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Synthesis of (*S*)-Imperanene by Using Allylic Substitution

Yuji Takashima and Yuichi Kobayashi*

Department of Biomolecular Engineering, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8501, Japan

ykobayas@bio.titech.ac.jp

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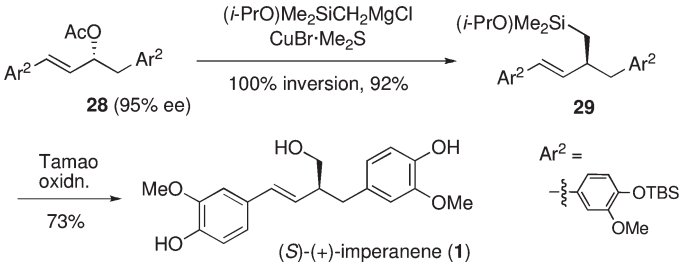
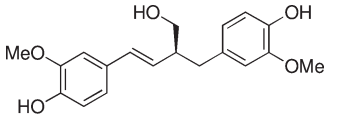


Synthesis of (*S*)-imperanene (**1**) was studied by using copper-assisted allylic substitution of ArCH=CHCH(L)CH_2Ar (L: leaving group) and (*i*-PrO)Me_2SiCH_2MgCl. Preliminary substitution between PhCH=CHCH(L)Me (L = AcO, PivO, $MeOCO_2$, (2-Py)CO_2) and Bu copper reagents derived from BuMgX (X = Br, Cl) and CuBr·Me_2S or CuCl in 1:1−40:1 ratios suggested acetate **28** as the best substrate. To prepare **28**, kinetic resolution of racemic (*E*)-TMSCH=CHCH(OH)CH_2Ar^2 (Ar^2 = (*p*-TBSO)(*m*-MeO)C_6H_3) carried out by using the asymmetric epoxidation with (−)-DIPT afforded the corresponding epoxy alcohol and (*S*)-allylic alcohol. After separation by chromatography, these products were converted to (*S*,*E*)-Bu_3SnCH=CHCH(OH)CH_2Ar^2, which upon palladium-catalyzed coupling with Ar^2-I followed by acetylation gave **28** (95−98% ee). Substitution of **28** with (*i*-PrO)Me_2SiCH_2MgCl and CuBr·Me_2S in a 4:1 ratio at 0 °C proceeded cleanly to produce **29** with 100% inversion in 92% yield. Finally, Tamao oxidation furnished **1**.

Introduction

In the past decade allylic substitution of secondary (optically active) allylic alcohol derivatives with copper reagents has much progressed with the finding of reactive leaving groups such as $C_6F_5CO_2$, *o*-(Ph_2P)$C_6H_4CO_2$, *o*-(Ph_2PO)$C_6H_4CO_2$, $(RO)_2P(O)O$, and (2-Py)CO_2. With these groups a wide range of allylic substrates have been shown to undergo γ-substitution with high efficiency in yield and in regio- and stereoselectivities.[1] However, there are a class of substrates that suffer from low regioselectivity by steric and/or electronic reason. For example, the γ-aryl allylic alcohol derivatives afford a mixture of regioisomers in varying ratios depending on copper reagents and reaction conditions.[2] Somewhat low percent inversion[3] for S_N2-type product observed with alkyl copper reagent is another problem to be solved.



(*S*)-(+)-imperanene (**1**)

To advance in this area, we have become interested in the synthesis of (*S*)-imperanene (**1**) by using γ- and α-selective allylic substitutions of esters **2** and **3** with masked "$HOCH_2$" copper reagents derived from (*i*-PrO)Me_2SiCH_2MgCl[4] and CuX to give **4**, which would furnish alcohol **5** by oxidation (Scheme 1). This target, isolated from *Imperata cylindrica* by Ohizumi,[5] inhibit platelet aggregation. Recently, inhibition

(1) (a) Negishi, E.; Liu, F. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Chapter 1.(b) Kar, A.; Argade, N. P. *Synthesis* **2005**, 2995–3022.

(2) (a) Goering, H. L.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 3986–3990. (b) Tseng, C. C.; Yen, S.-J.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2892–2895. (c) Norinder, J.; Bogár, K.; Kanupp, L.; Bäckvall, J.-E. *Org. Lett.* **2007**, *9*, 5095–5098.

(3) We define "% inversion" as (% ee of product/% ee of substrate) × 100.

(4) Tamao, K.; Ishida, N. *Tetrahedron Lett.* **1984**, *25*, 4245–4248.

(5) Matsunaga, K.; Shibuya, M.; Ohizumi, Y. *J. Nat. Prod.* **1995**, *58*, 138–139.

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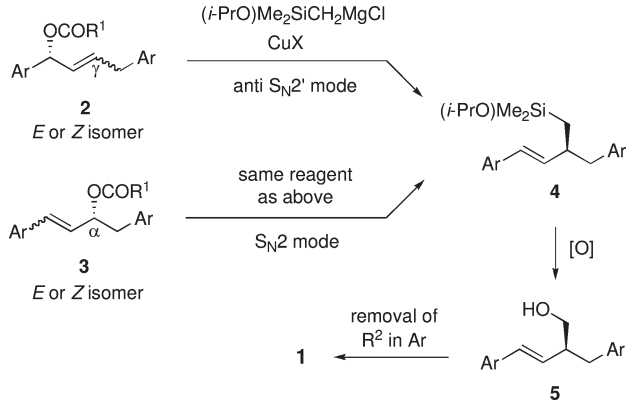
SCHEME 1. Two Approaches to Imperanene[a]



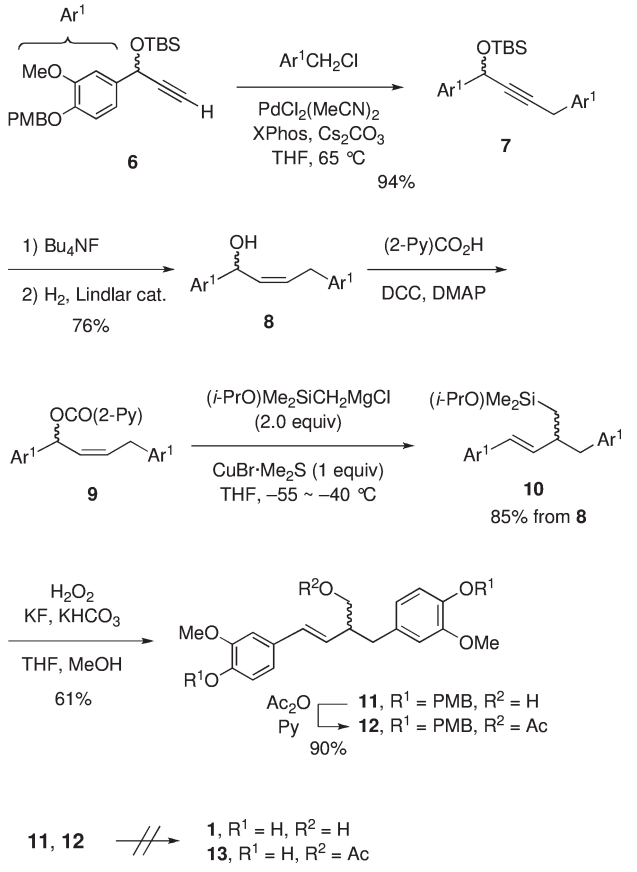
[a]Ar = (*m*-MeO)(*p*-R^{2}O)C$_6$H$_3$ (R^2 = PMB, TBS, TBDPS, Ts).

of tyrosinase activity was newly reported.[6] Four syntheses[7] of **1** and one synthesis[8] of the enantiomer have been reported to date. The key to the success in these syntheses was the proper control of the reactive oxygen-containing functional groups and suppression of side reactions induced by these groups. Herein, we report a different approach to **1** using allylic substitution.

Results and Discussion

The first approach to **4** from **2** was examined by using our protocol,[9] in which a cis allylic picolinate is required for high γ-selectivity. Thus, picolinate **9** with (*m*-MeO)(*p*-PMBO)C$_6$H$_3$ (abbreviated to Ar^1) was chosen as **2**, and synthesized in a racemic form by the method summarized in Scheme 2. Coupling of acetylene **6** and Ar^{1}CH$_2$Cl was accomplished with the Pd/XPhos catalyst to afford **7** in 94% yield.[10] Other attempts by using catalysts such as Co(acac)$_3$[11] and CuCN and by conducting the reaction in HMPA did not afford the product. Conversion of **7** to picolinate **9** proceeded well. Allylic substitution of picolinate **9** with ((*i*-PrO)Me$_2$SiCH$_2$)$_2$CuMgCl, synthesized from (*i*-PrO)Me$_2$SiCH$_2$MgCl (2 equiv) and CuBr·Me$_2$S (1 equiv) at 0 °C (30 min), proceeded smoothly to afford the γ-substitution product **10** regioselectively in good yield. Oxidation of **10** under the reported conditions successfully produced alcohol **11** in 61% yield. Finally, removal of the PMB group was

SCHEME 2. Investigation of the Anti S$_N$2′ Approach[a]



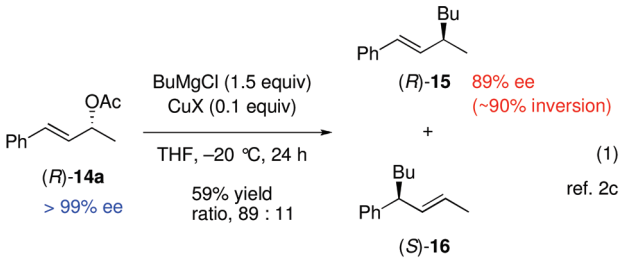
[a]XPhos: 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl.

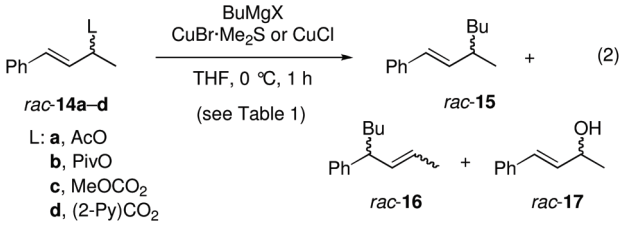
attempted with DDQ in wet CH$_2$Cl$_2$,[12] CF$_3$CO$_2$H in CH$_2$Cl$_2$,[13] NaB(CN)H$_3$/BF$_3$·Et$_2$O in THF at 80 °C,[14] Ph$_3$CBF$_4$ in CH$_2$Cl$_2$,[15] and Dowex in MeOH/THF.[16] However, these reagents unfortunately gave a mixture of unidentified products. Another attempt on acetate **12** derived from **11** with CF$_3$CO$_2$H in CH$_2$Cl$_2$[13] and ClSO$_2$NCO in CH$_2$Cl$_2$[17] produced a mixture. Next, the transformation of Scheme 2 was examined with compounds possessing the TBS, TBDPS, or Ts protective group in place of the PMB group. However, Pd/XPhos-catalyzed coupling of these acetylenes with ArCH$_2$Cl was unsuccessful, yielding $<26\%$ of the desired product or a mixture of unidentified products.

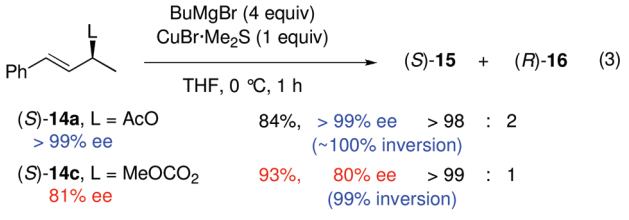
The second approach of Scheme 1 through the S$_N$2-type substitution (i.e., **3** to **4**) was investigated next. Allylic substitution of racemic ArCH=CHCH(L)R, which has the same structural type as **3**, has been well documented,[1] whereas reactions of the optically active substrates have been reported a little.[2] Unfortunately, percent inversion is at the 90% level with varying regioselectivity depending on the

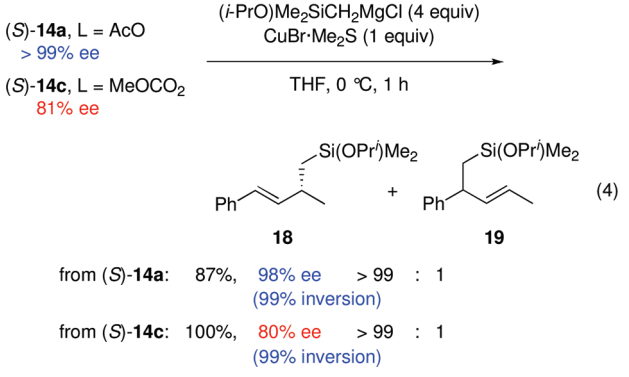
(6) Takara, K.; Iwasaki, H.; Ujihara, K.; Wada, K. *J. Oleo Sci.* **2008**, *57*, 191–196.
(7) (a) Shattuck, J. C.; Shreve, C. M.; Solomon, S. E. *Org. Lett.* **2001**, *3*, 3021–3023. (b) Doyle, M. P.; Hu, W.; Valenzuela, M. V. *J. Org. Chem.* **2002**, *67*, 2954–2959. (c) Davies, H. M. L.; Jin, Q. *Tetrahedron: Asymmetry* **2003**, *14*, 941–949. (d) Carr, J. A.; Bisht, K. S. *Org. Lett.* **2004**, *6*, 3297–3300.
(8) Eklund, P. C.; Riska, A. I.; Sjöholm, R. E. *J. Org. Chem.* **2002**, *67*, 7544–7546.
(9) (a) Kiyotsuka, Y.; Acharya, H. P.; Katayama, Y.; Hyodo, T.; Kobayashi, Y. *Org. Lett.* **2008**, *10*, 1719–1722. (b) Kiyotsuka, Y.; Kobayashi, Y. *Tetrahedron Lett.* **2008**, *49*, 7256–7259. (c) Kiyotsuka, Y.; Katayama, Y.; Acharya, H. P.; Hyodo, T.; Kobayashi, Y. *J. Org. Chem.* **2009**, *74*, 1939–1951.
(10) Larsen, C. H.; Anderson, K. W.; Tundel, R. E.; Buchwald, S. L. *Synlett* **2006**, *18*, 2941–2946.
(11) Kuno, A.; Saino, N.; Kamachi, T.; Okamoto, S. *Tetrahedron Lett.* **2006**, *47*, 2591–2594.
(12) (a) Vig, O. P.; Bari, S. S.; Sharma, A.; Sattar, M. A. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1990**, *29B*, 284–286. (b) Oikawa, Y.; Tanaka, T.; Horita, K.; Yonemitsu, O. *Tetrahedron Lett.* **1984**, *25*, 5397–5400. (c) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.* **1982**, *23*, 885–888.
(13) Fellows, I. M.; Kaelin, D. E., Jr.; Martin, S. F. *J. Am. Chem. Soc.* **2000**, *122*, 10781–10787.
(14) Srikrishna, A.; Viswajanani, R.; Sattigeri, J. A.; Vijaykmar, D. *J. Org. Chem.* **1995**, *60*, 5961–5962.
(15) Barton, D. H. R.; Magnus, P. D.; Streckert, G.; Zurr, D. *J. Chem. Commun.* **1971**, 1109–1111.
(16) Pletcher, J. M.; McDonald, F. E. *Org. Lett.* **2005**, *7*, 4749–4752.
(17) Kim, J. D.; Han, G.; Jeong, L. S.; Park, H.; Zee, O. P.; Jung, Y. H. *Tetrahedron* **2002**, *58*, 4395–4402.

reagents and reaction conditions as summarized in eq 1.[18] Due to this reason, we explored substitution between PhCH=CHCH(L)Me (L = AcO, PivO, $MeOCO_2$, (2-Py)-CO_2) and Bu copper reagents derived from BuMgX (X = Cl, Br) and CuBr·Me_2S or CuCl in 1:1−40:1 ratios (eq 2). As summarized in Table 1, the reaction of *rac*-**14a**−**c** with the copper reagents in >4:1 ratios in THF at 0 °C for 1 h was highly α-selective irrespective of the leaving groups (entries 3−8, 10, and 14), whereas substitution with the 1:1 reagent was γ-selective, but proceeded slowly (entries 1, 2, 11, and 12). Both BuMgBr and BuMgCl showed essentially the same regioselectivity and reactivity in reactions with acetate *rac*-**14a**. On the other hand, picolinate *rac*-**14d** was highly reactive with the 1:1 reagent, and gave the γ-product efficiently (entries 15 and 16).









(18) The copper catalyst used in ref 2c (CuX) is uncertain because of inconsistent description (Table 3, entry 2 and SI, CuCl vs. CuBr·Me_2S). As shown in Table 1 of the present MS, we confirmed essentially no difference between CuCl and CuBr·Me_2S.

TABLE 1. Preliminary Study of Allylic Substitution[a]

entry	substrate	L	BuMgX: X	equiv	CuBr·Me_2S equiv	**15**:**16**:**17**:SM[b]
1	*rac*-**14a**	AcO	Cl	2.0	2.2	0:18[c]:0:82
2	*rac*-**14a**	AcO	Br	2.0	2.3	0:29[c]:0:71
3	*rac*-**14a**	AcO	Cl	4.0	1.0	92: < 1:7:0
4	*rac*-**14a**	AcO	Br	4.0	1.0	94: < 2:4:0
5	*rac*-**14a**	AcO	Cl	4.0	0.4	92: < 1:7:0
6	*rac*-**14a**	AcO	Cl	4.0	0.1	94: < 1:6:0
7	*rac*-**14a**	AcO	Cl	1.4	CuCl,[d] 0.2	98: < 2:0:0
8	*rac*-**14a**	AcO	Br	1.4	CuCl,[d] 0.2	97: < 2: < 1:0
9	*rac*-**14b**	PivO	Cl	2.0	2.3	0:0:0:100
10	*rac*-**14b**	PivO	Cl	4.0	1.0	91:9:0:0
11	*rac*-**14c**	$MeOCO_2$	Cl	2.0	2.3	0:15[e]:0:85
12	*rac*-**14c**	$MeOCO_2$	Br	2.0	2.3	2:64[e]:0:34
13	*rac*-**14c**	$MeOCO_2$	Cl	4.0	1.0	89:11[e]:7:0
14	*rac*-**14c**	$MeOCO_2$	Br	4.0	1.0	99: < 1:0:0
15	*rac*-**14d**	(2-Py)CO_2	Cl	2.0	2.3	4:96[e]:0:0
16	*rac*-**14d**	(2-Py)CO_2	Br	2.0	2.2	4:96[e]:0:0
17	*rac*-**14d**	(2-Py)CO_2	Cl	4.0	1.0	64:29[e]:7:0
18	*rac*-**14d**	(2-Py)CO_2	Br	4.0	1.0	53:41[e]:6:0

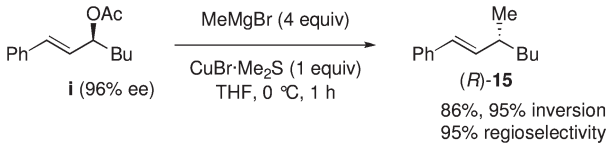
[a]Reactions were carried out at 0 °C for 1 h unless otherwise noted. [b]Starting material. [c]Cis:trans = ca. 1:2 by ^{1}H NMR spectroscopy. [d]At −20 °C for 2 h. [e]Cis:trans = ca. 2:1 by ^{1}H NMR spectroscopy.

With the above results in hand, we prepared optically active esters (*S*)-**14a** (>99% ee) and (*S*)-**14c** (81% ee) from the corresponding alcohol[19] of >99% ee (for (*S*)-**14a**, Ac_2O, DMAP, pyridine, CH_2Cl_2, rt, 100%; for (*S*)-**14c**, $ClCO_2Me$, pyridine, CH_2Cl_2, 0 °C−rt, 85%), though substantial drop in ee was observed with (*S*)-**14c**. These esters upon reaction with BuMgBr/CuBr·Me_2S (>4:1) under the optimized conditions produced (*S*)-**15** in good yields with high percent inversion and regioselectivity (eq 3). Similarly, reactions with (*i*-PrO)Me_2SiCH_2MgCl/CuBr·Me_2S (4:1) proceeded well to produce **18** quite efficiently (eq 4). On the basis of these results and the ee of (*S*)-**14a** and (*S*)-**14c** mentioned above, we decided to use acetate **28** with (*p*-TBSO)(*m*-MeO)C_6H_3 as Ar^2 in the real synthesis of imperanene (**1**) as shown in Scheme 3. In addition, we are pleased to conclude that highly efficient allylic substitution of ArCH=CHCH(OAc)R with R′MgBr/CuBr·Me_2S is now established.[20]

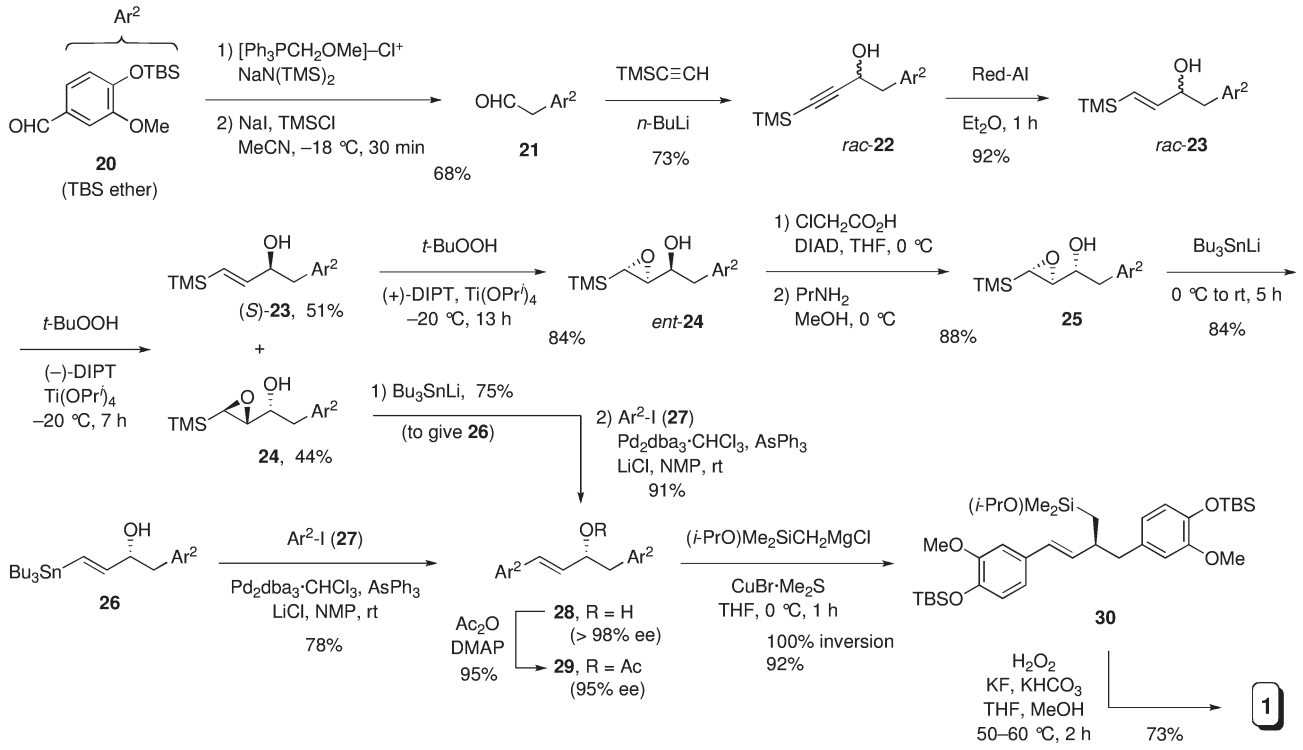
Successful synthesis of **1** and unsuccessful attempts for the preparation of intermediates are summarized in Schemes 3 and 4. TBS ether **20** was converted to homologue **21** and Ar^2-CCH (**31**) through the Wittig reaction and the Corey−Fuchs reaction, respectively, in good yields. An attempted asymmetric addition of **31** to **21** according to the literature

(19) Itoh, T.; Matsushita, Y.; Abe, Y.; Han, S.-H.; Wada, S.; Hayase, S.; Kawatsura, M.; Takai, S.; Morimoto, M.; Hirose, Y. *Chem.—Eur. J.* **2006**, *12*, 9228–9237.

(20) Additional example of successful substitution:



SCHEME 3. Synthesis of (*S*)-Imperanene



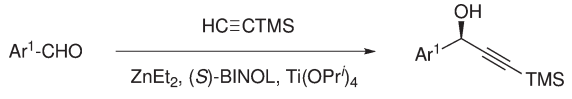
methods[21] was, however, unsuccessful, giving unidentified products (Scheme 4, attempt 1) probably due to the enolizable methylene moiety as suggested by Trost in his similar case.[22,23] In contrast, addition of the lithium anion of **31** to aldehyde **21** proceeded cleanly to produce racemic alcohol *rac*-**32**, which was subjected to oxidation in order to obtain ketone **33** for asymmetric hydrogen transfer reaction. However, oxidations with PCC, Dess-Martin, TPAP, $SO_3 \cdot Py$ resulted in formation of complex mixtures (attempt 2). In contrast, oxidation of racemic alcohol *rac*-**22** derived from **21** and TMS acetylene successfully afforded ketone **34** (attempt 3). Unfortunately, asymmetric hydrogen transfer reduction of **34** was quite slow, affording alcohol (*S*)-**22** in 24% yield after 24 h (attempt 3).[24,25]

Next, kinetic resolution of racemic allylic alcohol *rac*-**23** by asymmetric epoxidation[26] was investigated to create the asymmetric center for the allylic substitution. Under the reported conditions,[27] asymmetric epoxidation of *rac*-**23**, synthesized from *rac*-**22** by Red-Al reduction, afforded (*S*)-**23** and epoxide **24** in reasonable yields. Both of the products were separated by chromatography on silica gel, and converted to alcohol **27** separately. Epoxidation of (*S*)-**23** was followed by Mitsunobu inversion to afford **25** in 88% yield. Peterson reaction of **25** with Bu_3SnLi (prepared from Bu_3SnH and LDA) proceeded well to furnish γ-stannyl alcohol **26** stereoselectively in good yield. Palladium-catalyzed Stille coupling of **26** with (*p*-TBSO)(*m*-MeO)C_6H_3I (**27**, abbreviated to Ar^2-I)[28] was successful under modified conditions of Farina[29] with use of $Pd_2dba_3 \cdot CHCl_3$ (5 mol %), $AsPPh_3$ (20 mol %), and LiCl (4 equiv) in NMP at rt to afford alcohol **28** (99% ee) in 78% yield.[30] In a similar manner, epoxide **24** was converted to **28** (98% ee) via vinylstannane **26** in two steps. Finally, acetylation of alcohol **28** with

(21) (a) Gao, G.; Moore, D.; Xie, R.-G.; Pu, L. *Org. Lett.* **2002**, *4*, 4143–4146. (b) Gao, G.; Wang, Q.; Yu, X.-Q.; Xie, R.; Pu, L. *Angew. Chem., Int. Ed.* **2006**, *45*, 122–125.

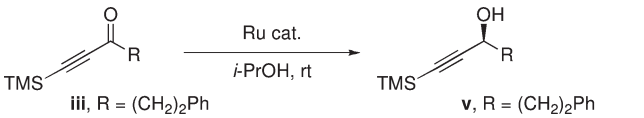
(22) Trost, B. M.; Ameriks, M. K. *Org. Lett.* **2004**, *6*, 1745–1748. Cf.: Anand, N. K.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 9687–9688.

(23) In contrast, the following reaction was successfully executed by the authors to produce **ii**, which was converted to (*S*)-**6** for the first approach (Scheme 2).



(24) Reaction at 35 °C produced a mixture of (*S*)-**22** and unidentified products.

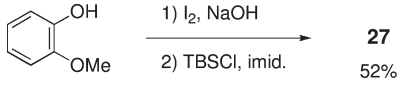
(25) In contrast, asymmetric hydrogen transfer reduction of ketones **iii** and **iv** executed by the authors gave alcohols **v** (90%, 98% ee) and **vi** (86%), respectively.



(26) (a) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237–6240. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780.

(27) Kinetic resolution of γ-silylallylic alcohols: Kitano, Y.; Matsumoto, T.; Sato, F. *Tetrahedron* **1988**, *44*, 4073–4086.

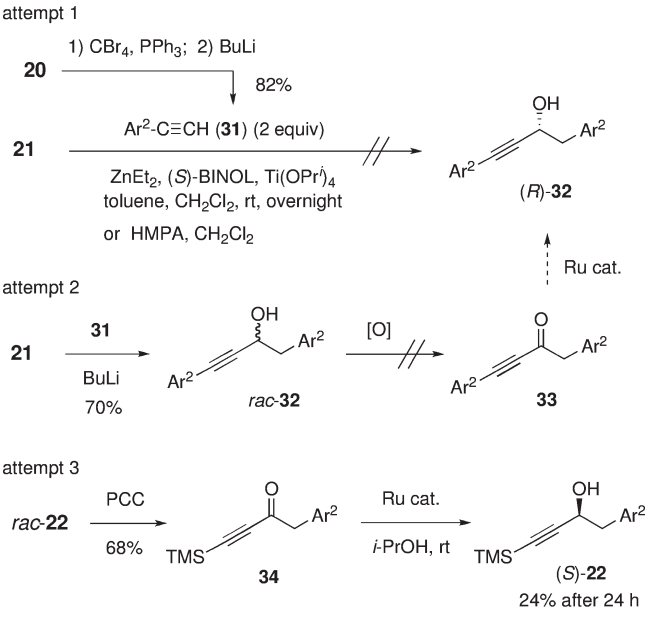
(28) Prepared as presented below. See the Experimental Section.



(29) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585–9595.

(30) Other conditions ($Pd_2dba_3 \cdot CHCl_3$/$AsPPh_3$ in THF at 50 °C, Pd(PPh_3)$_4$/CuI/CsF in DMF at 50 °C, and Pd(PPh_3)$_4$/LiCl in refluxing toluene) were unsuccessful, in our hand.

SCHEME 4. Attempted Preparation of Intermediates[a]



[a] Ar^2 = (*p*-TBSO)(*m*-MeO)C_6H_3. Ru cat. = Ru[(*S*,*S*)-TsDPEN](*p*-cymene).

Ac_2O and DMAP in CH_2Cl_2 afforded allylic acetate **29** in 95% yield, which was 95% ee by chiral HPLC. The coupling reaction of **29** with (*i*-PrO)Me_2SiCH_2MgCl/CuBr·Me_2S (4:1) at 0 °C completed within 1 h to furnish the α-substitution product **30** regioselectively in 92% yield. Finally, oxidation of **30** under the given conditions proceeded with concomitant desilylation of the TBS ether to produce (*S*)-imperanene (**1**) in 73% yield: 95% ee by chiral HPLC, $[\alpha]^{25}_D$ +98 (*c* 0.70, $CHCl_3$); lit. $[\alpha]^{25}_D$ +97 (*c* 0.68, $CHCl_3$) and $[\alpha]^{25}_D$ +103 (*c* 1.7, $CHCl_3$).[7b]

Conclusions

In summary, we have achieved the synthesis of (*S*)-imperanene (**1**) through α-selective allylic substitution of acetate **29** with the copper reagent derived from (*i*-PrO)Me_2SiCH_2MgCl/CuBr·Me_2S (4:1) under the reaction conditions established herein. Furthermore, several results unexpectedly encountered during the synthesis are disclosed as useful information for future study of transforming highly oxygenated aromatic compounds.

Experimental Section

1-(4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl)-4-(trimethylsilyl)but-3-yn-2-ol (*rac*-22). To a solution of vanillin (5.01 g, 32.9 mmol) and imidazole (4.52 g, 66.4 mmol) in CH_2Cl_2 (70 mL) was added TBSCl (7.58 g, 50.3 mmol). The mixture was stirred at room temperature for 1 h and poured into saturated NH_4Cl. The product was extracted with CH_2Cl_2 twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 1:0 to 20:1) to afford the known silyl ether **20**[31] (8.25 g, 94%) as a colorless oil.

To an ice-cold solution of (methoxymethyl)triphenylphosphonium chloride (3.12 g, 9.10 mmol) in THF (40 mL) was added $NaN(TMS)_2$ (9.00 mL, 1.0 M in THF, 9.00 mmol) under an argon atmosphere. After 20 min at 0 °C, a solution of **20** (2.04 g, 7.66 mmol) in THF (10 mL) was added to the reaction mixture. The mixture was allowed to warm slowly to ambient temperature, stirred for 14 h, and poured into saturated NH_4Cl. The product was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 1:0 to 20:1) to afford the corresponding enol ether (2.14 g, 95%) as a 65:35 mixture of trans and cis isomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 6 H), 0.99 (s, 9 H), 3.66 (s, 2 H), and 3.77 (s, 1 H), 3.80 (s, 3 H), 5.16 (d, *J* = 7 Hz, 0.35 H), and 5.76 (d, *J* = 13 Hz, 0.65 H), 6.05 (d, *J* = 7 Hz, 0.35 H), and 6.94 (d, *J* = 13 Hz, 0.65 H), 6.66−6.78 (m, 3 H).

To a solution of the above enol ether (114 mg, 0.387 mmol) and NaI (63 mg, 0.42 mmol) in MeCN (7 mL) was added TMSCl (0.043 mL, 0.34 mmol) at −18 °C under an argon atmosphere. After 30 min at −18 °C, the reaction mixture was poured into aqueous $Na_2S_2O_3$. The product was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 1:0 to 20:1) to afford aldehyde **21** (78 mg, 72%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 6 H), 0.99 (s, 9 H), 3.60 (d, *J* = 2.5 Hz, 2 H), 3.80 (s, 3 H), 6.63−6.70 (m, 2 H), 6.84 (d, *J* = 8 Hz, 1 H), 9.71 (t, *J* = 2.5 Hz, 1 H).

To a solution of trimethylsilylacetylene (0.62 mL, 4.39 mmol) in THF (12 mL) was added *n*-BuLi (2.73 mL, 1.55 M in THF, 4.23 mmol) at −78 °C under an argon atmosphere. After 0.5 h of stirring at −78 °C, a solution of aldehyde **21** (948 mg, 3.38 mmol) in THF (8 mL) was added to the solution. After 2 h of stirring at −50 °C, the mixture was poured into saturated NH_4Cl. The product was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was purified by chromatography on silica gel with hexane/EtOAc (from 1:0 to 20:1) to afford propargyl alcohol *rac*-**22** (931 mg, 73%) as a colorless oil: IR (neat) 3393, 1516, 1251, 1041, 841 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 6 H), 0.16 (s, 9 H), 0.99 (s, 9 H), 2.91 (dd, *J* = 13, 6 Hz, 1 H), 2.94 (dd, *J* = 13, 6 Hz, 1 H), 3.79 (s, 3 H), 4.53 (t, *J* = 6 Hz, 3 H), 6.69−6.73 (m, 1 H), 6.71−6.80 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5 (−), −0.08 (−), 18.5 (+), 25.8 (−), 43.8 (+), 55.5 (−), 63.7 (−), 90.3 (+), 106.1 (+), 113.8 (−), 120.8 (−), 122.2 (−), 129.8 (+), 144.1 (+), 150.8 (+); HRMS (FAB) calcd for $C_{20}H_{34}O_3Si_2Na$ [(M + Na)$^+$] 401.1944, found 401.1943.

(*E*)-1-(4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl)-4-(trimethylsilyl)but-3-en-2-ol (*rac*-23). To an ice-cold solution of propargyl alcohol *rac*-**22** (1.30 g, 3.43 mmol) in Et_2O (35 mL) was added Red-Al (1.91 mL, 70% toluene solution, 6.85 mmol) under an argon atmosphere. After 1 h of stirring at room temperature, the mixture was poured into saturated 1 N HCl with vigorous stirring. The product was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 1:0 to 10:1) to afford allylic alcohol *rac*-**23** (1.21 g, 92%) as a colorless oil: IR (neat) 3393, 1517, 1281, 1125, 839 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 9 H), 0.15 (s, 6 H), 0.99 (s, 9 H), 1.71 (br s, 1 H), 2.68 (dd, *J* = 13.5, 8 Hz, 1 H), 2.82 (dd, *J* = 13.5, 5 Hz, 1 H), 3.79 (s, 3 H), 4.24−4.34 (m, 1 H), 5.85 (dd, *J* = 19, 1 Hz, 1 H), 6.09 (dd, *J* = 19, 5 Hz, 1 H), 6.65 (dd, *J* = 8, 2 Hz, 1 H), 6.70 (d, *J* = 2 Hz, 1 H), 6.79 (d, *J* = 8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5 (−), −1.2 (−), 18.5 (+), 25.8 (−), 43.5 (+), 55.5 (−), 75.0 (−), 113.5 (−), 120.9 (−), 121.8 (−), 129.6 (−), 131.0 (+), 143.8 (+), 147.5 (−), 150.9 (+); HRMS (FAB) calcd for $C_{20}H_{36}O_3Si_2Na$ [(M + Na)$^+$] 403.2101, found 403.2097.

(31) Rao, P. N. P.; Chen, Q.-H.; Knaus, E. E. *J. Med. Chem.* **2006**, *49*, 1668–1683.

(*R*)-2-(4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl)-1-((2*R*,3*R*)-3-(trimethylsilyl)oxiran-2-yl)ethanol (24) and (*E*,*R*)-1-(4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl)-4-(trimethylsilyl)-but-3-en-2-ol ((*S*)-23). To a solution of Ti(O-*i*-Pr)$_4$ (0.88 mL, 2.97 mmol) in CH_2Cl_2 (22 mL) was added (−)-DIPT (0.74 mL, 3.53 mmol) at −10 °C under an argon atmosphere. After 50 min of stirring at −10 °C, a solution of allylic alcohol *rac*-**23** (1.13 g, 2.97 mmol) in CH_2Cl_2 (8 mL) was added to the solution. After 50 min of stirring at −10 °C, the solution was cooled to −40 °C, and *t*-BuOOH (0.56 mL, 5.86 M in CH_2Cl_2, 3.28 mmol) was added. The solution was stirred at −20 °C for 7 h, and Me_2S (0.24 mL, 3.27 mmol) was added. The solution was stirred at room temperature for 0.5 h, and 10% aqueous tartaric acid (0.5 mL) and NaF (174 mg, 4.14 mmol) were added. The resulting mixture was stirred for 30 min and filtered through a pad of Celite. The filtrate was concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 100:1 to 4:1) to afford allylic alcohol (*S*)-**23** (572 mg, 51%) and epoxy alcohol **24** (525 mg, 44%) as a colorless oil. Epoxy alcohol **24**: $[\alpha]^{27}_D$ −3.7 (*c* 0.22, $CHCl_3$); IR (neat) 3447, 1516, 1282, 1250, 841 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 9 H), 0.14 (s, 6 H), 0.99 (s, 9 H), 1.95 (d, *J* = 2 Hz, 1 H), 2.36 (d, *J* = 4 Hz, 1 H), 2.77−2.81 (m, 2H), 2.85 (t, *J* = 4 Hz, 1 H), 3.79 (s, 3 H), 3.96−4.04 (m, 1 H), 6.67 (dd, *J* = 8, 2 Hz, 1 H), 6.74 (d, *J* = 2 Hz, 1 H), 6.78 (d, *J* = 8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (−), −3.6 (−), 18.5 (+), 25.8 (−), 40.2 (+), 48.0 (−), 55.5 (−), 57.9 (−), 70.6 (−), 113.3 (−), 120.9 (−), 121.6 (−), 130.6 (+), 143.8 (+), 151.0 (+); HRMS (FAB) calcd for $C_{20}H_{36}O_4Si_2Na$ [(M + Na)$^+$] 419.2050, found 419.2045. Allylic alcohol (*S*)-**23**: $[\alpha]^{23}_D$ −9.3 (*c* 0.56, $CHCl_3$).

(*S*)-2-(4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl)-1-((2*S*,3*S*)-3-(trimethylsilyl)-oxiran-2-yl)ethanol (*ent*-24). To a solution of Ti(O-*i*-Pr)$_4$ (0.45 mL, 1.52 mmol) in CH_2Cl_2 (10 mL) was added (+)-DIPT (0.38 mL, 1.82 mmol) at −10 °C under an argon atmosphere. After 30 min of stirring at −10 °C, a solution of allylic alcohol (*S*)-**23** (577 mg, 1.52 mmol) in CH_2Cl_2 (5 mL) was added to the solution. After 45 min of stirring at −20 °C, the solution was cooled to −30 °C, and *t*-BuOOH (0.29 mL, 5.86 M in CH_2Cl_2, 1.70 mmol) was added. The solution was stirred at −20 °C for 13 h, and Me_2S (0.12 mL, 1.63 mmol) was added. The solution was stirred at room temperature for 0.5 h, and 10% aqueous tartaric acid (0.3 mL) and NaF (0.114 g, 2.74 mmol) were added. The resulting mixture was stirred for 30 min and filtered through a pad of Celite. The filtrate was concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 100:1 to 4:1) to afford epoxy alcohol *ent*-**24** (0.505 g, 84%) as a colorless oil: $[\alpha]^{25}_D$ +3.5 (*c* 0.63, $CHCl_3$).

(*R*)-2-(4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl)-1-((2*S*,3*S*)-3-(trimethylsilyl)-oxiran-2-yl)ethanol (25). To an ice-cold solution of epoxy alcohol *ent*-**24** (99 mg, 0.25 mmol), PPh_3 (104 mg, 0.397 mmol), and $ClCH_2COOH$ (31 mg, 0.31 mmol) in THF (1.5 mL) was added DIAD (0.15 mL, 0.305 mmol) dropwise. After 3 h of stirring at 0 °C, the mixture was allowed to warm to room temperature over 13 h. The reaction mixture was concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 1:0 to 20:1) to afford the corresponding chloroacetate (106 mg, 90%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.00 (s, 9 H), 0.14 (s, 6 H), 0.99 (s, 9 H), 1.95 (d, *J* = 3 Hz, 1 H), 2.89 (dd, *J* = 14, 8 Hz, 1 H), 2.94 (dd, *J* = 6, 3 Hz, 1 H), 3.01 (dd, *J* = 14, 6 Hz, 1 H), 3.79 (s, 3 H), 4.05 (d, *J* = 15 Hz, 1 H), 4.10 (d, *J* = 15 Hz, 1 H), 4.84 (dt, *J* = 6, 8 Hz, 1 H), 6.63 (dd, *J* = 8, 2 Hz, 1 H), 6.72 (d, *J* = 2 Hz, 1 H), 6.77 (d, *J* = 8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (−), −3.7 (−), 18.5 (+), 25.8 (−), 37.7 (+), 41.0 (+), 49.8 (−), 55.5 (−), 56.2 (−), 79.4 (−), 113.0 (−), 121.0 (−), 121.7 (−), 129.2 (+), 144.1 (+), 151.0 (+), 166.7 (+).

To an ice-cold solution of the above chloroacetate (327 mg, 0.691 mmol) in MeOH (3 mL) was added *n*-$PrNH_2$ (0.06 mL, 0.73 mmol). After 1.5 h of stirring at 0 °C, the mixture was poured into saturated NH_4Cl. The product was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 10:1 to 4:1) to afford epoxy alcohol **25** (269 mg, 98%) as a colorless oil: $[\alpha]^{24}_D$ −29 (*c* 0.18, $CHCl_3$); IR (neat) 3394, 1513, 1281, 1250, 841 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 9 H), 0.14 (s, 6 H), 0.99 (s, 9 H), 2.00 (d, *J* = 5 Hz, 1 H), 2.13 (d, *J* = 4 Hz, 1 H), 2.79 (dd, *J* = 13, 7 Hz, 1 H), 2.84−2.96 (m, 2 H), 3.59−3.69 (m, 1 H), 3.79 (s, 3 H), 6.66 (dd, *J* = 8, 2 Hz, 1 H), 6.72 (d, *J* = 2 Hz, 1 H), 6.78 (d, *J* = 8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (−), −3.6 (−), 18.5 (+), 25.8 (−), 40.7 (+), 49.7 (−), 55.6 (−), 58.7 (−), 74.3 (−), 113.3 (−), 120.9 (−), 121.6 (−), 130.7 (+), 143.8 (+), 151.0 (+); HRMS (FAB) calcd for $C_{20}H_{36}O_4Si_2Na$ [(M + Na)$^+$] 419.2050, found 419.2061.

(*R*,*E*)-1-(4-(*tert*-Butyldimethylsilyloxy)-3-methoxyphenyl-4-(tributylstannyl)but-3-en-2-ol (26). From 25:. To an ice-cold solution of *i*-Pr_2NH (0.32 mL, 2.28 mmol) in THF (4 mL) was added *n*-BuLi (1.14 mL, 1.55 M in THF, 1.77 mmol) under an argon atmosphere. After 0.5 h of stirring at 0 °C, Bu_3SnH (0.20 mL, 0.744 mmol) and, after 0.5 h at 0 °C, a solution of epoxy alcohol **25** (260 mg, 0.655 mmol) in THF (2.5 mL) were added to the solution. Stirring was continued at 0 °C for 1 h and at room temperature for 4 h. The solution was poured into saturated NH_4Cl. The product was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 1:0 to 20:1) to afford γ-stannyl alcohol **26** (330 mg, 84%) as an yellow oil: $[\alpha]^{23}_D$ −8.7 (*c* 0.62, $CHCl_3$); IR (neat) 3360, 1515, 1282, 840 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 6 H), 0.84−0.94 (m, 15 H), 0.99 (s, 9 H), 1.23−1.37 (m, 6 H), 1.43−1.53 (m, 6 H), 1.67 (d, *J* = 4 Hz, 1 H), 2.70 (dd, *J* = 14, 8 Hz, 1 H), 2.82 (dd, *J* = 14, 5 Hz, 1 H), 3.79 (s, 3 H), 4.23−4.32 (m, 1 H), 6.05 (dd, *J* = 19, 5 Hz, 1 H; $J_{Sn-H(cis)}$ = 65 Hz), 6.17 (dd, *J* = 19, 0.6 Hz, 1 H; $J_{Sn-H(gem)}$ = 71 Hz), 6.65 (dd, *J* = 8, 2.5 Hz, 1 H), 6.70−6.73 (m, 1 H), 6.75−6.81 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (−), 9.5 (+), 13.8 (−), 18.5 (+), 25.8 (−), 27.4 (+), 29.1 (+), 43.7 (+), 55.5 (−), 75.9 (−), 113.5 (−), 120.9 (−), 121.8 (−), 128.1 (−), 131.3 (+), 143.7 (+), 149.8 (−), 150.9 (+). **From 24:** To an ice-cold solution of *i*-Pr_2NH (0.70 mL, 4.99 mmol) in THF (5 mL) was added *n*-BuLi (2.51 mL, 1.55 M in THF, 3.89 mmol) under an argon atmosphere. After 0.5 h of stirring at 0 °C, Bu_3SnH (0.43 mL, 1.60 mmol) and, after 0.5 h at 0 °C, a solution of epoxy alcohol **24** (572 mg, 1.44 mmol) in THF (3 mL) were added to the solution. Stirring was continued at 0 °C for 1 h and at room temperature for 4 h. The solution was poured into saturated NH_4Cl. The product was extracted with EtOAc twice and purified as above to afford alcohol **26** (646 mg, 75%) as an yellow oil.

1-(*tert*-Butyldimethylsilyloxy)-4-iodo-2-methoxybenzene (27). To a solution of phenol 2-methoxyphenol (103 mg, 0.83 mmol) and NaOH (61 mg, 1.53 mmol) in MeOH (2 mL) was added I_2 (215 mg, 0.847 mmol) at −4 °C. The mixture was stirred at −4 °C for 1 h and poured into H_2O. The product was extracted with EtOAc twice. The combined organic layers were washed with aqueous Na_2S_2O and brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 1:0 to 10:1) to afford 4-iodo-2-methoxyphenol (120 mg, 70%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.88 (s, 3 H), 5.57 (s, 1 H), 6.68 (d, *J* = 8 Hz, 1 H), 7.13 (d, *J* = 2 Hz, 1 H), 7.18 (dd, *J* = 8, 2 Hz, 1 H). The ^{1}H NMR spectrum was identified with that reported.[32]

(32) Fryatt, T.; Botting, N. P. *J. Labelled Compd. Radiopharm.* **2005**, *48*, 951–969.

A solution of the above iodide (404 mg, 1.84 mmol), TBSCl (369 mg, 2.45 mmol), and imidazole (203 mg, 2.98 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 12 h and poured into saturated NH_4Cl. The product was extracted with CH_2Cl_2 twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane to afford **27** (454 mg, 74%) as a colorless oil: IR (neat) 1581, 1496, 1256, 1224, 831 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 6 H), 0.98 (s, 9 H), 3.78 (s, 3 H), 6.59 (d, J = 8 Hz, 1 H), 7.10 (d, J = 2.5 Hz, 1 H), 7.12 (dd, J = 8, 2.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (−), 18.5 (+), 25.7 (−), 55.7 (−), 83.4 (+), 121.2 (−), 122.9 (−), 130.0 (−), 145.3 (+), 152.0 (+).

(*R*,*E*)-1,4-Bis(4-(*tert*-butyldimethylsilyloxy)-3-methoxyphenyl)but-3-en-2-ol (28). To a solution of the above iodide (224 mg, 0.615 mmol), LiCl (69 mg, 1.63 mmol), Ph_3As (26 mg, 0.085 mmol), and $Pd_2(dba)_3 \cdot CHCl_3$ (21 mg, 0.020 mmol) in NMP (1 mL) was added a solution of γ-stannyl alcohol **26** (250 mg, 0.418 mmol) in NMP (3 mL) under an argon atmosphere. After 11 h of stirring at room temperature, the mixture was poured into saturated NH_4Cl. The product was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was purified by chromatography on silica gel with hexane/EtOAc (from 1:0 to 10:1) to afford allylic alcohol **28** (207 mg, 91%) as an yellow oil: >99% ee by HPLC analysis (Chiralcel OD-H, hexane/*i*-PrOH = 98/2, 0.3 mL/min, 40 °C; t_R/min = 51.7 (*S*), 55.2 (*R*)); $[\alpha]^{23}_D$ −22.7 (*c* 1.09, $CHCl_3$); IR (neat) 3373, 1513, 1281, 1125, 903 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.146 (s, 6 H), 0.152 (s, 6 H), 0.99 (s, 18 H), 2.78 (dd, J = 14, 8 Hz, 1 H), 2.90 (dd, J = 14, 5 Hz, 1 H), 3.77 (s, 3 H), 3.81 (s, 3 H), 4.41−4.50 (m, 1 H), 6.13 (dd, J = 16, 7 Hz, 1 H), 6.50 (d, J = 16 Hz, 1 H), 6.68−6.90 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (−), 18.6 (+), 25.8 (−), 44.1 (+), 55.50 (−), 55.53 (−), 73.7 (−), 109.9 (−), 113.6 (−), 119.6 (−), 120.96 (−), 121.01 (−), 121.8 (−), 129.6 (−), 130.4 (−), 130.7 (+), 131.1 (+), 143.9 (+), 145.0 (+),150.9 (+), 151.1 (+); HRMS (FAB) calcd for $C_{30}H_{48}O_5Si_2Na$ [(M+Na)$^+$] 567.2938, found 567.2940.

(*R*,*E*)-1,4-Bis(4-(*tert*-butyldimethylsilyloxy)-3-methoxyphenyl)but-3-en-2-yl Acetate (29). To a solution of allylic alcohol **28** (55 mg, 0.0937 mmol) and DMAP (14.5 mg, 0.119 mmol) in CH_2Cl_2 (0.5 mL) was added a solution of Ac_2O (0.011 mL, 0.12 mmol) in CH_2Cl_2 (0.7 mL) at −18 °C under an argon atmosphere. After 2 h of stirring at −18 °C, the mixture was poured into saturated $NaHCO_3$. The product was extracted with CH_2Cl_2 twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was purified by chromatography on silica gel with hexane/EtOAc (from 1:0 to 30:1) to afford acetate **29** (52 mg, 95%) as an yellow oil: 95% ee by HPLC analysis (Chiralcel OD-H, hexane/*i*-PrOH = 99/1, 0.3 mL/min, 40 °C; t_R/min = 24.1 (*R*), 38.7 (*S*)); $[\alpha]^{25}_D$ −12 (*c* 0.93, $CHCl_3$); IR (neat) 1735, 1508, 1281, 1235, 903 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.13 (s, 6 H), 0.14 (s, 6 H), 0.98 (s, 9 H), 0.99 (s, 9 H), 2.02 (s, 3 H), 2.88 (dd, J = 14, 6 Hz, 1 H), 2.97 (dd, J = 14, 7 Hz, 1 H), 3.75 (s, 3 H), 3.80 (s, 3 H), 5.56 (q, J = 7 Hz, 1 H), 5.99 (dd, J = 16, 7 Hz, 1 H), 6.46 (d, J = 16 Hz, 1 H), 6.64−6.85 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (−), 18.52 (+), 18.54 (+), 21.4 (−), 25.79 (−), 25.80 (−), 41.1 (+), 55.50 (−), 55.51 (−), 73.5 (−), 110.1 (−), 113.6 (−), 119.7 (−), 120.8 (−), 121.0 (−), 121.9 (−), 125.1 (−), 130.3 (+), 130.5 (+), 132.7 (−), 143.7 (+), 145.3 (+), 150.7 (+), 151.0 (+), 170.2 (+); HRMS (FAB) calcd for $C_{32}H_{50}O_6Si_2Na$ [(M + Na)$^+$] 609.3044, found 609.3045.

(*R*,*E*)-1,4-Bis(4-(*tert*-butyldimethylsilyloxy)-3-methoxyphenyl)-3-(isopropyloxydimethylsilyl)methylbut-3-en (30). To an ice-cold suspension of $CuBr \cdot Me_2S$ (32 mg, 0.156 mmol) in THF (2.4 mL) was added (*i*-PrO)Me_2SiCH_2MgCl (0.75 mL, 0.85 M in THF, 0.64 mmol) dropwise. After 0.5 h of stirring at 0 °C, a solution of acetate **29** (94 mg, 0.16 mmol) in THF (1.6 mL) was added to the mixture dropwise. After 1 h of stirring at 0 °C, the mixture was diluted with EtOAc and saturated NH_4Cl with vigorous stirring. The layers were separated and the aqueous layer was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 1:0 to 30:1) to afford olefin **30** (97.5 mg, 92%) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.01−0.19 (m, 2H), 0.09 (s, 6 H), 0.12 (s, 6 H), 0.14 (s, 6 H), 0.98 (s, 9 H), 0.99 (s, 9 H), 1.10 (d, J = 6 Hz, 1 H), 1.12 (d, J = 6 Hz, 1 H), 2.48−2.72 (m, 3 H), 3.70 (s, 3 H), 3.79 (s, 3 H), 3.88−4.00 (m, 1 H), 5.86 (dd, J = 16, 8 Hz, 1 H), 6.09 (d, J = 16 Hz, 1 H), 6.56−6.63 (m, 2 H), 6.72−6.79 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.60 (−), −4.57 (−), −0.58 (−), −0.08 (−), 18.52 (+), 18.54 (+), 22.8 (+), 25.8 (−), 25.9 (−), 40.9 (−), 45.4 (+), 55.5 (−), 64.8 (−), 109.7 (−), 113.7 (−), 118.8 (−), 120.5 (−), 120.9 (−), 121.7 (−), 128.6 (−), 131.9 (+), 133.8 (−), 134.2 (+), 134.3 (−), 143.0 (+), 144.3 (+), 150.4 (+), 150.9 (+).

(*S*)-Imperanene (1). To a solution of olefin **30** (97.5 mg, 0.148 mmol), KF (65.5 mg, 1.13 mmol), and $KHCO_3$ (95,6 mg, 0.955 mmol) in THF/MeOH (1:1, 4 mL) was added 35% H_2O_2 (0.43 mL, 4.94 mmol) dropwise at 60 °C. After 2 h of stirring at 60 °C, the reaction mixture was poured into aqueous $Na_2S_2O_3$. The product was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a residual oil, which was chromatographed on silica gel with hexane/EtOAc (from 20:1 to 1:1) to afford (*S*)-imperanene (**1**) (35.7 mg, 73%) as a colorless oil: 95% ee by HPLC analysis (Chiralcel OD-H, hexane/*i*-PrOH = 70/30, 0.3 mL/min, rt; t_R/min = 51.8 (*R*), 60.6 (*S*)); $[\alpha]^{25}_D$ +97.7 (*c* 0.70, $CHCl_3$); $[\alpha]^{25}_D$ +104 (*c* 0. 010, $CHCl_3$), $[\alpha]^{25}_D$ +97 (*c* 0. 68, $CHCl_3$);[7b,7d] ^1H NMR (300 MHz, $CDCl_3$) δ 1.77 (br s, 1 H), 2.56−2.78 (m, 3 H), 3.55 (dd, J = 11, 7 Hz, 1 H), 3.66 (dd, J = 11, 4 Hz, 1 H), 3.81 (s, 3 H), 3.87 (s, 3 H), 5.62 (s, 1 H), 5.78 (s, 1 H), 5.92 (dd, J = 16, 8 Hz, 1 H), 6.34 (d, J = 16 Hz, 1 H), 6.65−6.69 (m, 2 H), 6.78−6.86 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.7 (+), 47.6 (−), 55.9 (−), 65.3 (+), 108.3 (−), 111.8 (−), 114.2 (−), 114.5 (−), 119.7 (−), 121.9 (−), 128.4 (−), 129.7 (+), 131.6 (−), 132.2 (−), 143.9 (+), 145.3 (+), 146.4 (+), 146.7 (+). These ^1H and ^{13}C MMR spectra were identical with those reported.[7b,7d]

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Supporting Information Available: Experimental procedures and spectral data of compounds described herein. This material is available free of charge via the Internet at http://pubs.acs.org.