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Asymmetric cyclization–carbonylation of 2-alkyl-2-propargylcyclohexane-1,3-diones: facile access to optically active hydrindanes

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Abstract

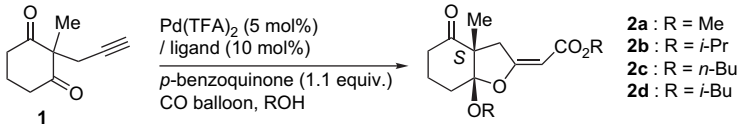
Oxidative cyclization–carbonylation of 2-alkyl-2-propargylcyclohexane-1,3-diones mediated by $Pd(TFA)_2$/2,2′-isopropylidenebis[(4*R*)-4-(3,4-dimethoxyphenyl)-2-oxazoline] **28** afforded bicyclic-β-alkoxyacrylates in 51–74% yields with 72–82% ee. The products containing quaternary carbon were converted to optically active hydrindanes **33**.

Keywords: Palladium; Bisoxazoline; Asymmetric; Wacker-type cyclization; Carbonylation; Hydrindane

1. Introduction

Palladium(II)-catalyzed reactions are of fundamental importance in the area of organic transformations.[1] Compared with the impressive development of Pd(II)-catalyzed oxidative asymmetric reactions of alkenes,[2] those of alkynes have received scant attention.[3] We previously reported the first examples of asymmetric cyclization–carbonylation of *meso*-2-alkyl-2-propargylcyclohexane-1,3-diol[3a,c] and 2-methyl-2-propargylcyclohexane-1,3-dione[3b] catalyzed by Pd(II) with chiral bisoxazoline (box) ligands. In this paper, we report the screening of several types of box ligand for the latter reaction (Scheme 1); the ligand 2,2′-isopropylidenebis[(4*R*)-4-(3,4-dimethoxyphenyl)-2-oxazoline] (**28**) was found to be the most effective.

Many biologically important natural products, such as chiloscyphones,[4a] acutifolone A,[4b] pinguisenes,[4c] and bakkenolides,[4d] contain a highly functionalized bicyclo[4.3.0]nonane framework with a substituent at one of the ring junctions. We also report the synthesis of **33**, which contains a bicyclo[4.3.0]-nonane framework with a quaternary carbon junction.



Scheme 1.

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2. Results and discussion

2.1. Cyclization–carbonylation of *1*: screening of ligands[5]

As shown in Table 1 (entry 1), asymmetric cyclization–methoxycarbonylation of 2-methyl-2-propargylcyclohexane-1,3-dione **1** in the presence of $Pd(CF_3CO_2)_2$, ligand **3**, and *p*-benzoquinone in methanol at −30 °C under a carbon monoxide atmosphere (balloon) afforded 8% ee of *cis*-**2a** as a single diastereomer in 90% yield. The bulkiness of the alcohol used in the reaction affected the yield and enantioselectivity of the products **2**, as shown in entries 2–4. The use of bulkier alcohols resulted in the formation of the corresponding products with greater enantiomeric excess (*n*-BuOH 27% ee<*i*-PrOH 33% ee<*i*-BuOH 43% ee). In order to evaluate the influence of substituents at the C4 positions of the bisoxazoline rings, we tested a further three box ligands **4**–**6**, and found that none of these were effective; only ligand **3** (R=Ph) was effective, giving a 43% ee of bicyclic-β-alkoxyacrylate **2d** in 48% yield (Table 1, entries 4–7; Scheme 1). Based on the above results, further ligand screening was performed using box ligands with aromatic substituents at the C4 positions of the oxazoline rings, with *i*-BuOH as a solvent. We first examined variations in the spacer between the two rings, using one or two carbon atoms (**7** and **8**), a pyridine ring (**9** and **10**), a binaphthyl skeleton (**11**), and a cyclohexane ring (**12** and **13**) (entries 8–14). Among these, the cyclohexane-linked box ligand **12** gave the best result (entry 13). Phosphine-based ligands seemed to be ineffective for reactions of this type;[3a,c] a palladium complex of (*S*)-BINAP **14** and bis(phosphino)ferrocene complexes **15** did not show any catalytic activity, and the use of **16** and **17** gave racemic **2a** in 10–13% yield (Fig. 1).

Table 1
Cyclization–carbonylation of **1**: ligand screening (Scheme 1 and Fig. 1)[a]

Entry	Ligand	Conditions	Product	ROH (solvent)	Yield (%)	% ee (config.)[b]
1	**3**	−30 °C, 24 h	**2a**	MeOH	90	8 (*R*)
2	**3**	0–10 °C, 20 h	**2b**	*i*-PrOH	54	33 (*S*)
3	**3**	0 °C, 23 h	**2c**	*n*-BuOH	62	27 (*S*)
4	**3**	0 °C, 20 h	**2d**	*i*-BuOH	48	43 (*S*)
5	**4**	0 °C, 23 h	**2d**	*i*-BuOH	25	31 (*S*)
6	**5**	0 °C to rt, 26 h	**2d**	*i*-BuOH	47	0 (–)
7	**6**	0 °C, 48 h	**2d**	*i*-BuOH	N.R.	—
8	**7**	0 °C, 48 h	**2d**	*i*-BuOH	25	29 (*R*)
9	**8**	0 °C to rt, 23 h	**2d**	*i*-BuOH	21	3 (*R*)
10	**9**	0 °C to rt, 24 h	**2d**	*i*-BuOH	42	19 (*R*)
11	**10**	0 °C to rt, 24 h	**2d**	*i*-BuOH	40	24 (*S*)
12	**11**	0 °C, 23 h	**2d**	*i*-BuOH	36	6 (*R*)
13	**12**	0 °C, 22 h	**2d**	*i*-BuOH	54	59 (*R*)
14	**13**	rt, 72 h	**2d**	*i*-BuOH	27	11 (*R*)
15	**18**	0 °C, 72 h	**2d**	*i*-BuOH	74	18 (*S*)
16	**19**	0 °C, 45 h	**2d**	*i*-BuOH	53	28 (*R*)
17	**20**	0 °C, 24 h	**2d**	*i*-BuOH	76	50 (*S*)
18	**21**	−20 °C, 72 h	**2d**	*i*-BuOH	52	48 (*S*)
19	**22**	0 °C, 72 h	**2d**	*i*-BuOH	41	6 (*S*)
20	**23**	0 °C, 24 h	**2d**	*i*-BuOH	59	52 (*S*)
21	**24**	0 °C, 24 h	**2d**	*i*-BuOH	73	42 (*R*)
22	**25**	0 °C, 24 h	**2d**	*i*-BuOH	77	48 (*R*)
23	**26**	0 °C, 24 h	**2d**	*i*-BuOH	81	5 (*R*)
24	**27**	0 °C, 12 h	**2d**	*i*-BuOH	78	51 (*R*)
25	**28**	0 °C, 20 h	**2d**	*i*-BuOH	71	69 (*R*)
26	**28**	−20 °C, 48 h	**2d**	*i*-BuOH	74	76 (*R*)

[a] All reactions were performed using 5 mol % of $Pd(TFA)_2$ and 10 mol % of ligand in ROH.
[b] Absolute configuration of quaternary carbon bearing a methyl group.

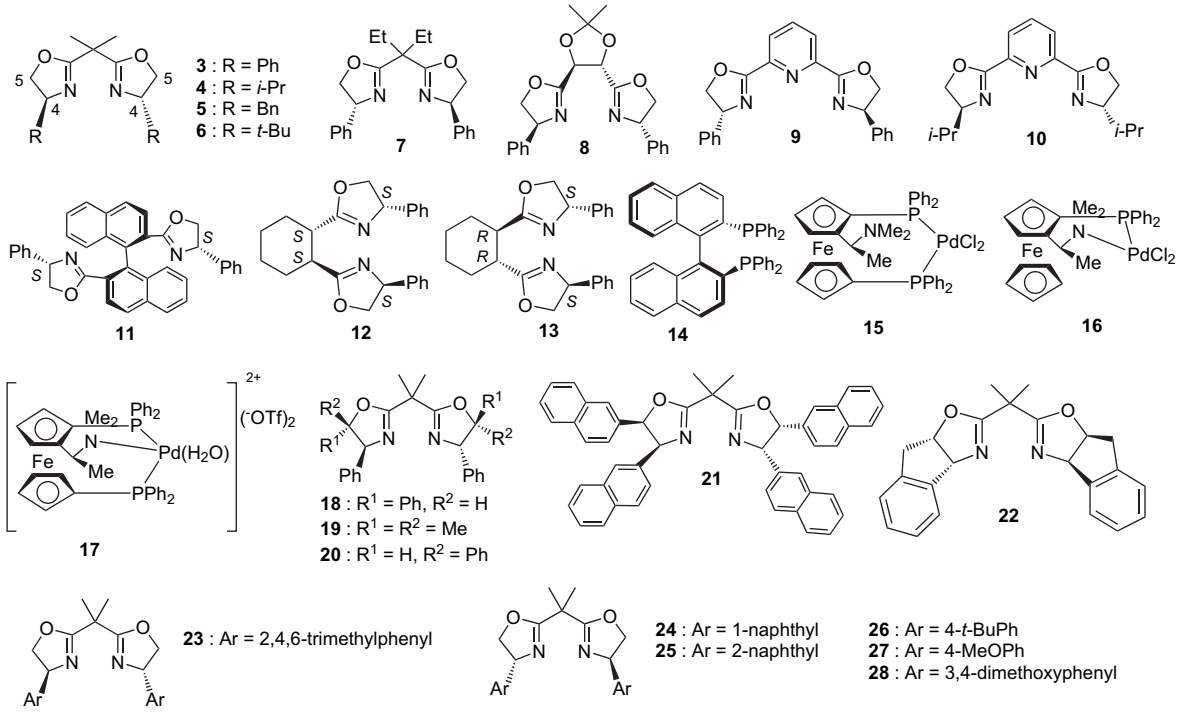


Figure 1. Screening of ligands.

We next examined the influence of the substituents at the C5 positions of the bisoxazoline rings (Table 1, entries 15–19; Scheme 1). Although the presence of *trans*-phenyl groups (**18**) and dimethyl groups (**19**) at the C5 position resulted in reduced enantioselectivity (entries 15 and 16), the results were improved slightly by the use of ligands **20** and **21**, bearing *cis*-phenyl groups at the C5 position, or 2-naphthyl groups at the C4 and C5 positions (entries 17 and 18). Ligand **22**, which contains phenyl groups fixed to the oxazoline rings in parallel at the C4 and C5 positions, showed poor selectivity (entry 19).

Next, the use of various aromatic substituents at the C4 position of the bisoxazoline ring was investigated (Table 1, entries 20–26; Scheme 1). Replacement of the phenyl group of **3** with mesityl, 1-naphthyl or 2-naphthyl groups resulted in increased yields, and except for 1-naphthyl, slightly increased selectivities (entries 20–22) were observed. However, the use of **26** bearing the bulky *tert*-butyl group resulted in reduced enantioselectivity (entry 23), while ligands **27** and **28**, with methoxy groups attached to the phenyl group, caused improvements in enantioselectivity (entries 24–26). Ligand **28** showed the best results, giving the product in 74% yield with 76% ee.

2.2. Cyclization–carbonylation of *1*: effect of additives

From the results of entries 1–4 in Table 1 (solvent effect), it was suggested that hemiacetal formation plays an important role in the present reaction. Thus the effects of various Lewis acid additives on the cyclization–carbonylation reaction were examined, and the results are shown in Table 2 (Scheme 1). In all cases, the addition of a Lewis acid resulted in an improved yield. The use of $Sn(OTf)_2$, $Cu(OTf)_2$, and $In(OTf)_3$ reduced enantioselectivity in the reaction (entries 1–3), whereas $ZnCl_2$, Me_2SnCl_2, and $InCl_3$ caused a little loss of enantioselectivity (entries 4–8). In an attempt to rationalize the different effects of $In(OTf)_3$ and $InCl_3$, we carried out ^1H NMR studies of a mixture of **3** (2 equiv), $Pd(TFA)_2$ (1 equiv), and additives ($In(OTf)_3$ or $InCl_3$; 1 equiv) in CD_2Cl_2 at room temperature. The mixture containing $In(OTf)_3$ gave a complex spectrum whose signals could not be assigned; this was thought to result from decomposition of the complex [$Pd(TFA)_2$-**3**]. In the case of $InCl_3$, however, the signals corresponding to [$Pd(TFA)_2$-**3**] disappeared and signals due to [$PdCl_2$-**3**] appeared, presumably due to replacement of triflate with chloride. The resulting ^1H NMR spectrum was identical to that previously reported for [$PdCl_2$-**3**]. When the present reaction was performed in the presence of [$PdCl_2$-**3**], a similar result (yield and ee) to that using [$Pd(TFA)_2$-**3**] was obtained.[6] Eventually, the addition of a Lewis acid ($ZnCl_2$, Me_2SnCl_2, and $InCl_3$) resulted in an improved yield with a little loss of enantioselectivity.

Table 2
Cyclization–carbonylation of **1**: effect of additives (Scheme 1)[a]

Entry	Additive (5 mol %)	Ligand	Conditions	Yield (%) of **2d**	% ee (config.)[b]
1	$Sn(OTf)_2$	**3**	0 °C, 39 h	81	17 (*S*)
2	$Cu(OTf)_2$	**3**	0 °C, 12 h	71	25 (*S*)
3	$In(OTf)_3$	**3**	0 °C, 16 h	70	15 (*S*)
4	$ZnCl_2$	**3**	0 °C, 17 h	77	40 (*S*)
5	Me_2SnCl_2	**3**	0 °C, 41 h	78	43 (*S*)
6	$InCl_3$	**3**	0 °C, 21 h	80	42 (*S*)
7	$ZnCl_2$	**28**	−20 °C, 43 h	81	73 (*S*)
8	Me_2SnCl_2	**28**	−20 °C, 22 h	81	75 (*S*)

[a] All reactions were performed using 5 mol % of $Pd(TFA)_2$ and 10 mol % of ligand in *i*-BuOH.
[b] Absolute configuration of quaternary carbon bearing a methyl group.

2.3. Cyclization–carbonylation of *1* and *29–32*: synthesis of optically active hydrindanes *33*

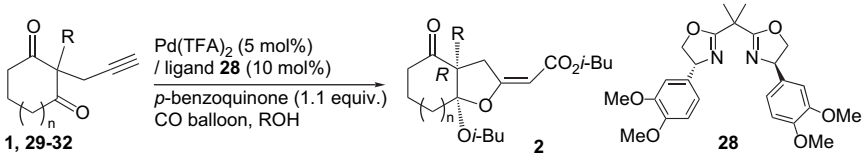
Next, we investigated the reaction of **1** and **29–32**, which are analogs of **1** bearing propyl, allyl, and propargyl groups and with various values of *n*, using ligand **28** (Table 3 and Scheme 2). Replacement of the methyl group with a propyl group (entry 2) resulted in a slight decrease in selectivity, but the presence of an allyl or propargyl group (entries 3–5) increased the selectivity. In the case of the bis-propargyl substrate **31**, the reaction proceeded slowly, and the product was obtained in 51% yield with the aid of an additive (entries 4 and 5). The reaction of cycloheptane derivative **32** gave **2h** in moderate yield with 82% ee (entry 6).

The relative stereochemistry of product **2a** was determined by X-ray crystallographic analysis.[3b] The absolute stereochemistry of products **2d** and **2e** was determined by conversion to hydrindanes **33d** and **33e**: Wittig reactions of **2d** and **2e** followed by acid hydrolysis afforded the corresponding β-ketoesters, which were subjected to Knoevenagel condensation to give the corresponding hydrindanes. The authentic hydrindanes *ent*-**33d** and *ent*-**33e** were prepared from known

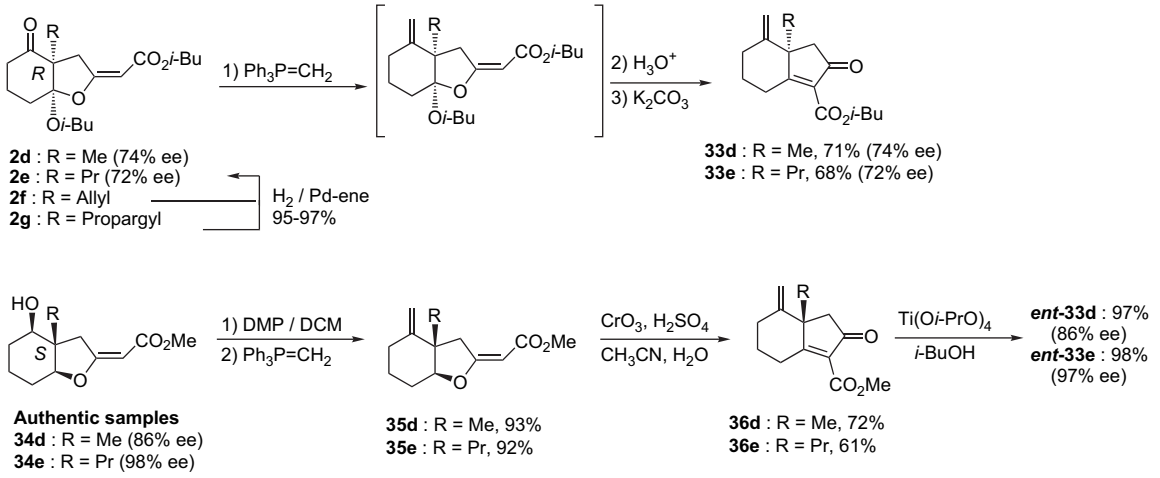
Table 3
Cyclization–carbonylation of **1** using ligand **28** (Scheme 2)

Entry	Substrate	*n*	R	Conditions	Product	Yield (%)	% ee (config.)[a]
1	**1d**	1	Me	−20 °C, 2 days	**2d**	74	76 (*R*)
2	**29**	1	Propyl	−30 °C, 2.2 days	**2e**	57	72 (*R*)
3	**30**	1	Allyl	−20 to 0 °C, 4.5 days	**2f**	60	82 (*R*)
4	**31**	1	Propargyl	−20 °C, 4 days	**2g**	28	80 (*R*)
5[b]	**31**	1	Propargyl	−15 to −10 °C, 6 days	**2g**	51	82 (*R*)
6	**32**	2	Me	−30 to −15 °C, 1.7 days	**2h**	52	82 (*R*)

[a] Absolute configuration of quaternary carbon bearing an R group.
[b] 5 mol % of $InCl_3$ was added.



Scheme 2.

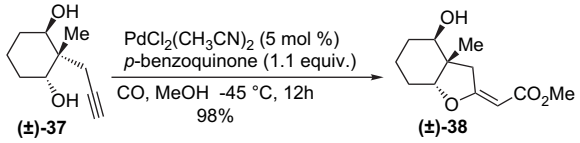


Scheme 3.

alcohols **34d** and **34e**[3c] via oxidation of the alcohols followed by Wittig reaction to give **35d** and **35e**, which were treated with Jones reagent to give hydrindanes **36d** and **36e**, followed by ester exchange reactions. The absolute stereochemistry of products **2f** and **2g** was determined by conversion to **2e**, and the absolute stereochemistry of product **2h** was estimated by a modified Mosher's method[7] after conversion to the MTPA ester of the corresponding secondary alcohol (Scheme 3).

2.4. Plausible mechanism

The obtained experimental results were analyzed in order to elucidate the mechanism of the cyclization–carbonylation reaction. A possible mechanism is proposed in Scheme 4 based on the following points. (I) The bulkiness of the alcohols used in the reaction affected the enantioselectivities and yields of **2**, as shown in Table 1 (entries 1–4), which suggests that the alcohol is incorporated into the substrate as a hemiacetal before cyclization. (II) We previously reported that the cyclization–carbonylation reaction of 2-propargylcyclohexane-1,3-diol (±)-**37** afforded the product (±)-**38** in 98% yield as a single diastereomer (Scheme 5).[3a] This result suggests that the hydroxyl group with a cis-relationship to the propargyl group was more reactive than the trans hydroxyl group. At first, two types of hemiacetal intermediate, with hydroxyl groups that are either trans or cis

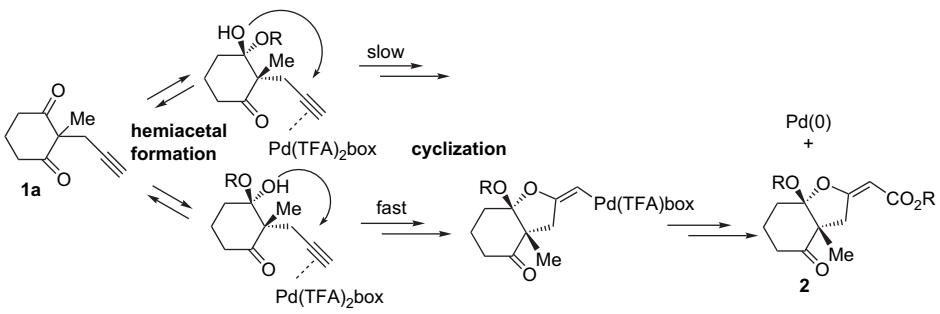


Scheme 5.

with respect to the propargyl group, should be produced. Coordination of the alkyne to Pd(II) may be induced by an attack by the cis hydroxyl group, producing a vinyl palladium intermediate, followed by CO insertion, and subsequent reaction with ROH to provide *cis*-**2** as a single diastereomer (Scheme 4). (III) Addition of a Lewis acid generally improved the yield, which means that hemiacetal formation may be accelerated by such additives (Table 2). Although some Lewis acid additives caused a decrease in enantioselectivity, selectivity was not affected by the addition of Me_2SnCl_2 or $InCl_3$. These results suggest that the asymmetric induction step seems to be cyclization.

3. Conclusion

Oxidative cyclization–carbonylation of 2-alkyl-2-propargylcyclohexane-1,3-diones mediated by $Pd(TFA)_2$/2,2′-isopropylidenebis[(4*R*)-4-(3,4-dimethoxyphenyl)-2-oxazoline] **28**



Scheme 4.

afforded bicyclic-β-alkoxyacrylates in 51–74% yield with 72–82% ee. The products containing quaternary carbons were converted to optically active hydrindanes. The present reaction offers facile access to optically active hydrindanes. Investigation of further synthetic application of this method is now in progress.

4. Experimental section

4.1. General experimental methods

All melting points were measured on a Yanaco MP-3S micromelting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR, COSY, HMQC, and HMBC spectra were recorded on JEOL AL 400 and JEOL Lambda 500 spectrometers in $CDCl_3$ with Me_4Si as an internal reference. In the case of acetone-d_6, solvent peak was used as a reference (δ 2.04 for ^{1}H and δ 29.8 for ^{13}C). High-resolution mass spectra (HRMS) and the fast atom bombardment mass spectra (FABMS) were obtained with a JEOL GC mate II, a JMS-SX102, and a JEOL JMS 600 H spectrometers. IR spectra were recorded with a JASCO FT/IR-300 spectrometer. All reagents were purchased from commercial sources and used without purification. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed. The substrates **1** and **29**–**32** were known compounds.[3c,8,9]

4.2. Preparation of *23* and *28*

Ligands **23** and **28** were prepared from (2*S*)-2-amino-2-(2,4,6-trimethyphenyl)ethan-1-ol[10b] and (2*R*)-2-amino-2-(3,4-dimethoxyphenyl)ethan-1-ol[10a] according to the reported procedure.[3c]

4.2.1. (4*S*,4′*S*)-2,2′-(1-Methylethylidene)bis[4,5-dihydro-4-(2,4,6-trimethyphenyl)]oxazole (*23*)

Colorless amorphous, $[\alpha]_D^{29}$ −115.2 (*c* 0.545, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.63 (6H, s), 2.24 (6H, s), 2.30 (12H, s), 4.12 (2H, dd, *J*=8.4, 10.4 Hz), 4.63 (2H, dd, *J*=8.4, 11.2 Hz), 5.65 (2H, t, *J*=11.2 Hz), 6.82 (4H, s); ^{13}C NMR ($CDCl_3$) δ 20.6, 20.7, 23.9, 38.9, 66.1, 72.3, 130.2, 133.0, 137.0, 168.8; IR (KBr) 1659, 1475, 1111 cm^{-1}; HRMS-EI *m/z*: [M$^+$] calcd for $C_{27}H_{34}N_2O_2$ 418.2620; found 418.2629.

4.2.2. (4*R*,4′*R*)-2,2′-(1-Methylethylidene)bis[4,5-dihydro-4-(3,4-dimethoxyphenyl)]oxazole (*28*)

Colorless needles, mp 129–130 °C (hexane), $[\alpha]_D^{25}$ +173.8 (*c* 0.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.68 (6H, s), 3.78 (6H, s), 3.85 (6H, s), 4.15 (2H, t, *J*=7.4 Hz), 4.62 (2H, t, *J*=10.0 Hz), 5.17 (2H, dd, *J*=10.0, 7.4 Hz), 6.80 (6H, s); ^{13}C NMR ($CDCl_3$) δ 24.5, 39.0, 55.7, 56.0, 69.3, 75.6, 110.0, 111.2, 118.9, 135.2, 148.6, 149.3, 170.2; IR (KBr) 1664, 1519, 1256 cm^{-1}; HRMS-EI *m/z*: [M$^+$] calcd for $C_{25}H_{30}N_2O_6$ 454.2104; found 454.2103.

4.3. General procedure for the cyclization–carbonylation of *1* and *29*–*32*

A 30 mL two-necked round-bottomed flask, containing a magnetic stirring bar, $Pd(TFA)_2$ (0.015 mmol), ligand (0.03 mmol), *p*-benzoquinone (0.33 mmol), and ROH (3–4 mL), was fitted with a rubber septum and a three-way stopcock connected to a balloon filled with carbon monoxide. (In some cases, the mixture of $Pd(TFA)_2$ and ligand was sonicated in ROH for 1–5 min before adding *p*-benzoquinone.) The apparatus was purged with carbon monoxide by pumping–filling via the three-way stopcock. The substrate (0.3 mmol) dissolved in ROH (3×1 mL) was added dropwise to the stirred mixture via a syringe at −40 °C. After being stirred for the period of time at appropriate temperature, the mixture was diluted with CH_2Cl_2 (30 mL), washed with 5% NaOH aq (40 mL), and dried over $MgSO_4$. The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (30 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/ethyl acetate (100/1 to 50/1) afforded **2**. Enantiomeric excess was determined by HPLC analysis.

4.3.1. Methyl (2E)-[(3aR,7aS)-hexahydro-7a-methoxy-3a-methyl-4-oxo-2(3H)-benzofuranylidene]acetate (*2a*)

Colorless needles, mp 75–76 °C (hexane), $[\alpha]_D^{25}$ −7.5 (*c* 1.3, $CHCl_3$); 7.5% ee (Chiralcel OD, hexane/EtOH=30/1, 1 mL/min, t_R=10 min, 12 min); ^{1}H NMR (CD_3COCD_3) δ 1.26 (3H, s), 1.42–1.55 (1H, m), 1.94–2.05 (2H, m), 2.21–2.27 (1H, m), 2.55–2.60 (1H, m), 2.60 (1H, dd, *J*=2.4, 17.6 Hz), 2.70 (1H, dt, *J*=14.4, 5.6 Hz), 3.32 (3H, s), 3.60 (3H, s), 4.02 (1H, br d, *J*=17.6 Hz), 5.22 (1H, dd, *J*=2.4, 1.6 Hz); ^{13}C NMR (CD_3COCD_3) δ 18.0, 19.9, 26.7, 37.6, 38.3, 49.9, 50.8, 58.8, 92.6, 113.0, 168.2, 173.7, 209.6; IR (KBr) 1720, 1655, 1136 cm^{-1}; FABMS *m/z*: 255 (M$^+$+H). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found: C, 61.27; H, 7.21; X-ray crystallographic analysis (Fig. 2): X-ray diffraction data for **2a** were collected on a Rigaku AFC-7R four-circle diffractometer equipped with a graphite crystal and incident beam monochromator using Mo Kα radiation (λ=0.71073 Å) at room

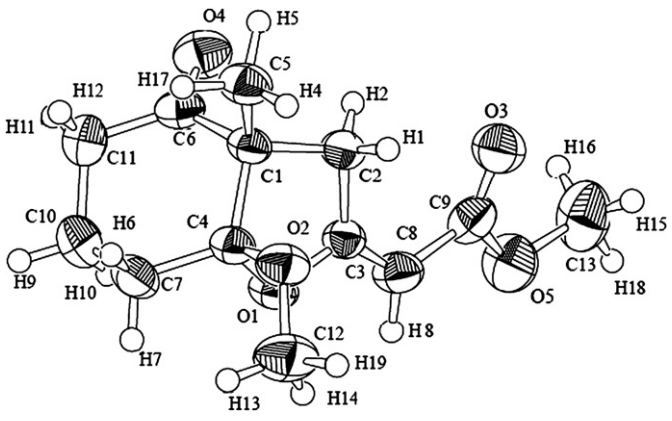


Figure 2. X-ray structure of **2a**.

temperature. The structures were solved by direct method[11] and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. The unit cell contains two crystallographically independent molecules. Crystallographic parameters: $C_{13}H_{18}O_5$, M_W=254.28, monoclinic, space group $P2_1/n$, with unit cell a=7.836(2) Å, b=24.352(3) Å, c=7.818(1) Å, β=116.74(1) and V=1332.4(4) Å^3. Z=4, D_{calcd}=1.268 g cm^{-3}, $R1(I>2\sigma(I))$=0.042, $wR2$=0.151, refinement using 3063 reflections with $F^2>-10.0\sigma(F^2)$, 236 parameters refined on F^2. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 206137.

*4.3.2. 1-Methylethyl (2E)-[(3aS,7aR)-hexahydro-3a-methyl-7a-(1-methylethoxy)-4-oxo-2(3H)-benzofuranylidene]acetate (**2b**)*

Colorless oil, $[\alpha]_D^{24}$ +35.0 (*c* 1.0, $CHCl_3$); 33% ee (Chiralcel OC, hexane/EtOH=100/1, 1 mL/min, t_R=12 min, 15 min); ^{1}H NMR (CD_3COCD_3) δ 1.04 (3H, d, J=6.2 Hz), 1.16 (3H, d, J=6.0 Hz), 1.19 (3H, d, J=6.2 Hz), 1.19 (3H, d, J=6.2 Hz), 1.25 (3H, s), 1.45–1.55 (1H, m), 2.20–2.26 (2H, m), 2.23 (1H, m), 2.56–2.60 (1H, m), 2.60 (1H, dd, J=17.6, 2.4 Hz), 2.66 (1H, dt, J=14.4, 6.0 Hz), 4.04 (1H, d, J=17.6 Hz), 4.20 (1H, sept, J=6.2 Hz), 4.95 (1H, sept, J=6.2 Hz), 5.14 (1H, dd, J=2.4, 1.2 Hz); ^{13}C NMR (CD_3COCD_3) δ 18.0, 20.0, 22.2, 22.2, 24.3, 24.3, 28.3, 37.7, 38.5, 58.9, 66.0, 66.7, 93.0, 113.2, 167.4, 173.8, 209.8; IR (KBr) 1707, 1648, 1105 cm^{-1}; FABMS *m/z*: 311 (M^++H). Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44. Found: C, 65.74; H, 8.40.

*4.3.3. Butyl (2E)-[(3aS,7aR)-7a-butoxyhexahydro-3a-methyl-4-oxo-2(3H)-benzofuranylidene]acetate (**2c**)*

Colorless oil, $[\alpha]_D^{22}$ +21.8 (*c* 1.1, $CHCl_3$); 28% ee (Chiralcel OC, hexane/EtOH=100/1, 0.5 mL/min, t_R=21 min, 26 min); ^{1}H NMR (CD_3COCD_3) δ 0.89 (3H, t, J=7.2 Hz), 0.93 (3H, t, J=7.6 Hz), 1.29 (3H, s), 1.31–1.43 (4H, m), 1.45–1.63 (5H, m), 1.93–2.07 (2H, m), 2.25 (1H, br d, J=15.2 Hz), 2.56–2.73 (3H, m), 3.54–3.67 (2H, m), 4.05 (2H, t, J=6.4 Hz), 4.06 (1H, br d, J=17.2 Hz), 5.20 (1H, dd, J=1.6, 2.4 Hz); ^{13}C NMR (CD_3COCD_3) δ 14.0, 14.0, 18.0, 19.9, 19.9, 20.0, 27.6, 31.7, 32.6, 37.7, 38.4, 58.9, 62.1, 63.5, 92.8, 112.8, 167.8, 173.6, 209.7; IR (KBr) 1717, 1636 cm^{-1}; FABMS (NaCl) *m/z*: 361 (M^++Na). Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.93. Found: C, 67.14; H, 8.93.

*4.3.4. 2-Methylpropyl (2E)-[(3aR,7aS)-hexahydro-3a-methyl-7a-(2-methylpropoxy)-4-oxo-2(3H)-benzofuranylidene]acetate (**2d**)*

Colorless oil, $[\alpha]_D^{22}$ −52.9 (*c* 0.67, $CHCl_3$); 76% ee (Chiralcel OD-H, hexane/EtOH=200/1, 0.4 mL/min, t_R=29 min, 35 min); ^{1}H NMR ($CDCl_3$) δ 0.87 (6H, t, J=6.8 Hz), 0.94 (6H, d, J=6.7 Hz), 1.28 (3H, s), 1.59–1.98 (5H, m), 2.34–2.54 (3H, m), 2.72 (1H, dd, J=17.8, 2.3 Hz), 3.28–3.34 (2H, m), 3.83–3.91 (2H, m), 4.09 (1H, d, J=17.8 Hz), 5.28 (1H, dd, J=1.9, 1.3 Hz); ^{13}C NMR ($CDCl_3$) δ 17.9, 19.2, 19.2, 19.2, 27.2, 27.8, 28.6, 37.3, 37.8, 58.4, 68.3, 69.8, 92.9, 111.3, 167.9, 172.4, 209.6; IR (KBr) 1710, 1653, 1128 cm^{-1}; FABMS *m/z*: 339 (M^++H). Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.93. Found: C, 67.45; H, 8.91.

*4.3.5. 2-Methylpropyl (2E)-[(3aR,7aS)-hexahydro-7a-(2-methylpropoxy)-3a-propyl-4-oxo-2(3H)-benzofuranylidene]acetate (**2e**)*

Colorless oil, $[\alpha]_D^{21}$ −70.0 (*c* 0.89, $CHCl_3$); 72% ee (Chiralcel OD, hexane/EtOH=250/1, 0.5 mL/min, t_R=22 min, 46 min); ^{1}H NMR ($CDCl_3$) δ 0.78 (3H, d, J=6.8 Hz), 0.80 (3H, d, J=6.8 Hz), 0.82 (3H, t, J=7.2 Hz), 0.87 (6H, d, J=6.8 Hz), 0.94–1.19 (2H, m), 1.49–1.90 (7H, m), 2.27–2.46 (3H, m), 2.58 (1H, dd, J=17.6, 2.4 Hz), 3.19–3.26 (2H, m), 3.77–3.90 (2H, m), 4.04 (1H, d, J=17.6 Hz), 5.21 (1H, dd, J=1.4, 2.4 Hz); ^{13}C NMR ($CDCl_3$) δ 14.5, 18.5, 19.2 (2C), 19.2 (2C), 19.6, 27.3, 27.8, 28.6, 34.0, 36.0, 38.0, 62.7, 68.3, 69.7, 93.0, 111.8, 167.9, 172.8, 208.6; IR (KBr) 1703, 1653, 1119 cm^{-1}; HRMS-EI *m/z*: [M^+] calcd for $C_{21}H_{34}O_5$ 366.2406; found 366.2394.

*4.3.6. 2-Methylpropyl (2E)-[(3aR,7aS)-hexahydro-7a-(2-methylpropoxy)-3a-(2-propenyl)-4-oxo-2(3H)-benzofuranylidene]acetate (**2f**)*

Colorless oil, $[\alpha]_D^{21}$ −84.2 (*c* 0.66, $CHCl_3$); 82% ee (Chiralcel AS, hexane/EtOH=300/1, 0.5 mL/min, t_R=13 min, 17 min); ^{1}H NMR ($CDCl_3$) δ 0.80 (3H, d, J=6.8 Hz), 0.81 (3H, d, J=6.8 Hz), 0.87 (6H, d, J=6.8 Hz), 1.50–1.90 (5H, m), 2.31–2.57 (5H, m), 2.66 (1H, dd, J=17.6, 2.4 Hz), 3.22–3.28 (2H, m), 3.76–3.84 (2H, m), 4.02 (1H, d, J=17.6 Hz), 4.95–4.99 (2H, m), 5.22 (1H, s), 5.49–5.59 (1H, m); ^{13}C NMR ($CDCl_3$) δ 19.2 (2C), 19.2, 19.2, 19.4, 27.6, 27.8, 28.5, 36.6, 37.0, 38.5, 62.2, 68.4, 69.8, 93.0, 111.3, 118.2, 132.9, 167.8, 172.3, 208.0; IR (KBr) 1705, 1652, 1124 cm^{-1}; HRMS-EI *m/z*: [M^+] calcd for $C_{21}H_{32}O_5$ 364.2250; found 364.2244.

*4.3.7. 2-Methylpropyl (2E)-[(3aR,7aS)-hexahydro-7a-(2-methylpropoxy)-3a-(2-propynyl)-4-oxo-2(3H)-benzofuranylidene]acetate (**2g**)*

Colorless oil, $[\alpha]_D^{21}$ −59.9 (*c* 0.6, $CHCl_3$); 82% ee (Chiralcel AD, hexane/EtOH=300/1, 0.5 mL/min, t_R=29 min, 37 min); ^{1}H NMR ($CDCl_3$) δ 0.87 (3H, d, J=6.4 Hz), 0.89 (3H, d, J=6.8 Hz), 0.94 (6H, d, J=6.8 Hz), 1.59–1.69 (1H, m), 1.76–1.83 (1H, m), 1.90–1.99 (2H, m), 2.04–2.12 (1H, m), 2.10 (1H, t, J=2.6 Hz), 2.48–2.55 (2H, m), 2.58–2.78 (4H, m), 3.30–3.38 (2H, m), 3.83–3.91 (2H, m), 4.13 (1H, d, J=18.0 Hz), 5.29 (1H, dd, J=1.6, 2.4 Hz); ^{13}C NMR ($CDCl_3$) δ 19.0, 19.2, 19.2 (2C), 22.7, 27.7, 27.8, 28.5, 38.0, 39.4, 60.4, 68.6, 69.9, 72.2, 79.9, 93.0, 110.8, 167.8, 171.3, 207.7; IR (KBr) 1702, 1651, 1125 cm^{-1}; HRMS-EI *m/z*: [M^+] calcd for $C_{21}H_{30}O_5$ 362.2093; found 362.2094.

*4.3.8. Hydrogenation of **2f** and **2g***

To a solution of **2** (0.11 mmol) in MeOH (4 mL) was added Pd/C ethylenediamine complex (10 mg). The apparatus was purged with hydrogen. After being stirred for 24 h, the mixture was filtered through a pad of Celite and concentrated in vacuo.

The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/ethyl acetate (100/1 to 80/1) afforded **2e** as a colorless oil. From **2f**: 90% yield, $[\alpha]_D^{23}$ −78.8 (*c* 0.71, $CHCl_3$); from **2g**: 94% yield, $[\alpha]_D^{27}$ −81.4 (*c* 0.65, $CHCl_3$).

*4.3.9. 2-Methylpropyl (2E)-[(3aR,8aS)-3a-methyl-8a-(2-methylpropoxy)-4-oxo-octahydrocyclohepta[b]-furanylidene]acetate (**2h**)*

Colorless oil, $[\alpha]_D^{28}$ +24.9 (*c* 0.47, $CHCl_3$); 82% ee (Chiralcel AD, hexane/EtOH=300/1, 0.5 mL/min, t_R=29 min, 37 min); ^{1}H NMR ($CDCl_3$) δ 0.94 (6H, d, *J*=6.8 Hz), 0.95 (3H, d, *J*=6.8 Hz), 0.96 (3H, d, *J*=6.8 Hz), 1.27 (3H, s), 1.58−1.71 (4H, m), 1.84−1.97 (3H, m), 2.10−2.14 (1H, m), 2.32−2.37 (1H, m), 2.79 (1H, dt, *J*=2.8, 11.2 Hz), 3.22 (1H, dd, *J*=18.8, 1.6 Hz), 3.36−3.48 (3H, m), 3.86 (2H, d, *J*=6.4 Hz), 5.27 (1H, dd, *J*=2.0, 1.6 Hz); ^{13}C NMR ($CDCl_3$) δ 19.2 (2C), 19.3, 19.4 (2C), 23.0, 27.6, 27.9, 28.8, 33.1, 39.4, 40.0, 60.9, 69.1, 69.7, 91.2, 110.4, 168.3, 171.2, 211.5; IR (KBr) 1708, 1646, 1123 cm^{-1}; HRMS-EI *m/z*: [M^+] calcd for $C_{20}H_{32}O_5$ 352.2250; found 352.2253.

*4.3.10. Conversion of **2h** to MTPA ester*

To a solution of **2h** (53 mg, 0.15 mmol) at 0 °C in MeOH (2 mL) was added $NaBH_4$ (17 mg, 0.45 mmol), and the mixture was stirred for 15 min at the same temperature. The mixture was diluted with water (20 mL) and EtOAc (20 mL). The layers were separated, the aqueous layer was extracted with EtOAc (20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by preparative TLC. The corresponding secondary alcohol was obtained in 91% yield, which was converted to (*R*)- and (*S*)-MTPA esters. The stereochemistry of the corresponding secondary alcohol was confirmed by NOE experiment. *Secondary alcohol*: ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, d, *J*=6.7 Hz), 0.87 (3H, d, *J*=6.7 Hz), 0.94 (6H, d, *J*=6.7 Hz), 1.24 (3H, s), 1.48−1.78 (8H, m), 1.86−1.97 (2H, m), 2.11−2.17 (1H, m), 2.80 (1H, dd, *J*=2.0, 19 Hz), 3.20−3.27 (2H, m), 3.59 (1H, dd, *J*=1.2, 19 Hz), 3.63 (1H, br s), 3.82−3.89 (2H, m), 5.24 (1H, m); ^{13}C NMR ($CDCl_3$) δ 19.2 (2C), 19.3 (2C), 21.7, 22.0, 26.5, 27.9, 28.8, 29.9, 32.4, 40.9, 52.5, 67.5, 69.6, 78.0, 89.7, 113.1, 168.9, 175.2; IR (neat) 3459, 1686, 1635 cm^{-1}; HRMS-EI *m/z*: [M^+] calcd for $C_{20}H_{34}O_5$ 354.2406; found 354.2388. *(S)-MTPA ester of secondary alcohol*: ^{1}H NMR ($CDCl_3$) δ 0.84 (3H, d, *J*=6.6 Hz), 0.85 (3H, d, *J*=6.6 Hz), 0.92 (3H, d, *J*=6.6 Hz), 0.93 (3H, d, *J*=6.6 Hz), 1.07 (3H, s), 1.59−1.94 (9H, m), 2.14 (1H, dd, *J*=6.0, 15.0 Hz), 2.78 (1H, dd, *J*=2.1, 19 Hz), 3.19−3.26 (2H, m), 3.48 (1H, d, *J*=19 Hz), 3.53 (3H, s), 3.81−3.89 (2H, m), 4.93 (1H, d, *J*=8.0 Hz), 5.25 (1H, br s), 7.37−7.41 (3H, m), 7.51−7.54 (2H, m). *(R)-MTPA ester of secondary alcohol*: ^{1}H NMR ($CDCl_3$) δ 0.84 (3H, d, *J*=6.4 Hz), 0.85 (3H, d, *J*=6.4 Hz), 0.93 (6H, d, *J*=6.8 Hz), 1.19 (3H, s), 1.54−1.95 (9H, m), 2.04 (1H, dd, *J*=5.6, 15 Hz), 2.86 (1H, dd, *J*=2.0, 19 Hz), 3.19−3.25 (2H, d, *J*=5.7 Hz), 3.43 (1H, d, *J*=19 Hz), 3.51 (3H, s), 3.81−3.88 (2H, d, *J*=5.6 Hz), 4.95 (1H, d, *J*=8.4 Hz), 5.23 (1H, s), 7.36−7.40 (3H, m), 7.51−7.52 (2H, m).

*4.4. Conversion of **2d** and **2e** to authentic hydrindanes **33d** and **33e***

$Ph_3P{=}CH_2$ solution: a solution of $MePPh_3Br$ (3.97 g, 11.1 mmol) and *t*-BuOK (1.25 g, 11.1 mmol) in toluene (40 mL) was refluxed for 3 h under an argon atmosphere. The solution was cooled to room temperature and used for the following reactions.

To a solution of **2** (0.31 mmol) in toluene (5 mL) was added toluene solution of $Ph_3P{=}CH_2$ (4 mL) at 0 °C and stirred for 2 h. The mixture was diluted with satd NH_4Cl aq (20 mL). The layers were separated, the aqueous layer was extracted with EtOAc (20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. A solution of the crude product in CH_3CN/H_2O/10% HCl (3 mL/1 mL/2 mL) was stirred for 2 h. The mixture was diluted with satd $NaHCO_3$ aq (20 mL) and EtOAc (20 mL). The layers were separated, the aqueous layer was extracted with EtOAc (20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. A mixture of the crude product and K_2CO_3 (43 mg, 0.31 mmol) in MeOH (5 mL) was stirred for 10 min. The mixture was diluted with H_2O (20 mL) and EtOAc (20 mL). The layers were separated, the aqueous layer was extracted with EtOAc (20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/EtOAc (50/1) afforded **33d** and **33e** in 71% and 68% yields, respectively.

*4.4.1. 2-Methylpropyl (7aR)-2,4,5,6,7,7a-hexahydro-7a-methyl-7-methylene-2-oxo-1H-indene-3-carboxylate (**33d**)*

Colorless oil, $[\alpha]_D^{23}$ +20.9 (*c* 0.59, $CHCl_3$); 74% ee (Chiralcel AS, hexane/EtOH=200/1, 1.0 mL/min, t_R=13.2 min, 17.0 min); ^{1}H NMR ($CDCl_3$) δ 4.85 (1H, d, *J*=1.6 Hz), 4.79 (1H, d, *J*=1.6 Hz), 4.02 (2H, d, *J*=6.6 Hz), 3.48−3.43 (1H, m), 2.92 (1H, d, *J*=17.9 Hz), 2.58−2.35 (4H, m), 2.13−1.97 (2H, m), 1.62−1.50 (1H, m), 1.44 (3H, s), 0.98 (6H, d, *J*=6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 201.0, 190.4, 163.4, 152.1, 128.3, 109.0, 71.0, 48.7, 48.5, 31.6, 28.8, 27.8, 27.5, 26.5, 19.2, 19.2; IR (KBr) 1715, 1631 cm^{-1}; HRMS-EI *m/z*: [M^+] calcd for $C_{16}H_{22}O_3$ 262.1569; found 262.1573.

*4.4.2. 2-Methylpropyl (7aR)-2,4,5,6,7,7a-hexahydro-7a-propyl-7-methylene-2-oxo-1H-indene-3-carboxylate (**33e**)*

Colorless oil, $[\alpha]_D^{24}$ −2.24 (*c* 0.58, $CHCl_3$); 72% ee (Chiralcel AS, hexane/EtOH=250/1, 1.0 mL/min, t_R=11.3 min, 13.7 min); ^{1}H NMR ($CDCl_3$) δ 4.91 (1H, d, *J*=1.6 Hz), 4.73 (1H, s), 4.02 (2H, d, *J*=6.6 Hz), 3.48−3.41 (1H, m), 2.76 (1H, d, *J*=18 Hz), 2.51−2.33 (4H, m), 2.11−1.96 (2H, m), 1.85−1.78 (1H, m), 1.62−1.42 (2H, m), 1.27−1.04 (2H, m), 0.98 (6H, d, *J*=6.6 Hz), 0.89 (3H, t, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 201.3, 190.0, 163.6, 150.5, 128.9, 110.3, 71.0, 52.8, 45.8, 41.1, 31.7, 27.8, 27.5, 26.6, 19.2, 19.2, 18.2, 14.2; IR (KBr) 1715, 1629 cm^{-1}; HRMS-EI *m/z*: [M^+] calcd for $C_{18}H_{26}O_3$ 290.1882; found 290.1883.

4.5. Synthesis of authentic hydrindanes (*ent*-**33d** and *ent*-**33e**)

To a solution of **34** (0.4 mmol) in CH_2Cl_2 (5 mL) was added Dess–Martin periodinane (341 mg, 0.80 mmol). After being stirred at room temperature for 3 h, the reaction mixture was diluted with satd $NaHCO_3$ aq (20 mL) and EtOAc (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was treated with $Ph_3P{=}CH_2$ in a manner similar to that described for the preparation of **33**. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/EtOAc (100/1) afforded **35d** and **35e** in 93% and 92% yields, respectively.

4.5.1. Methyl (2E)-[(3aS,7aS)-hexahydro-3a-methyl-4-methylene-2(3H)-benzofuranylidene]acetate (**35d**)

Colorless oil, $[\alpha]_D^{28}$ +16.8 (*c* 0.73, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.40 (1H, br s), 4.78 (1H, s), 4.75 (1H, s), 3.68 (3H, s), 3.61 (1H, dd, *J*=12, 3.6 Hz), 3.37 (1H, d, *J*=17 Hz), 2.77 (1H, br d, *J*=17 Hz), 2.36–2.27 (1H, m), 2.15 (1H, dd, *J*=15, 4.9 Hz), 2.04–1.91 (2H, m), 1.81–1.72 (1H, m), 1.47–1.35 (1H, m), 1.00 (3H, s); ^{13}C NMR ($CDCl_3$) δ 175.5, 168.9, 150.6, 107.0, 92.1, 87.9, 50.8, 46.9, 41.9, 29.8, 24.3, 23.6, 18.0; IR (KBr) 1712, 1645, 1130 cm^{-1}; HRMS-EI *m*/*z*: [M^+] calcd for $C_{13}H_{18}O_3$ 222.1256; found 222.1253.

4.5.2. Methyl (2E)-[(3aS,7aS)-hexahydro-3a-propyl-4-methylene-2(3H)-benzofuranylidene]acetate (**35e**)

Colorless oil, $[\alpha]_D^{27}$ −2.61 (*c* 0.58, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.39 (1H, br s), 4.83 (1H, s), 4.69 (1H, s), 3.68 (3H, s), 3.68–3.64 (1H, m), 3.56 (1H, d, *J*=17 Hz), 2.60 (1H, br d, *J*=17 Hz), 2.16–2.12 (2H, m), 2.01–1.83 (3H, m), 1.59–1.36 (2H, m), 1.21–0.98 (3H, m), 0.88 (3H, t, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 175.6, 168.9, 148.8, 108.5, 92.0, 88.7, 50.7, 50.5, 38.6, 30.0, 29.9, 24.2, 23.0, 16.9, 14.7; IR (KBr) 1710, 1648, 1126 cm^{-1}; HRMS-EI *m*/*z*: [M^+] calcd for $C_{15}H_{22}O_3$ 250.1569; found 250.1569.

To a solution of **35** (0.36 mmol) in CH_3CN/H_2O (2 mL/0.5 mL) was added Jones reagent (3.56 mol/L, 0.4 mL) at 0 °C, and the resulting mixture was stirred for 1 h. The reaction mixture was quenched with satd NaCl aq (20 mL) and $NaHCO_3$. The mixture was extracted with EtOAc (30 mL) and the aqueous layer was extracted with EtOAc (20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/EtOAc (20/1 to 12/1) afforded **36d** and **36e** in 72% and 61% yields, respectively.

4.5.3. Methyl (7aS)-2,4,5,6,7,7a-hexahydro-7a-methyl-7-methylene-2-oxo-1H-indene-3-carboxylate (**36d**)

Colorless needles, mp 77–78 °C (hexane), $[\alpha]_D^{25}$ −26.7 (*c* 0.94, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 4.86 (1H, s), 4.79 (1H, s), 3.84 (3H, s), 3.54–3.48 (1H, m), 2.92 (1H, d, *J*=18 Hz), 2.58–2.36 (4H, m), 2.14–2.07 (1H, m), 1.62–1.50 (1H, m), 1.44 (3H, s); ^{13}C NMR ($CDCl_3$) δ 201.1, 191.9, 163.7, 152.0, 127.8, 109.1, 51.9, 48.8, 48.6, 31.6, 28.9, 27.5, 26.5; IR (KBr) 1712, 1619 cm^{-1}; HRMS-EI *m*/*z*: [M^+] calcd for $C_{13}H_{16}O_3$ 220.1100; found 220.1098.

4.5.4. Methyl (7aS)-2,4,5,6,7,7a-hexahydro-7a-propyl-7-methylene-2-oxo-1H-indene-3-carboxylate (**36e**)

Colorless oil, $[\alpha]_D^{23}$ +5.11 (*c* 0.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 4.91 (1H, s), 4.73 (1H, s), 3.83 (3H, s), 3.50 (1H, br d, *J*=15 Hz), 2.76 (1H, d, *J*=18 Hz), 2.51–2.33 (4H, m), 2.12–2.04 (1H, m), 1.85–1.78 (1H, m), 1.62–1.42 (2H, m), 1.26–1.04 (2H, m), 0.89 (3H, t, *J*=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 201.4, 191.4, 163.7, 150.4, 128.5, 110.3, 52.9, 51.9, 45.9, 41.2, 31.7, 27.4, 26.6, 18.2, 14.2; IR (KBr) 1716, 1624 cm^{-1}; HRMS-EI *m*/*z*: [M^+] calcd for $C_{15}H_{20}O_3$ 248.1413; found 248.1411.

To a solution of **36** (0.26 mmol) and *i*-BuOH (0.49 mL) in toluene (25 mL) was added Ti(*i*-PrO)$_4$ (7.7 mL, 0.02 mmol), and the resulting mixture was refluxed for 23 h. The reaction mixture was quenched with $NaHCO_3$ aq (20 mL) and EtOAc (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/EtOAc (50/1 to 12/1) afforded *ent*-**33d** and *ent*-**33e** in 97% and 98% yields, respectively.

4.5.5. 2-Methylpropyl (7aS)-2,4,5,6,7,7a-hexahydro-7a-methyl-7-methylene-2-oxo-1H-indene-3-carboxylate (*ent*-**33d**)

Colorless oil, $[\alpha]_D^{21}$ −23.2 (*c* 0.51, $CHCl_3$, 86% ee).

4.5.6. 2-Methylpropyl (7aS)-2,4,5,6,7,7a-hexahydro-7a-propyl-7-methylene-2-oxo-1H-indene-3-carboxylate (*ent*-**33e**)

Colorless oil, $[\alpha]_D^{22}$ +2.97 (*c* 0.75, $CHCl_3$, 97% ee).

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