Highly Stereoselective Syntheses of the Sex Pheromone Components of the Southern Green Stink Bug *Nezara viridula* (L.) and the Green Stink Bug *Acrosternum hilare* (Say)

Xin Chen, Levi Gottlieb, Jocelyn G. Millar

Department of Entomology, University of California Riverside CA 92521, USA
E-mail: jocelyn.millar@ucr.edu

Received 29 June 1999; revised 24 September 1999

Abstract: Diastereoisomeric (*Z*)-(1*R*,2*S*,4*S*)- and (*Z*)-(1*S*,2*R*,4*S*)-epoxybisabolenes (**1** and **2**), sex pheromone components of the stink bugs *Nezara viridula* and *Acrosternum hilare* were synthesized stereoselectively in three steps from commercially available (–)-limonene oxide **3**. Two other stereoisomers, (*E*)-(1*R*,2*S*,4*S*)- and (*E*)-(1*S*,2*R*,4*S*)-epoxybisabolenes (**7** and **9**) were obtained in two steps from the same starting material. The other four stereoisomers are also accessible by simply substituting (+)-limonene oxide for **3**, providing short, stereoselective routes to all eight possible stereoisomers.

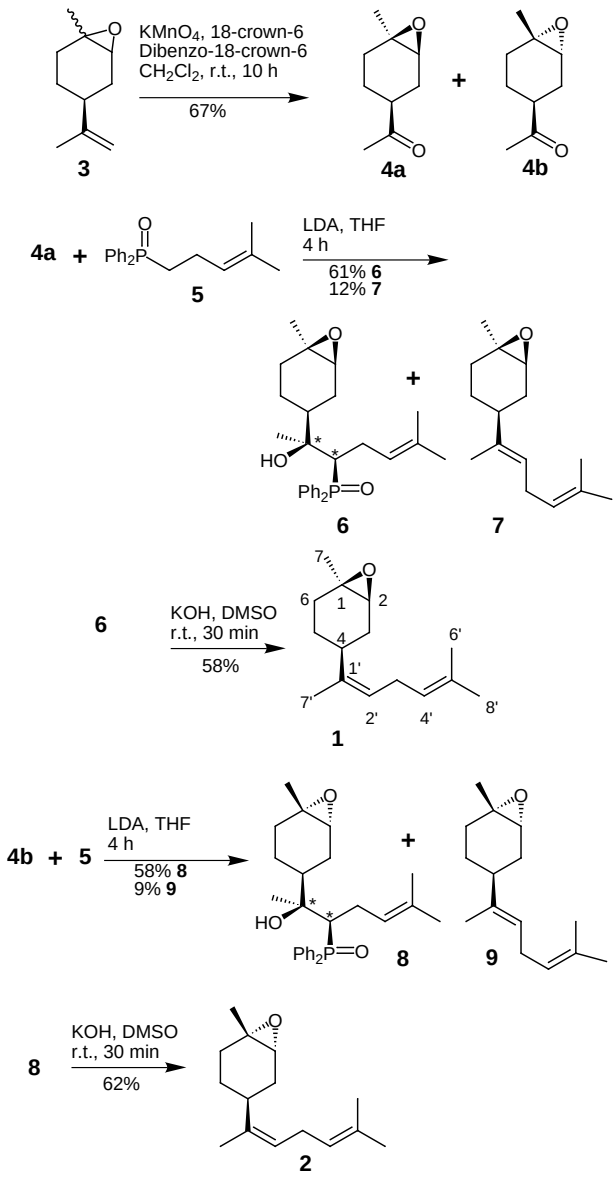
Key words: stink bug, pheromone, Horner–Wittig reaction

The southern green stink bug *Nezara viridula* (L.), a notorious agricultural pest with a worldwide distribution, attacks a wide range of vegetable, fruit and cereal crops.[1] The polyphagous nature and mobility of the bug have made its control extremely difficult. The closely related green stink bug *Acrosternum hilare* is found frequently with *N. viridula* as part of a complex of stink bugs infesting soybeans and other legumes, cotton, and alfalfa.[1] Sex attractant pheromones released by males of both species attract conspecific females. The pheromone blend produced by *A. hilare* consists mainly of *cis*-(*Z*)-(1*R*,2*S*,4*S*)-epoxybisabolene **1** mixed with lesser amounts of the corresponding *trans*-isomer **2**[2] whereas the attractant blend of *N. viridula* is composed of the opposite ratio, with **2** as the major and **1** as the minor component.[2-4] In view of the importance of these insects as agricultural pests, and the important role that the pheromones could play in the development of attractant-based methods of monitoring and controlling these bugs, **1** and **2** have attracted the interest of synthetic chemists, and at least six syntheses have been described.[3-8] However, all the reported syntheses have major drawbacks, varying from the production of the epoxybisabolenes as mixtures of several or all possible stereoisomers,[4,6] to the production of small quantities of compounds from lengthy syntheses requiring highly toxic and/or expensive reagents.[3,5,7,8] The resulting lack of significant quantities of stereochemically pure compounds has delayed the determination of the optimal pheromone blend for each species, and field testing of the blends to assess their potential for development into pest management tools. Our objective was to develop straightforward preparative scale methods for synthesizing the target compounds in high chemical and isomeric purity, to provide sufficient quantities of pure materials for laboratory bioassays and field tests. We report here the convenient syntheses of **1** and **2** in three steps from commercially available (–)-limonene oxide **3**.

The biggest challenge in constructing both **1** and **2** proved to be controlling the stereochemistry of the trisubstituted double bond. Marron and Nicolaou[5] used stereospecific cuprate addition to an alkynoate to establish the required *Z*-stereochemistry, but the overall synthetic route required 8 steps. In our hands, a much shorter alternate route was developed that took advantage of the stability of the intermediates formed from the Horner–Wittig reaction of a ketone with a carbanion stabilized by an attached diphenylphosphine oxide group.[9] In particular, a mixture of *erythro*- and *threo*-diastereomers results, the *erythro*-isomers of which are stable enough to be isolated, whereas under the reaction conditions, the *threo* intermediates collapse to produce the trisubstituted (*E*)-alkene. Furthermore, the ratio of *erythro*:*threo* intermediates can be manipulated; at lower reaction temperatures, the reaction gives a preponderance of the desired *erythro*-diastereomer,[10] which upon treatment with base, undergoes a stereospecific *syn* elimination of diphenylphosphinic acid, producing the desired (*Z*)-alkene.

Our synthesis began with (–)-limonene oxide **3**, commercially available as a 42:58 mixture of α- and β-epoxides. Phase transfer catalyzed oxidation of **3** with $KMnO_4$ gave the epoxy ketones **4a** and **4b**. Optimization of the catalyst proved to be critical for this oxidative cleavage. The catalysts triethylbenzylammonium chloride,[11] 18-crown-6, or dibenzo-18-crown-6,[7] when used alone, resulted in incomplete conversion. However, when a mixture of 18-crown-6 and dibenzo-18-crown-6 was used, the oxidation went to completion, giving **4a** and **4b** (58:42) in an overall yield of 67%. Compounds **4a** and **4b**[12] were separated by chromatography, and each isomer was processed separately through the rest of the sequences (Scheme).

Horner–Wittig reaction between the lithium salt of (4-methyl-3-pentenyl)diphenylphosphine oxide (**5**)[7] and β-epoxy ketone **4a** in THF at –78 °C afforded the desired *erythro*-adduct **6** as the major product,[10] together with (*E*)-(1*R*,2*S*,4*S*)-epoxybisabolene **7** as a minor product. However, the choice of base was critical: with *n*-butyllithium,[7] the yield of **6** was poor, and most of the unreacted ketone **4a** was racemized at C-4. An improvement in yield (61%) was achieved by substituting LDA for *n*-BuLi, with no epimerization of the small amounts of unreacted ketone



Scheme

4a. The crystalline adduct **6** was obtained as a pair of *erythro*-diastereoisomers (ratio 3:1), which apparently separated into pure crystals of each stereoisomer during crystallization, as evidenced by two observed melting ranges (172–174 °C and 181–183 °C). Preliminary attempts to separate the two stereoisomers by fractional crystallization or flash chromatography on silica were not successful, and were not pursued because the two new chiral centers would be lost anyway during the next elimination step. The proton NMR spectra of the two diastereoisomers showed distinctly different signals for the proton at C-2 (doublets at 3.00 and 2.90 ppm, respectively).

The base-induced elimination of diphenylphosphinic acid[10,13] from **6** was highly stereoselective. However, the reaction was very sensitive to the conditions used, with unwanted isomers and other non-volatile degradation products being formed readily. Employing the previously reported standard conditions (NaH in DMF),[7,13] considerable amounts of retro-addition products **5** and epimerized **4a** resulted. After lengthy experimentation with different bases (KOBu^t, KN(TMS)$_2$, KOH, NaOH, BuLi, NaH), solvents (THF, DMSO, DMF) and temperatures (75 °C, 50 °C and 25 °C), the optimal conditions for the elimination were determined to be the rapid addition of powdered KOH to a DMSO solution of **6** at room temperature, and quenching the reaction by adding ice-cold water as soon as all the starting materials had been consumed (approximately 30 minutes). Under these conditions, pure *cis*-(*Z*)-epoxybisabolene **1** was obtained in 58% yield, free of the undesired *cis*-(*E*)-isomer or other diastereoisomers. Furthermore, this result confirmed the stereochemistry of *erythro*-**6**.

The spectral data of **1** were identical with those reported in the literature.[3,8] The NMR spectra of (*Z*)-**1** and (*E*)-**7** display features allowing unambiguous differentiation between them. In the ^{1}H spectra, a multiplet from the proton at C-4 in (*Z*)-**1** appears at 2.40 ppm, whereas in (*E*)-**7**, the corresponding proton is observed at 1.92 ppm. In the ^{13}C NMR spectra, the diagnostic signals are those from C-4 and C-7′. The C-4 signal is significantly more shielded in **1** (34.60 ppm for **1**, 42.50 ppm for **7**), and the C-7′ signal is deshielded by about 4 ppm in **1** (17.76 ppm for **1**, 13.59 ppm for **7**). These results agree well with those previously reported.[3]

In an analogous manner, *trans*-(*Z*)-epoxybisabolene **2** and its *E*-isomer **9** were prepared from α-epoxy ketone **4b** (Scheme). The NMR spectra of **2** and **9** were in good agreement with literature data.[3,7]

In conclusion, short, simple, and highly stereoselective syntheses of *cis*-(*Z*)-epoxybisabolene **1** and the *trans*-(*Z*)-isomer **2** have been developed. The corresponding *cis*-(*E*)- and *trans*-(*E*)-epoxybisabolenes **7** and **9** have also been synthesized in two steps from the same starting material. Furthermore, the routes developed for **1**, **2**, **7** and **9** can be applied equally well to the syntheses of the other four stereoisomers by substitution of (–)-limonene oxide **3** with commercially available (+)-limonene oxide.

Mps are uncorrected. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a General Electric QE-300 instrument, using $CDCl_3$ as solvent. EIMS (70 eV) were recorded with a Hewlett–Packard (HP, Palo Alto CA) 5970 mass selective detector interfaced to a HP 5890 GC fitted with a DB-5 column (20m × 0.25mm i.d.; J&W Scientific, Folsom CA). High resolution exact mass measurements were made with a VG 7070E double focusing magnetic sector instrument (EI, 50 eV), using a direct insertion probe. Routine GC analyses were carried out on an HP 5890 GC fitted with a DB-5 column (20m × 0.32mm i.d.). THF was purified by distillation from sodium/benzophenone ketyl under Ar. Solvents (hexane and EtOAc) for flash chromatography were distilled prior to use. All other solvents and reagents were used as received. Flash chromatography was conducted on 32–63μ silica gel (Scientific Adsorbents Inc., Atlanta GA). Moisture-sensitive reactions were carried out in oven-dried glassware under Ar atm. Unless otherwise stated, extracts were dried over anhyd Na_2SO_4, and concentrated by rotary

evaporation under reduced pressure. (4-Methyl-3-pentenyl) diphenylphosphine oxide (**5**) was prepared as previously described.[7]

(1*R*,2*S*,4*S*)-4-Acetyl-1,2-epoxy-1-methylcyclohexane (4a) and (1*S*,2*R*,4*S*)-4-Acetyl-1,2-epoxy-1-methylcyclohexane (4b)

To a stirred suspension of (–)-limonene oxide **3** (20.4 g, 132 mmol; Aldrich) and $KMnO_4$ (88 g, 556 mmol) in anhyd CH_2Cl_2 (900 mL) was added 18-crown-6 (2.4 g, 9.1 mmol, 0.07 equiv) and dibenzo-18-crown-6 (2.9 g, 8.0 mmol, 0.06 equiv) at r.t. Stirring was continued for 10h, then the resulting gray-brown suspension was filtered through a pad of Celite, rinsing the solids with CH_2Cl_2 (200 mL) and EtOAc (150 mL). The combined filtrate was concentrated, and the residue was purified in batches by flash chromatography (4–15% EtOAc in hexane) to afford **4b** (5.9 g, 29% yield) followed by **4a** (7.7 g, 38% yield) as colorless oils.

4a: R_f = 0.14 (silica gel, 15% EtOAc in hexanes).

^{1}H NMR: δ = 1.32 (s, 3H), 1.40–1.78 (m, 3H), 2.03–2.10 (m, 3H), 2.13 (s, 3H), 2.18–2.32 (m, 1H), 3.01 (d, 1H, *J* = 4.2 Hz).

^{13}C NMR: δ = 21.62, 22.88, 25.87, 27.76, 29.53, 46.12, 57.31, 58.04, 210.20.

MS: *m/z* = 154 (M^+, 1), 136 (1), 121 (2), 111 (8), 96 (12), 83 (13), 71 (8), 55 (9), 43 (100).

4b: R_f = 0.20.

^{1}H NMR: δ = 1.30 (s, 3H), 1.35–1.45 (m, 1H), 1.71–2.15 (m, 5H), 2.14 (s, 3H), 2.59 (m, 1H), 3.08 (br s, 1H).

^{13}C NMR: δ = 22.80, 23.88, 26.62, 27.77, 28.17, 43.30, 57.25, 59.51, 211.15.

MS: *m/z* = 154 (M^+,1), 136 (1), 121 (1), 111(4), 96 (9), 83 (6), 71 (3), 55 (7), 43 (100).

^{1}H and ^{13}C spectra of **4a** and **4b** matched those previously reported.[12]

***erythro*-(1*R*,2*S*,4*S*)-4-(1′,5′-Dimethyl-2′-diphenylphosphinoyl-1′-hydroxyhex-4′-enyl)-1,2-epoxy-1-methylcyclohexane (6) and *(E)*-(1*R*,2*S*,4*S*)-4-(1′,5′-Dimethylhexa-1′,4′-dienyl)-1,2-epoxy-1-methylcyclohexane (7)**

LDA (80 mL, 1.5M in hexanes; 120 mmol) was added dropwise to a stirred soln of (4-methyl-3-pentenyl) diphenylphosphine oxide (**5**)[7] (25.5g, 90 mmol) in anhyd THF (450 mL) at 0 °C. The resulting dark brown mixture was stirred at 0 °C for 30 min, then cooled to –78 °C, and a solution of **4a** (9.3 g, 60 mmol) in dry THF (50 mL) was added dropwise over 1h, maintaining the reaction temperature below –73 °C. After the addition was complete, the mixture was stirred at –78 °C for 1h, then warmed gradually to r.t., and maintained at the same temperature for an additional 2h. The reaction was quenched by addition of sat. NH_4Cl (200 mL), and the resulting mixture was extracted with EtOAc (500 mL). The EtOAc extract was dried, concentrated and purified by flash chromatography (30% EtOAc in hexanes), yielding (*E*)-epoxybisabolene **7** (1.58 g, 12%) as a colorless liquid, followed by unreacted **4a** (1.7 g). Further elution with 50% EtOAc in hexanes afforded **6** (16.1 g, 61% yield) as a white solid. GC analysis indicated two diastereoisomeric products in a ratio of 3:1. The solid was recrystallized from 20% EtOAc in hexane (200 mL) at –20 °C, yielding a white crystalline product (14.2 g) with two distinct melting ranges (172–174 °C and 181–183 °C).

***erythro* Adduct 6 (the major isomer)**

^{1}H NMR: δ = 0.96 (s, 3H, 7′-Me), 1.16 (s, 3H, 7-Me), 1.55 (br s, 3H, 6′-Me), 1.71 (br s, 3H, 8′-Me), 1.70–2.72 (m, 10H, ring protons, 2′,3′-H), 3.00 (d, 1H, *J* = 5.4 Hz, 2-H), 4.69 (br s, 1H, OH), 4.87 (m, 1H, 4′-H), 7.37–7.51 (m, 6H, Ar-H), 7.68–7.88 (m, 4H, Ar-H).

^{13}C NMR: δ = 17.58, 17.94, 21.21, 23.04, 23.84, 24.12, 25.76, 25.81 (J_{PC} = 8.5 Hz), 30.56, 39.34 (J_{PC} = 9.6 Hz), 43.35 (J_{PC} = 66.7 Hz), 57.46, 59.70, 119.86, 124.33 (J_{PC} = 8.0 Hz), 128.42 (J_{PC} = 11.5 Hz), 128.81 (J_{PC} = 11.0 Hz), 129.72 (J_{PC} = 8.6 Hz), 130.70, 132.27, 135.82 (J_{PC} = 90.8 Hz).

HRMS: *m/z* calc for $C_{27}H_{36}O_3P$ ($M+1^+$, from self-protonation on probe) 439.2402. Found: 439.2388.

***cis*-(*E*)-Epoxybisabolene 7**

^{1}H NMR: δ = 1.32 (s, 3H, 7-Me), 1.41 (m, 1H, ring proton), 1.56 (s, 3H, 6′-Me), 1.62 (s, 3H, 7′-Me), 1.69 (d, 3H, *J* = 0.8 Hz, 8′-Me), 1.64–1.85 (m, 4H, ring protons), 1.92 (m, 1H, 4-H), 2.05 (m, 1H, ring proton), 2.66 (t, 2H, *J* = 7.2 Hz, 3′-H), 2.98 (d, 1H, *J* = 5.2 Hz, 2-H), 5.07–5.12 (m, 2H, 2′, 4′-H).

^{13}C NMR: δ = 13.59(C-7′), 17.71 (C-6′), 23.15 (C-5), 24.34 (C-7), 25.69 (C-8′), 26.87 (C-6), 29.79 (C-3′), 30.84 (C-3), 42.50 (C-4), 57.51 (C-1), 59.46 (C-2), 122.50 (C-4′), 123.22 (C-2′), 131.43 (C-5′), 138.31 (C-1′).

MS: *m/z* = 220 (M^+, 2), 205 (1), 187 (3), 176 (3), 151 (5), 133 (8), 125 (9), 109 (45), 93 (64), 81 (40), 67 (61), 55 (40), 43 (100).

HRMS: *m/z* calc for $C_{15}H_{24}O$ (M^+) 220.1827. Found: 220.1833.

(*Z*)-(1*R*,2*S*,4*S*)-4-(1',5'-Dimethylhexa-1',4'-dienyl)-1,2-epoxy-1-methylcyclohexane (1)

To a stirred solution of **6** (10.6 g, 24.2 mmol) in anhyd DMSO (120 mL) was added powdered KOH (1.8 g, 88% purity, 28.8 mmol) in one portion at r.t., and the reaction solution was stirred at r.t. for 30 min. The reaction was quenched by adding ice-cold H_2O (150 mL), and the resulting mixture was diluted with brine (150 mL) and extracted with Et_2O (500 mL). The ethereal solution was washed with H_2O (2 × 80 mL) and brine (100 mL), dried, and concentrated. The crude products were purified by flash chromatography (5% Et_2O in hexane) to give **1** (3.1 g, 58% yield) as a colorless liquid.

^{1}H NMR: δ = 1.12–1.20 (m, 1H, ring proton), 1.33 (s, 3H, 7-Me), 1.49 (qd, 1H, *J* = 12.8, 4.2 Hz, ring proton), 1.56 (br s, 3H, 6′-Me), 1.63 (br s, 3H, 7′-Me), 1.69 (br s, 3H, 8′-Me), 1.65–1.82 (m, 3H, ring protons), 2.02 (m, 1H, ring proton), 2.40 (m, 1H, 4-H), 2.67 (t, 2H, *J* = 7.0 Hz, 3′-H), 2.98 (d, 1H, *J* = 3.8 Hz, 2-H), 5.03–5.11 (m, 2H, 2′, 4′-H).

^{13}C NMR: δ = 17.76 (C-7′), 19.10 (C-6′), 23.26 (C-7), 23.89 (C-8′), 25.75 (C-3′), 26.41 (C-5), 28.50 (C-3), 30.80 (C-6), 34.60 (C-4), 57.43 (C-1), 59.43 (C-2), 123.43 (C-4′), 123.91 (C-2′), 131.44 (C-5′), 138.10 (C-1′).

MS: *m/z* = 220 (M^+, 8), 205 (3), 202 (6), 187 (12), 176 (11), 151 (13), 133 (24), 121 (21), 109 (62), 93 (69), 81 (41), 67 (54), 55 (47), 43 (100).

HRMS: *m/z* calc for $C_{15}H_{24}O$ (M^+) 220.1827. Found: 220.1830.

***erythro*-(1*S*,2*R*,4*S*)-4-(1′,5′-Dimethyl-2′-diphenylphosphinoyl-1′-hydroxyhex-4′-enyl)-1,2-epoxy-1-methylcyclohexane (8) and *(E)*-(1*S*,2*R*,4*S*)-4-(1′,5′-dimethylhexa-1′,4′-dienyl)-1,2-epoxy-1-methylcyclohexane (9)**

Employing the same procedure used for **6**, Horner–Wittig reaction of α-epoxy ketone **4b** (4.9 g, 32 mmol) with **5** (13.6 g, 48 mmol) gave **8** (8.2 g, 58%) as a solid and **9** (0.68 g, 9%) as a colorless liquid. Compound **8** was recrystallized from 30% EtOAc in hexane (100 mL) at –20 °C to afford white crystals (7.2 g), mp 157–159 °C.

***erythro* Adduct 8 (the major isomer)**

^{1}H NMR: δ = 0.99 (s, 3H, 7′-Me), 1.19 (s, 3H, 7-Me), 1.23 (br s, 3H, 6′-Me), 1.54 (br s, 3H, 8′-Me), 1.77–2.75 (m, 10H, ring protons, 2′, 3′-H), 2.98 (br s, 1H, 2-H), 4.70 (br s, 1H, 4′-H), 4.81 (br s, 1H, OH), 7.37–7.53 (m, 6H, Ar-H), 7.68–7.92 (m, 4H, Ar-H).

^{13}C NMR: δ = 17.60, 21.70, 23.23, 23.72, 24.42, 25.32, 25.82 (J_{PC} = 8.1 Hz), 27.85, 29.07, 35.10 (J_{PC} = 10.5 Hz), 43.68 (J_{PC} = 66.9 Hz), 56.87, 60.54, 124.16 (J_{PC} = 7.7 Hz), 128.22, 128.42

(J_{PC} = 11.1 Hz), 128.83 (J_{PC} = 11.5 Hz), 129.88 (J_{PC} = 8.4 Hz), 131.33, 132.68, 136.10 (J_{PC} = 90.6 Hz).

HRMS: *m/z* calc for $C_{27}H_{35}O_3P$ (M^+) 438.2324. Found: 438.2314.

***trans*-(*E*)-Epoxybisabolene 9**

^{1}H NMR: δ = 1.30 (s, 3H, 7-Me), 1.43–1.53 (m, 1H, ring proton), 1.58 (br s, 3H, 6′-Me), 1.63 (br s, 3H, 7′-Me), 1.70 (d, 3H, *J* = 0.8 Hz, 8′-Me), 1.75–1.92 (m, 4H, ring protons), 2.02–2.15 (m, 2H, ring protons), 2.68 (t, 2H, *J* = 7.0 Hz, 3′-H), 3.04 (br s, 1H, 2-H), 5.05–5.14 (m, 2H, 2′, 4′-H).

^{13}C NMR: δ = 14.54 (C-7′), 17.71 (C-6′), 24.32 (C-5), 25.67 (C-7), 26.05 (C-8′), 26.94 (C-6), 28.76 (C-3′), 30.71 (C-3), 37.67 (C-4), 57.32 (C-1), 60.73 (C-2), 122.35 (C-4′), 123.27 (C-2′), 131.39 (C-5′), 137.91 (C-1′).

MS: *m/z* = 220 (M^+, 1), 205 (1), 191 (3), 177 (4), 159 (10), 151 (5), 121 (15), 109 (52), 93 (50), 82 (60), 55 (35), 43 (100).

HRMS: *m/z* calc for $C_{15}H_{24}O$ (M^+) 220.1827. Found: 220.1826.

(*Z*)-(1*S*,2*R*,4*S*)-4-(1',5'-Dimethylhexa-1',4'-dienyl)-1,2-epoxy-1-methylcyclohexane (2)

Under the same reaction conditions used for **1**, the base-induced elimination of **8** (6.4 g, 14.6 mmol) gave **2** (2.0 g, 62% yield) as a colorless liquid.

^{1}H NMR: δ = 1.24–1.32 (m, 2H, ring protons), 1.31 (s, 3H, 7-Me), 1.58 (d, 3H, *J* = 1.0 Hz, 6′-Me), 1.62 (br s, 3H, 7′-Me), 1.67 (d, 3H, *J* = 0.8 Hz, 8′-Me), 1.72–1.94 (m, 4H, ring protons), 2.68 (m, 3H, 3′,4-H), 3.04 (br s, 1H, 2-H), 5.03–5.14 (m, 2H, 2′,4′-H).

^{13}C NMR: δ = 17.69 (C-7′), 19.20 (C-6′), 24.56 (C-7), 25.69 (C-8′), 26.19 (C-3′), 26.37 (C-5), 29.21 (C-3), 29.90 (C-6), 30.09 (C-4), 57.06 (C-1), 60.81 (C-2), 123.27 (C-4′), 124.48 (C-2′), 131.33 (C-5′), 137.64 (C-1′).

MS: *m/z* = 220 (M^+, 1), 205 (1), 191 (1), 177 (2), 164 (10), 159 (10), 149 (6), 131 (15), 121 (13), 109 (54), 93 (68), 82 (45), 67 (50), 55 (44), 43 (100).

HRMS: *m/z* calc for $C_{15}H_{24}O$ (M^+) 220.1827. Found: 220.1838.

Acknowledgement

We thank the University of California Integrated Pest Management Program and the California Pistachio Commission for financial support of this work, and the UC Riverside Analytical Chemistry Instrumentation Facility for the high resolution mass spectra.

References

(1) (a) Todd, J. W. *Ann. Rev. Entomology* **1989**, 34, 273.
(b) Panizzi, A. R. *Ann. Rev. Entomology* **1997**, 42, 99.
(c) Metcalf, R. L.; Metcalf, R. A. *Destructive and Useful Insects*, 5th ed. McGraw-Hill: New York, 1993.
(2) (a) Aldrich, J. R.; Lusby, W. R.; Marron, B. E.; Nicolau, K. C.; Hoffmann, M. P.; Wilson, L. T. *Naturwissenschaften* **1989**, *76*, 173.
(b) Millar, J. G.; McBrien, H. Unpublished data.
(3) Baker, R.; Borges, M.; Cooke, N. G.; Herbert, R. H., *J. Chem. Soc., Chem. Commun*. **1987**, 414.
(4) Brézot, P.; Malosse, C.; Mori, K.; Renou, M. *J. Chem. Ecol*. **1994**, *20*, 3133.
(5) Marron, B. E.; Nicolaou, K. C. *Synthesis* **1989**, 537.
(6) Tomioka, H.; Mori, K. *Biosci. Biotech. Biochem*. **1992**, *56*, 1001.
(7) Baptistella, L. H. B.; Aleixo, A. M. *Liebigs Ann. Chem*. **1994**, 785.
(8) (a) Kuwahara, S.; Itoh, D.; Leal, W. S.; Kodama, O. *Tetrahedron Lett*. **1998**, *39*, 1183.
(b) Kuwahara, S.; Itoh, D.; Leal, W. S.; Kodama, O. *Tetrahedron* **1998**, *54*, 11421-11430.
(9) Buss, A. D.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 3931.
(10) Buss, A. D.; Warren, S. *J. Chem. Soc., Perkin Trans. I* **1985**, 2307.
(11) Ogino, T.; Mochizuki, K. *Chem. Lett.* **1979**, 443.
(12) Delay, F.; Ohloff, G. *Helv. Chim. Acta* **1979**, *62*, 2168.
(13) Buss, A. D.; Greeves, N.; Mason, R.; Warren, S. *J. Chem. Soc., Perkin Trans. I* **1987**, 2569.

Article Identifier:
1437-210X,E;2000,0,02,0269,0272,ftx,en;M01699SS.pdf