg; IR (neat) *ν* 3326, 2926, 2855, 1597, 1464

cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (3H, t, J 6.6, CH_3), 1.20–1.40 (20H, m, CH_2), 1.60–1.70 (1H, br s, OH), 2.05–2.12 (2H, m, CH_2), 4.10 (2H, d, J 5.0, CH_2), 5.45-5.70 (2H, m, CH=CH); MS (EI) m/z 226 (M^+) [Calc. for $C_{15}H_{30}O$ (226.3981): C, 79.58; H, 13.36. Found: C, 79.50; H, 13.47%].

Typical reaction procedure for the preparation of triols 3

(2*S*,3*S*)-Tetradecane-1,2,3-triol 3g. To a stirred mixture of K_2CO_3 (0.83 mg, 6 mmol), $K_3Fe(CN)_6$ (2 g, 6 mmol), $NaHCO_3$ (0.51 g, 6 mmol) and $CH_3SO_2NH_2$ (0.2 mg, 2 mmol) in a mixture of 10 ml water and 10 ml *t*-BuOH were added $(DHQ)_2$-PHAL (16 mg, 0.02 mmol) and $K_2OSO_2(OH)_2$ (7.5 mg, 0.02 mmol) and the reaction mixture was cooled to 0 °C. Compound **2g** (424 mg, 2 mmol) was added into the reaction mixture, which was stirred for 6 h at 0 °C. The reaction was quenched by adding 3 g of anhydrous Na_2SO_3 at room temperature and the mixture was stirred for 30 min. After filtration the mixture was extracted with EtOAc several times, the combined extracts were washed successively with 5% HCl and brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatograph (eluent: petroleum spirit–EtOAc 1 : 10) to obtain **3g** as a white solid (443 mg, 90%); mp 82–83 °C; $[a]_D$ −6.8 (*c* 1.0, CH_3OH); IR (KBr) ν 3330, 2928, 1230, 563 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.9 (3H, t, J 7.0, CH_3), 1.15–1.40 (18H, m, CH_2), 1.50–1.60 (2H, m, CH_2), 2.12–2.30 (2H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.57 (1H, m), 3.60–3.90 (3H, m); MS (EI) m/z 247 (MH^+), 229 ($M - H_2O$) [Calc. for $C_{14}H_{30}O_3$ (246.3862): C, 68.25; H, 12.27. Found: C, 68.20; H, 12.13%].

Compounds **3a**–**f** and **3h** were prepared in the same manner to that described above.

(2*S*,3*S*)-Octane-1,2,3-triol 3a. A white solid (220 mg, 68%); mp 62–64 °C; $[a]_D$ −5.8 (*c* 1.0, CH_3OH); IR (KBr) ν 3324, 2928, 1145, 546 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.9 (3H, t, J 7.0, CH_3),1.15–1.42 (6H, m, CH_2), 1.50–1.60 (2H, m, CH_2), 2.12–2.30 (2H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.60 (1H, m), 3.60–3.90 (3H, m); MS (EI) m/z 162 (M^+), 144 ($M - H_2O$) [Calc. for $C_8H_{18}O_3$ (162.2267): C, 59.23; H, 11.18. Found: C, 59.12; H, 11.02%].

(2*S*,3*S*)-Nonane-1,2,3-triol 3b. A white solid (264 mg, 75%); mp 73–75 °C; $[a]_D$ −6.0 (*c* 1.0, CH_3OH); IR (KBr) ν 3335, 2928, 1230, 563 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (3H, t, J 7.0, CH_3), 1.14–1.42 (8H, m, CH_2), 1.47–1.58 (2H, m, CH_2), 2.12–2.30 (2H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.45–3.58 (1H, m), 3.60–3.90 (3H, m); MS (EI) m/z 177 (MH^+), 159 ($MH - H_2O$) [Calc. for $C_9H_{20}O_3$ (176.2533): C, 61.33; H, 11.44. Found: C, 61.52; H, 11.26%].

(2*S*,3*S*)-Decane-1,2,3-triol 3c. A white solid (297 mg, 78%); mp 76–77 °C; $[a]_D$ −6.2 (*c* 1.0, CH_3OH); IR (KBr) ν 3341, 2928, 1225, 569 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (3H, t, J 7.0, CH_3), 1.14–1.42 (10H, m, CH_2), 1.47–1.60 (2H, m, CH_2), 2.12–2.30 (2H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.48–3.58 (1H, m), 3.60–3.90 (3H, m); MS (EI) m/z 191 (MH^+), 173 ($MH - H_2O$) [Calc. for $C_{10}H_{22}O_3$ (190.2799): C, 63.12; H, 11.65. Found: C, 63.22; H, 11.67%].

(2*S*,3*S*)-Undecane-1,2,3-triol 3d. A white solid (322 mg, 79%); mp 79–80 °C; $[a]_D$ −6.8 (*c* 1.3, CH_3OH); IR (KBr) ν 3330, 2928, 1250, 543 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, t, J 7.0, CH_3), 1.14–1.40 (12H, m, CH_2), 1.50–1.56 (2H, m, CH_2), 2.12–2.30 (2H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.58 (1H, m), 3.60–3.92 (3H, m); MS (EI) m/z 205 (MH^+), 187 ($MH - H_2O$) [Calc. for $C_{11}H_{24}O_3$ (204.3065): C, 64.67; H, 11.84. Found: C, 64.52; H, 11.87%].

(2*S*,3*S*)-Dodecane-1,2,3-triol 3e. A white solid (349 mg, 84%); mp 79–80 °C; $[a]_D$ −6.8 (*c* 1.0, CH_3OH); IR (KBr) ν 3328, 2928, 1267, 547 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t, J 7.0, CH_3), 1.14–1.42 (14H, m, CH_2), 1.50–1.56 (2H, m, CH_2), 2.12–2.30 (2H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.58 (1H, m), 3.60–3.92 (3H, m); MS (EI) m/z 219 (MH^+), 201 ($MH - H_2O$) [Calc. for $C_{12}H_{26}O_3$ (218.3330): C, 66.01; H, 12.00. Found: C, 66.22; H, 12.11%].

(2*S*,3*S*)-Tridecane-1,2,3-triol 3f. A white solid (408 mg, 88%); mp 80–81 °C; $[a]_D$ −7.0 (*c* 1.3, CH_3OH); IR (KBr) ν 3330, 2928, 1272, 551 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (3H, t, J 7.0, CH_3), 1.14–1.40 (16H, m, CH_2), 1.50–1.58 (2H, m, CH_2), 2.12–2.30 (2H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.58 (1H, m), 3.62–3.90 (3H, m); MS (EI) m/z 233 (MH^+), 215 ($MH - H_2O$) [Calc. for $C_{13}H_{28}O_3$ (232.3596): C, 67.20; H, 12.15. Found: C, 67.08; H, 12.27%].

(2*S*,3*S*)-Pentadecane-1,2,3-triol 3h. A white solid (438 mg, 89%); mp 85–87 °C; $[a]_D$ −7.0 (*c* 1.0, CH_3OH); IR (KBr) ν 3329, 2927, 1230, 562 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (3H, t, J 7.0, CH_3), 1.14–1.40 (20H, m, CH_2), 1.52–1.62 (2H, m, CH_2), 2.12–2.30 (2H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.57 (1H, m), 3.60–3.90 (3H, m); MS (EI) m/z 247 (MH^+), 229 ($MH - H_2O$) [Calc. for $C_{15}H_{32}O_3$ (260.4128): C, 69.18; H, 12.39. Found: C, 69.22; H, 12.37%].

Typical reaction procedure for the preparation of 1,2-chiral epoxides 4

(2*S*,3*S*)-1,2-Epoxy-3-(tosyloxy)tetradecane 4g. To a solution of **3g** (246 mg, 1 mmol) in dry THF was added 95% NaH (72 mg, 3 mmol) and the mixture was stirred for 30 min at room temperature. Then Tos-Im was added into the reaction solution, which was further stirred for 6 h before being poured into ice–water and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatograph (eluent: EtOAc–petroleum spirit 1 : 6) to give compound **4g** as a colorless solid (241 mg, 63%); mp 71–72 °C, $[a]_D$ +8.6 (*c* 1, $CHCl_3$); IR (KBr) ν 3202, 1599, 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, t, J 6.5, CH_3), 1.25–1.50 (18H, m, CH_2), 1.65–1.85 (2H, m, CH_2), 2.45 (3H, s, CH_3), 2.60 (1H, dd, J 5.0, 2.5), 2.78 (1H, t, J 5.0), 3.05–3.12 (1H, m), 4.35 (1H, q, J 6.0, CH), 7.35 (2H, d, J 7.5, ArH), 7.8 (2H, d, J 7.5, ArH); MS (EI) m/z 383 (MH^+), 227 ($M^+ - C_{11}H_{23}$) [Calc. for $C_{21}H_{34}O_4S$ (382.5583): C, 65.93; H, 8.96. Found: C, 65.82; H, 8.97%].

Compounds **4a**–**f** and **4h** were prepared in the same manner to that described above.

(2*S*,3*S*)-1,2-Epoxy-3-(tosyloxy)octane 4a. A colorless oil (158 mg, 53%); $[a]_D$ +8.5 (*c* 1.0, $CHCl_3$); IR (KBr) ν 3200, 1597, 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (3H, t, J 6.5, CH_3), 1.25–1.50 (6H, m, CH_2), 1.65–1.85 (2H, m, CH_2), 2.44 (3H, s, CH_3), 2.65 (1H, dd, J 4.6, 2.5, CH), 2.75 (1H, t, J 4.5, CH), 3.0–3.10 (1H, m, CH), 4.35 (1H, q, J 6.0), 7.35 (2H, d, J 7.5, ArH), 7.85 (2H, d, J 7.5, ArH); MS (EI) m/z 299 (MH^+) [Calc. for $C_{15}H_{22}O_4S$ (298.3988): C, 60.38; H, 7.43. Found: C, 60.52; H, 7.33%].

(2*S*,3*S*)-1,2-Epoxy-3-(tosyloxy)nonane 4b. A colorless oil (172 mg, 55%); $[a]_D$ +8.2 (*c* 1.0, $CHCl_3$); IR (KBr) ν 3200, 1597, 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (3H, t, J 6.5, CH_3), 1.25–1.50 (8H, m, CH_2), 1.65–1.85 (2H, m, CH_2), 2.43 (3H, s, CH_3), 2.65 (1H, dd, J 4.6, 2.5, CH), 2.75 (1H, t, J 4.5, CH), 3.0–3.10 (1H, m, CH), 4.35 (1H, q, J 6.0, 15.0, CH), 7.35 (2H, d, J 7.6, ArH), 7.85 (2H, d, J 7.5, ArH); MS (EI) m/z 313 (MH^+) [Calc. for $C_{16}H_{24}O_4S$ (312.4254): C, 61.51; H, 7.74. Found: C, 61.46; H, 7.70%].

(2*S*,3*S*)-1,2-Epoxy-3-(tosyloxy)decane 4c. A white solid (186 mg, 57%); mp 54–55 °C; $[a]_D$ +8.5 (*c* 1.0, $CHCl_3$); IR (KBr)

ν 3205, 1597, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3H, t, J 6.5, CH_3), 1.25–1.50 (10H, m, CH_2), 1.65–1.85 (2H, m, CH_2), 2.45 (3H, s, CH_3), 2.65 (1H, dd, J 4.6, 2.6, CH), 2.78 (1H, t, J 4.6, CH), 3.10 (1H, m, CH), 4.35 (1H, q, J 6.0, 15.0, CH), 7.35 (2H, d, J 7.5, ArH), 7.85 (2H, d, J 7.5, ArH); MS (EI) m/z 327 (MH^+) [Calc. for $C_{17}H_{26}O_4S$ (326.4519): C, 62.55; H, 8.03. Found: C, 62.52 ; H, 8.17%].

(2*S*,3*S*)-1,2-Epoxy-3-(tosyloxy)undecane 4d. A white solid (204 mg, 60%); mp 57–58 °C; $[\alpha]_D$ +8.0 (c 1.0, $CHCl_3$); IR (KBr) ν 3205, 1597, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3H, t, J 6.5, CH_3), 1.25–1.50 (12H, m, CH_2), 1.65–1.85 (2H, m, CH_2), 2.45 (3H, s, CH_3), 2.65 (1H, dd, J 4.6, 2.6, CH), 2.78 (1H, t, J 4.6, CH), 3.0–3.10 (1H, m, CH), 4.35 (1H, q, J 6.0, CH), 7.35 (2H, d, J 7.5, ArH), 7.85 (2H, d, J 7.5, ArH); MS (EI) m/z 341 (MH^+) [Calc. for $C_{18}H_{28}O_4S$ (340.4785): C, 63.50; H, 8.29. Found: C, 63.72; H, 8.07%].

(2*S*,3*S*)-1,2-Epoxy-3-(tosyloxy)dodecane 4e. A white solid (205 mg, 58%); mp 59–60 °C; $[\alpha]_D$ +8.7 (c 1.0, $CHCl_3$); IR (KBr) ν 3205, 1597, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3H, t, J 6.5, CH_3), 1.25–1.50 (14H, m, CH_2), 1.70–1.90 (2H, m, CH_2), 2.45 (3H, s, CH_3), 2.65 (1H, dd, J 4.6, 2.5, CH), 2.75 (1H, t, J 4.5, CH), 3.0-3.10 (1H, m, CH), 4.35 (1H, q, J 6.0, CH), 7.35 (2H, d, J 7.5, ArH), 7.85 (2H, d, J 7.5, ArH); MS (EI) m/z 355 (MH^+) [Calc. for $C_{19}H_{30}O_4S$ (354.5051): C, 64.37; H, 8.53. Found: C, 64.33; H, 8.67%].

(2*S*,3*S*)–1,2-Epoxy-3-(tosyloxy)tridecane 4f. A white solid (206 mg, 56%); mp 72–74 °C; $[\alpha]_D$ +8.3 (c 1.0, $CHCl_3$); IR (KBr) ν 3205, 1597, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3H, t, J 6.5, CH_3), 1.27–1.52 (16H, m, CH_2), 1.70–1.90 (2H, m, CH_2), 2.43 (3H, s, CH_3), 2.65 (1H, dd, J 4.6, 2.5, CH), 2.75 (1H, t, J 4.5, CH), 3.0–3.10 (1H, m, CH), 4.35 (1H, q, J 6.0, CH), 7.35 (2H, d, J 7.5, ArH), 7.85 (2H, d, J 7.5, ArH); MS (EI) m/z 369 (MH^+) [Calc. for $C_{20}H_{32}O_4S$ (368.5317): C, 65.18; H, 8.75. Found: C, 65.11; H, 8.91%].

(2*S*,3*S*)-1,2-Epoxy-3-(tosyloxy)pentadecane 4h. A white solid (262 mg, 66%); mp 85–86 °C; $[\alpha]_D$ +8.0 (c 1.0, $CHCl_3$); IR (KBr) ν 3205, 1597, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3H, t, J 6.5, CH_3), 1.25–1.50 (20H, m, CH_2), 1.65–1.85 (2H, m, CH_2), 2.43 (3H, s, CH_3), 2.60 (1H, dd, J 5.0, 2.5, CH), 2.78 (1H, t, J 4.5, CH), 3.0–3.10 (1H, m, CH), 4.35 (1H, q, J 5.0, CH), 7.35 (2H, d, J 7.5, ArH), 7.85 (2H, d, J 7.5, ArH); MS (EI) m/z 397 (MH^+) [Calc. for $C_{22}H_{36}O_4S$ (396.5848): C, 66.63; H, 9.15. Found: C, 66.78; H, 9.27%].

The preparation of diols 6

The reaction procedure is the same as that described in the preparation of diol **3**, but starting from the *E*-allyl chlorides **5**.

(2*S*,3*S*)-1-Chlorooctane-2,3-diol 6a. A white solid (302 mg, 84%); mp 76–78 °C; $[\alpha]_D$ −9.5 (c 1.0, CH_3OH); IR (KBr) ν 3324, 2928, 1145, 546 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3H, t, J 7.0, CH_3), 1.15–1.42 (6H, m, CH_2), 1.50–1.60 (2H, m, CH_2), 2.12–2.30 (1H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.48–3.60 (2H, m), 3.60–3.96 (2H, m); MS (EI) m/z 178, 180 (M^+), 162 ($M - H_2O$) [Calc. for $C_8H_{17}ClO_2$ (180.6721): C, 53.18; H, 9.48. Found: C, 53.02; H, 9.32%].

(2*S*,3*S*)-1-Chlorononane-2,3-diol 6b. A white solid (330 mg, 85%); mp 82–84 °C; $[\alpha]_D$ −9.0 (c 1.0, CH_3OH); IR (KBr) ν 3335, 2928, 1230, 563 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (3H, t, J 7.0, CH_3), 1.14–1.42 (8H, m, CH_2), 1.47–1.58 (2H, m, CH_2), 2.12–2.30 (1H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.45–3.60 (2H, m), 3.70–3.97 (2H, m); MS (EI) m/z 192, 194 (M^+), 176 ($M - H_2O$) [Calc. for $C_9H_{19}ClO_2$ (194.6987): C, 55.52; H, 9.84. Found: C, 55.62; H, 9.98%].

(2*S*,3*S*)-1-Chlorodecane-2,3-diol 6c. A white solid (363 mg, 88%); mp 86–87 °C; $[\alpha]_D$ −9.6 (c 1.0, CH_3OH); IR (KBr) ν 3341, 2928, 1225, 569 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (3H, t, J 7.0, CH_3), 1.14–1.42 (10H, m, CH_2), 1.47–1.60 (2H, m, CH_2), 2.12–2.30 (1H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.48–3.58 (2H, m), 3.70–4.0 (2H, m); MS (EI) m/z 206, 208 (M^+), 192 ($M - H_2O$) [Calc. for $C_{10}H_{21}ClO_2$ (208.7252): C, 57.54; H, 10.14. Found: C, 57.29; H, 10.27%].

(2*S*,3*S*)-1-Chloroundecane-2,3-diol 6d. A white solid (382 mg, 86%); mp 87–89 °C; $[\alpha]_D$ −9.6 (c 1.3, CH_3OH); IR (KBr) ν 3330, 2928,1250, 543 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (3H, t, J 7.0, CH_3), 1.14–1.40 (12H, m, CH_2), 1.50–1.56 (2H, m, CH_2), 2.12–2.30 (1H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.47–3.58 (2H, m), 3.70–3.97 (2H, m); MS (EI) m/z 220, 222 (M^+), 204 ($M - H_2O$) [Calc. for $C_{11}H_{23}ClO_2$ (222.7518): C, 59.31; H, 10.41. Found: C, 59.42; H, 10.67%].

(2*S*,3*S*)-1-Chlorododecane-2,3-diol 6e. A white solid (394 mg, 84%); mp 89–90 °C; $[\alpha]_D$ −9.8 (c 1.0, CH_3OH); IR (KBr) ν 3328, 2928, 1267, 547 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (3H, t, J 7.0, CH_3), 1.14–1.42 (14H, m, CH_2), 1.50–1.56 (2H, m, CH_2), 2.12–2.30 (1H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.62 (2H, m), 3.70–3.98 (2H, m); MS (EI) m/z 234, 236 (M^+), 218 ($M - H_2O$) [Calc. for $C_{12}H_{25}ClO_2$ (236.7784): C, 60.87; H, 10.64. Found: C, 60.72; H, 10.61%].

(2*S*,3*S*)-1-Chlorotridecane-2,3-diol 6f. A white solid (440 mg, 88%); mp 90–91 °C; $[\alpha]_D$ −9.7 (c 1.3, CH_3OH); IR (KBr) ν 3330, 2928, 1272, 551 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (3H, t, J 7.0, CH_3), 1.14–1.40 (16H, m, CH_2), 1.50–1.58 (2H, m, CH_2), 2.12–2.30 (1H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.60 (2H, m), 3.72–3.97 (2H, m); MS (EI) m/z 248, 250 (M^+), 232 ($M - H_2O$) [Calc. for $C_{13}H_{27}ClO_2$ (250.8050): C, 62.26; H, 10.85. Found: C, 62.14; H, 10.67%].

(2*S*,3*S*)-1-Chlorotetradecane-2,3-diol 6g. A white solid: yield 454 mg, 86%); mp 89–90 °C; $[\alpha]_D$ −6.8 (c 1.0, CH_3OH); IR (KBr) ν 3330, 2928, 1230, 563 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3H, t, J 7.0, CH_3), 1.15–1.40 (18H, m, CH_2), 1.50–1.60 (2H, m, CH_2), 2.12–2.30 (1H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.50–3.60 (2H, m), 3.60–3.98 (2H, m); MS (EI) m/z 262, 264 (M^+), 246 ($M - H_2O$) [Calc. for $C_{14}H_{29}ClO_2$ (264.8316): C, 63.49; H, 11.04. Found: C, 63.31; H, 11.11%].

(2*S*,3*S*)-1-Chloropentadecane-2,3-diol 6h. A white solid (478 mg, 86%); mp 92–93 °C; $[\alpha]_D$ −7.0 (c 1.0, CH_3OH); IR (KBr) ν 3329, 2927, 1230, 562 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (3H, t, J 7.0, CH_3), 1.14–1.40 (20H, m, CH_2), 1.52–1.62 (2H, m, CH_2), 2.12–2.30 (1H, br s, OH), 2.60–2.70 (1H, br s, OH), 3.53–3.62 (2H, m), 3.64–4.0 (2H, m); MS (EI) m/z 276, 278 (M^+), 260 ($M - H_2O$) [Calc. for $C_{15}H_{31}ClO_2$ (278.8581): C, 64.61; H, 11.21. Found: C, 64.46; H, 11.42%].

Compounds **6a**–**h** can be easily transformed into the corresponding epoxy tosyl esters **4a**–**h** upon treatment with K_2CO_3–MeOH and NaH–Tos-im. The typical procedure is as follows.

To a solution of 1.74 g of **6g** (6.64 mmol) in methanol (10 ml) was added potassium carbonate (1.08 g, 7.82 mmol) and the reaction mixture was stirred at room temperature for 8 h. The reaction was quenched by addition of water (20 ml) and the mixture was extracted with ethyl acetate (10 ml × 3). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was treated with NaH (60%) (266 mg, 6.64 mmol) in anhydrous THF (20 ml) at 0 °C and the mixture was stirred at room temperature for 15 min. Tos-Im (1.45 g, 6.64 mmol) was added and the mixture was stirred for 1.5 h. The mixture was poured into ice–water and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (eluent:

EtOAc–petroleum spirit 1:6) to obtain compound **4g** as a colorless solid (1.28 g, 50%); mp 53–56 °C; $[\alpha]_D$ +8.4 (*c* 1, $CHCl_3$).

The synthesis of insect pheromone (6*Z*,9*S*,10*R*)-9,10-epoxyhenicosadec-6-ene 9

(8*S*,9*S*)-9-Hydroxy-10-(tosyloxy)icos-6-yne 7. To a solution of hept-1-yne (300 mg, 3.6 mmol) in 5 ml of anhydrous THF was added a solution of n-BuLi (2.0 M; 1.8 ml, 3.6 mmol) in hexane at −78 °C. The resulting dark yellow solution was stirred for 30 min and then treated with boron trifluoride–diethyl ether (0.45 ml, 511 mg, 3.6 mmol) with syringe. After stirring of the mixture for another 30 min, a solution of **4g** (500 mg, 1.3 mmol) in anhydrous THF (5 ml) was added and the mixture was stirred for 2 h at −78 °C. The reaction mixture was quenched by adding water, washed with aq. NH_4Cl and extracted with diethyl ether. The organic layer was washed successively with water and brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography to afford **7** (425 mg, 70%) as a colorless liquid, $[\alpha]_D$ +6.4 (*c* 1, $CHCl_3$) IR(neat) *ν* 3400, 2210 cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 0.89 (3H, t, *J* 6.0, CH_3), 0.91 (3H, t, *J* 6.0, CH_3), 1.10–1.70 (26H, m, CH_2), 2.10–2.25 (2H, m, CH_2), 2.27 (1H, br s, OH), 2.30–2.40 (2H, m, CH_2), 2.45 (3H, s, CH_3), 3.80 (1H, m, CH), 4.60–4.70 (1H, m, CH), 7.30 (2H, d, *J* 7.5, ArH), 7.80 (2H, d, *J* 7.5, ArH); MS (EI) *m*/*z* 479 (MH^+) [Calc. for $C_{28}H_{46}O_4S$ (478.7284): C, 70.25; H, 9.69. Found: C, 70.56; H, 9.77%].

(9*S*,10*R*)-9,10-Epoxyhenicosadec-6-yne 8. To a solution of **7** (580 mg, 1 mmol) in anhydrous methanol (20 ml) was added, in small portions, anhydrous potassium carbonate (5 mol equiv.) at room temperature. After 30 min, the solvent was removed under reduced pressure and the mixture was directly purified by flash chromatography (eluent: ethyl acetate–petroleum spirit 10:90) to give the pure compound **8** (180 mg, 60%), $[\alpha]_D$ +26.2 (*c* 1.2, CH_2Cl_2); IR (neat) 2940, 2210 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.89 (3H, t, *J* 6.5, CH_3), 0.91 (3H, t, *J* 6.5, CH_3), 1.10–1.40 (24H, m, CH_2), 1.42–1.60 (2H, m, CH_2), 2.17 (2H, tt, *J* 7.2, 2.1, CH_2), 2.22 (1H, ddt, *J* 16.5, 7.7, 2.4, CH), 2.56 (1H, ddt, *J* 16.5, 5.4, 2.1, CH), 2.95 (1H, dt, *J* 5.7, 2.4, oxirane CH), 3.08–3.17 (1H, m, oxirane CH); MS (EI) *m*/*z* 307 (MH^+) [Calc. for $C_{21}H_{38}O$ (306.5258): C, 82.28; H, 12.50. Found: C, 82.12; H, 12.76%].

(6*Z*,9*S*,10*R*)-9,10-Epoxyhenicosadec-6-ene 9. To a solution of **8** (300 mg, 1 mmol) in methanol (20 ml) was added Lindlar catalyst (10 mg). The reaction mixture was stirred under a hydrogen atmosphere for 1 h. After filtration off of the catalyst and concentration under reduced pressure, the residue was purified by flash chromatography (eluent: ethyl acetate–hexane 10:90) to give the pure insect pheromone **9** (241 mg, 80%), $[\alpha]_D$ +8.7 (*c* 0.97, $CHCl_3$); IR (neat) *ν* 2910, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 0.91 (6H, t, *J* 6.0, CH_3), 1.10–1.60 (26H, m, CH_2), 1.90–2.50 (4H, m, CH_2), 2.80–3.10 (2H, m), 5.40–5.70 (2H, m, HC=CH); MS (EI) *m*/*z* 309 (MH^+) [Calc. for $C_{21}H_{40}O$ (308.5417): C, 81.75; H, 13.07. Found: C, 81.80; H, 13.12%].

Acknowledgements

We thank the National Natural Sciences Foundation of China for financial support.

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Paper a907396e