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cis-Oxypalladation Complexes Derived from (1*R*,5*R*)-2(10),3-Pinadiene and Their Utilization in Pd(II)-catalyzed Enantioselective Cyclization of 2-(*trans*-2-Butenyl)phenols

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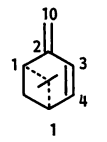
(1*R*,5*R*)-2(10),3-Pinadiene, when treated with either Na_2PdCl_4 in MeOH or $Pd(OAc)_2$ in AcOH and NaCl, gives di-μ-chloro-bis[(3,2,10-η-*cis*-4-methoxy or acetoxypinene)palladium(II)] (**4a**) or (**4b**), respectively. These complexes represent the firstly isolated *cis*-oxypalladation adduct. The ligand exchange of **4b** with AgOAc affords di-μ-acetato-bis[(3,2,10-η-*cis*-4-acetoxypinene)palladium(II)] (**5b**) which serves as the catalyst for the asymmetric cyclization of 2-(*trans*-2-butenyl)phenols leading to 2-vinyl-2,3-dihydrobenzofurans (**13**). Although the enantioselectivities induced in this asymmetric cyclization are not high (1—29% ee), noteworthy is that the *cis*-complex **5b** affords (*R*)-(−)-enantiomer of **13** while the parent di-μ-acetato-bis[(3,2,10-η-pinene)palladium-(II)] give the (*S*)-isomer. As an application of the present asymmetric cyclization, attempts to synthesize (*S*)-(+)-tremetone have been made.

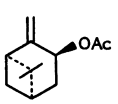
During the course of our study on the asymmetric cyclization of 2-allylphenols using (η^3-pinene)palladium(II) catalyst,[1,2] our interest has been extended to prepare η^3-allylpalladium(II) complexes bearing functionalized pinanyl ligands. For this purpose, (1*R*,5*R*)-2(10), 3-pinadiene (**1**) (verbenene) has been chosen as a precursor of the pinanyl ligand, since the reactions of 1,3-dienes with Pd(II) compounds in the presence of nucleophiles gives functionalized η^3-allylpalladium(II) complexes.[3] This type of reactions with oxygen nucleophiles such as alcohol[4] has been known to proceed by *trans*-addition; however, η^3-allylpalladium(II) complexes **4** obtained from **1** were the products derived from *cis*-addition. Although the stereochemistry of oxypalladation of alkenes has been extensively studied,[5] there has been no unambiguous examples of *cis*-oxypalladation complexes.[6] Described herein are the preparation and structural elucidation of the *cis*-oxypalladium complexes **4a**—**c**,[7] and their utilization as the catalyst for the asymmetric cyclization of 2-(*trans*-2-butenyl)-phenols.

Results and Discussion

Preparation of Di-μ-chloro-bis[3,2,10-η-cis-4-methoxy or Acetoxypinene)palladium(II)] (4). The synthesis of pinadiene **1** has been previously performed by bromination of α- or β-pinene with NBS followed by dehydrobromination.[8] Although this procedure seems to be a reasonable manipulation, the diene **1** was synthesized by utilizing palladium-catalyzed elimination of allylic acetates to dienes.[9] Thus, when a mixture of allylic acetates **2** and **3** (**2**/**3**=2/1), prepared from (−)-β-pinene and $Pb(OAc)_4$,[10] was treated with $Pd(OAc)_2$ (5 mol%) in the presence of PPh_3 (0.5 equiv), diene **1** was obtained in 72% yield {$[\alpha]_D$ +106° (CCl_4)}. The overall yield of **1** (32%) from β-pinene in this procedure is comparable to that in the previous method.[8]



1



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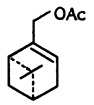
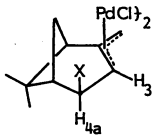
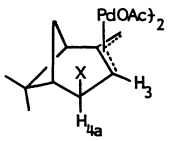


3

When the diene **1** thus obtained was allowed to react with an equimolar amount of Na_2PdCl_4 in MeOH, the *cis*-complex **4a** was formed as a single product in 66% isolated yield. The reaction of **1** with $Pd(OAc)_2$ in AcOH followed by addition of NaCl gave the complex **4b** (71%). The use of $Pd(OAc)_2$ in MeOH under otherwise the same conditions afforded two complexes **4a** (12%) and **4b** (14%). Also, the reaction of **1** with $Pd(OCOCF_3)(OOBu^t)$ in acetone and subsequent addition of NaCl gave the complex **4c** (85%).



4a; X=OMe
4b; X=OAc
4c; X=OBu^t

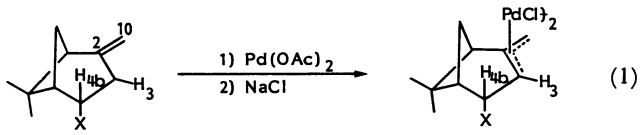


5a; X=OMe
5b; X=OAc
5c; X=H

The chloride ligand of complexes **4a** and **4b** is readily exchanged to acetate upon treatment with an equimolar amount of AgOAc. The complexes **5a** and **5b** thus obtained serve as the catalyst for the asymmetric cyclization of 2-(*trans*-2-butenyl)phenols (**12**). The results will be compared to those obtained by using the parent complex **5c** (X=H) (*vide infra*).

Structural Characterization. The structural elucidation of **4a**—**c** was undertaken by comparing the spectral data of **4a** and **4b** with those of the corresponding *trans*-isomers **7a** and **7b**. The authentic complexes **7a** and **7b** were prepared as

follows. The β-pinenes **6a** and **6b** bearing the substituent (X=OMe or OAc) at the C(4),*endo*-position were prepared from (−)-α-pinene by the reported method.[11,12] The reaction of **6a** with an equimolar amount of $Pd(OAc)_2$ in MeOH followed by addition of NaCl gave a 58% yield of complex **7a** (Eq. 1). Likewise, the *trans*-complex **7b** was obtained from **6b** in 52% yield. The reaction of β-pinene (**6c**) with $PdCl_2$ has been shown to proceed by the *exo*-attack of palladium at sterically less-hindered site of C(2)=C(10) olefin to give the complex **7c**.[13] The β-pinenes **6a** and **6b** react similarly with Pd(II) to afford the *trans*-complexes **7a** and **7b** as depicted in Eq. 1.



(1)

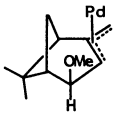
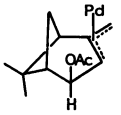
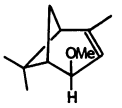
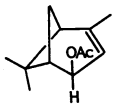
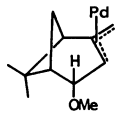
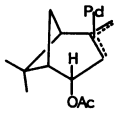
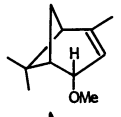
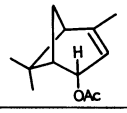
6a; X=OMe
6b; X=OAc
6c; X=H

7a; X=OMe
7b; X=OAc
7c; X=H

Comparison of the ^1H NMR spectral data shown in Table 1 unambiguously indicates the configurational difference between **4a** and **7a** or **4b** and **7b** (Entries 1, 2, 5, and 6), respectively. The following data in Table 1 support that the palladium is situated at the *exo*-position of all these complexes. Thus, the difference in chemical shifts between *gem*-dimethyl groups (Δδ Me-8,9) of the *exo*-α-pinenes **4a**, **4b**, **8**, and **9** (group i) fall into the region of 0.36—0.48, whereas those of the *endo*-isomers **7a**, **7b**, **10**, and **11** (group ii) are in 0.26—0.36. Although these values tend to be lowered upon complexation, no significant difference was observed between the value of η^3-allyl complex and the corresponding α-pinene (*e.g.*, **4a** and **8**). If palladium in these complexes occupies the site opposite to that depicted, the relative chemical shift must differ greatly owing to the proximity of palladium to one of the Me group.[14] These considerations allow us to assign the *cis*-configuration of **4a** and **4b**.

The ^1H NMR spectrum of *trans*-complex **7a**

Table 1. ^1H NMR chemical shifts[a] of π-allyl complexes and α-pinene derivatives

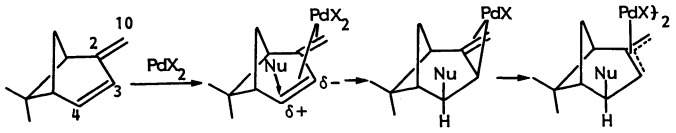
Entry	Compd		H-10	H-3	H-4	J_{34}	J_{45}	Me-8	Me-9	Δδ Me-8,9
	group (i)									
1		**4a**	3.03 3.73	3.99	3.52	4.5	2.5	0.99	1.39	0.40
2		**4b**	3.08 3.69	4.15	4.88	5.0	2.6	1.04	1.40	0.36
3		**8**	—	5.30	3.67	NA[b]	NA	0.85	1.33	0.48
4		**9**	—	5.32	5.32	NA	NA	0.92	1.36	0.44
	group (ii)									
5		**7a**	3.08 3.75	3.96	3.65	0	2.4	1.11	1.38	0.27
6		**7b**	3.09 3.77	3.89	5.07	0	2.4	1.13	1.39	0.26
7		**10**	—	5.33	3.88	NA	NA	0.94	1.31	0.37
8		**11**	—	5.33	5.33	NA	NA	0.99	1.35	0.36

a) ^1H NMR spectra of complexes were obtained on a JEOL FX-100 ($CDCl_3$), and those of α-pinenes on a JEOL MH-100 (CCl_4) spectrometer. b) Not ascertainable.

showed no coupling between H-3 and H-4b (Table 1, Entry 5), while the coupling constant of 4.5 Hz was observed between H-3 and H-4a in the *cis*-complex **4a** (Entry 1). Similar observation was also made between the complexes **7b** and **4b**. The dihedral angle between H-3 and H-4b protons estimated by using a stereochemical model is roughly 80—90°, while that between H-3 and H-4a is around 30—40° because of the structural distortion of the pinanyl ligand. These angles, when applied to the Karplus equation, are in good agreement with the observed coupling constants. This also supports the configurational assignment of the complexes.

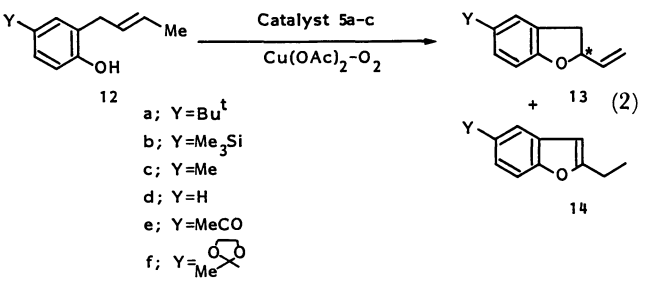
The present oxypalladation proceeds *via* π-coordination of Pd(II) to the C(3)=C(4) olefin (Scheme 1). The coordination is probably "slipped" away from the symmetrical position because of the steric factors. This allows the C(4) carbon to be more positive.[15] The *cis*-, *exo*-attack of nucleophiles on this carbon could be favorable,[16] similarly to the *cis*-oxymercuration of strained olefins such as norbornenes.[17]

*Asymmetric Cyclization of 2-(*trans*-2-Butenyl)phenols.* The results of the asymmetric cyclization of 2-(*trans*-2-butenyl)phenols (**12**) using the *cis*-complex **5b** (X=OAc) as the catalyst are shown in Table 2,



Scheme 1.

together with those obtained by using the parent complex **5c** (Eq. 2). Although the induced enantioselectivities (% ee) of product **13** are not much high in either case, the following two points are of noteworthy. 1) The acetoxy complex **5b** leads to the predominant formation of (*R*)-enantiomer of **13**, opposite to that with the complex **5c**. 2) The electron-withdrawing substituent (Y) of phenoxyl group provides a relatively higher enantiomer excess in either case, as has been observed previously,[2] and the enantioselectivity is not much affected by the steric factor of substituent Y.

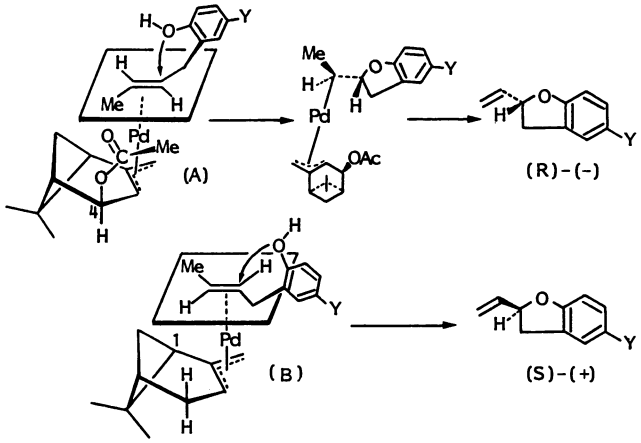


The mechanistic implication of these results may deserve comments. The internal chelation of the *cis*-OAc group in **5b** to palladium(II) blocks the front side corner of the pinanyl ligands. Accordingly, the bulky phenoxyl substituent of olefin **12** prefers to be far apart from the OAc group in the stage where the substrate approaches palladium. The π-complexation A shown in Scheme 2 is thus attained at the expence of steric interference between the Me substituent of

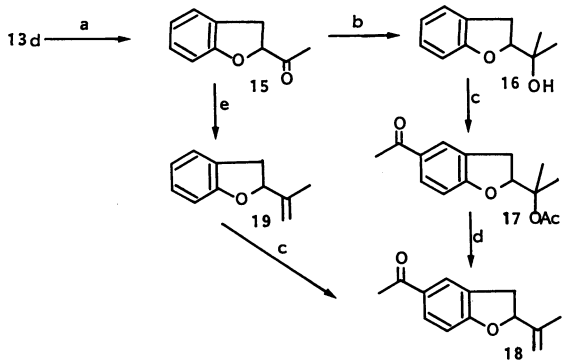
Table 2. Pd(II)-catalyzed asymmetric cyclization of 2-(*trans*-2-butenyl)phenols **12**[a]

Entry	Substrate, Y	Catalyst	Time[b] h	Cyclized product: Yield[c] %	Product ratio **13**/**14**	$[\alpha]_D$ of **13**[d] deg, (*c*, CCl_4)	Conf	ee[e] %
1	**12a**, 4-Bu^t	**5b** (X=OAc)	13	74	78/22	−6.34, (9.84)	*R*	25
2		**5c** (X=H)	4.8	78	82/18	+3.73, (10.8)	*S*	15
3	**12b**, 4-Me_3Si	**5b**	31	78	78/22	−5.04, (16.3)	*R*	17
4		**5c**	29	65	81/19	+4.40, (17.9)	*S*	15
5	**12c**, 4-Me	**5b**	12	51	78/22	−4.29, (9.46)	*R*	13
6		**5c**	11	76	83/17	+6.84, (3.86)	*S*	21[f]
7	**12d**, 4-H	**5b**	13	61	80/20	−4.58, (6.62)	*R*	18
8		**5c**	4.5	77	83/17	+4.53, (5.19)	*S*	18[g]
9	**12e**, 4-MeCO	**5b**	23	48	96/4	−0.79, (5.33)	*R*	~1
10		**5c**	11	74	96/4	+0.89, (2.71)	*S*	1[f]
11	**12f**, 4-	**5b**	23	79	80/20	−9.40, (4.31)	*R*	29
12	**12a**, 4-Bu^t	**5a** (X=OMe)	16	72	79/21	+0.24, (12.5)	*S*	1
13	**12d**, 4-H	**5a**	13	66	85/15	+0.92, (6.88)	*S*	4

a) The reaction conditions are shown in the text. b) Reaction time required for >98% completion. c) Isolated yield by Kugelrohr distillation. d) Measured at 25—29 °C. e) Determination of % ee for **13a**, **13b**, and **13f** is described in Experimental Section, and for others, see Ref. 2. f) Data from Ref. 2. g) Data from Ref. 1.



Scheme 2.



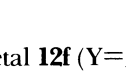
a, $Bu^tOOH/Pd(OCOCF_3)(OOBu^t)$; b, MeMgBr; c, $Ac_2O/SnCl_4$; d, 330 °C; e, $Ph_3P=CH_2$

Scheme 3.

olefin and the blocking OAc group. In the parent complex **5c**, the least steric hindrance is achieved if the Me group is situated in the "pocket" existing over the C(1) bridgehead hydrogen[2] (B in Scheme 2). *trans*-Oxypalladation from these arrangements followed by Pd–H elimination results in the formation of (*R*)- or (*S*)-enantiomer of **13**, respectively, as shown in Scheme 2.[18] The observed substituent (Y) effect common to both of the complexes suggests that the OAc group of pinanyl ligand does not alter the reaction pathways themselves.

In the case of complex **5a** (X=OMe), the two types of π-complexation (A and B) will be involved because the front-side corner must be less effectively blocked by the OMe group. In fact, the use of complex **5a** gives rise to poor enantioselectivity (1—4% ee) in the cyclization of **12a** and **12d** (Table 2, Entries 12 and 13).

As an application of the present asymmetric cyclization, the synthesis of optically active tremetone (**18**) was attempted. The oxidation of (+)-**13d** {$[\alpha]_D$ +4.11°, 16% ee} with Bu^tOOH in the presence of $Pd(OCOCF_3)(OOBu^t)$ as the catalyst gave (−)-2-acetyl-2,3-dihydrobenzofuran (**15**) {48%, $[\alpha]_D$ −9.30°} which was transformed into (*S*)-(+)-tremetone (**18**) by the following sequences (Scheme 3). Conversion of (−)-**15** into tertiary alcohol **16** with MeMgBr followed by acetylation ($SnCl_4$, Ac_2O) afforded 1-(5-acetyl-2,3-dihydro-2-benzofuranyl)-1-methylethyl acetate (**17**) (82%). Pyrolysis of the acetate **17** (330 °C, 1.5 min) gave (*S*)-(+)-tremetone (**18**) {$[\alpha]_D$ +10.4°, 17% ee[19,20]} in 76% yield. Alternatively, the Wittig reaction of (+)-**15** ($Ph_3P=CH_2$, 40 °C, 19 h, 33%) followed by acetylation ($SnCl_4$, Ac_2O, 89%) led to the formation of (*S*)-(+)-**18** {$[\alpha]_D$ +10.5°, 17% ee}.

The asymmetric cyclization of acetal **12f** (Y= ) using *cis*-complex **5b** gave (*R*)-(−)-**13f** in 29% ee. Thus, the natural (*R*)-(−)-tremetone (**18**), one of biologically active components in the white snakeroot and others, which induces "tremble" in cattle and "milksickness" in higher animals and humans,[19,20] can be derived from either (*R*)-acetals **13f** or (*R*)-(−)-**13d** (Y=H).

Experimental

Optical rotation were measured with JASCO DIP-4 polarimeter with 1 dm-long cell at room temperature. ^1H NMR spectra were recorded on JMN-MH-60 (JEOL) and JMN FX-100 (JEOL) spectrometers. GLC analysis was performed on a JEOL Model JGC-20KFP flame ionization chromatograph using a 1 m×4 mm, 10% PEG 20 M on 80—100 mesh Celite column under the conditions of injection temperature (200 °C) and column temperature (100—230 °C). Preparative GLC was carried out on a JEOL Model JGC-20KT thermal conductive chromatograph using a 2 m×4 mm or 1 m×4 mm, 10% PEG 20 M on Celite column. Preparative thin-layer chromatography plates were made of silica gel 60 PF254 (Merck).

Palladium(II) acetate $[Pd(OAc)_2]$,[21] sodium tetrachloropalladate(II) (Na_2PdCl_4),[22] and (*t*-butyldioxy) (trifluoroacetato)palladium(II) $[Pd(OCOCF_3)(OOBu^t)]$[23] were prepared as the reported method. *t*-Butyl hydroperoxide (80%) is commercially avairable [Maruwaka Chemical Ind., Ltd. (Osaka)].

Preparation of (1R,5R)-2(10),3-Pinadiene (Verbenene) (1): A mixture of 2(10)-pinen-3-yl acetate (**2**) and 2-pinen-10-yl acetate (**3**) (**2**/**3**=2/1) (12.0 g, 61.8 mmol) prepared from (−)-β-pinene {$[\alpha]_D$ −20°, Tokyo Kasei} and $Pb(OAc)_4$,[10] was added to a stirred solution of $Pd(OAc)_2$ (0.690 g, 3.08 mmol) and PPh_3 (8.10 g, 30.8 mmol) in dry dioxane (72 mL) under argon. After the mixture was refluxed for 24 h, pentane (200 mL) was added to the reaction mixture. The resulting precipitate was removed by filtration, and the filtrate was washed with water (50 mL×2), 5% aqueous $NaHCO_3$ solution (50 mL), and brine (50 mL), and dried over Na_2SO_4. Evaporation followed by distillation gave pinadiene **1** (6.00 g, 72%): bp 60—65 °C (20 mmHg) (1 mmHg=133.322 Pa); $[\alpha]_D^{22}$ +106° (*c* 0.47, CCl_4); IR (neat) 3050, 2945, 1632, 1582, 1370, and 878 (C=CH_2) cm^{-1};

^{1}H NMR (100 MHz, CCl_4) δ=0.87 (3H, s, *gem*-Me), 1.36 (3H, s, *gem*-Me), 1.46 (1H, d, J=8.0 Hz), 2.25—2.65 (3H, m), 4.66 (2H, s, H-10), 6.02 (1H, d, J=8.0 Hz, H-3), and 6.32 (1H, dd, J=8.0 and 6.5 Hz, H-4).

Found: C, 89.17; H, 10.66%. Calcd for $C_{10}H_{14}$: C, 89.49; H, 10.51%. This compound has been reported to be prepared by dehydrobromination of 10-bromo-2-pinene with γ-collidine in 46—64% yields.[8]

Reaction of Pinadiene 1 with Na_2PdCl_4 in MeOH: Into a 0.1 M (1 M=1 mol dm^{-3}) solution of Na_2PdCl_4 in MeOH (10.0 mL, 1.00 mmol) was added pinadiene **1** (0.134 g, 1.00 mmol), and the solution was stirred for 1 h at room temperature. After removal of the solvent, the residue was extracted with CH_2Cl_2 (20 mL), and the extract was washed with brine (10 mL) and dried over Na_2SO_4. Evaporation followed by Al_2O_3 column chromatography (eluent CH_2Cl_2) afforded di-μ-chloro-bis[(3,2,10-η-*cis*-4-methoxypinene)palladium(II)] (**4a**) (0.204 g, 66%): mp 145—158 °C (decomp); IR (Nujol) 1356, 1250, 1104 (C–O), 982, and 788 cm^{-1}; The ^{1}H NMR spectral data of this compound **4a** are listed in Table 1, together with those of **4b**, **7a**, **7b**, **8**, **9**, **10**, and **11** described below.

Found: C, 43.69; H, 5.62; Cl, 11.32%. Calcd for $C_{11}H_{17}ClOPd$: C, 43.02; H, 5.58; Cl, 11.54%.

Reaction of Pinadiene 1 with $Pd(OAc)_2$ in AcOH: Into a suspended solution of $Pd(OAc)_2$ (0.449 g, 2.00 mmol) in AcOH (10 mL) was added pinadiene **1** (0.268 g, 2.00 mmol). After the solution was stirred for 1 h at room temperature, NaCl (0.350 g, 6.00 mmol) was added into the solution, and stirring was further continued for 30 min. The reaction mixture was extracted with CH_2Cl_2 (50 mL), washed with 5% aqueous $NaHCO_3$ solution (20 mL×2), and brine (20 mL) and dried over Na_2SO_4. Evaporation followed by Al_2O_3 column chromatography (eluent CH_2Cl_2) to give di-μ-chloro-bis[(3,2,10-η-*cis*-4-acetoxypinene)palladium(II)] (**4b**) (0.476 g, 71%): mp 117 °C; $[\alpha]_D^{22}$ −237° (c 0.22, MeOH); IR (Nujol) 1737 (C=O), 1241 (C–O), 1030, and 781 cm^{-1}.

Found: C, 43.36; H, 5.26; Cl, 10.72%. Calcd for $C_{12}H_{17}ClO_2Pd$: C, 43.01; H, 5.11; Cl, 10.58%.

Reaction of Pinadiene 1 with $Pd(OAc)_2$ in MeOH: The reaction of pinadiene **1** (0.460 g, 3.43 mmol) with $Pd(OAc)_2$ (0.770 g, 3.43 mmol) in MeOH (15 mL) was carried out according to the procedure described above. After usual workup, the crude oil was purified by preparative TLC [SiO_2, benzene-acetone (9:1)] to give **4a** (0.130 g, 12%, R_f 0.49) and **4b** (0.163 g, 14%, R_f 0.57).

Preparation of Di-μ-chloro-bis[(3,2,10-η-cis-4-t-butoxypinene)-palladium(II)] (4c): The reaction of pinadiene **1** (0.067 g, 0.50 mmol) with $Pd(OCOCF_3)(OOBu^t)$ (0.154 g, 0.50 mmol) in acetone (2.5 mL) was carried out according to the procedure described above. After usual workup, Al_2O_3 column chromatography (eluent CH_2Cl_2) afforded complex **4c** (0.149 g, 85%): ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.03 (3H, s, *gem*-Me), 1.25 (9H, s, Bu^t), 1.41 (3H, s, *gem*-Me), 2.00—2.75 (4H, m), 3.13 (1H, br), 3.75 (1H, br), 3.85—3.95 (1H, m), and 4.16—4.25 (1H, m).

Found: C, 48.29; H, 6.47%. Calcd for $C_{14}H_{23}ClOPd$: C, 48.15; H, 6.64%.

Ligand Exchange of Complex 4a and 4b with AgOAc: The reaction of chloride complex **4a** and **4b** with AgOAc in $CHCl_3$ was carried out according to the procedure described previously.[1]

Di-μ-acetato-bis[(3,2,10-η-cis-4-methoxypinene)palladium(II)] (5a): Yield 64%; IR (KBr) 1570, 1412, 1342, 1096, 976, 920, and 780 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.00 (3H, s, *gem*-Me), 1.41 (3H, s, *gem*-Me), 1.87—2.73 (4H, m), 2.01 (3H, s, OAc), 2.83 (1H, s, *syn*-H-10), 3.30 (3H, s, OMe), 3.47 (1H, dd, J=5 and 2 Hz, H-4), 3.66 (1H, s, *anti*-H-10), and 3.98 (1H, d, J=5 Hz, H-3).

Found: C, 47.17; H, 6.19%. Calcd for $C_{13}H_{20}O_3Pd$: C, 47.22; H, 6.10%.

Di-μ-acetato-bis[(3,2,10-η-cis-4-acetoxypinene)palladium(II)] (5b): Yield 84%; $[\alpha]_D^{27}$ −75° (c 0.25, MeOH); IR (KBr) 1730, 1570, 1416, 1240, and 1024 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.05 (3H, s, *gem*-Me), 1.43 (3H, s, *gem*-Me), 1.80—2.03 (1H, m), 1.96 (6H, s, OAc), 2.23—2.80 (3H, m), 3.35 (1H, s, *syn*-H-10), 3.52 (1H, d, J=2 Hz, *anti*-H-10), 3.85 (1H, d, J=5 Hz, H-3), and 4.72 (1H, dd, J=5 and 3 Hz, H-4).

Found: C, 47.29; H, 5.78%. Calcd for $C_{14}H_{20}O_4Pd$: C, 46.88; H, 5.62%.

Preparation of (1S,4S,5S)-2(10)-Pinen-4-yl Methyl Ether (6a): According to the sequence of G. Ohloff *et. al.*,[12] (−)-(1S,4S,5S)-2(10)-pinen-4-ol (**20**) was firstly prepared starting from (−)-α-pinene {$[\alpha]_D$ −29° (neat), Tokyo Kasei}. In this procedure, isomerization of (1S,5S)-2-pinen-4-one (verbenone) to (1S,5S)-2(10)-pinen-4-one was performed by Herrmann's method.[24] The alcohol **20** obtained in this way was transformed into the methyl ether **6a** by the following procedure.

Sodium hydride (0.068 g, 2.83 mmol) was added to a solution of alcohol **20** (0.400 g, 2.63 mmol) and MeI (0.436 g, 3.07 mmol) in dry DME (1.5 mL) over a period of 10 min with stirring at room temperature. After stirring for 10 min, a further quantity of MeI (0.100 g, 0.705 mmol) was added, and stirring was continued for additional 2 h. The DME and excess MeI were then removed by distillation at atmospheric pressure. To the remaining mixture was added ether (5 mL), and the resulting NaI was filtered off and washed with additional ether (10 mL). Evaporation of ether followed by distillation gave 2(10)-pinen-4-yl methyl ether (**6a**) (0.357 g, 82%): bp 90—95 °C (35 mmHg); IR (neat) 2935 (C-H), 1648, 1468, 1372, 1092, 874, and 846 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ=0.93 (3H, s, *gem*-Me), 1.25 (3H, s, *gem*-Me), 1.63—1.75 (1H, m), 2.18—2.93 (5H, m), 3.28 (3H, s, OMe), 3.63—3.98 (1H, m, H-4), and 4.63 (2H, d, J=2 Hz, H-10).

Preparation of (1S,4S,5S)-2(10)-Pinen-4-yl Acetate (6b): The alcohol **20** (0.584 g, 3.84 mmol) was acetylated by using Ac_2O (0.431 g, 4.22 mmol) in the presence of pyridine (0.455 g, 5.76 mmol). Usual workup followed by distillation gave 2(10)-pinen-4-yl acetate (**6b**) (0.653 g, 88%): bp 70—75 °C (2 mmHg); IR (neat) 2940 (C-H), 1738 (C=O), 1648, 1472, 1372, 1242, 1042, 1024, 880, and 852 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ=0.93 (3H, s, *gem*-Me), 1.30 (3H, s, *gem*-Me), 1.73—2.60 (6H, m), 1.96 (3H, s, OAc), 4.66 (2H, t, J=2 Hz, H-10), and 5.05—5.50 (1H, m, H-4).

Preparation of Di-μ-chloro-bis[(3,2,10-η-trans-4-methoxy-pinene)palladium(II)] (7a): Into a suspended solution of $Pd(OAc)_2$ (0.225 g, 1.00 mmol) in anhydrous MeOH (5 mL) was added methyl ether **6a** (0.166 g, 1.00 mmol). After the mixture was stirred for 30 min, NaCl (0.174 g, 3.00 mmol) was added to the solution, and stirring was continued for further 30 min. The solvent was then removed under reduced pressure, and the residue was extracted with

CH_2Cl_2 (50 mL×2), washed with brine (20 mL×2), and dried over Na_2SO_4. After evaporation of the solvent, the residual yellow oil was chromatographed on Al_2O_3 (15 g). Elution with $CHCl_3$ (100 mL) gave oily material which was purified by preparative TLC [benzene–EtOAc (4:1)] to give complex **7a** (0.179 g, 58%): R_f 0.75; mp 147—151 °C (decomp); IR ($CHCl_3$) 1470, 1252, 1086, 948, and 822 cm^{-1}.

Found: C, 43.02; H, 5.58; Cl, 11.54%. Calcd for $C_{11}H_{17}ClOPd$: C, 43.39; H, 5.69; Cl, 11.03%.

Preparation of Di-μ-chloro-bis[(3,2,10-η-trans-4-acetoxypinene)palladium(II)] (7b): The reaction of acetate **6b** (0.194 g, 1.00 mmol) and $Pd(OAc)_2$ (0.225 g, 1.00 mmol) was carried out according to the procedure described above. Chromatographic purification of the resulting oil followed by preparative TLC [benzene–EtOAc (4:1)] gave complex **7b** (0.174 g, 51%): R_f 0.70; mp 145 °C (decomp); $[\alpha]_D$ −94° (*c* 0.19, MeOH); IR ($CHCl_3$) 1740 (C=O), 1045, 1023, and 980 cm^{-1}.

Found: C, 43.65; H, 5.21; Cl, 10.32%. Calcd for $C_{12}H_{17}ClO_2Pd$: C, 43.00; H, 5.11; Cl, 10.58%.

(1S,4R,5S)-2-Pinen-4-yl Acetate (9): The pinene **9** bearing OAc group at the C(4),*exo*-position was prepared by the reaction of α-pinene with $Pb(OAc)_4$ followed by isomerization in AcOH[11] in 47% yield from α-pinene; bp 96—98 °C (8 mmHg); IR (neat) 2930, 1730 (C=O), 1372, 1240 (C–O), 1018, 970, and 773 cm^{-1}.

(1S,4R,5S)-2-Pinen-4-yl Methyl Ether (8): The pinene **8** bearing OMe group at the C(4),*exo*-position was synthesized by the hydrolysis of the acetate **9** followed by treatment with MeI in 61% yield from **9**; bp 83—85 °C (23 mmHg); IR (neat) 2920, 2815, 1468, 1445, 1192, 1138, 1086, and 959 cm^{-1}.

(1S,4S,5S)-2-Pinen-4-yl Methyl Ether (10): The pinene **10** bearing OMe group at the C(4),*endo*-position was prepared by treatment of (1*S*,4*S*,5*S*)-2-pinen-4-ol (**21**) with MeI in 84% yield. The alcohol **21** was obtained by MnO_2 oxidation of (1*S*,4*R*,5*S*)-2-pinen-4-ol followed by $LiAlH_4$ reduction;[12] bp 80—83 °C (20 mmHg); IR (neat) 2930, 2810, 1446, 1368, 1354, 1190, 1088, and 952 cm^{-1}.

(1S,4S,5S)-2-Pinen-4-yl Acetate (11): The esterification of alcohol **21** with Ac_2O gave the pinene **11** bearing OAc group at the C(4),*endo*-position in 89% yield: bp 90—95 °C (8 mmHg); IR (neat) 2940, 1740 (C=O), 1662, 1450, 1375, 1242, 1022, 976, and 810 cm^{-1}.

Found: C, 74.15; H, 9.40%. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%.

*Preparation of 4-Substituted 2-(*trans*-2-Butenyl)phenols 12*: 4-*t*-Butyl-2-(*trans*-2-butenyl)phenol (**12a**) was prepared by *C*-alkylation of *p*-*t*-butylphenol with *trans*-1-chloro-2-butene (Tokyo Kasei). 4-Trimethylsilyl-2-(*trans*-2-butenyl)-phenol (**12b**) was synthesized by the silylation of 4-bromo-2-(*trans*-2-butenyl)phenol prepared by *O*-alkylation of *p*-bromophenol with 3-chloro-2-butene followed by the Claisen rearrangemet (200 °C, *N*,*N*-diethylaniline). The silylation procedure is as follows. Into a solution of 4-bromo-2-(*trans*-2-butenyl)phenol (3.40 g, 15.0 mmol) in dry THF (20 mL) was dropwise added Bu^nLi (1.6 M in hexane, 31 mL, 50 mmol) at −78 °C, and then chlorotrimethylsilane (5.7 mL, 45 mmol) was added to the solution at −78 °C. The mixture was warmed up to room temperature, stirred overnight, quenched with 2 M HCl (30 mL), and extracted with ether. Usual workup followed by distillation gave **12b** (2.56 g, 78%); bp 95—102 °C (1 mmHg); IR (neat) 3460 (OH) and 960 (C=C) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ=0.00 (9H, s, $SiMe_3$), 1.35—1.55 (3H, m, Me), 2.90—3.23 (2H, m, CH_2), 5.10 (1H, br s, OH), and 5.18—5.50 (2H, m, CH=CH). The acetal **12f** was synthesized as follows. A mixture of 4-acetyl-2-(*trans*-2-butenyl)phenol (**12e**) (1.14 g, 6.0 mmol), ethylene glycol (18.6 g, 300 mmol), and fumaric acid (0.06 g, 0.5 mmol) in dry benzene (20 mL) was refluxed with stirring. The water formed during the reaction was removed azeotropically (Dean-Stark trap) for 72 h. After the mixture was cooled to room temperature, benzene (200 mL) and K_2CO_3 was added until drying agent was coagulated. The solid was filtered off by suction. The filtrate was washed with 5% aqueous $NaHCO_3$ solution (20 mL) and brine (20 mL), and dried over Na_2SO_4. Evaporation of the solvent and addition of pentane induced crystallization to give ethylene acetal **12f** (1.07 g, 76%): IR (Nujol) 3370, 2930, 1611 (C=C), 1504, 1377, 1275, 1204, 1097, 1036, 971, 860, and 820 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ=1.65 (3H, s, Me), 1.68—1.78 (3H, m, Me), 3.38 (2H, br s), 3.75—4.10 (4H, m, OCH_2CH_2O), 4.20—5.10 (1H, m, OH), 5.60—5.78 (2H, m, CH=CH), 6.81 (1H, d, *J*=9 Hz, ArH), and 7.20—7.40 (2H, m, ArH). Preparation of other phenols **12c—e** was described previously.[1,2]

Asymmetric Cyclization of 12: The cyclization of **12** (2.5 mmol) was performed by using di-μ-acetato-bis[(3,2,10-η-pinene)palladium(II) **5a—c** (0.125 mmol as a dimer) and $Cu(OAc)_2$ (0.0454 g, 0.25 mmol) in anhydrous MeOH (5 mL) under an atmosphere of O_2 (1 atm) at 35 °C according to the general procedure described previously.[1,2] The cyclized products **13** and **14** were isolated by Kugelrohr distillation and purified by either preparative GLC (20% PEG 20 M, 2 m) or TLC. The spectral and analytical data of newly obtained products are listed below.

2-Vinyl-5-t-butyl-2,3-dihydrobenzofuran (13a): Kugelrohr distillation, bp 120—129 °C (6 mmHg); IR (neat) 2970, 1500, 1240, 930, and 810 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ=1.15 (9H, s, Bu^t), 2.69 (1H, dd, *J*=15 and 8 Hz, H-3), 3.13 (1H, dd, *J*=15 and 9 Hz, H-3), 4.75—5.35 (3H, m, H-2 and CH_2=C), 5.57—6.12 (1H, m, CH=C), 6.35 (1H, d, *J*=9 Hz, ArH), and 6.78—7.02 (2H, m, ArH).

Found: C, 83.16; H, 8.87%. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97%.

5-t-Butyl-2-ethylbenzofuran (14a): Kugelrohr distillation, bp 135 °C (6 mmHg); IR (neat) 2970, 1480, 1370, 1270, and 800 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ=1.32 (9H, s, Bu^t), 1.35 (3H, t, *J*=8 Hz, Me), 2.73 (2H, q, *J*=8 Hz, CH_2), 6.20 (1H, br s, H-3), and 7.12—7.41 (3H, m, ArH).

Found: C, 83.03; H, 8.84%. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97%.

5-Trimethylsilyl-2-vinyl-2,3-dihydrobenzofuran (13b): TLC [SiO_2, hexane–$CHCl_3$ (4:1)], R_f 0.51; IR (neat) 2950, 1600, 1480, 1250, 1240, and 815 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ=0.00 (9H, s, $SiMe_3$), 2.88 (1H, dd, *J*=18 and 8 Hz, H-3), 3.40 (1H, dd, *J*=18 and 10 Hz, H-3), 5.05—5.83 (3H, m, H-2 and CH_2=C), 7.11 (1H, d, *J*=9 Hz, ArH), and 7.37—8.07 (2H, m, ArH).

5-Trimethylsilyl-2-ethylbenzofuran (14b): TLC (the same conditions as above), R_f 0.64; IR (neat) 2950, 1598, 1250, and 820 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ=0.00 (9H, s, $SiMe_3$), 1.15 (3H, t, *J*=8 Hz, Me), 2.80 (2H, q, *J*=8Hz, CH_2), 6.60 (1H, br s, CH=C), and 7.68—8.10 (3H, m, ArH).

5-Acetyl-2-vinyl-2,3-dihydrobenzofuran Ethylene Acetal (13f): TLC [SiO_2, hexane–EtOAc (5:1)], R_f 0.70; bp 122—124 °C (1 mmHg); $[\alpha]_D$ −9.40° (*c* 4.31, CCl_4); ^1H NMR (60 MHz, CCl_4) δ=1.48 (3H, s, Me), 2.83 (1H, dd, *J*=13 and 7 Hz, H-3), 3.28 (1H, dd, *J*=13 and 8 Hz, H-3), 3.53—3.91 (4H, m, OCH_2CH_2O), 4.78—5.39 (3H, m, H-2 and CH_2=), 5.92 (1H, ddd, *J*=15, 9, and 5 Hz, -CH=), 6.50 (1H, d, *J*=9 Hz, ArH), and 6.91—7.16 (2H, m, ArH).

Found: C, 72.39; H, 6.88%. Calcd for $C_{14}H_{16}O_3$: C, 72.40; H, 6.94%.

5-Acetyl-2-ethylbenzofuran Ethylene Acetal (14f): TLC (the same conditions as above), R_f 0.80; ^1H NMR (60 MHz, CCl_4) δ=1.31 (3H, t, *J*=8 Hz, Me), 1.61 (3H, s, Me), 2.78 (2H, q, *J*=8 Hz, CH_2), 3.64—4.05 (4H, m, OCH_2CH_2O), 6.30 (1H, s, H-3), and 7.23—7.34 (3H, m, ArH).

Determination of Enantiomer Excess of 13a (Y=Bu^t): The % ee determination of **13a** (Y=Bu^t) was attempted by using Eu(tfc)$_3$ through the NMR spectrum of methyl ester derived from $KMnO_4$ oxidation of **13a** followed by esterification.[2] However, during the workup process of $KMnO_4$ oxidation performed in MeCN–glyme solution, unreproducible results were obtained for this compound, because of the difference in solubility of the resulting enantiomeric potassium 5-*t*-butyl-2,3-dihydrobenzofuran-2-carboxylate into aqueous NaOH solution.[25] Hence, the enantiomer excess of **13a** was determined through the NMR spectrum of 2-(5-*t*-butyl-2,3-dihydro-2-benzofuranyl)-2-propanol (**22**) prepared by the same manner as that of **16** (see Scheme 3).

a) Transformation of 13a (Y=Bu^t) into Tertiary Alcohol 22: A solution of 2-vinyl-5-*t*-butyl-2,3-dihydrobenzofuran (**13a**) {0.270 g, 1.3 mmol, $[\alpha]_D^{21}$ −4.54° (*c* 8.58, CCl_4)}, $Pd(OCOCF_3)(OOBu^t)$ (0.040 g, 0.13 mmol), and Bu^{t}OOH (0.30 mL, 1.3 mmol) in benzene (6 mL) was stirred at 50 °C for 65 h. Evaporation of the solvent followed by addition of pentane afforded brown precipitate which was removed by filtration. Concentration of the filtrate followed by Kugelrohr distillation gave a 60:40 mixture (0.155 g) of 2-acetyl-5-*t*-butyl-2,3-dihydrobenzofuran (**23**) and unreacted **13a**. The compound **23** purified by preparative TLC [SiO_2, hexane–EtOAc (7:3)] showed the following characteristics: R_f 0.40; IR (neat) 2952, 2860, 1812, 1756, 1720, 1494, 1362, 1239, 1216, 1160, 1064, 962, and 829 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ=1.29 (9H, s, Bu^t), 2.23 (3H, s, COMe), 3.29 (1H, d, *J*=8 Hz, H-3), 3.31 (1H, d, *J*=10 Hz, H-3), 4.95 (1H, dd, *J*=10 and 8 Hz, H-2), and 6.63—7.30 (3H, m, ArH). The acetylbenzofuran **23** (0.090 g, 0.41 mmol) was treated with MeMgBr (0.50 mmol) in dry ether (4 mL) at 0 °C. Usual workup followed by preparative TLC [SiO_2, benzene–EtOAc (4:1)] gave tertiary alcohol **22** (0.040 g, 42%): R_f 0.45; ^1H NMR (60 MHz, $CDCl_3$) δ=1.23 (3H, s, Me), 1.34 (3H, s, Me), 1.31 (9H, s, Bu^t), 2.03 (1H, br, OH), 3.18 (2H, d, *J*=9 Hz, H-3), 4.67 (1H, t, *J*=9 Hz, H-2), and 6.73—7.49 (3H, m, ArH).

b) Determination of Enantiomer Excess of 13a through tert-Alcohol 22: The ^1H NMR spectra ($CDCl_3$) of tertiary alcohol **22** (0.013 g) obtained above showed a triplet signal due to the C(2) proton at δ=4.67 (*J*=9 Hz). The proton was separated clearly into two sets of triplets (*J*=9 Hz) by addition of Eu(tfc)$_3$ (0.004 g). The relative peak areas of the three sets of splitting signals led to 18% ee for this compound. Thus, the maximum rotation of **13a** is estimated to be 25.4° (CCl_4). Using **13a** with different $[\alpha]_D$ values, the experiment was repeated three times, and the results were shown to be reproducible.

Application of this procedure to **13c** (Y=Me) led to the % ee in good agreement with that obtained by the previous method.[2]

Determination of Enantiomer Excess of 13b (Y=SiMe$_3$): Optically active **13b** (0.209 g, 0.96 mmol) of $[\alpha]_D^{23}$ −5.04° (*c* 16.3, CCl_4) was dissolved in CCl_4 (3 mL), into which was added trifluoroacetic acid (5 mL) at room temperature. After stirring for 24 h, the mixture was diluted with ether, poured into saturated $NaHCO_3$ solution (20 mL), and extracted with ether. Preparative TLC [SiO_2, hexane–EtOAc (4:1), R_f 0.80] followed by Kugelrohr distillation [bp 80—82 °C (1 mmHg)] gave **13d** (Y=H) (0.023 g, 17%), the $[\alpha]_D$ of which was −4.32° (*c* 1.16, CCl_4). This value corresponds to 17% ee based on the previously reported maximum rotation.[1] The maximum rotation of **13b** is thus estimated to be −30.3° (CCl_4).

Determination of Enantiomer Excess of 13f: Into a solution of **13f** {0.182 g, 0.78 mmol, $[\alpha]_D$ −9.40°} in ether (20 mL) was added 2 M HCl solution (20 mL). After the mixture was stirred at room temperature overnight, the ether layer was washed with water and brine, and dried over Na_2SO_4. Evaporation followed by preparative TLC [SiO_2, hexane–EtOAc (4:1), R_f 0.45] gave 4-acetyl-2-vinyl-2,3-dihydrobenzofuran (**13e**) (0.085 g, 58%), the $[\alpha]_D$ of which was −25.0° (CCl_4). This value corresponds to 29% ee.[2]

Preparation of 2-Acetyl-2,3-dihydrobenzofuran (15): A solution of 2-vinyl-2,3-dihydrobenzofuran **13d** {1.00 g, 6.84 mmol, $[\alpha]_D^{23}$ +4.11° (*c* 5.55, CCl_4)}, $Pd(OCOCF_3)(OOBu^t)$ (0.210 g, 0.68 mmol), and Bu^{t}OOH (1.76 mL, 14.7 mmol) in benzene (30 mL) was stirred at 50 °C for 16 h. The mixture was extracted with CH_2Cl_2, washed with a 10% aqueous Na_2SO_3 and brine, and dried over Na_2SO_4. Evaporation of the solvent gave oily material, which was dissolved into a small amount of ether. Addition of pentane to this solution afforded brown precipitate which was removed by filtration. Evaporation followed by Kugelrohr distillation gave 2-acetyl-2,3-dihydrobenzofuran **15** (0.532 g, 48%). Analytically-pure **15** was obtained by preparative GLC; bp 100—110 °C (2 mmHg); $[\alpha]_D^{24}$ −9.30° (*c* 1.52, CCl_4); IR (neat) 1720 (C=O) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ=2.27 (3H, s, COMe), 3.37 (2H, br d, *J*=9 Hz, H-3), 4.93 (1H, t, *J*=9 Hz, H-2), and 6.53—7.26 (4H, m, ArH).

Found: C, 73.58; H, 6.18%; M^+, 162. Calcd for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22%; M, 162.

Preparation of 2-(2,3-Dihydro-2-benzofuranyl)-2-propanol (16): Into a solution of MeMgBr (11.6 mmol) in ether (30 mL) was slowly added a solution of **15** (0.754 g, 4.6 mmol) in ether (10 mL). The mixture was stirred for 1 h at room temperature and then acidified by 2 M HCl. Extraction with ether followed by Kugelrohr distillation gave tertiary alcohol **16** (0.580 g, 70%) which was purified by preparative GLC: bp 78—80 °C (0.1 mmHg); $[\alpha]_D^{24}$ +5.87° (*c* 1.02, EtOH); IR (neat) 3400 (OH) cm^{-1}; ^1H MNR (60 MHz, $CDCl_3$) δ=1.12 (3H, s, Me), 1.25 (3H, s, Me), 3.05 (2H, br d, *J*=9 Hz, H-3), 3.17—3.83 (1H, m, OH), 4.51 (1H, dd, *J*=10 and 9 Hz, H-2), and 6.60—7.25 (4H, m, ArH).

Preparation of 1-(5-Acetyl-2,3-dihydro-2-benzofuranyl)-1-methylethyl Acetate (17): A mixture of tertiary alcohol **16** (0.514 g, 2.88 mmol) and Ac_2O (0.894 g, 8.76 mmol) in

benzene (20 mL) was stirred at 0 °C while a solution of $SnCl_4$ (2.25 g, 8.64 mmol) in benzene (10 mL) was added dropwise over a period of 20 min. After stirring for further 30 min, the solution was poured into ice-water, extracted with ether until neutral, and dried over Na_2SO_4. Evaporation of the solvent gave acetate **17** (0.623 g, 82%) as solid which was recrystallized from pentane; mp 95.5—97.0 °C; IR (Nujol) 1730, 1664, 1610, 1270, 1250, 966, and 820 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ=1.48 (3H, s, Me), 1.55 (3H, s, Me), 1.94 (3H, s, OAc), 2.51 (3H, s, COMe), 3.17 (2H, d, J=9 Hz, H-3), 5.02 (1H, t, J=9 Hz, H-2), 6.73 (1H, d, J=9 Hz, ArH), and 7.57—7.92 (2H, m, ArH).

Found: 68.58; H, 6.83%. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92%.

Preparation of Tremetone (18): The acetate **17** (0.117 g, 0.45 mmol) was pyrolyzed at 330 °C for 1.5 min according to the procedure of Bonner *et al.*[20] The crude tremetone (**18**) formed in 76% yield (0.091 g, 75% pure) was purified by preparative GLC: $[\alpha]_D^{21}$ +10.4° (*c* 0.87, EtOH); IR (neat) 1678, 1608, and 1264 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ=1.73 (3H, s, Me), 2.40 (3H, s, COMe), 2.95 (1H, dd, J=16 and 9 Hz, H-3), 3.35 (1H, dd, J=16 and 9 Hz, H-3), 4.85 (1H, br s, =CH_2), 5.03 (1H, br s, =CH_2), 5.15 (1H, t, J=9 Hz, H-2), 6.68 (1H, d, J=9 Hz, ArH), and 7.57—7.83 (2H, m, ArH). The spectral data agrees well with that reported previously.[26] The $[\alpha]_D$ value of +10.4° corresponding to 17% ee based on the reported maximum rotation.[19]

Found C, 76.80; H, 7.07%. Calcd for $C_{13}H_{14}O$: C, 77.20; H, 6.98%.

Tremetone (18) Prepared via *Wittig Reaction*: Into a solution of Bu^{n}Li (1.6 M in hexane, 2.10 mL, 3.36 mmol) in ether (8 mL) was added $[Ph_3PMe]^+Br^-$ (1.32 g, 3.70 mmol) by portions, and the mixture was stirred for 4 h at room temperature under argon. Into this mixture was added dropwise a solution of 2-acetyl-2,3-dihydrobenzofuran (**15**) {0.600 g, 3.70 mmol, $[\alpha]_D$ −9.30°} in ether (2 mL). The whole mixture was then heated at 40 °C for 19 h under argon, and the resulting solid was removed by filtration. The ether layer was washed with water until neutral, and dried over $CaCl_2$. Evaporation followed by Kugelrohr distillation gave 2-isopropenyl-2,3-dihydrobenzofuran (**19**) (0.180 g, 33%): bp 105—120 °C (2 mmHg); ^1H NMR (60 MHz, $CDCl_3$) δ=1.74 (3H, d, J=1 Hz, Me), 2.96 (1H, dd, J=16 and 9 Hz, H-3), 3.34 (1H, dd, J=16 and 9 Hz, H-3), 4.83—5.33 (3H, m, C=CH_2 and H-2), and 6.67—7.42 (4H, m, ArH). The dihydrobenzofuran **19** (0.174 g, 1.17 mmol) was converted into tremetone (**18**) (0.223 g, 94% pure) in 89% yield by the procedure using Ac_2O (0.364 g, 3.57 mmol) and $SnCl_4$ (0.917 g, 3.52 mmol) in benzene (15 mL). Preparative TLC (SiO_2, $CHCl_3$, R_f 0.27) followed by Kugelrohr distillation [bp 170 °C (2 mmHg)], gave pure **18** of $[\alpha]_D^{24}$ +10.5° (*c* 2.64, EtOH) in 17% ee.[19]

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