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Synthesis of both enantiomers of *cis*-α-irone and *cis*-γ-irone, principal constituents of iris oil, via resolution of (±)-2,2,4-trimethyl-3-cyclohexene-1-carboxylic acid

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Abstract

The principal constituents of iris oil, (−)-*cis*-α-irone and (−)-*cis*-γ-irone, and their enantiomers, were synthesized from (−)- and (+)-2,2,4-trimethyl-3-cyclohexene-1-carboxylic acids. The racemic acid was resolved by recrystallization of its salt with a chiral amine, or by enzymatic hydrolysis of the corresponding alcohol. The fragrances of (−)-(1*R*,5*S*)-*cis*-α-irone and (−)-(1*R*,5*S*)-*cis*-γ-irone were superior to those of (+)-(1*S*,5*R*)-*cis*-α-irone and (+)-(1*S*,5*R*)-*cis*-γ-irone.

1. Introduction

cis-α-Irone **1** and *cis*-γ-irone **2** are the principal constituents of iris rhizome which is an important perfume with its scent like violets (Fig. 1). Both enantiomers of these compounds exist in a variety of natural iris oils.[1] Although the olfactory activities of the enantiomers of chiral *cis*-irones were investigated by GC–sniff analysis[2] of the corresponding racemates separated with chiral stationary phases,[2,3] quite a few syntheses of single enantiomers of *cis*-irones have been reported to date.[4–6] However, comparison of the olfactory characteristics of the enantiomerically pure forms have not yet been examined. For this purpose, we planned to synthesize both enantiomers. Among the stereoselective syntheses of racemic *cis*-irones,[7–9] we took notice of (±)-2,2,4-trimethyl-3-cyclohexene-1-methanol [(±)-**3**],[10,11] a key intermediate of Nussbaumer and Fráter's method,[7] as an attractive substrate for resolution and total syntheses of our targets (Scheme 1). Here we describe the resolution of (±)-**3** and synthesis of both enantiomers of *cis*-α- and *cis*-γ-irones from homochiral **3**.

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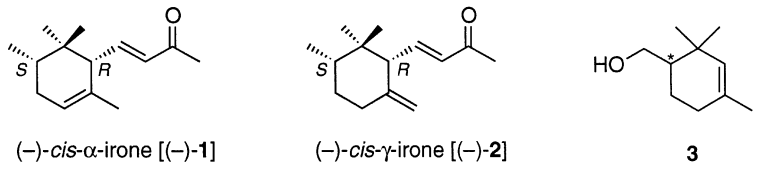
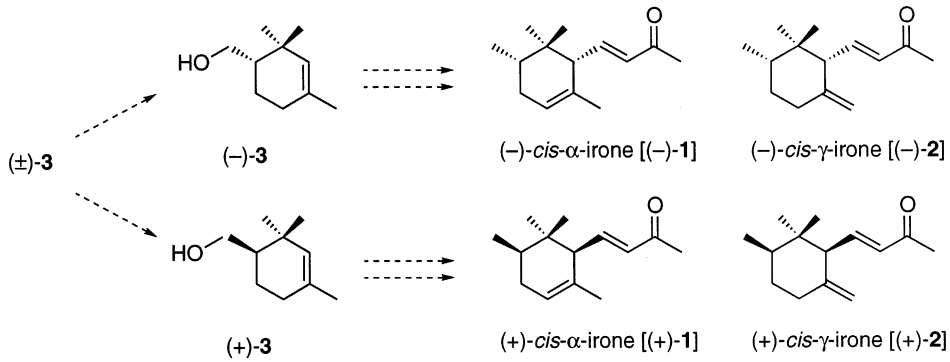


Figure 1.

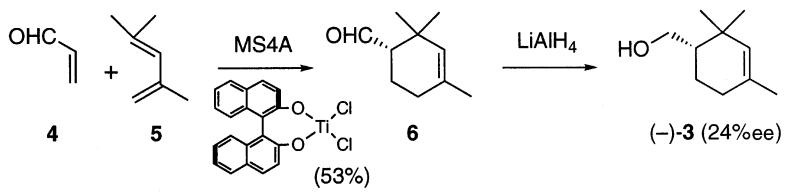


Scheme 1. Synthetic plan for enantiomerically pure irones

2. Results and discussion

2.1. Asymmetric Diels–Alder reaction

Jitkow and Bogert prepared (±)-**3** via a Diels–Alder reaction of 2,4-dimethyl-1,3-pentadiene **4** with acrolein **5**.[10] Therefore we first tried an application of this reaction under asymmetric conditions (Scheme 2).[12] Some asymmetric induction occurred in the presence of (*R*)-1,1′-binaphthoxydichlorotitanium[13] to give (–)-**6**,[11,14,15] however, the enantiomeric excess of (–)-**3** was only 24% ee.



Scheme 2. Asymmetric Diels–Alder reaction

2.2. Enzymatic reaction

Next we examined the resolution of (±)-**3** using hydrolytic enzymes.[16] Transesterification was carried out with vinyl acetate as an acyl donor. Table 1 summarizes the results of the enzyme

Table 1
Enzyme-catalyzed transesterification of alcohol (±)-**3**

Enzyme	Source	Time	Temp. (°C)	Acetate (**7**) yield % (% enantiomeric excess[a])		Alcohol (**3**) yield % (% enantiomeric excess)		*E* value[b]
Lipase PS-30 (Amano)	*Pseudomonas cepacia*	2 d	30	*S*	27 (43)	*R*	64 (22)	3.1
Lipase P (Amano)	*Pseudomonas cepacia*	9 h	30	*S*	19 (44)	*R*	72 (13)	2.9
Lipase P (Nagase)	*Pseudomonas* sp.	25 h	30	*S*	17 (44)	*R*	72 (11)	2.9
Lipase 2G (Nagase)	*Pseudomonas* sp.	16 h	30	*R*	71 (21)	*S*	21 (73)	3.0
Immobilized lipase (TOYOBO)	*Pseudomonas* sp.	2.5 h	20	*R*	47 (35)	*S*	53 (24)	2.6
Lipase, immobilized (Nacalai)	*Pseudomonas fluorescens*	8 d	20	*S*	17 (20)	*R*	71 (5)	1.6
CHIRAZYME® L-1, c.f., (Roche)	*Burkholderia cepacia*	2 h	5	*S*	13 (6)	*R*	71 (2)	1.1
CHIRAZYME® L-2, c.f., C2 (Roche)	*Candida antarctica*	2 h	5	*R*	16 (26)	*S*	73 (7)	1.8
Lipase MY (Meito)	*Candida cylindracea*	9 h	30	*S*	28 (12)	*R*	78 (2)	1.3
CHIRAZYME® L-9, c.f., C2 (Roche)	*Mucor miehei*	20 h	30	*S*	70 (21)	*R*	18 (**84**)	3.4
Rhilipase (Nagase)	*Rhizopus japonicus*	41 h	30	*S*	13 (38)	*R*	86 (4)	2.3
Pancreatin (Nacalai)	Porcine pancreas	8 d	20	*S*	20 (68)	*R*	76 (17)	6.2
PPL (SIGMA type II)	Porcine pancreas	3 d	20	*S*	39 (**79**)	*R*	59 (52)	**14**

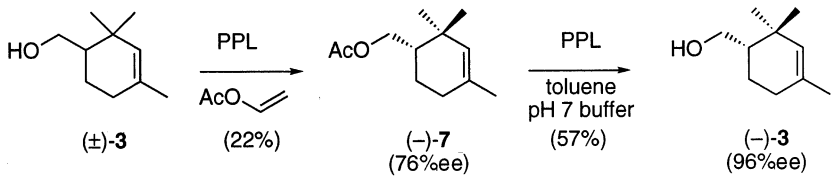
[a] Enantiomeric excesses (ee) were calculated from the specific rotation values of the enantiomerically pure samples: (+)-**3**, $[\alpha]_D^{24}$ +46 (*c* 1.6, $CHCl_3$); (+)-**7**, $[\alpha]_D^{22}$ +34 (*c* 1.6, $CHCl_3$).

[b] *E* values were calculated on the basis of the equation as follows: $E=\ln[ee_p(1-ee_s)/(ee_s+ee_p)]/\ln[ee_p(1+ee_s)/(ee_s+ee_p)]$, conversion $=ee_s/(ee_p+ee_s)$.

Table 2
Enzyme-catalyzed hydrolysis of acetate (±)-**7**

Enzyme	Source	Time	Temp. (°C)	Alcohol (**3**) yield % (% enantiomeric excess)[a]		Acetate (**7**) yield % (% enantiomeric excess)		*E* value
Lipase PS-30 (Amano)	*Pseudomonas cepacia*	1 d	30	*S*	6 (2)	*R*	88 (5)	1.1
Immobilized lipase (TOYOBO)	*Pseudomonas* sp.	7 d	20	*R*	16 (51)	*S*	56 (15)	3.6
Lipase 2G (Nagase)	*Pseudomonas* sp.	8 h	20	*R*	28 (26)	*S*	61 (9)	1.9
CHIRAZYME® L-9, c.f., C2 (Roche)	*Mucor miehei*	7 h	20	*S*	14 (17)	*R*	75 (3)	1.5
Pancreatin (Nacalai)	Porcine pancreas	8 h	20	*R*	25 (16)	*S*	61 (9)	1.5
PPL (SIGMA type II)	Porcine pancreas	2 d	20	*S*	30 (**89**)	*R*	50 (56)	**30**

[a] Enantiomeric excesses (ee) were calculated from the specific rotation values: see footnote a for Table 1.



Scheme 3. Enzymatic resolution of (±)-**3**

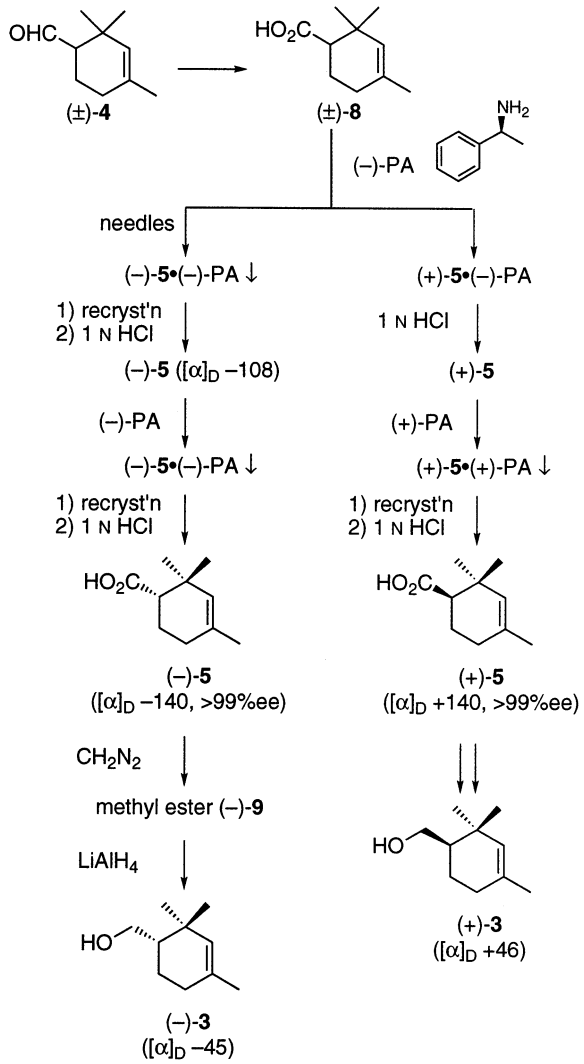
screening: PPL (Sigma), lipase 2G (Nagase) and CHIRAZYME® L-9 exhibited moderate selectivity. Table 2 also shows the results of hydrolysis of the corresponding acetate (±)-**7**[17] with pH 7 phosphate buffer. In this case, PPL (Sigma) selectively catalyzed the hydrolysis to give (–)-(*S*)-**3** (89% ee). To obtain the enantiomerically enriched compound, these reactions were combined: the transesterification of (±)-**3**, followed by the hydrolysis of the intermediary acetate (–)-**7** (76% ee) gave (–)-(*S*)-**3** (96% ee) (Scheme 3).

2.3. Resolution of chiral amine salt

Finally, resolution using a resolving agent was attempted. Esterification of (±)-**3** with chiral carboxylic acid, such as (*S*)-5-oxo-2-pyrrolidinecarboxylic acid, gave inseparable diastereomers, and therefore the resolution as the corresponding carboxylic acid (±)-**8** was examined. The aldehyde (±)-**4** was oxidized to give (±)-**8**.[18–20] The resolution pathway is summarized in Scheme 4. A solution of (±)-**8** in 2-propanol was treated with 1 equiv. of (–)-1-phenylethylamine [(–)-PA], and the resulting needles were recrystallized twice with 2-propanol to give (–)-**8**·(–)-PA salt. This was treated with 1N HCl to give (–)-**8** ($[\alpha]_D^{27}$ –108), which was treated again with (–)-PA, recrystallized and acidified to afford enantiomerically pure (–)-**8** ($[\alpha]_D^{22}$ –140). The other diastereomer (+)-**8**·(–)-PA remaining in solution was acidified to afford (+)-**8**, which was then treated with 1 equiv. of (+)-PA. The resulting needles (+)-**8**·(+)-PA were recrystallized from 2-propanol and acidified to give (+)-**8** ($[\alpha]_D^{23}$ +140). The enantiomeric purity of this (+)-**8** was determined by HPLC analysis (Chiralcel® OD) of the corresponding *p*-bromophenacyl ester to be >99% ee. Both enantiomers were treated with diazomethane to give **9**[18] {(–)-**9**, $[\alpha]_D^{22}$ –112 (*c* 1.00, $CHCl_3$); (+)-**9**, $[\alpha]_D^{22}$ +113 (*c* 1.20, $CHCl_3$)}, followed by reduction with $LiAlH_4$ to afford (–)-**3** {$[\alpha]_D^{27}$ –45 (*c* 1.2, $CHCl_3$); lit.,[11] $[\alpha]_D^{25}$ –37.5 (*c* 1.18, $CHCl_3$)} and (+)-**3**, respectively.

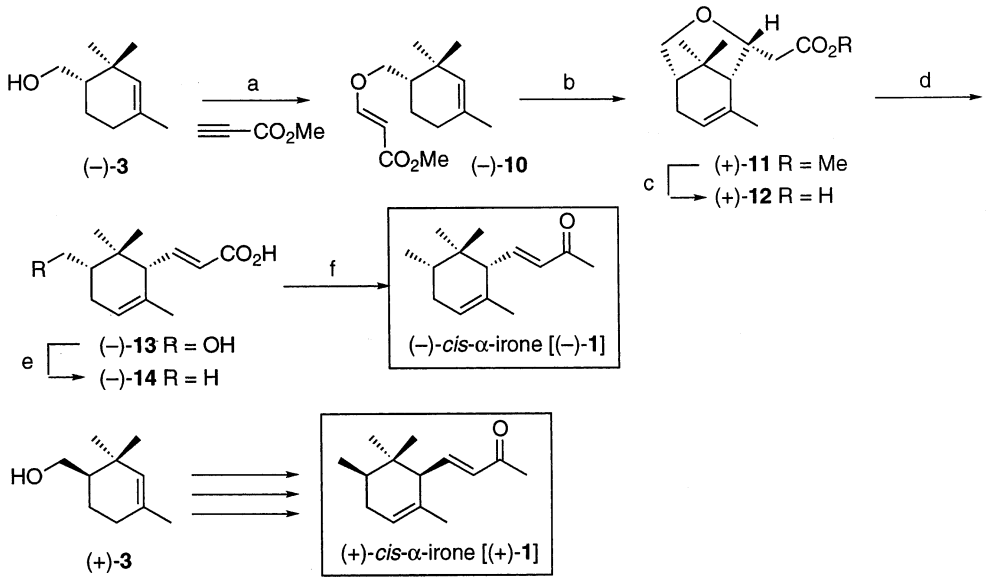
2.4. Synthesis of both enantiomers of cis-α*-irone and* cis-γ*-irone*

The next stage was the conversion of (–)- and (+)-**3** to homochiral *cis*-irones. The transformation to *cis*-α-irones was carried out according to the method reported by Nussbaumer and Fráter[7] (Scheme 5). Intramolecular ene reaction of the vinyl ether **10** derived from (–)-**3** gave cyclic ether (+)-**11**. After hydrolysis of the methyl ester, the resulting carboxylic acid (+)-**12** was treated with LDA to give (–)-**13**. The newly formed hydroxy group was removed by mesylation followed by reduction with zinc to afford (–)-**14**. Finally, the carboxy group was converted to methyl ketone with MeLi to give (–)-*cis*-α-irone {(–)-**1**, $[\alpha]_D^{24}$ –119 (*c* 0.925, $CHCl_3$)}. Similarly, (+)-**3** gave (+)-*cis*-α-irone {(+)-**1**, $[\alpha]_D^{19}$ +133 (*c* 1.42, $CHCl_3$); lit.,[21] $[\alpha]_D^{20}$ +109 (*c* 1.26, $CHCl_3$)}.

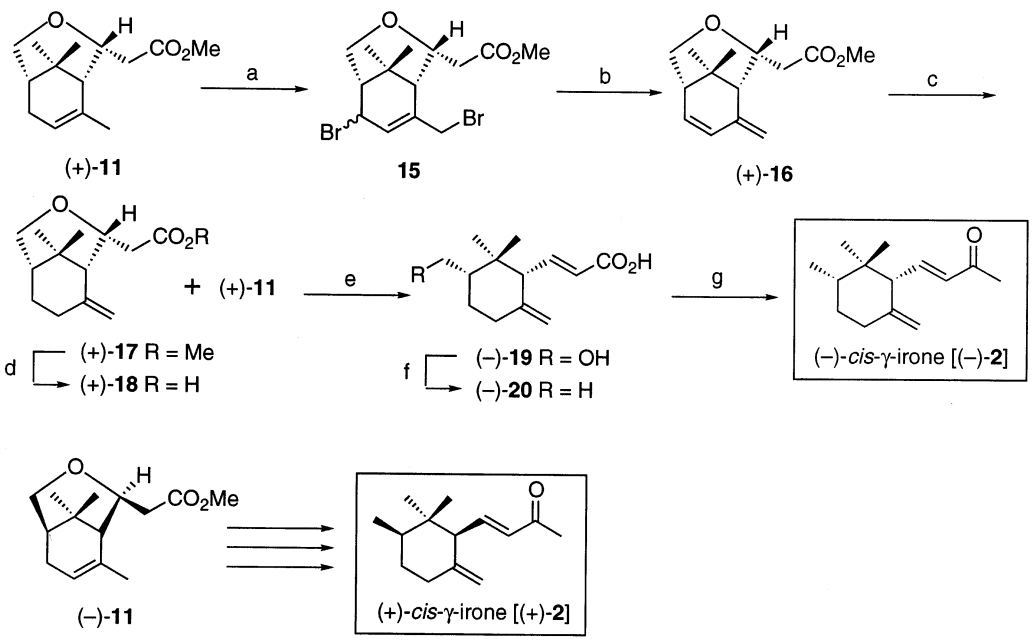


Scheme 4. Resolution using (–)- and (+)-1-phenylethylamines

As *cis*-γ-irones are the *exo* olefin isomers of *cis*-α-irones, we intended to prepare the corresponding *exo* isomers of **11**. Attempts of cyclization of **10** using other acids, such as $BF_3 \cdot OEt_2$ and HBr gave exclusively the *endo* isomers.[8] Thermal conditions over 270°C[8] gave the desired *exo* isomer **17**, however, the yield was low (<23%). Migration of the *endo* double bond of (+)-**11** by epoxidation followed by base-catalyzed cleavage also failed. Finally, the shift of the double bond was achieved in the following manner (Scheme 6). Bromination of (+)-**11** with *N*-bromosuccinimide (NBS) gave dibromide **15**, which was treated with zinc to afford diene (+)-**16**. Hydrogenation of the *endo* double bond was carried out using Adam's catalyst to give (+)-**17** together with (+)-**11**. Conversion of (+)-**17** to (–)-*cis*-γ-irone (–)-**2** was achieved by the known procedure as shown in Scheme 6.[8] (+)-*cis*-γ-Irone (+)-**2** was prepared from (+)-**3** in the same manner. Enantiomeric purity of (–)-**2** was determined by HPLC analysis (Chiralcel® OD)



Scheme 5. Synthesis of (–)- and (+)-α-irones. (a) *N*-Methylmorpholine, Et_2O (quant.). (b) Methanesulfonic acid (MsOH), Et_2O (67%). (c) NaOH, MeOH (quant.). (d) LDA, THF. (e) (i) MsCl, Py, CH_2Cl_2; (ii) Zn, NaI, DME, reflux [66% from (+)-**12**]. (f) MeLi, Et_2O (68%)



Scheme 6. Synthesis of (–)- and (+)-γ-irones. (a) NBS, $CHCl_3$. (b) Zn, DME, reflux [78% from (+)-**11**]. (c) H_2, PtO_2, MeOH [31% for (+)-**17**; 37% for (+)-**11**]. (d) NaOH, MeOH (quant.). (e) LDA, THF. (f) (i) MsCl, Py, CH_2Cl_2; (ii) Zn, NaI, DME, reflux [40% from (+)-**18**]. (g) MeLi, Et_2O (36%)

Table 3
Olfactory evaluation of both enantiomers of *cis*-α-irone and *cis*-γ-irone

Compound	Odor description
(+)-(1*S*,5*R*)-*cis*-α-Irone [(+)-**l**]	Green, light; weak
(−)-(1*R*,5S)-*cis*-α-Irone [(−)-**l**]	Single-floral, ionone-like
(+)-(1*S*,5*R*)-*cis*-γ-Irone [(+)-**2**]	Floral, green; weak
(−)-(1*R*,5*S*)-*cis*-γ-Irone [(−)-**2**]	Floral, sweet, ionone-like

to be >99% ee. Since the specific rotation value of chiral *cis*-γ-irone was small ($|[\alpha]_D|<2$), the absolute configuration of (−)-**2** was confirmed from the CD spectrum.[22]

2.5. Odors of both enantiomers of cis-α-irone and cis-γ-irone

The odors of the synthetic irones were tested, and the results are shown in Table 3. In both α- and γ-irones, the fragrances of (−)-(1*R*,5*S*)-isomers were superior to those of (+)-(1*S*,5*R*)-isomers. The (1*R*,5*S*)-configuration rather than the geometry of the double bond was important for the fragrant activity. These results were similar to those reported by Brenna et al.[2,5]

3. Conclusion

Synthesis of both enantiomers of *cis*-α-irone **1** and *cis*-γ-irone **2** in enantiomerically pure forms (>99% ee) was achieved via resolution of (±)-2,2,4-trimethyl-3-cyclohexene-1-carboxylic acid **5** using homochiral 1-phenylethylamine as a resolving agent. Enzyme-catalyzed resolution of the corresponding alcohol **3**, transesterification followed by hydrolysis with PPL, also gave (−)-**3** (96% ee). The fragrances of (−)-(1*R*,5*S*)-**1** and (−)-(1*R*,5*S*)-**2** were superior to those of (+)-(1*S*,5*R*)-**1** and (+)-(1*S*,5*R*)-**2**.

4. Experimental

4.1. General

Melting point values are uncorrected. Optical rotations were measured on HORIBA SEPA-300. CD spectrum was recorded on JASCO J-720WI. IR spectra were recorded on JASCO IR Report-100. ^{1}H and ^{13}C NMR spectra were recorded on Varian GEMINI 2000/300 (300 MHz for ^{1}H) and Varian Unity INOVA 500 (125 MHz for ^{13}C) in $CDCl_3$ using Me_4Si as an internal standard. Mass spectra were recorded on a Jeol JMS-700. HPLC analyses were done with a HITACHI L-6000 pump and an L-4200H UV–vis detector. Column chromatography was performed with Merck Silica gel 60, mesh size 0.063–0.200 mm. Preparative TLC plates (0.75 mm thickness) were made of Merck silica gel 60 PF_{254}.

4.2. (−)-(S)-2,2,4-Trimethyl-3-cyclohexene-1-carbaldehyde (−)-6: asymmetric Diels–Alder reaction

To a suspension of powdered MS4A (2.0 g) in dry toluene (10 ml) were added (+)-(*R*)-1,1′-bi-2-naphthol (100 mg, 0.35 mmol) and $TiCl_2(Oi\text{-}Pr)_2$ in toluene (0.88 M, 0.4 ml, 0.35 mmol). The resulting mixture was stirred at room temperature under N_2 for 1 h and then cooled to −70°C. Then acrolein (**4**, 0.5 ml, 7.5 mmol) followed by a solution of 2,4-dimethyl-1,3-pentadiene (**5**, 350 mg, 3.7 mmol) in dry toluene (1 ml) was added dropwise to the mixture. The resulting mixture was stirred at −70°C for 20 min and then warmed up to 5°C during 4 h. The reaction mixture was poured into aq. 5% $NaHCO_3$ soln (100 ml) and then filtered through a Celite pad. The filtrate was extracted with ether (50 ml×3) and washed with brine. The organic extract was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel (hexane:ethyl acetate = 10/1) to afford (−)-**6** (297 mg, 1.95 mmol, 53%) as a colorless oil. Spectra of this compound were identical with those reported,[11,14,15] $[\alpha]_D^{24}$ −16 (*c* 1.6, $CHCl_3$). This aldehyde **6** was reduced with $LiAlH_4$ (82 mg) in ether to give alcohol (−)-**3**. The enantiomeric excess was determined to be 24% ee from comparison of the specific rotation value {$[\alpha]_D^{23}$ −11 (*c* 1.5, $CHCl_3$)} with that of an enantiomerically pure sample.

4.3. General procedure of enzymatic transesterification of (±)-3

A suspension of (±)-**3** (200 mg, 1.3 mmol), vinyl acetate (3.7 ml), diisopropyl ether (25 ml), hexane (25 ml)) and enzyme (20–50 mg) was stirred vigorously. The reaction was monitored by TLC. The suspension was filtered through a Celite pad and the filtrate was concentrated in vacuo. Purification by silica gel column chromatography (hexane:ethyl acetate = 10/1–5/1) afforded acetate **7** and recovered **3**.

4.4. General procedure for enzymatic hydrolysis of (±)-7

A suspension of (±)-**7** (0.2 g, 1.0 mmol) and enzyme (20–50 mg) in toluene (0.5 ml) and 0.1 M phosphate buffer (pH 7.0, 4 ml) was stirred vigorously. The reaction was monitored by TLC. The suspension was filtered through a Celite pad. The filtrate was extracted with ether (20 ml×3) and washed with brine, dried over $MgSO_4$ and concentrated in vacuo. Purification by silica gel column chromatography (hexane:ethyl acetate = 10/1–5/1) afforded **3** and recovered **7**.

4.5. Resolution of (±)-8 with 1-phenylethylamine

Both (±)-**8** (12 g, 71 mmol) and (*S*)-(−)-1-phenylethylamine [(−)-PA, 8.6 g, 71 mmol] were dissolved in 2-propanol (100 ml) and the resulting precipitates were recrystallized three times with 2-propanol to afford (−)-**8**·(−)-PA. This salt was dissolved in ether and washed with 1N HCl three times. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo to give (−)-**8** as white plates, $[\alpha]_D^{27}$ −108 (*c* 1.70, $CHCl_3$). The enantiomeric purity was 75% ee by HPLC analysis of the corresponding *p*-bromophenacyl ester (Chiralcel® OD, 4.6×250 mm; hexane:2-propanol = 200/1, 0.5 ml/min; 254 nm; t_R = 59, 63 min). These plates were purified by repeating the same procedure as described above to give enantiomerically pure (−)-**8** (1.5 g, 8.8 mmol, 12%, >99% ee), $[\alpha]_D^{22}$ −140 (*c* 1.60, $CHCl_3$).

The enantiomer (+)-**8** was obtained from the mother liquor, and purified with the similar manner as for (−)-**8** using (+)-PA. (+)-**8** (2.0 g, 12 mmol, 17%, >99% ee); mp 58.9–59.9°C, $[\alpha]_D^{23}$ +140 (*c* 1.60, $CHCl_3$) {lit.,[20] $[\alpha]_D$ +52.8 (*c* 12.5, EtOH), ee unknown}.

4.6. (−)-(S)-2,2,4-Trimethyl-3-cyclohexene-1-methanol (−)-3

To a suspension of $LiAlH_4$ (350 mg, 9.1 mmol) in dry ether (30 ml) was added dropwise (−)-**9** (2.2 g, 12 mmol) in dry ether (12 ml) at 0°C. The resulting mixture was stirred under N_2 at room temperature for 20 min and quenched with EtOH, water and 1N HCl. The mixture was extracted with ether (50 ml×3), washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (hexane:ethyl acetate = 2/1) afforded (−)-**3** (1.90 g (12 mmol, quant.) as a colorless oil, $[\alpha]_D^{27}$ −45 (*c* 1.2, $CHCl_3$) {lit.,[11] $[\alpha]_D^{25}$ −37.5 (*c* 1.18, $CHCl_3$)}. The spectral data were identical with those reported.[11]

For (+)-**3**, $[\alpha]_D^{24}$ +46 (*c* 1.6, $CHCl_3$).

4.7. Methyl (1S,2R,5S)-(9,9-dimethyl-8-methylene-3-oxabicyclo[3.3.1]non-6-en-2-yl)acetate: (+)-16

To a solution of (+)-**11** (394 mg, 1.65 mmol) in $CHCl_3$ (20 ml) was added *N*-bromosuccinimide (619 mg, 3.48 mmol) and stirred at room temperature for 12 h. To the mixture was added additional *N*-bromosuccinimide (350 mg, 1.97 mmol) and stirred at room temperature for 5 h. The resulting mixture was poured into water and extracted with ether (50 ml×3). The organic layer was washed with brine and dried over $MgSO_4$. Then to this was added a small amount of cyclohexene to remove bromine. The resulting suspension was then filtered and concentrated in vacuo to give **15**. To a solution of this crude dibromide **15** in 1,2-dimethoxyethane (DME, 50 ml) was added zinc powder (7.9 g, 12 mmol) and the mixture was refluxed for 2 h. After being cooled to room temperature, the suspension was filtered through a Celite pad, and the remaining solid was washed with ether and water. The filtrate was extracted with ether (50 ml×3). The organic layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. Purification by silica gel column chromatography (hexane:ethyl acetate = 20/1–10/1) and preparative TLC (hexane:ethyl acetate = 5/1) afforded (+)-**16** [305 mg, 1.29 mmol, 78% from (+)-**11**] as a colorless oil; $[\alpha]_D^{23}$ +94 (*c* 1.5, $CHCl_3$). IR (film) ν_{max}: 3070, 3020, 2880, 1730, 1630, 1590, 1170, 1090, 1000, 890 cm^{-1}. ^1H NMR (300 MHz) δ: 0.95 (s, 3H), 1.26 (s, 3H), 1.8–1.9 (2H), 2.31 (dd, 1H, J = 5.4, 15.8 Hz), 2.46 (dd, 1H, J = 8.0, 15.9 Hz), 3.40 (dd, 1H, J = 1.4, 11.5 Hz), 3.68 (s, 3H), 4.07 (dd, 1H, J = 1.8, 11.4 Hz), 4.39 (ddd, 1H, J = 2.0, 5.6, 7.7 Hz), 4.69 (s, 1H), 5.09 (d, 1H, J = 1.9 Hz), 5.74 (dd, 1H, J = 6.7, 9.6 Hz), 6.34 (d, 1H, J = 9.6 Hz). ^{13}C NMR (125 MHz) δ: 24.2, 28.4, 32.6, 39.2, 41.5, 50.7, 51.6, 64.6, 70.6, 115.6, 129.3, 131.7, 142.6, 172.2. HREIMS m/z (M^+): calcd for $C_{14}H_{20}O_3$: 236.1412; found: 236.1414.

4.8. Methyl (1S,2R,5S)-(9,9-dimethyl-8-methylene-3-oxabicyclo[3.3.1]non-2-yl)acetate: (+)-17

A suspension of (+)-**16** (248 mg, 1.05 mmol) and $PtO_2 \cdot (H_2O)_{1-3}$ (0.04 g) in MeOH (20 ml) was stirred under H_2 at 27°C until 36 ml of H_2 (1.5 mmol) was absorbed. The resulting suspension was filtered through a Celite pad and the filtrate was concentrated in vacuo. Purification by silica gel column chromatography (hexane:ethyl acetate = 20/1) and preparative TLC (hexane:ethyl acetate = 5/1) afforded (+)-**17** {78 mg, 0.33 mmol, 31%; $[\alpha]_D^{24}$ +62 (*c* 1.6, $CHCl_3$)} and

(+)-**11** (98 mg, 0.39 mmol, 37%) as colorless oils. The spectral data were identical with those reported.[8]

4.9. HPLC analysis of cis-γ-irones

Column, Daicel Chiralcel® OD 4.6×250 mm; solvent, hexane:2-propanol = 500/1; flow rate, 1.0 ml/min; detect, 254 nm; $t_R = 8.4$ [(+)-**2**] and 10.0 [(−)-**2**] min.

4.10. CD spectrum of (+)-cis-γ-irone (+)-*2*

λ_{max} ($\Delta\varepsilon$) 329 (+0.08), 224 (+2.3), 210 (+1.9); 2.3 mmol/l in CH_3CN {lit.[22] λ_{max} ($\Delta\varepsilon$) 372 (+0.05), 354 (+0.15), 340 (+0.22), 326 (+0.21), 315 (+0.15), 223 (+3.86); 5.2 mmol/l in CH_3CN}.

4.11. Optical rotation values of other compounds reported as racemates[7,8]

Compound (−)-**10**, $[\alpha]_D^{24}$ −18 (*c* 1.8, $CHCl_3$); (+)-**11**, $[\alpha]_D^{23}$ +31 (*c* 1.8, $CHCl_3$); (−)-**14**, $[\alpha]_D^{24}$ −114 (*c* 3.28, $CHCl_3$); (−)-**20**, $[\alpha]_D^{20}$ −10 (*c* 1.4, $CHCl_3$).

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