Tetrahedron 72 (2016) 6578–6588

Contents lists available at ScienceDirect

Tetrahedron

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

Pheromone synthesis. Part 260: Synthesis of (±)-(*anti*-1,2-dimethyl-3-methylenecyclopentyl)acetaldehyde, the racemate of the female-produced sex pheromone of the pineapple mealybug (*Dysmicoccus brevipes*), and its *syn*-isomer☆

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ARTICLE INFO

Article history:
Received 19 July 2016
Received in revised form 23 August 2016
Accepted 24 August 2016
Available online 25 August 2016

Keywords:
Dysmicoccus brevipes
Ireland–Claisen rearrangement
Monoterpene aldehyde
Pheromone
Ring-closing metathesis

ABSTRACT

(±)-(*anti*-1,2-Dimethyl-3-methylenecyclopentyl)acetaldehyde, the racemate of the female-produced sex pheromone of the pineapple mealybug, was synthesized in four different ways. Ireland–Claisen rearrangement or conjugate addition was employed for the construction of the quaternary carbon center, while ring-closing olefin metathesis or cationic cyclization was used for the construction of the five-membered carbocycle.

1. Introduction

Recent studies by Millar and co-workers culminated in the identifications of three monoterpenes **A**, **B** and **C** (Fig. 1) with a five-membered carbocycle as the sex pheromones of the mealybugs.[2] In 2005, **A** was identified as the pheromone of the obscure mealybug (*Pseudococcus viburni*).[3] Then in 2007, the pheromone of the grape mealybug (*Pseudococcus maritimus*) was shown to be **B**.[4] Finally in 2009, **C** was proved to be the pheromone of the longtailed mealybug (*Pseudococcus longispinus*).[5] Their unique structures including stereochemistry were all confirmed by syntheses.[2]

In Japan, Tabata et al. are working on the identification of the female produced sex pheromone of the pineapple mealybug [*Dysmicoccus brevipes* (Cockerell), Homoptera: Pseudococcidae], which is a pest infesting pineapples in Okinawa.[6] Dr. Tabata asked me to synthesize samples with the proposed structure **1** of the pheromone (Tabata, J. personal communication). My synthesis provided both (±)-*anti*- and *syn*-**1**. Their NMR and GC–MS comparisons with the natural pheromone as well as their bioassay established the structure of the pheromone as *anti*-**1**, although its absolute configuration still remains unknown.[7]

This paper describes in detail the synthesis of (±)-*anti*- and *syn*-**1** as achieved by several different approaches.

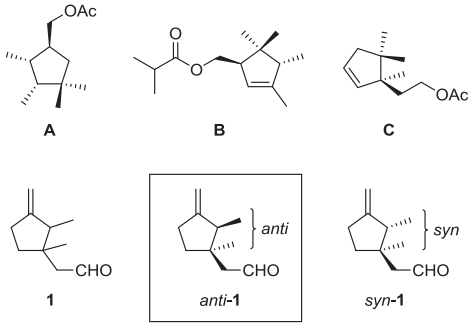

Fig. 1. Structures of the mealybug pheromones. **A**: the obscure mealybug (*Pseudococcus viburni*); **B**: the grape mealybug (*Pseudococcus maritimus*); **C**: the longtailed mealybug (*Pseudococcus longispinus*); **1**: the pineapple mealybug (*Dysmicoccus brevipes*). The structures depicted for *anti*- and *syn*-**1** show relative configuration.

☆ For Part 259, see Ref. 1. This work was orally reported by K.M. as a part of his lecture at International Chemical Ecology Conference 2016 (July 5, 2016) in Iguassu Falls, Brazil.

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http://dx.doi.org/10.1016/j.tet.2016.08.072
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2. Results and discussion

2.1. Retrosynthetic analyses of 1

Fig. 2 shows the retrosynthetic analyses of **1**, all of which could be realized later to give (±)-**1**. The most direct route to **1** is route (a), making the ring first and then generating the quaternary carbon center. Conjugate addition of allylsilane[8] is employed as the key step for conversion of the known **E** to **1** via **D**. This route was examined first, and gave both (±)-*anti*- and *syn*-**1** used for the identification of the natural pheromone.[7]

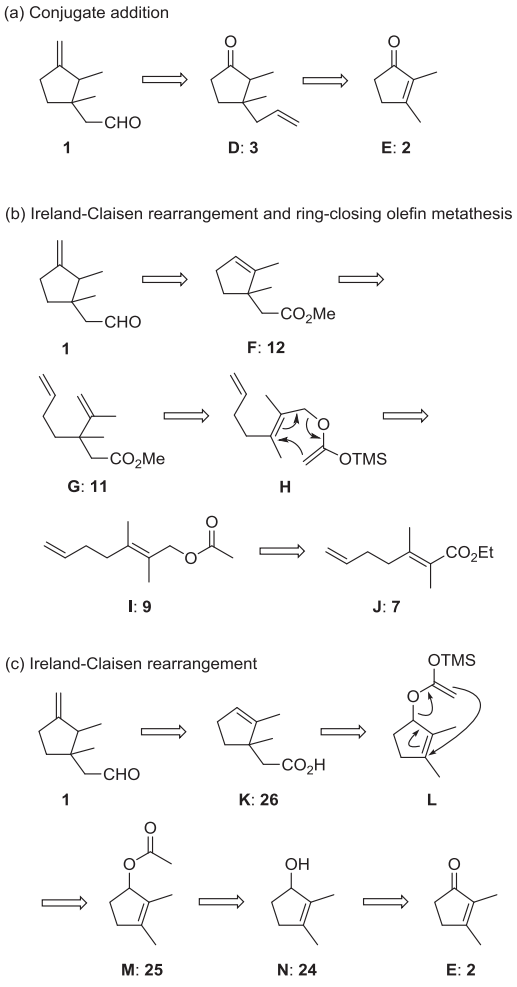


Fig. 2. Retrosynthetic analyses of **1**.

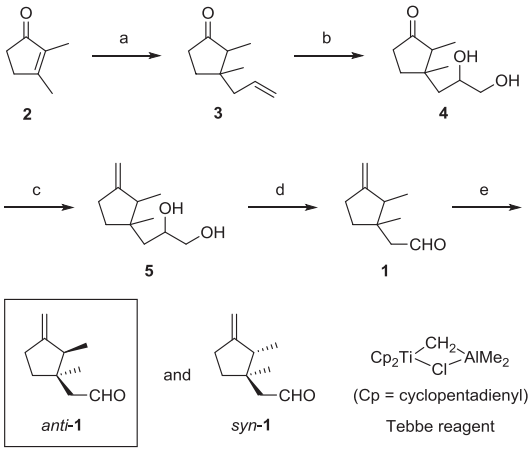
Practical difficulties encountered in the course of the realization of route (a) forced me to adopt route (b) as the more reliable one. Ireland's ester-enolate Claisen rearrangement[9] and Grubbs's ring-closing olefin metathesis[10,11] serve as the two key reactions. The five-membered ring is to be closed by olefin metathesis (**G**→**F**), and the quaternary carbon center is to be constructed by Ireland–Claisen rearrangement (**I**→**H**→**G**). Ester **J** will give **I** in two steps.

In future it will be necessary to prepare both the enantiomers of *anti*-**1** so as to determine the absolute configuration of the natural pheromone. Route (c) can be used for that purpose, because the resolution of **N** may be feasible to give the enantiomers of **N**. The Ireland–Claisen rearrangement of acetate **M** via **L** gives **K**, which is structurally equivalent to **F** in route (b). Accordingly, **K** can readily be converted to **1**. It must be mentioned that the construction of the quaternary center in cyclopentanoids by means of route (c) was first reported by Jäger and co-workers in their polycyclopentanoid synthesis,[12] and then Zou and Millar in their synthesis of the pheromone **C**.[13]

The rest of the present paper details the realization of these three retrosynthetic analyses to achieve three different syntheses of **1** as well as a formal synthesis of **1** via **K**.

2.2. First synthesis of the pheromone 1

The first synthesis of **1** was accomplished as shown in Scheme 1. Synthesis of the starting material, 2,3-dimethyl-2-cyclopenten-1-one (**2**) have been reported repeatedly.[14–18] Polyphosphoric acid (PPA)-mediated cyclization of 4-methyl-4-hexenoic acid was most reliable to give over 10 g of **2**.[12,14] Methylation of the enol phosphate of 2-methyl-1,3-cyclopentanedione with Me_2CuLi was also a good method to prepare **2**.[15] Isopropylmagnesium chloride-promoted unilateral addition of MeMgBr to 2-methyl-1,3-cyclopentanedione according to Yuan et al.[19] afforded **2**, but in a low yield of 14% after distillation.



Scheme 1. First synthesis of (±)-*anti*-**1**. Reagents: (a) CH_2=$CHCH_2TMS$, $TiCl_4$, CH_2Cl_2, −78 to −30 °C; then SiO_2 chromatography (12%); (b) OsO_4, NMO, *t*-BuOH, Me_2CO,H_2O (58%); (c) Tebbe reagent, toluene, THF; (d) $NaIO_4$, THF, H_2O; then SiO_2 chromatography (18%, two steps); (e) $AgNO_3/SiO_2$ chromatography.

Conjugate addition of allyltrimethylsilane to **2** was achieved according to Hosomi and Sakurai,[8] employing $TiCl_4$ as the catalyst. The desired allylated ketone **3** (diastereomer ratio=ca. 1:1) was obtained in 12% yield after SiO_2 chromatography. Although the yield was quite unsatisfactory, **3** could be obtained repeatedly, confirming the reproducibility of the reaction. An attempt was made to increase the yield by employing $InCl_3$ as the catalyst,[20] which unfortunately did not work at all. Additional unsuccessful attempts were made to construct the quaternary carbon center by means of copper(I)-catalyzed conjugate addition to **2** of allyl Grignard reagent in the presence of conventional CuI or CuBr/Me_2S, LiCl and TMSCl.[21] Conjugate addition of dimethyl malonate to **2** in the presence of NaOMe in MeOH was not fruitful, either.

Dihydroxylation of the allylated ketone **3** with OsO_4 and *N*-methylmorpholine *N*-oxide (NMO)[22] yielded dihydroxy ketone **4**, which was treated with excess Tebbe reagent[23] to give methylenated diol **5**. Finally, cleavage of the glycol system of **5** with $NaIO_4$ afforded a crude oil (540 mg), which was purified by SiO_2 chromatography to give 132 mg of **1** (44.4% GC purity) as a stereoisomeric mixture. The overall yield of **1** was 0.6% based on **2** (four steps).

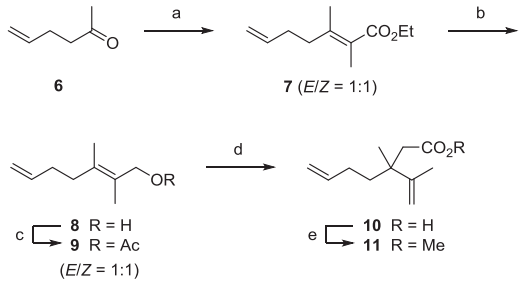
The mixture could be further purified by $AgNO_3/SiO_2$ chromatography[24] to separate (±)-*anti*-**1** from its *syn*-isomer. After the separation, the ^1H NMR spectra of the two isomers were compared, and the relative configuration of the two methyl groups was

studied by NOESY to find out NOE in the case of the later eluting isomer. Accordingly, the later eluting one must be (±)-*syn*-**1**, while the earlier eluting one was (±)-*anti*-**1**. The retention time (t_R) of (±)-*anti*-**1** was identical to that of the natural pheromone. The ^{1}H, ^{13}C NMR and MS spectra of (±)-*anti*- and (±)-*syn*-**1** were different from each other (see 4.6), and the spectra of (±)-*anti*-**1** was identical to those of the natural pheromone. The structure and the relative configuration of the natural pheromone was therefore determined as *anti*-**1**.

Field bioassay of the synthetic (±)-*anti*- and (±)-*syn*-**1** as well as their mixture was carried out by Dr. J. Tabata at National Agriculture and Food Research Organization, Japan. The racemic *anti*-**1** was bioactive as the pheromone of *D. brevipes*, while *syn*-**1** was devoid of bioactivity. Fortunately, *syn*-**1** did not inhibit the pheromone activity of (±)-*anti*-**1**.[7] Therefore, a stereoisomeric mixture **1** of the two isomers can be used sufficiently for the practical purpose of population monitoring or communication disruption.

2.3. Construction of the quaternary carbon center by means of Ireland–Claisen rearrangement

Since it was difficult to improve the miserable 10–12% yield of the conjugate allylation step (**2**→**3**, Scheme 1), efforts were made to employ Ireland–Claisen rearrangement for the construction of the quaternary carbon center (Scheme 2).

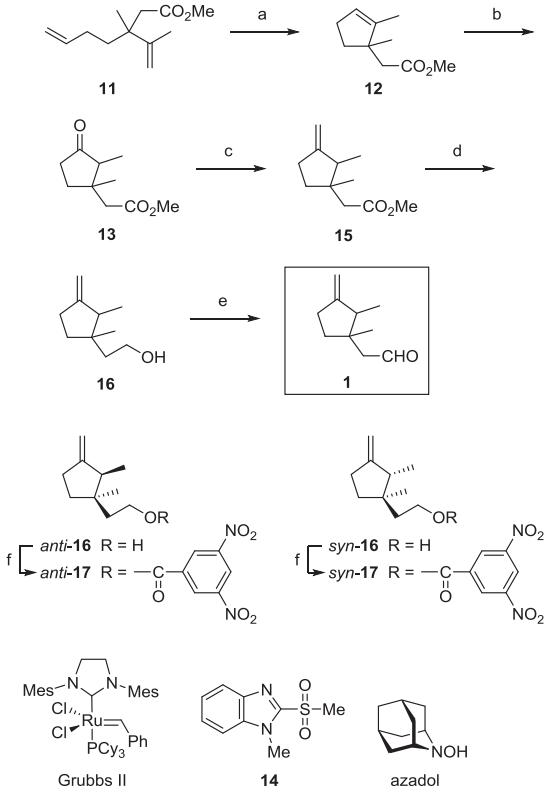


Scheme 2. Synthesis of **11**. Reagents: (a) $(EtO)_2P(O)CHMeCO_2Et$, NaH, THF (95%); (b) $LiAlH_4$, Et_2O; (c) Ac_2O, DMAP, C_5H_5N (94%, two steps); (d) $LiN(i\text{-}Pr)_2$, TMSCl, THF; heat at 70 °C, 4 h; MeOH; then dil HCl (86%); (e) K_2CO_3, MeI, DMF (66%).

The required substrate **9** for the rearrangement was synthesized from commercially available 5-hexen-2-one (**6**). Treatment of **6** with triethyl 2-phosphonopropanoate and NaH in THF furnished **7** as an *E*/*Z* mixture. The dienoic ester **7** was reduced with $LiAlH_4$ to give **8**, which was acetylated to afford **9**. The acetate **9** was treated with $LiN(i\text{-}Pr)_2$ and TMSCl to give TMS-enolate (**H** in Fig. 2), which was heated at 70 °C for 4 h to effect the rearrangement.[9] The TMS group was removed by methanolysis, and the resulting acid **10** could be isolated in 86% yield. Methylation of **10** with K_2CO_3 and MeI afforded methyl ester **11** in 66% yield. Its ^{1}H NMR spectrum was consistent with the structure **11**, exhibiting three 3H singlets at δ=1.19, 2.07 and 3.62 together with signals due to five olefinic protons. The overall yield of the acid **10** was 77% based on **6** (four steps).

2.4. Second synthesis of the pheromone 1

The next thing to do was to execute the ring-closing olefin metathesis of **11** and subsequent conversion of the product **12** to **1** (Scheme 3). Treatment of **11** with 0.3 mol % of the second generation Grubbs catalyst (Grubbs II)[10,11] in refluxing CH_2Cl_2 gave **12** with a single olefinic proton (δ=5.31) in 76% yield. Hydroboration–oxidation of the double bond of **12** with $BH_3\cdot SMe_2$ followed by Jones CrO_3 afforded **13** in 47% yield. The next step, methylenation of the CO group of **13**, was problematic, because its facile enolization rendered conventional methylenation with $Ph_3P{=}CH_2$ impractical. Accordingly, attempts were made to employ Ando's new olefination reagent [1-methyl-2-(methylsulfonyl)benzimidazole (**14**)][25] for the methylenation.



Scheme 3. Second synthesis of (±)-**1**. Reagents: (a) Grubbs II (0.3 mol %), CH_2Cl_2, reflux, 2 h (76%); (b) $BH_3\cdot SMe_2$, Et_2O; then Jones CrO_3, Me_2CO (47%); (c) **14**, NaHMDS, DMF (27%; 51% based on the consumed **13**); (d) $LiAlH_4$, Et_2O (quant.); (e) $NaOCl\cdot 5H_2O$, Bu_4NHSO_4, azadol, H_2O, CH_2Cl_2 (63% after distillation); (f) 3,5-dinitrobenzoyl chloride, DMAP, C_5H_5N; then recrystallization from EtOAc/hexane.

When sodium hexamethyldisilazide (NaHMDS) was added to a solution of **13** and **14** in DMF, the desired **15** was obtained. The yield, however, was only 27% (or 51% based on the consumed **13**) with a substantial amount of the recovered **13**, reflecting the large extent of enolization prior to the nucleophilic addition of the anion derived from **14**. When *t*-BuOK was used as the base instead of NaHMDS,[25] the product (28% yield) was not **15** but the corresponding *tert*-butyl ester generated by the nucleophilic attack of *t*-BuO^- to the ester CO group.

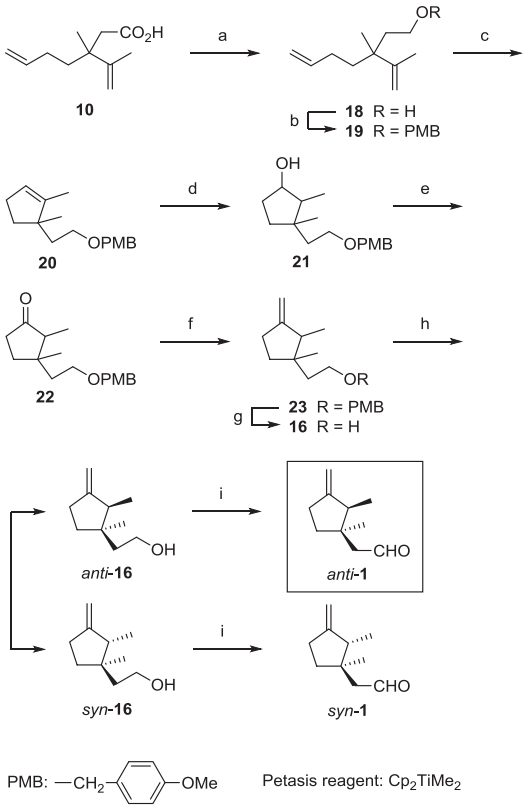
Reduction of the ester **15** with $LiAlH_4$ furnished alcohol **16**, which was oxidized with sodium hypochlorite pentahydrate[26] and azadol[27] to give a stereoisomeric mixture of **1** [*anti*/*syn*=1:1.3; 669 mg (78% GC purity)]. The overall yield of **1** was 2.4% based on **6** (10 steps). The present route enabled the preparation of **1** useful for further field bioassays.

Since the separation of (±)-*anti*-**1** from (±)-*syn*-**1** by $AgNO_3/SiO_2$ chromatography was rather tedious, separation of (±)-*anti*- and (±)-*syn*-**16** was attempted. 3,5-Dinitrobenzoate **17** of the stereoisomeric mixture **16** was first prepared. Unfortunately, its fractional crystallization failed, and neither pure (±)-*anti*-**17** nor (±)-*syn*-**17** could be secured. Chromatographic separation over SiO_2 of a stereoisomeric mixture of the alcohol **16** was more fruitful, and almost pure (±)-*anti*-**16** (*anti*/*syn*=97:3) and (±)-*syn*-**16** (*anti*/*syn*=4:96) could be obtained. Their separate derivatizations to the corresponding 3,5-dinitrobenzoates gave (±)-*anti*-**17** as leaflets, mp 55–56 °C, and (±)-*syn*-**17** as prisms, mp 58–59 °C. Their ^{13}C NMR

spectra confirmed their high purities (see 4.17.3 and 4.17.4), and their mixture melting point determination resulted in the depression of the mp (mmp 41–46 °C). It became clear that pure (±)-*anti*- and (±)-*syn*-**16** would be obtained, if we couple SiO_2 chromatography of **16** with recrystallization of the corresponding **17**. Hydrolysis of the pure 3,5-dinitrobenzoates (±)-*anti*- and *syn*-**17** would give pure (±)-*anti*- and *syn*-**16**, whose separate oxidation would furnish pure (±)-*anti*- and *syn*-**1**. However, as reported in 2.2, there is no practical need to secure pure (±)-*anti*-**1**, because (±)-*syn*-**1** does not inhibit the bioactivity of (±)-*anti*-**1**.

2.5. Third synthesis of the pheromone 1

The low yield (27%) of the methylenation step (**13**→**15**, Scheme 3) made me modify the synthetic route as shown in Scheme 4: namely, to reduce the carboxy group of **10** and protect the hydroxy group of the resulting **18** as *p*-methoxybenzyl (PMB) ether **19**.



Scheme 4. Third synthesis of (±)-**1**. Reagents: (a) $LiAlH_4$, THF (73%); (b) PMBCl, *t*-BuOK, THF, DMF (99%); (c) Grubbs II (0.44 mol %), CH_2Cl_2, reflux, 2 h (87%); (d) $BH_3{\cdot}SMe_2$, THF; then NaOH, H_2O_2 (68%); (e) Jones CrO_3, Me_2CO (93%); (f) Petasis reagent, THF, toluene, 70 °C, 25 h (85%); (g) DDQ, H_2O, CH_2Cl_2 (65%); (h) SiO_2 chromatography; (i) azadol, $PhI(OAc)_2$, CH_2Cl_2 (60% for *anti*-rich **1**; 72% for *syn*-rich **1**).

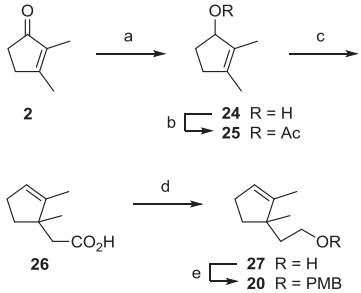
Treatment of **10** with $LiAlH_4$ in THF yielded **18**, and its PMB ether **19** was subjected to ring-closing metathesis in the presence of 0.44 mol % of Grubbs II catalyst. The ring-closure took place in a satisfactory yield of 87% to give **20**. Hydroboration of **20** with $BH_3{\cdot}SMe_2$ was followed by oxidation with H_2O_2/NaOH to give **21**. Jones CrO_3 oxidized **21** cleanly to ketone **22**. Methylenation was then executed by treatment of **22** with commercially available Petasis reagent (Cp_2TiMe_2)[28] to furnish **23** in an excellent yield of 85%. Methylenation reagents employed so far (i.e., Tebbe, Ando, and Petasis reagents) are all commercially available and easy to handle. Lombardo reagent ($Zn/CH_2Br_2/TiCl_4$ in THF),[29] which must be prepared prior to use, may also work efficiently,[30] and will be examined in future to achieve a synthesis of the enantiomers of **1**.

Deprotection of **23** was effected in 65% yield with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and water in CH_2Cl_2[31] to give **16**. Purification of **16** by SiO_2 chromatography gave 456 mg of *anti*-rich **16** (*anti*/*syn*=81.3:15.4) and 397 mg of ca. 1:1 mixture of *anti*- and *syn*-**16**. By adding another batch of *syn*-rich **16**, 1.67 g of *syn*-rich **16** (*anti*/*syn*=2:3) was secured. These were separately oxidized with azadol and diacetoxyiodobenzene (DAIB)[27] to give (±)-*anti*-rich **1** (243 mg, 99.6% GC purity, *anti*/*syn*=85.6:14.0) and (±)-*syn*-rich **1** (1.19 g, 99.6% GC purity, *anti*/*syn*=38.0:61.6). The amounts obtained were sufficient for future field bioassay. The overall yield of **1** was 12% based on **6** (12 steps), in comparison to 0.6% in the case of the first synthesis and 2.4% in the case of the second synthesis. Accordingly, the present third synthesis was 20 times more efficient than the first one and five times more efficient than the second one, although the protection/deprotection strategy in the third synthesis increased the number of the steps from 10 in the second one to twelve.

2.6. Alternative synthesis of the intermediate 20

It is important to develop a synthetic route applicable to the preparation of both the enantiomers of *anti*-**1** so as to determine the absolute configuration of the naturally occurring *anti*-**1**. Reproducibility of the synthesis of **26** as reported by Jäger and coworkers in 1984[12] was therefore examined as shown in Scheme 5.

Alcohol (±)-**24** might possibly be resolved by enzymatic means, because (±)-2,4,4-trimethyl-2-cyclohexen-1-ol could be resolved by asymmetric hydrolysis of its acetate with pig liver esterase.[32] The synthesis in Scheme 5 was straightforward. Reduction of **2** with $LiAlH_4$ gave **24**, which was acetylated to give acetate **25**. Ireland–Claisen rearrangement of the TMS-enol ether of **25** gave **26** in 33% yield. Treatment of **26** with $LiAlH_4$ in THF gave **27**. Of course resolution of (±)-**26** or (±)-**27** might be another option to obtain the enantiomers of *anti*-**1**. Finally, **27** was treated with PMBCl and *t*-BuOK to give **20**, whose IR, ^1H NMR and MS spectra were identical with those of **20** obtained by ring-closing metathesis of **19** (Scheme 4). The overall yield of **20** was 9.1% based on **2** (five steps). Since **20** had been converted to (±)-*anti*-**1** as shown in Scheme 4, the present route constituted the fourth synthesis of (±)-*anti*-**1** in a formal sense.



Scheme 5. Alternative synthesis of **20**. Reagents: (a) $LiAlH_4$, Et_2O; (b) Ac_2O, C_5H_5N (40%, 2 steps); (c) $LiN(i\text{-}Pr)_2$, TMSCl, THF; then heat at 65 °C, 2.5 h; MeOH; then dil HCl (33%); (d) $LiAlH_4$, THF (69%); (e) PMBCl *t*-BuOK, THF, DMF (quant.).

3. Conclusion

Both *anti*- and *syn*-isomers of (±)-(1,2-dimethyl-3-methylenecyclopentyl)acetaldehyde (**1**) were synthesized. The isomer (±)-*anti*-**1** showed ^1H, ^{13}C NMR and MS spectra identical to those of the female-produced sex pheromone of the pineapple mealybug, *D. brevipes*. Synthetic (±)-*anti*-**1** was pheromonally active in the field test in Okinawa. A mixture of (±)-*anti*- and *syn*-**1** was also bioactive, while (±)-*syn*-**1** was biologically inactive.

Accordingly, (±)-*syn*-**1** does not inhibit the pheromone activity of (±)-*anti*-**1**. The synthesis of **1** was executed in four different ways, and over 1 g of (±)-**1** was secured for future biological studies. Synthesis of the enantiomers of *anti*-**1** is in progress, and will be published in due course.

4. Experimental

4.1. General

Melting points are uncorrected values. Refractive indices were measured on an Atago DMT-1 refractometer. IR spectra were measured on a Jasco FT/IR-410 spectrometer. ^{1}H NMR spectra (400 MHz, TMS at δ=0.00 as the internal standard) and ^{13}C NMR spectra (100 MHz, $CDCl_3$ at δ=77.0 as the internal standard) were recorded on a Jeol JNM-ECZ 400S/L1 spectrometer. GC–MS were measured on Agilent Technologies 5975 inert XL. HRMS were recorded on Jeol JMS-SX 102A or Waters Synapt G2 HDMS. Column chromatography was carried out on Merck Kieselgel 60 Art 1.00734.

4.2. 2,3-Dimethyl-2-cyclopenten-1-one (2)

Eighty five percent H_3PO_4 (75 mL) was added to P_2O_5 (135 g), and the mixture was stirred for 30 min at 200 °C to obtain a viscous liquid of PPA. 4-Methyl-4-hexenoic acid (20.0 g, 156 mmol)[12] was added to the hot and stirred PPA in one portion at 110 °C, and the mixture was stirred and heated at 110 °C for 2 h. The dark PPA solution was then poured into ice, saturated with NaCl, and extracted with hexane/Et_2O. The extract was washed successively with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The above process was repeated twice, and the residue from 40.0 g of the acid was distilled to give **2** (10.15 g, 30%) as a slightly yellow oil, bp 105–107 °C/56 Torr; ν_{max} (film): 2919 (m), 2864 (w), 1698 (s), 1651 (s), 1442 (m), 1388 (m), 1330 (m), 1302 (w), 1181 (w), 1065 (m), 938 (w), 862 (w), 810 (w), 650 (w); δ_H ($CDCl_3$): 1.69 (3H, s), 2.05 (3H, s), 2.30–2.40 (2H, m), 2.44–2.54 (2H, m); GC–MS [column: HP-5MS, 5% phenylmethylsiloxane, 0.25 mm i.d.×30 m; carrier gas, He; press 60.7 kPa; temp: 70–230 °C (+10 °C/min)]; t_R 3.11 (impurity, 5.1%), 5.56 min (88.4%); MS (70 eV, EI): *m*/*z*: 110 (76) [M^+], 95 (25), 81 (11), 67 (100), 54 (8), 39 (21).

4.3. 3-Allyl-2,3-dimethylcyclopentan-1-one (3)

A solution of $TiCl_4$ in CH_2Cl_2 (TCI, 1.0 M, 12 mL, 12 mmol) was added dropwise to a stirred and cooled solution of **2** (1.10 g, 10 mmol) and CH_2=$CHCH_2TMS$ (2.28 g, 20 mmol) in dry CH_2Cl_2 (10 mL) at −40 to −30 °C under argon. The brown-colored mixture was stirred for 2 h at −40 to −30 °C. It was then quenched by adding NH_4Cl solution, and extracted with Et_2O. The extract was washed successively with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residual oil (1.73 g) was chromatographed over SiO_2 (20 g). Careful fractionation was necessary to obtain **3** as a stereoisomeric mixture (176 mg, 12%) by elution with hexane/EtOAc (100:1–50:1). The above process was repeated twice and 347 mg of ca. 86.8% pure **3** (ca. 1:1 mixture of isomers) could be secured as a colorless oil, ν_{max} (film): 3070 (w), 2959 (s), 2934 (s), 2874 (m), 2840 (w), 1741 (s), 1638 (m), 1455 (m), 1382 (m), 1250 (m), 1145 (m), 1038 (m), 996 (m), 915 (s), 842 (m); δ_H ($CDCl_3$): 0.79 (1.5H, s), 0.94 (1.5H, d, *J*=6.8 Hz), 0.96 (1.5H, d, *J*=6.8 Hz), 1.11 (1.5H, s), 1.35–1.56 (1H, m), 1.60–1.80 (2H, m), 1.90–2.06 (2H, m), 2.06–2.34 (2H, m), 4.99–5.11 (2H, m), 5.70–5.90 (1H, m); GC–MS (same conditions as those used for **2**); t_R 7.37 (44.0%), 7.49 (42.8%), 11.36 min (impurity, 8.6%); MS of **3** with t_R=7.37 min (70 eV, EI): *m*/*z*: 152 (18) [M^+], 111 (41), 110 (44), 95 (12), 83 (88), 69 (100), 55 (55), 41 (43), 39 (24); MS of **3** with t_R=7.49 min (70 eV, EI): *m*/*z*: 152 (14) [M^+], 111 (41), 110 (55), 95 (11), 83 (85), 69 (100), 55 (55), 41 (43), 39 (23).

4.4. 3-(1,2-Dimethyl-3-oxocyclopentyl)propane-1,2-diol (4)

A solution of OsO_4 in *t*-BuOH [1%, 2 mL=20 mg (0.08 mmol)] and 50% NMO in H_2O (2.0 g, 8 mmol) were added to a stirred solution of **3** (340 mg, 2.2 mmol) in a mixture of *t*-BuOH (5 mL), acetone (10 mL) and H_2O (3 mL). The dark mixture was stirred for 3 d at room temperature (22 °C) to give a clear solution. Solid Na_2SO_3 (2.0 g) was added to reduce both NMO and OsO_4, and the mixture was concentrated in vacuo. The residue was diluted with brine, and extracted with EtOAc. The EtOAc extract was dried ($MgSO_4$), and concentrated in vacuo to give 240 mg (58%) of crude **4** as an oil, ν_{max} (film): 3421 (br s), 2953 (s), 2871 (s), 1736 (s), 1455 (m), 1249 (m), 1118 (m), 1072 (m), 1038 (m), 863 (m), 837 (m), 681 (s). This oil was employed in the next step without further purification.

4.5. 3-(1,2-Dimethyl-3-methylenecyclopentyl)propane-1,2-diol (5)

A solution of Tebbe reagent in toluene (TCI, 0.5 M, 10 mL) was added dropwise via syringe to a stirred and ice-cooled solution of **4** (240 mg, 1.3 mmol) in dry THF (10 mL) at 0–5 °C under argon. The mixture was stirred for 1 h at 0–5 °C. It was then quenched with NaOH solution (200 mg in 20 mL H_2O), diluted with EtOAc, and filtered through Celite. The filtrate was extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give 0.75 g of the residue containing **5**. Its IR [ν_{max} at 1654 (m)] and ^{1}H NMR spectra (olefinic protons at δ 3.3–4.0) showed the presence of the methylene group. This oil was employed in the next step without further purification.

4.6. (1,2-Dimethyl-3-methylenecyclopentyl)acetaldehyde (1)

$NaIO_4$ (2.0 g, 10 mmol) was added to a solution of crude **5** (750 mg, ca. 4 mmol) in THF (10 mL) and H_2O (5 mL). The mixture was stirred for 40 min at room temperature (22 °C). It was then diluted with water, and extracted with Et_2O. The Et_2O extract was washed successively with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give 540 mg of the residue, which was chromatographed over SiO_2 (7.5 g). Elution with hexane/EtOAc (50:1) gave 132 mg (18%) of crude **1** as a clear oil, ν_{max} (film); 3074 (w), 2956 (s), 2870 (m), 2730 (w), 1721 (s), 1655 (w), 1456 (m), 1380 (m), 880 (m); GC–MS (same conditions as used for **2**): t_R 7.21 (18.0%; identical t_R with that of the natural pheromone) 7.35 min (26.4%); MS of *anti*-**1** with t_R=7.21 min (70 eV, EI): *m*/*z*: 152 (<1) [M^+], 109 (33), 108 (100), 93 (76), 91 (30), 79 (24), 77 (24), 67 (52), 55 (21), 53 (24), 41 (55), 39 (33); MS of *syn*-**1** with t_R=7.35 min (70 eV, EI): *m*/*z*: 152 (<1) [M^+], 109 (21), 108 (100), 93 (90), 91 (20), 79 (17), 77 (20), 67 (23), 55 (14), 53 (17), 41 (34), 39 (24). The mixture **1** could be separated by $AgNO_3/SiO_2$ chromatography to give *anti*-**1** and *syn*-**1**. NMR data of *anti*-**1**: δ_H (600 MHz, C_6D_6): 0.70 (3H, d, *J*=6.6 Hz), 0.86 (3H, s), 1.06–1.40 (1H, m), 1.56–1.62 (1H, m), 1.60–1.74 (2H, m), 1.74–1.80 (1H, m), 2.06–2.14 (1H, m), 2.16–2.24 (1H, m), 4.77 (1H, m), 4.85 (1H, m), 9.47 (1H, t, *J*=2.4 Hz); δ_C (150 MHz, C_6D_6): 12.06, 24.78, 28.94, 35.52, 43.27, 47.20, 50.36, 105.73, 155.76, 201.38. The spectra were identical with those of the natural pheromone and no NOE was observed between the protons of the two Me groups. NMR data of *syn*-**1**: δ_H (600 MHz, C_6D_6): 0.56 (3H, s), 0.72 (3H, d, *J*=7.2 Hz), 1.20–1.29 (1H, m), 1.38–1.44 (1H, m), 1.72 (1H, dd, *J*=3, 14 Hz), 1.78–1.84 (1H, m), 2.01 (1H, dd, *J*=3.6, 15 Hz), 2.07–2.17 (1H, m), 2.17–2.23 (1H, m), 4.78–4.82 (1H, q-like), 4.87–4.89 (1H, q-like), 9.48 (1H, t, *J*=3 Hz); δ_C (150 MHz, C_6D_6): 11.50, 18.69, 29.28, 36.27, 42.73, 48.52, 54.06, 105.51, 155.10, 200.85. The spectra were different from those of the natural

pheromone, and the NOESY spectrum of *syn*-**1** indicated the *cis*-relationship of the two Me groups of *syn*-**1**.

4.7. Ethyl (*E*,*Z*)-2,3-dimethyl-2,6-heptadienoate (7)

A solution of triethyl 2-phosphonopropanoate (50.1 g, 210 mmol) in dry THF (50 mL) was added dropwise to a stirred and ice-cooled suspension of 60% NaH in mineral oil (8.42 g, 210 mmol) in dry THF (100 mL) under argon. After the completion of H_2 evolution to give a homogeneous solution of the sodio enolate, a solution of **6** (20.5 g, 210 mmol) in dry THF (30 mL) was added dropwise. No exothermic reaction could be observed. The mixture was stirred for 3 d at room temperature (20 °C). It was then diluted with ice and water, and extracted with Et_2O. The Et_2O extract was washed successively with water and brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was distilled to give 36.2 g (95%) of **7** [an almost 1:1 mixture of its (*E*)- and (*Z*)-isomers] as a colorless oil, bp 85–95 °C/7 Torr; n_D^{18}=1.4618; ν_{max} (film): 3078 (w), 2980 (m), 2932 (m), 2871 (w), 1714 (s), 1640 (m), 1446 (m), 1365 (m), 1277 (s), 1210 (s), 1101 (s), 911 (m), 772 (m); δ_H ($CDCl_3$): 1.297 (1.5H, t, *J*=6.8 Hz), 1.303 (1.5H, t, *J*=6.8 Hz), 1.78 (1.5H, s), 1.85 (1.5H, s), 1.87 (1.5H, s), 1.98 (1.5H, s), 2.12–2.28 (3H, m), 2.43 (1H, t, *J*=7.2 Hz), 4.18 (1H, q, *J*=7.2 Hz), 4.20 (1H, q, *J*=7.2 Hz), 4.90–5.10 (2H, m), 5.77–5.90 (1H, m); GC–MS [column: HP-5MS, 0.25 mm i.d.×30 m; carrier gas, He; press 61 kPa; temp: 70–230 °C (+10 °C/min)]: t_R 8.32 (49.3%), 8.69 min (47.4%) (total 96.7%); MS of **7** with t_R=8.32 min (70 eV, EI): *m*/*z*: 182 (5) [M^+], 167 (2), 153 (38), 137 (33), 113 (65), 109 (100), 95 (26), 93 (23), 81 (18), 79 (14), 67 (38), 43 (27); MS of **7** with t_R=8.69 min (70 eV, EI): *m*/*z*: 182 (6) [M^+], 167 (3), 153 (40), 137 (59), 125 (22), 113 (92), 109 (100), 95 (27), 93 (25), 81 (22), 79 (16), 67 (58), 55 (18), 53 (17), 43 (33). HRMS calcd for $C_{11}H_{18}O_2$: 182.1307, found: 182.1305 (short t_R) and 182.1322 (long t_R).

4.8. (*EZ*)-2,3-Dimethyl-2,6-heptadien-1-ol (8)

A solution of **7** (33.0 g, 181 mmol) in dry Et_2O (50 mL) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (4.00 g, 105 mmol) in dry Et_2O (200 mL) at 10–15 °C. After the addition, the mixture was stirred for 2 h at 0–5 °C. Then excess $LiAlH_4$ was destroyed by slowly adding water to the stirred mixture with ice-cooling. The mixture was acidified with ice and dil. HCl, and extracted with Et_2O. The Et_2O extract was washed successively with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 28.4 g (quant.) of **8** as a colorless oil. An analytical sample of **8** was obtained by distillation, bp 81–82 °C/6 Torr; n_D^{20}=1.4755; ν_{max} (film): 3326 (br m), 3077 (w), 2978 (m), 2925 (s), 2864 (m), 1663 (w), 1640 (m), 1442 (m), 996 (s), 910 (s); δ_H ($CDCl_3$): 1.37 (1H, br s), 1.67 (1.5H, s), 1.72 (1.5H, s), 1.74 (3H, s), 2.08–2.25 (4H, m), 4.10 (2H, d, *J*=14 Hz), 4.90–5.08 (2H, m), 5.72–5.88 (1H, m); GC–MS (same conditions as used for **7**); t_R 6.67 (48.6%), 6.81 min (47.5%) (total 96.1%); MS of **8** with t_R=6.67 min (70 eV, EI): *m*/*z*: 140 (<1) [M^+], 125 (10), 109 (40), 107 (29), 93 (16), 91 (18), 85 (18), 81 (21), 79 (28), 67 (16), 57 (8), 55 (23), 43 (100). The MS spectrum of **8** with t_R=6.81 min was almost identical with the above described one. HRMS calcd for $C_9H_{16}O$: 140.1201, found: 140.1218 (short t_R), 140.1220 (long t_R).

4.9. (*EZ*)-2,3-Dimethyl-2,6-heptadienyl acetate (9)

Ac_2O (60 mL=78 g, 765 mmol) and DMAP (0.2 g) were added to a stirred solution of **8** (28.3 g, 180 mmol) in dry C_5H_5N (100 mL). When the exothermic reaction subsided, the mixture was stirred and heated at 80 °C for 30 min. After cooling, the mixture was diluted with ice and water, and extracted with Et_2O. The Et_2O extract was washed successively with dil HCl, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated at atmospheric pressure. The residue was distilled to give 31.0 g (94% based on **7**, two steps) of **9** as a colorless oil, bp 83–90 °C/6 Torr; n_D^{21}=1.4582; ν_{max} (film): 3078 (w), 2979 (m), 2927 (m), 2865 (m), 1740 (s), 1666 (w), 1640 (m), 1443 (m), 1376 (m), 1232 (s), 1022 (m), 911 (m); δ_H ($CDCl_3$): 1.70 (4.5H, s), 1.74 (1.5H, s), 2.04 (3H, s), 2.02–2.25 (4H, m), 4.58 (2H, d, *J*=5.6 Hz), 4.92–5.06 (2H, m), 5.72–5.86 (1H, m); GC–MS (same conditions as used for **7**); t_R 8.53 (48.5%), 8.65 min (46.9%) (total 95.4%); MS of **9** with t_R=8.53 min (70 eV, EI): *m*/*z*: 182 (1) [M^+], 164 (2), 141 (4), 122 (18), 107 (58), 99 (28), 94 (22), 93 (27), 91 (23), 81 (24), 79 (46), 67 (16), 53 (13), 43 (100). The MS spectrum of **9** with t_R=8.65 min was almost identical with the above data. HRMS calcd for $C_{11}H_{18}O_2$: 182.1307, found: 182.1326 (short t_R), 182.1326 (long t_R).

4.10. 3-Isopropenyl-3-methyl-6-heptenoic acid (10)

TMSCl (37.0 *g*=42 mL, 340 mmol) was added to a stirred and cooled solution of **9** (15.5 g, 85 mmol) in dry THF (60 mL) at −78 °C under argon. A solution of LiN(*i*-Pr)$_2$ in THF/PhEt/heptane (TCI, 1.5 M, 100 mL, 150 mmol) was added dropwise over 15 min to the stirred solution at −78 to −60 °C. Then the dry ice/acetone bath was removed, and the mixture was allowed to reach room temperature over 1 h. The mixture was stirred and heated at 70 °C (bath temperature) for 4 h. After cooling, MeOH (40 mL) was added to the mixture, which was stirred for 10 min at room temperature. The mixture was then transferred to a separatory funnel, and extracted with 5% NaOH aqueous solution (60 mL×3). The aqueous extract was transferred into another separatory funnel, and washed with Et_2O to remove neutral impurities. The aqueous layer was acidified with dil. HCl with ice-cooling, and the separated oily **10** was extracted with Et_2O. The Et_2O extract was washed successively with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give 13.3 g (86%) of **10** as an oil, ν_{max} (film): 3078 (w), 2976 (s), 2939 (s), 2684 (br w), 1708 (s), 1640 (m), 1447 (m), 1410 (m), 1380 (m), 1309 (m), 1227 (m), 898 (s); δ_H ($CDCl_3$): 1.22 (3H, s), 1.44–1.66 (2H, m), 1.74 (3H, s), 1.82–2.00 (2H, m), 2.36 (1H, d, *J*=13.6 Hz), 2.48 (1H, d, *J*=13.6 Hz), 4.75 (1H, s), 4.88 (1H, t-like, *J*=1.6 Hz), 4.91–5.02 (2H, m), 5.74–5.84 (1H, m); This oil was used in the next step without further purification.

4.11. Methyl 3-isopropenyl-3-methyl-6-heptenoate (11)

K_2CO_3 (34.5 g, 250 mmol) and MeI (54.0 g 380 mmol) were added to a stirred solution of **10** (24.3 g, 134 mmol) in dry DMF (160 mL). After the initial exothermic reaction, the mixture was stirred for 3 d at room temperature (21 °C). It was then diluted with ice and water, and extracted with Et_2O. The Et_2O extract was washed successively with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 17.4 g (66%) of **11** as a colorless oil, bp 93–96 °C/8 Torr; n_D^{24}=1.4532; ν_{max} (film): 3079 (w), 2975 (m), 2950 (m), 1739 (s), 1639 (m), 1436 (m), 1379 (m), 1337 (m), 1311 (m), 1252 (m), 1196 (s), 1120 (m), 1015 (m), 898 (s), 845 (w); δ_H ($CDCl_3$): 1.19 (3H, s), 1.41–1.49 (1H, m), 1.54–1.66 (1H, m), 2.07 (3H, s), 1.81–1.98 (2H, m), 2.34 (1H, d, *J*=14 Hz), 2.47 (1H, d, *J*=14 Hz), 3.62 (3H, s), 4.72 (1H, s), 4.86 (1H, s-like), 4.90–5.04 (2H, m), 5.74–5.86 (1H, m); GC–MS (same conditions as used for **7**); t_R 9.03 min (87.1%); MS (70 eV, EI): *m*/*z*: 197 (<1) [$(M+H)^+$], 181 (20), 142 (42), 122 (54), 110 (42), 109 (39), 107 (42), 99 (19), 95 (43), 82 (81), 81(100), 67 (41), 59 (19), 55 (35), 41 (38). HRMS calcd for $C_{12}H_{20}O_2$: 196.1463, found: 196.1491.

4.12. Methyl (1,2-dimethyl-2-cyclopentenyl)acetate (12)

Grubbs II catalyst (190 mg, 0.22 mmol, 0.4 mol %) was added to a solution of **11** (17.3 g, 88 mmol) in CH_2Cl_2 (400 mL) under argon.

The mixture was stirred and heated under gentle reflux. After 2 h, when the evolution of ethylene ceased, the mixture was concentrated in vacuo. The residue was chromatographed over SiO_2 (100 g). Elution with hexane/EtOAc(30:1) gave 15.0 g of crude **12**, which was distilled to furnish 11.3 g (76%) of **12** as a colorless oil, bp 72–75 °C/7 Torr; n_D^{25}=1.4542; ν_{max} (film): 3038 (w), 2953 (m), 2851 (m), 1739 (s), 1437 (m), 1218 (m); δ_H ($CDCl_3$): 1.09 (3H, s), 1.63 (3H, s-like), 1.66–1.76 (1H, m), 2.06–2.14 (1H, m), 2.16–2.22 (2H, m), 2.28 (1H, d, *J*=13 Hz), 2.36 (1H, d, *J*=13 Hz), 3.64 (3H, s), 5.31 (1H, br s); GC–MS (same conditions as used for **7**): t_R 6.95 min (94.6%); MS (70 eV, EI): *m*/*z*: 168 (19) [M^+], 136 (4), 121 (3), 95 (98), 94 (100), 79 (35), 65 (18), 55 (7), 41 (7), 39 (7). HRMS calcd for $C_{10}H_{16}O_2$: 168.1150, found: 168.1168.

4.13. Methyl (1,2-dimethyl-3-oxocyclopentyl)acetate (13)

$BH_3{\cdot}Me_2S$ (7.2 mL=5.7 g, 75 mmol) was added dropwise to a stirred and ice-cooled solution of **12** (11.3 g, 88 mmol) in dry Et_2O (80 mL) at 5–10 °C under argon. The mixture was stirred for 3 h at room temperature (21 °C). Water (30 mL) was slowly added dropwise to the stirred and ice-cooled mixture at 5–10 °C to destroy excess BH_3. Subsequently, the mixture was diluted with acetone (60 mL). Jones CrO_3 (50 mL) was added dropwise over 20 min to the stirred and ice-cooled mixture at 5–10 °C. After adding MeOH (5 mL) to destroy the excess CrO_3, the mixture was concentrated in vacuo. The residue was diluted with water, and extracted with Et_2O. The extract was washed successively with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 9.73 g of crude hydroxy ester, ν_{max} (film): 3460 (br m), 2956 (s), 2874 (m), 1737 (s), 1438 (m), 1348 (m), 1213 (m), 1010 (m). This oil was dissolved in acetone (120 mL), and treated with Jones CrO_3 (14 mL) under ice-cooling at 5–10 °C. After 10 min, the mixture was quenched with MeOH (5 mL), and concentrated in vacuo. The residue was diluted with water and extracted with Et_2O. The Et_2O extract was washed successively with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 5.8 g (47%) of **13** as a colorless oil, bp 110–115 °C/7 Torr; n_D^{24}=1.4594; ν_{max} (film): 2957 (m), 2876 (m), 1739 (s), 1455 (m), 1438 (m), 1239 (m), 1213 (m), 1170 (m), 1119 (m), 1009 (m); δ_H ($CDCl_3$): 0.96 (1H, d, *J*=7.6 Hz), 0.98 (2H, d, *J*=7.6 Hz), 1.26 (3H, s), 1.60–1.74 (2H, m), 1.90–2.40 (5H, m), 3.67 (2H, s), 3.69 (1H, s); GC–MS (same conditions as used for **7**); t_R 9.90 (56.5%), 10.09 min (24.0%) (total 80.5%); MS of the major isomer (70 eV, EI): *m*/*z*: 184 (7) [M^+], 169 (5), 153 (12), 127 (10), 111 (100), 95 (11), 83 (12), 74 (11), 69 (24), 55 (17), 41 (17); MS of the minor isomer (70 eV, EI): *m*/*z*: 184 (1), 169 (5), 153 (8), 127 (6), 111 (100), 96 (7), 83 (7), 69 (18), 55 (13), 41 (13). HRMS calcd for $C_{10}H_{16}O_3$: 184.1099, found: 184.1112 (major isomer), 184.1107 (minor isomer).

4.14. Methyl (1,2-dimethyl-3-methylenecyclopentyl)acetate (15)

A solution of NaHMDS in THF (TCI, 1.9 M, 22.6 mL, 43 mmol) was added over 5 min to a stirred and cooled solution of **13** (6.14 g, 33 mmol) and **14** (8.41 g, 40 mmol) in dry DMF (90 mL) at −70 to −60 °C under argon. The mixture was stirred for 10 min at −78 °C, and then the cooling bath was removed to raise the temperature gradually to room temperature in the course of 1 h. The mixture was stirred for 40 min at room temperature (22 °C). The reaction was quenched by adding ice and NH_4Cl solution and the mixture was extracted with Et_2O. The Et_2O solution was washed successively with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (80 g). Elution with hexane/EtOAc (30:1) gave 2.42 g of crude **15**. Further elution with the same eluent furnished 2.88 g (47% recovery) of **13**. The crude **15** was purified by distillation to give 1.65 g (27%; 51% based on the consumed **13**) of **15** as a colorless oil, bp 83–85 °C/7 Torr; n_D^{24}=1.4590; ν_{max} (film): 3074 (w), 2961 (m), 2873 (w), 1739 (s), 1656 (w), 1436 (m), 1201 (m), 1124 (m), 1013 (m), 880 (m); δ_H ($CDCl_3$): 0.78 (1.8H, s), 0.93 (3H, d, *J*=6.8 Hz), 1.13 (1.2H, s), 1.02–1.44 and 1.86–1.94 (total 1H, m), 1.56–1.70 (2H, m), 2.06–2.20 and 2.30–2.40 (total 2H, m), 2.22 (1H, d, *J*=13 Hz), 2.42 (1H, d, *J*=13 Hz), 3.65 and 3.66 (total 3H, each s), 4.78 (1H, s-like), 4.87 (1H, s-like); GC–MS (same conditions as used for **7**); t_R 8.41 (32.7%), 8.58 min (50.0%) (total 82.7%); MS of the minor isomer (70 eV, EI): *m*/*z*: 182 (<1) (M^+), 151 (6), 123 (4), 109 (33), 108 (100), 93 (35), 67 (15), 41 (9); MS of the major isomer (70 eV, EI): *m*/*z*: 183 (<1) [$(M+H)^+$], 151 (4), 109 (53), 108 (100), 93 (58), 91 (12), 67 (14), 41 (10). HRMS calcd for $C_{11}H_{18}O_2$: 182.1307, found: 182.1322 (minor isomer), 182.1323 (major isomer).

When *t*-BuOK, instead of NaHMDS, was employed as the base, the products (28% yield) were mainly the two isomeric *t*-Bu esters generated by the nucleophilic attack of *t*-BuO^- to the ester C=O of **15**. The *t*-Bu esters, bp 93–97 °C/7 Torr, n_D^{24}=1.4538, showed a signal due to *t*-Bu at δ=1.45, while the signal due to CO_2Me at δ 3.66 was almost absent. Its GC–MS showed two peaks at t_R=10.41 (24.7%) and 10.53 (40.4%) both with M^+=224 ($C_{14}H_{24}O_2$).

4.15. 2-(1,2-Dimethyl-3-methylenecyclopentyl)ethanol (16)

A solution of **15** (1.80 g, 10 mmol) in dry Et_2O (10 mL) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (380 mg, 10 mmol) in dry Et_2O (10 mL). The mixture was stirred for 1 h at 5–10 °C. Then water was added dropwise to the stirred and ice-cooled mixture to destroy excess $LiAlH_4$. The mixture was acidified with dil. HCl and ice, and extracted with Et_2O. The Et_2O extract was washed successively with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 1.60 g (quant.) of **16** as a colorless oil, ν_{max} (film): 3345 (br m), 3073 (w), 2959 (s), 1655 (w), 1454 (m), 1379 (m), 1054 (m), 1037 (m), 1009 (m), 876 (m); δ_H ($CDCl_3$): 0.69 (1.9H, s), 0.93 (1.9H, d, *J*=6.8 Hz), 0.94 (1.1H, d, *J*=6.8 Hz), 1.01 (1.1H, s), 1.20–1.80 (5H, m), 2.05 (1H, br), 2.15–2.45 (2H, m), 3.65–3.80 (2H, m), 4.77 (1H, m), 4.84–4.88 (1H, m); GC–MS (same conditions as those used for **7**): t_R 8.33 (30.9%), 8.49 min (48.2%); MS of the minor isomer (70 eV, EI): *m*/*z*: 154 (<1) [M^+], 139 (6), 125 (15), 121 (24), 110 (47), 109 (100), 95 (25), 93 (38), 91 (19), 81 (24), 79 (27), 67 (46), 55 (22), 53 (15), 41 (30); MS of the major isomer (70 eV, EI): *m*/*z*: 155 (<1) [$(M+H)^+$], 139 (4), 121 (13), 109 (100), 93 (25), 81 (12), 79 (14), 67 (19), 55 (10), 53 (8), 41 (15). HRMS calcd for $C_{10}H_{18}O$: 154.1358, found: 154.1374 (minor isomer), 154.1372 (major isomer).

4.16. (1,2-Dimethyl-3-methylenecyclopentyl)acetaldehyde (1)

Crystalline $NaOCl{\cdot}5H_2O$ (TCI, 1.60 g, 10 mmol) was added in one portion to a stirred and ice-cooled mixture of **16** (1.08 g, 7 mmol), Bu_4NHSO_4 (0.12 g, 0.35 mmol), azadol (30 mg, 0.2 mmol) and water (0.3 mL) in CH_2Cl_2 (30 mL) at 5–10 °C. The mixture was stirred for 1 h at 5–10 °C, when it became turbid. The mixture was shaken with an aqueous solution of $Na_2S_2O_3$ and $NaHCO_3$, the organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic solution was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give **1** (669 mg, 63%) as a colorless oil, bp 74–77 °C/7 Torr; GC–MS (same conditions as those used for **7**); t_R 7.02 (33.8%, *anti*-**1**), 7.16 min (44.2%, *syn*-**1**). Its IR, NMR and MS data were identical to those reported in 4.6 and 4.25.

4.17. 2-(1,2-Dimethyl-3-methylenecyclopentyl)ethyl 3,5-dinitrobenzoate (17)

*4.17.1. A mixture of anti- and syn-**17**.* Solid 3,5-dinitrobenzoyl chloride (1.40 g, 6 mmol) was added to a stirred and ice-cooled solution of **16** (mixture, 910 mg, 5 mmol) in dry C_5H_5N (2 mL) containing DMAP (10 mg). The mixture was stirred for 1.5 h at room temperature (22 °C), then diluted with ice and water, and extracted with Et_2O. The Et_2O solution was washed successively with dil. HCl, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 2.00 g (97%) of **17** as a slightly yellow-colored oil. This was dissolved in Et_2O/pentane, and left for 2 d at −20 °C. The separated solid (1.273 g) was collected on a glass filter, and recrystallized twice from Et_2O/pentane to give 484 mg (23%) of a mixture of *anti*- and *syn*-**17** as a solid, mp 39–41 °C, ν_{max} (film): 3104 (w), 2960 (m), 2931 (m), 2872 (m), 1733 (s), 1630 (w), 1548 (s), 1462 (m), 1345 (s), 1280 (s), 1167 (m), 1075 (w), 965 (w), 921 (w), 881 (w), 722 (m). The IR spectrum was very similar to that of *syn*-**17**. Its ^{1}H NMR spectrum was complicated as that of a mixture of *anti*- and *syn*-**17**, while its ^{13}C NMR spectrum clearly showed that the sample was a mixture of *anti*- and *syn*-**17**: δ_C ($CDCl_3$): 11.54, 12.07, 18.45, 24.73, 29.00, 29.28, 31.60, 35.02, 36.50, 39.09, 42.69, 48.63, 50.51, 60.41, 64.83, 64.88, 105.22, 105.35, 122.34, 129.41, 134.11, 148.69, 155.66, 156.18, 162.57.

*4.17.2. Chromatographic separation of the alcohol mixture **16**..* The alcohol mixture **16** (2.42 g) was purified by chromatography over SiO_2 (80 g). Elution with hexane (300 mL) gave nothing. Further elution with hexane/EtOAc (20:1) gave the following six fractions (each 300 mL), whose *anti*-**16** (short t_R)/*syn*-**16** (long t_R) ratio was determined by GC–MS analysis: (1) 303 mg (97:3)+several impurities with shorter t_Rs, (2) 424 mg (67:33), (3) 369 mg (34:66), (4) 285 mg (19:81), (5) 181 mg (8:92), (6) 140 mg (4:96). Fraction 1 was nearly pure *anti*-**16**, and fraction 6 was nearly pure *syn*-**16**. These were converted to the corresponding 3,5-dinitrobenzoates, *anti*-**17** and *syn*-**17**, and fractions 2–5 were combined and oxidized to give **1** as a stereoisomeric mixture.

*4.17.3. 2-(anti-1,2-Dimethyl-3-methylenecyclopentyl)ethyl 3,5-dinitrobenzoate (anti-**17**).* Alcohol *anti*-**16** (303 mg, 2 mmol) was esterified with 3,5-dinitrobenzoyl chloride (500 mg, 2.2 mmol) and dry C_5H_5N (4 mL) containing DMAP (10 mg) as described in 4.17.1. The resulting solid (617 mg) was recrystallized from EtOAc/hexane to give 199 mg of *anti*-**17** as leaflets, mp 55–56 °C; ν_{max} (Nujol): 3089 (m), 1720 (vs), 1655 (w), 1631 (m), 1598 (w), 1550 (vs), 1463 (s), 1351 (s), 1287 (s), 1170 (m), 966 (m), 926 (m), 869 (w), 776 (w), 722 (s); δ_H ($CDCl_3$): 1.01 (3H, d, J=6.8 Hz), 1.11 (3H, s), 1.60–1.65 (2H, m), 1.65–1.72 (1H, m), 1.76–1.84 (1H, m), 2.08–2.16 (1H, br), 2.30–2.40 (1H, m), 2.40–2.52 (1H, m), 4.50 (2H, t, J=7.2 Hz), 4.82 (1H, d, J=2 Hz), 4.89 (1H, d, J=2 Hz), 9.15 (2H, m), 9.23 (1H, t, J=2 Hz); δ_C ($CDCl_3$): 12.08, 24.74, 29.00, 31.60, 35.02, 42.69, 50.51, 64.88, 105.36, 122.32, 129.41, 134.12, 148.69, 156.16, 162.56. HRMS calcd for $C_{17}H_{20}O_6N_2$: 348.1321, found: 348.1344.

*4.17.4. 2-(syn-1,2-Dimethyl-3-methylenecyclopentyl)ethyl 3,5-dinitrobenzoate (syn-**17**).* Similarly, alcohol *syn*-**16** (140 mg, 1 mmol) was esterified with 3,5-dinitrobenzoyl chloride (250 mg, 1.1 mmol) and dry C_5H_5N (2 mL) containing DMAP (5 mg) to give 221 mg of a solid. This was recrystallized from EtOAc/hexane to give 162 mg of *syn*-**17** as prisms, mp 58–59 °C; ν_{max} (Nujol): 3108 (m), 1727 (vs), 1655 (w), 1631 (m), 1598 (w), 1547 (vs), 1460 (m), 1380 (w), 1344 (vs), 1316 (w), 1279 (s), 1166 (m), 1074 (m), 959 (m), 919 (m), 891 (m), 880 (m), 731 (s), 719 (s); The IR spectrum was different from that of *anti*-**17**. δ_H ($CDCl_3$): 0.79 (3H, s), 0.98 (3H, d, J=6.8 Hz), 1.52–1.66 (2H, m), 1.72–1.82 (1H, m), 1.98–2.06 (1H, m), 2.10–2.18 (1H, br), 2.28–2.40 (1H, m), 2.40–2.52 (1H, m), 4.48–4.62 (2H, m), 4.81 (1H, d, J=2 Hz), 4.90 (1H, d, J=2 Hz), 9.16 (2H, d, J=2 Hz), 9.23 (1H, t, J=2 Hz); δ_C ($CDCl_3$): 11.55, 18.46, 29.27, 36.50, 39.09, 42.69, 48.62, 64.83, 105.22, 122.34, 129.41, 134.12, 148.71, 155.65, 162.56. HRMS calcd for $C_{17}H_{20}O_6N_2$: 348.1321, found: 348.1340. Melting point depression was observed when *anti*-**17** and *syn*-**17** were mixed: mixture mp 41–46 °C.

4.18. 3-Isopropenyl-3-methyl-6-hepten-1-ol (18)

A solution of **10** (4.47 g, 24.6 mmol) in dry THF (15 mL) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (1.40 g, 37 mmol) in dry THF (35 mL) at 5–15 °C. After the addition, the mixture was stirred and heated under reflux for 1.5 h. It was then ice-cooled, and excess $LiAlH_4$ was destroyed by dropwise addition of water. The mixture was acidified with dil HCl and ice, and extracted with Et_2O. The Et_2O extract was washed successively with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 3.03 g (73%) of **18** as a colorless oil, bp 104–107 °C/7 Torr, n_D^{24}=1.4742; ν_{max} (film): 3328 (br m), 3087 (w), 2972 (s), 2940 (s), 1639 (m), 1447 (m), 1377 (m), 1138 (w), 1034 (m), 994 (m), 908 (s), 894 (s); δ_H ($CDCl_3$): 1.08 (3H, s), 1.30–1.40 (1H, m), 1.42 (1H, br s), 1.49–1.59 (2H, m), 1.72 (3H, s), 1.75–1.86 (2H, m), 1.87–2.00 (1H, m), 3.60 (2H, t, J=7.2 Hz), 4.73 (1H, d, J=1.2 Hz), 4.87 (1H, t, J=1.6 Hz), 4.90–5.02 (2H, m), 5.74–5.86 (1H, m); GC–MS (same conditions as those used for **7**): t_R 8.96 min (94.4%); MS (70 eV, EI): m/z: 169 (<1) [$(M+H)^+$], 153 (22), 135 (7), 124 (16), 114 (26), 95 (94), 83 (100), 81 (98), 67 (74), 55 (80), 41 (64). HRMS calcd for $C_{11}H_{20}O$: 168.1514, found; 168.1532.

4.19. 3-Isopropenyl-3-methyl-6-heptenyl *p*-methoxybenzyl ether (19)

t-BuOK (11.0 g, 90 mmol) was added in one portion to a solution of **18** (12.2 g, 72.6 mmol) in dry DMF (72 mL), and the mixture was stirred at room temperature to make a homogeneous solution. *p*-Methoxybenzyl chloride (PMBCl, 14.1 g, 90 mmol) was added to the stirred solution, and stirring was continued for 1 h at 65 °C. After cooling, the mixture was diluted with ice and water, and extracted with Et_2O. The Et_2O extract was washed successively with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue (26.8 g) was chromatographed over SiO_2 (100 g). Elution with hexane/EtOAc (30:1) gave 20.6 g (99%) of **19** as a colorless oil, n_D^{21}=1.5112; ν_{max} (film): 3076 (w), 2971 (s), 2937 (s), 2862 (m), 1638 (m), 1614 (s), 1586 (w), 1514 (vs), 1464 (m), 1362 (m), 1302 (m), 1248 (vs), 1173 (m), 1096 (m), 1038 (m), 894 (m), 822 (m); δ_H ($CDCl_3$): 1.04 (3H, s), 1.35–1.40 (1H, m), 1.46–1.55 (1H, m), 1.50–1.65 (1H, m), 1.68 (3H, s), 1.75–1.88 (2H, m), 1.88–1.98 (1H, m), 3.30–3.46 (2H, m), 3.80 (3H, s), 4.39 (2H, s), 4.68 (1H, s), 4.83 (1H, s), 4.89–5.00 (2H, m), 5.75–5.83 (1H, m), 6.87 (2H, d, J=7 Hz), 7.24 (2H, d, J=7 Hz); GC–MS (same conditions as those used for **7**); t_R 18.53 min (93.5%); MS (70 eV, EI): m/z: 288 (1) [M^+], 137 (12), 136 (12), 121 (100), 109 (8), 83 (13), 55 (6). HRMS calcd for $C_9H_{28}O_2$: 288.2089, found; 288.2106.

4.20. 2-(1,2-Dimethyl-2-cyclopentenyl)ethyl *p*-methoxybenzyl ether (20)

Grubbs II catalyst (280 mg, 0.32 mmol, 0.44 mol % for **19**) was added to a solution of **19** (20.6 g, 71.6 mmol) in CH_2Cl_2 (400 mL) under argon. The solution was stirred and heated under reflux for 2 h. Then the mixture was concentrated in vacuo. The residue was chromatographed over SiO_2 (100 g). Elution with hexane gave 1.33 g of impurities. Further elution with hexane/EtOAc (30:1) gave 16.2 g (87%) of **20** as a colorless oil, n_D^{22}=1.5156; ν_{max} (film): 3034 (w), 2952 (m), 2932 (m), 2853 (m), 1614 (m), 1586

(w), 1514 (s), 1456 (m), 1362 (m), 1302 (m), 1248 (s), 1173 (m), 1096 (s), 1038 (s), 821 (s); δ_H ($CDCl_3$): 1.00 (3H, s), 1.58 (3H, s), 1.60–1.76 (3H, m), 1.82–1.90 (1H, m), 2.12–2.25 (2H, m), 3.37–3.49 (2H, m), 3.80 (3H, s), 4.41 (2H, s), 5.25 (1H, br s), 6.87 (2H, d, J=6.8 Hz), 7.24 (2H, d, J=6.8 Hz); GC–MS (same conditions as those used for **7**); t_R 17.22 min (90.2%); MS (70 eV, EI): m/z: 259 (<1) [$(M\text{-}H)^+$], 231 (2), 163 (2), 137 (4), 121 (100), 97 (8), 77 (5), 57 (3), 41 (4). HRMS calcd for $C_{17}H_{24}O_2$: 260.1776, found; 260.1788.

4.21. 2-(3-Hydroxy-1,2-dimethylcyclopentyl)ethyl *p*-methoxybenzyl ether (21)

$BH_3{\cdot}Me_2S$ (10 mL, 8.0 g, 105 mmol) was added dropwise over 10 min to a stirred and ice-cooled solution of **20** (14.2 g, 55 mmol) in dry THF (140 mL) at 0–10 °C under argon. The mixture was stirred for 30 min at 0–5 °C and 2.5 h at room temperature. It was then ice-cooled again, and water (20 mL) was slowly added dropwise (H_2 evolution) to destroy excess borane. Then a solution of NaOH (4.6 g, 115 mmol) in water (32 mL) was added dropwise to the stirred and ice-cooled mixture. Subsequently 34.5% H_2O_2 (40 mL) was slowly added (exothermic), and stirring was continued for 1 h at 0–5 °C. The mixture was diluted with water, and extracted with Et_2O. The Et_2O extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue (20.3 g) was chromatographed over SiO_2 (100 g). Elution with hexane and hexane/EtOAc (10:1) gave 2.08 g of impurities. Further elution with hexane/EtOAc (4:1) furnished 10.4 g (68%) of **21** as a colorless and viscous oil, n_D^{22}=1.5060; ν_{max} (film): 3401 (br m), 2955 (s), 2869 (s), 1613 (m), 1586 (w), 1514 (s), 1463 (m), 1363 (m), 1302 (m), 1248 (s), 1173 (m), 1093 (s), 1037 (s), 821 (m); δ_H ($CDCl_3$): 0.76 (1.4H, s), 0.93–0.95 (3H, m), 0.98 (1.6H, s), 1.36–1.60 (5H, m), 1.60–1.80 (3H, m), 1.98–2.10 (1H, m), 3.80 (3H, s), 3.44–3.54 (2H, m), 4.42 (2H, s), 6.87 (2H, d, J=8.6 Hz), 7.25 (2H, d, J=8.6 Hz); GC–MS (same conditions as those used for **7**); t_R 19.77 (40.5%), 19.84 min (57.3%) (total 97.8%); MS of **21** with t_R=19.77 min (70 eV, EI): m/z: 278 (<1) [M^+], 137 (22), 121 (100), 95 (19), 77 (5), 57 (2); MS of **21** with t_R=19.84 min (70 eV, EI): m/z: 278 (<1) [M^+], 137 (4), 121 (100), 95 (10), 77 (5), 57 (3). HRMS calcd for $C_{17}H_{26}O_3$: 278.1882, found: 278.1899.

4.22. 2-(1,2-Dimethyl-3-oxocyclopentyl)ethyl *p*-methoxybenzyl ether (22)

Jones chromic acid (8 N, 8 mL, 64 meq) was added dropwise to a stirred and ice-cooled solution of **21** (9.51 g, 34 mmol) in acetone (150 mL) at 5–15 °C. The mixture was stirred for further 10 min after the addition. MeOH (5 mL) was added to destroy the excess CrO_3, and the mixture was concentrated in vacuo. The residue was diluted with water, and extracted with Et_2O. The Et_2O extract was washed successively with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was sufficiently pure **22** (8.80 g, 93%) obtained as a colorless oil, n_D^{20}=1.5042; ν_{max} (film): 2956 (m), 2934 (m), 2871 (m), 1737 (m), 1613 (m), 1586 (w), 1514 (m), 1463 (m), 1372 (m), 1302 (m), 1248 (s), 1174 (m), 1095 (m), 1037 (m), 821 (m); δ_H ($CDCl_3$): 0.80 (1.5H, s), 0.94 (1.5H, d, J=7.6 Hz), 0.95 (1.5H, d, J=7 Hz), 1.12 (1.5H, s), 1.35–1.60 (2H, m), 1.66–1.98 (2H, m), 1.98–2.32 (3H, m), 3.49 (1H, t, J=6.8 Hz), 3.58 (1H, t, J=6.8 Hz), 3.80 (3H, s), 4.41 (1H, s), 4.44 (1H, s), 6.85–6.90 (2H, m), 7.22–7.27 (2H, m); GC–MS (same conditions as those used for **7**): t_R 19.69 (48.5%), 19.83 min (46.8%) (total 95.3%); MS of **22** with t_R=19.69 min (70 eV, EI): m/z: 276 (2) [M^+], 137 (28), 121 (100), 111 (12), 77 (5), 55 (4); MS of **22** with t_R=19.83 min (70 eV, EI): m/z: 276 (1) [M^+], 231 (3), 137 (7), 121 (100), 111 (11), 77 (4), 55 (3). HRMS calcd for $C_{17}H_{24}O_3$: 276.1725, found: 276.1740 (short t_R), 276.1740 (long t_R).

4.23. 2-(1,2-Dimethyl-3-methylenecyclopentyl)ethyl *p*-methoxybenzyl ether (23)

A solution of dimethyltitanocene (Petasis reagent, TCI, 5 wt% solution in THF/toluene, 230 g, 56 mmol) was added to **22** (8.80 g, 32 mmol) under argon. The flask was wrapped with aluminum foils to keep inside dark, and the orange-colored mixture was stirred and heated at 70 °C for 25 h. After cooling, $NaHCO_3$ (2.4 g, 30 mmol), water (1.5 mL) and MeOH (30 mL) were added to the mixture, which was stirred overnight at room temperature (22 °C). Then the stirring bar was removed from the dark green-colored mixture to which was added SiO_2 (20 g). The mixture was concentrated in vacuo to give yellow-colored powder, which was transferred to the top of a column of SiO_2 (70 g) in hexane. Elution with hexane gave 0.18 g of hydrocarbon impurities. Further elution with hexane/EtOAc (30:1) gave 2.45 g of **23** (*anti*/*syn*=66.5:31.2) and then 3.52 g of **23** (*anti*/*syn*=43.1:55.9). Total yield of **23** was 5.97 g (68%). In another occasion, 85% yield could be observed. These two fractions were employed separately in the next step. Properties of **23** (*anti*/*syn*=ca. 1:1): n_D^{20}=1.5040; ν_{max} (film): 3071 (w), 2958 (s), 2934 (s), 2866 (m), 1654 (w), 1613 (m), 1586 (w), 1514 (s), 1464 (m), 1363 (m), 1302 (m), 1248 (s), 1173 (m), 1097 (s), 1038 (s), 876 (m), 821 (m); δ_H ($CDCl_3$): 0.66 (1.5H, s), 0.91 (1.5H, d, J=6.8 Hz), 0.93 (1.5H, d, J=6.8 Hz), 0.99 (1.5H, s), 1.25–1.60 (3H, m), 1.66–1.86 (1H, m), 1.95–2.10 (1H, m), 2.21–2.45 (2H, m), 3.45–3.58 (2H, m), 3.80 (3H, s), 4.41 (1H, s), 4.43 (1H, s), 4.75 (1H, s-like), 4.81–4.84 (1H), 6.87 (2H, d, J=11 Hz), 7.24–7.27 (2H, m); GC–MS (same conditions as those used for **7**); t_R=18.25 min (43.1%), 18.40 min (55.9%) (total 99.0%); MS of **23** with t_R=18.25 min (70 eV, EI): m/z: 274 (<1) [M^+], 136 (13), 121 (100), 109 (9), 95 (4), 77 (5), 67 (3), 41 (3); MS of **23** with t_R=18.40 min (70 eV, EI): m/z: 229 (8), 121 (100), 109 (12), 77 (4), 41 (2). HRMS calcd for $C_{18}H_{26}O_2$: 274.1933, found: 274.1947 (short t_R), 274.1945 (long t_R).

4.24. 2-(1,2-Dimethyl-3-methylenecyclopentyl)ethanol (16)

DDQ (2.95 g, 13 mmol) was added portionwise over 8 min to a stirred and ice-cooled solution of **23** [*anti*/*syn*=66.5:31.2, 2.34 g (8.5 mmol)] in CH_2Cl_2 (70 mL) and water (7 mL) at 5–10 °C. The dark-colored mixture was stirred for 30 min at room temperature (22 °C). It was then diluted with $NaHCO_3$ solution, and extracted with Et_2O. The organic solution was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The dark-colored residue was chromatographed over SiO_2 (50 g). Elution with hexane/EtOAc (50:1–30:1) gave *p*-methoxybenzaldehyde (ca. 1 g). Further elution with hexane/EtOAc (20:1) gave 853 mg (65%) of **16** (rich in *anti*-**16**), which comprised of the following three fractions. The first (456 mg) of these was a mixture of *anti*-**16** and *syn*-**16** in a GC ratio of 81.3:15.4, n_D^{22}=1.4788; ν_{max} (film): 3227 (br m), 3073 (w), 2959 (s), 2938 (s), 2871 (m), 1655 (m), 1454 (m), 1379 (m), 1054 (m), 1037 (s), 1008 (m), 876 (s). The second one (278 mg) was a 56.3:38.4 mixture, and the third one (119 mg) was a 31.8:64.8 mixture. Comparison of the ^1H NMR spectra of these three fractions allowed the assignment of the data to each of the isomers. ^1H NMR data of *anti*-**16**: δ_H ($CDCl_3$): 0.95 (3H, d, J=7.6 Hz), 1.01 (3H, s), 1.16–1.21 (1H, br s), 1.30–1.40 (4H, m), 1.68–1.76 (1H, m), 2.24–2.44 (2H, m), 3.69 (2H, t, J=7.6 Hz), 4.77 (1H, m), 4.84 (1H, m); ^1H NMR data of *syn*-**16**; δ_H ($CDCl_3$): 0.69 (3H, s), 0.93 (3H, d, J=6.8 Hz), 1.18–1.30 (1H, br), 1.30–1.56 (4H, m), 1.68–1.83 (1H, m), 2.24–2.46 (2H, m), 3.66–3.80 (2H, m), 4.77 (1H, m), 4.86 (1H, m); GC–MS (same conditions as those used for **7**): t_R 8.38 (*anti*-**16**), 8.51 min (*syn*-**16**); MS of *anti*-**16** (70 eV, EI): m/z: 154 (1) [M^+], 139 (6), 121 (26), 110 (47), 109 (100), 108 (30), 107 (26), 95 (25), 93 (40), 81 (25), 79 (27), 67 (45), 55 (18), 53 (15), 41 (27); MS of *syn*-**16** (70 eV, EI): m/z: 154 (<1) [M^+], 139 (4), 121 (13), 110 (10), 109 (100), 108 (16), 107 (12), 95 (9), 93 (35), 81 (12), 79 (15), 67 (26), 55

(11), 41 (16). HRMS calcd for $C_{10}H_{18}O$: 154.1358, found: 154.1374 (*anti*-**16**), 154.1372 (*syn*-**16**).

4.25. (1,2-Dimethyl-3-methylenecyclopentyl)acetaldehyde (1)

*4.25.1. anti-Rich **1**.* Diacetoxyiodobenzene (DAIB, 1.13 g, 3.5 mmol) was added to a stirred solution of **16** (*anti*/*syn*=81.3:15.4, 411 mg, 2.7 mmol) and azadol (TCI, 30 mg, 0.2 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 45 min at room temperature (22 °C). The oxidation was slightly exothermic. Then the solution was washed with an aqueous solution of $NaHCO_3$ and $Na_2S_2O_3$. The CH_2Cl_2 layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic solution was dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc (50:1) gave 332 mg (82%) of *anti*-rich **1**, which was distilled to give 243 mg (69%) of *anti*-rich **1** (*anti*/*syn*=85.6:14.0) as a colorless oil, bp 70–72 °C/6 Torr; n_D^{23}=1.4708; ν_{max} (film): 3074 (w), 2959 (m), 2873 (m), 2731 (w), 1721 (s), 1655 (w), 1455 (w), 1382 (w), 881 (m). The following NMR data show signals due to *anti*-**1**. δ_H (400 MHz, C_6D_6): 0.70 (3H, d, *J*=7.6 Hz), 0.87 (3H, s), 1.06–1.15 (1H, m), 1.57–1.62 (1H, m), 1.68–1.73 (2H, m), 1.74–1.84 (1H, m), 2.02–2.26 (2H, m), 4.78 (1H, m), 4.85 (1H, m), 9.48 (1H, t, *J*=2.4 Hz); δ_C (100 MHz, C_6D_6): 12.06, 24.78, 28.95, 35.49, 43.29, 47.15, 50.39, 105.77, 155.77, 201.51; GC–MS (same conditions as those used for **7**): t_R 7.04 (85.6%, *anti*-**1**), 7.16 min (14.0%, *syn*-**1**); MS of *anti*-**1** (70 eV, EI): *m*/*z*: 152 (<1) [M^+], 137 (3), 134 (2), 123 (3), 119 (7), 109 (32), 108 (100), 95 (19), 93 (63), 92 (18), 81 (16), 79 (16), 77 (14), 67 (36), 55 (13), 53 (15), 41 (25). HRMS of *anti*-**1** calcd for $C_{10}H_{16}O$: 152.1201, found: 152.1212.

*4.25.2. syn-Rich **1**.* In the same manner, 1.67 g (10.9 mmol) of *syn*-rich **16** (*anti*/*syn*=2:3) was oxidized with azadol (60 mg, 0.4 mmol) and DAIB (4.70 g, 14.6 mmol) in CH_2Cl_2 (30 mL) to give 1.19 g (72%) of *syn*-rich **1** (*anti*/*syn*=38:0:61.6) as a colorless oil, bp 75–77 °C/7 Torr; n_D^{24}=1.4690; δ_H ($CDCl_3$): 0.83 (2H, s), 0.96 (3H, d, *J*=6.8 Hz), 1.19 (1H, s), 1.44–1.90 (3H, s), 2.00–2.20 (1H, m), 2.24–2.54 (3H, m), 4.80 (1H, m), 4.90 (1H, m), 9.84 (0.4H, m), 9.88 (0.6H, m); GC–MS (same conditions as those used for **7**): t_R 7.04 (38.0%), 7.18 min (61.6%); MS of *syn*-rich **1** (70 eV, EI): *m*/*z*: 152 (<1) [M^+], 119 (2), 109 (19), 108 (100), 93 (80), 91 (16), 79 (11), 77 (11), 67 (21), 55 (9), 53 (11), 41 (16). HRMS of *syn*-**1** calcd for $C_{10}H_{16}O$: 152.1201, found: 152.1215.

4.26. 2,3-Dimethyl-2-cyclopenten-1-ol (24)

A solution of **2** (3.30 g, 30 mmol) in dry Et_2O (10 mL) was added dropwise over 20 min to a stirred and ice-cooled suspension of $LiAlH_4$ (570 mg, 15 mmol) in dry Et_2O (30 mL) at 5–10 °C. The mixture was stirred for 2 h at 5–10 °C. Then excess $LiAlH_4$ was destroyed by the addition of water. The mixture was acidified with ice and dil. HCl/NH_4Cl solution, and extracted with Et_2O. The Et_2O solution was washed successively with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 3.66 g (quant) of crude **24** as an oil, ν_{max} (film): 3300 (br s), 2964 (s), 2914 (s), 2855 (s), 1684 (w), 1442 (m), 1380 (m), 1330 (m), 1182 (m), 1063 (s), 1029 (s), 993 (s).

4.27. 2,3-Dimethyl-2-cyclopentenyl acetate (25)

Acetic anhydride (10 mL) was added to a solution of crude **24** (3.60 g, 30 mmol) in dry C_5H_5N (25 mL). The mixture was stirred and heated at 40–50 °C for 2 h. Conventional work-up was followed by distillation to give 1.85 g (40% based on **2**, two steps) of **25** as a colorless oil, bp 60–63 °C/5 Torr; n_D^{21}=1.4602; ν_{max} (film): 2970 (m), 2917 (m), 2853 (m), 1735 (s), 1441 (m), 1371 (m), 1243 (s), 1015 (m), 990 (m), 968 (m), 876 (m); δ_H ($CDCl_3$): 1.94 (6H, s), 2.05 (2H, m), 2.09 (3H, s), 2.81 (2H, m), 6.01 (1H, br s). HRMS calcd for $C_9H_{14}O_2$: 154.0994, found: 154.1012.

4.28. 2-(1,2-Dimethyl-2-cyclopentenyl)acetic acid (26)

A solution of **25** (1.71 g, 11 mmol) in dry THF (5 mL) was added over 2 min to a stirred solution of LiN(*i*-Pr)$_2$ (TCI, 1.5 M in THF, PhEt and heptane, 8.7 mL, 13 mmol) at −78 °C under argon. Then TMSCl (1.5 mL=1.18 g, 11 mmol) was added in one portion to the stirred mixture at −78 °C. The mixture was stirred and heated at 65 °C for 2.5 h, and the reaction was quenched by adding MeOH (3 mL). The mixture was stirred for 10 min at room temperature (20 °C), and extracted with 5% NaOH solution (10 mL×3). The aqueous solution was washed with Et_2O, acidified with dil HCl, and extracted with Et_2O. The Et_2O solution was washed successively with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give 0.56 g (33%) of **26** as an oil, ν_{max} (film): 3040–2690 (br m), 2961 (m), 2934 (m), 1706 (s), 1442 (m), 1408 (m), 1312 (m), 1287 (m), 1235 (m); δ_H ($CDCl_3$): 1.13 (3H, s), 1.63 (3H, s), 1.66–1.78 (1H, m), 2.09–2.18 (1H, m), 2.18–2.26 (2H, m), 2.30 (1H, d, *J*=14 Hz), 2.39 (1H, d, *J*=14 Hz), 5.32 (1H, br s).

4.29. 2-(1,2-Dimethyl-2-cyclopentenyl)ethanol (27)

A solution of **26** (0.56 g, 3.6 mmol) in dry THF (2 mL) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (0.25 g, 6.5 mmol) in dry THF (8 mL). The mixture was stirred and heated under reflux for 1.5 h. After cooling, the mixture was acidified with ice and dil HCl, and extracted with Et_2O. The Et_2O extract was washed successively with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 0.35 g (69%) of **27** as a colorless oil, n_D^{22}=1.4738; ν_{max} (film): 3236 (br m), 3037 (w), 2952 (s), 2852 (s), 1655 (w), 1453 (m), 1378 (w), 1055 (m), 1012 (m), 797 (w); δ_H ($CDCl_3$): 1.02 (3H, s), 1.35–1.50 (1H, br), 1.62 (3H, d, *J*=2 Hz), 1.64–1.70 (2H, m), 1.85–1.90 (2H, m), 2.15–2.22 (2H, br m), 3.60–3.68 (2H, m), 5.28 (1H, d, *J*=2 Hz). HRMS calcd for $C_9H_{16}O$: 140.1201, found: 140.1201.

4.30. 2-(1,2-Dimethyl-2-cyclopentenyl)ethyl PMB ether (20) from 27

t-BuOK (366 mg, 3 mmol) and *p*-methoxybenzyl chloride (0.41 mL=470 mg, 3 mmol) were added to a solution of **27** (350 mg, 2.5 mmol) in dry THF (5 mL) and dry DMF (1 mL). The mixture was stirred and heated at 60 °C for 1 h. Work-up as reported for **19** in 4.19 gave 1.01 g of crude **20**, which was chromatographed over SiO_2 (8 g). Elution with hexane/EtOAc (50:1) afforded 596 mg (quant.) of **20** as a colorless oil. Its IR, ^1H NMR and MS spectra were identical with those of **20** obtained by ring-closing metathesis of **19** as described in 4.20.

Acknowledgements

I thank Mr. M. Kimura (President, Toyo Gosei Co., Ltd) and Mr. Y. Kimura (CEO, Toyo Gosei Co., Ltd) for their support. I am indebted to Dr. J. Tabata (National Agriculture and Food Research Organization, Tsukuba) for kindly sharing the structure **1** with me prior to publication, and also for carrying out the $AgNO_3/SiO_2$ chromatography and bioassay of (±)-**1**. Mr. Y. Shikichi and Ms. Y. Yamaguchi (Toyo Gosei Co., Ltd) are thanked for NMR and GC–MS measurements. Drs. T. Nakamura and Y. Hongo (RIKEN) kindly carried out the HRMS analyses. Dr. T. Tashiro (Niigata University of Pharmacy and Applied Life Sciences) and Mr. K. Kikusato (RIKEN) helped me in preparing the manuscript.

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