Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 4725–4736

TETRAHEDRON:
ASYMMETRY

Asymmetric [2,3] Wittig rearrangement of crotyl furfuryl ethers

Masayoshi Tsubuki,* Teruyoshi Kamata, Michiyu Nakatani, Keiko Yamazaki,
Tomomi Matsui and Toshio Honda*

Faculty of Pharmaceutical Sciences, Hoshi University, Ebara 2-4-41, Shinagawa, Tokyo 142-8501, Japan

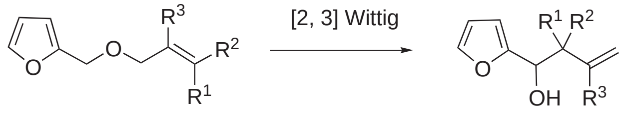
Received 19 October 2000; accepted 20 November 2000

Abstract

Asymmetric Wittig rearrangement of crotyl furfuryl ethers was investigated in diastereo- and enantioselective manners. Both (2*S*,3*Z*)- and (2*S*,3*E*)-3-penten-2-yl furfuryl ethers **3** and **9** rearranged with complete chirality transfer to give the *syn*- and *anti*-isomers **4** and **10**, respectively. Enantioselective Wittig rearrangement of both (*Z*)-and (*E*)-crotyl furfuryl ethers **15** and **17** using butyllithium and (−)-sparteine was examined to afford (1*S*,2*R*)-1-(2-furyl)-2-methyl-3-buten-ol **16** in up to 43% ee. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

The [2,3] Wittig rearrangement, the [2,3] sigmatropic rearrangement of allyl α-oxycarbanions, is a useful synthetic transformation for stereocontrolled carbon–carbon bond formation.[1] Various variants of the [2,3] Wittig rearrangement have been explored and applied to natural product synthesis. Recent studies[2] on the Wittig rearrangement of allyl furfuryl ethers **1** in our laboratories have demonstrated its utility for the synthesis of 2-furylcarbinols **2** (Scheme 1). In a continuation of these efforts, we were interested in the asymmetric [2,3] Wittig rearrangement of crotyl furfuryl ethers leading to chiral *syn*- and *anti*-1-(2-furyl)-2-methyl-3-buten-1-ols, since



Scheme 1.

---

* Corresponding authors. Fax: +81-3-3787-0036; e-mail: tsubuki@hoshi.ac.jp; honda@hoshi.ac.jp

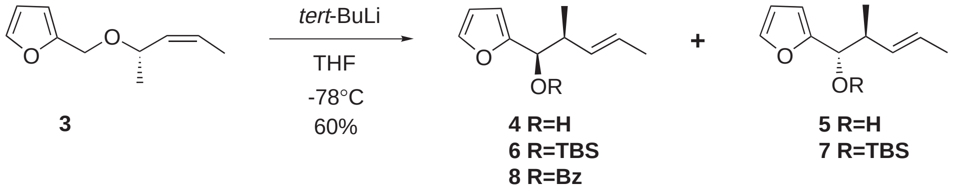
0957-4166/00/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0957-4166(00)00467-5

both *syn*- and *anti*-homoallyl alcohols could be versatile intermediates in synthetic transformations.[3] Here we report the preparation of enantioenriched *syn*- and *anti*-furylcarbinols employing the asymmetric [2,3] Wittig rearrangement of crotyl furfuryl ethers in diastereo- and enantioselective manners.

2. Results and discussion

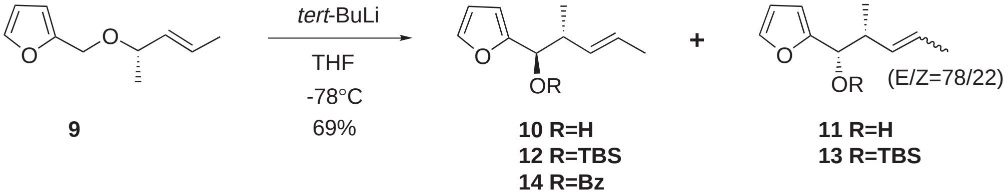
2.1. Chirality transfer via the [2,3] Wittig rearrangement of crotyl furfuryl ethers

Because the [2,3] Wittig rearrangement takes place through the highly-ordered five-membered transition state, the configuration at C-1 of the allylic moiety could be transferred into the newly generated stereogenic center in the product. Several asymmetric [2,3] Wittig rearrangements have been developed successfully to provide chiral homoallyl alcohols.[1] Initially, we investigated the asymmetric [2,3] Wittig rearrangement of chiral crotyl furfuryl ethers **3** and **9**. The [2,3] Wittig rearrangement of (2*S*,3*Z*)-3-penten-2-yl furfuryl ether **3** was shown in Scheme 2. Chiral (*Z*)-crotyl furfuryl ether **3** was prepared by the reaction of (2*S*,3*Z*)-3-penten-2-ol[4] with furfuryl chloride[5] using sodium hydride in DMF in 51% yield and 87% ee. Based on our previous results,[2] a combination of *tert*-butyllithium in THF was the solvent of choice for the rearrangement. Thus, chiral (*Z*)-crotyl furfuryl ether **3** was treated with *tert*-butyllithium (5 equiv.) in THF at −78°C to give an inseparable mixture of diastereoisomers **4** and **5** in a 93/7 ratio. Both *syn*- and *anti*-isomers **4** and **5** were obtained in pure form by silylation of the mixture, and careful separation of silyl ethers **6** and **7** on silica gel, and then deprotection of the silyl moiety in **6** and **7**. The enantiomeric purities of **4** and **5** were determined by HPLC analysis using Chiralcels AS and OJ as 87% ee and 45% ee, respectively. Although the reason for the observed low enantiospecificity in the minor product **5** was not clear, a similar result was found in the rearrangement of (2*S*,3*E*)-3-penten-2-yl benzyl ether.[6]



Scheme 2. Chirality transfer via Wittig rearrangement of the furfuryl ether **3**

Next, we examined the [2,3] Wittig rearrangement of (2*S*,3*E*)-3-penten-2-yl furfuryl ether **9** as shown in Scheme 3. Etherification of (2*S*,3*E*)-3-penten-2-ol,[4b,7] with furfuryl chloride, under the



Scheme 3. Chirality transfer via Wittig rearrangement of the furfuryl ether **9**

same conditions as above, afforded the ether **9** in 55% yield and 87% ee. Reaction of **9** with *tert*-butyllithium in THF at −78°C gave an inseparable mixture of isomers **10** and **11** in a 61/39 ratio. The mixture was separated by the same procedure as above via silyl ethers **12** and **13**. The ee of the major *anti*-isomer **10** was 87%, whereas the ee of the minor *syn*-isomer **11** could not be determined because **11** was an inseparable mixture of geometrical isomers ($E/Z=78/22$).

Thus, the [2,3] Wittig rearrangement of **3** and **9** proceeded with complete chirality transfer in the major products **4** and **10**.

The absolute configuration of **4** and **10** was established by the exciton chirality method as shown in Table 1. Gawronski et al. reported that the benzoate derivatives of 2-furylcabinols, having an (*R*)-configuration, gave a negative CD band near 230 nm and a positive band between 214 and 220 nm.[8] Based on their findings, both benzoates **8** and **14**, derived from **4** and **10**, respectively, showed negative Cotton effects in the CD spectra, thus having the (*R*)-configuration at the C-1 position. Further confirmation of the stereochemistry of **4** was made by transformation of **6** into aldehyde **21**, which was also prepared by the asymmetric aldol reaction[3d] as shown in the latter.

Table 1
Chiroptical data for benzoates **8** and **14**[a]

Benzoate	Config.[b]	CD $\Delta\varepsilon$ (nm)
8	*R*	+11.1 (215), −5.1 (231)
14	*R*	+10.1 (213), −1.8 (232)

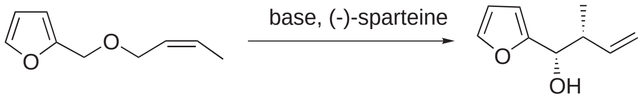
[a] The CD spectra were measured in acetonitrile solution.
[b] The absolute configuration at the C-1 position was indicated.

2.2. Enantioselective [2,3] Wittig rearrangement of crotyl furfuryl ethers

Despite the great success of asymmetric [2,3] Wittig rearrangements involving chiral auxiliaries, enantioselective [2,3] Wittig rearrangements employing an achiral substrate and a chiral ligand have been much less successful.[9] High enantioselectivities for benzyl crotyl ethers were obtained using norpseudoephedrine (64% ee)[9d] and a chiral base (up to 96% ee).[9f] On the basis of the precedents from Beak et al.[10] and Hoppe et al.[11] directed toward the asymmetric deprotonation mediated by (−)-sparteine, we intended to explore the enantioselective [2,3] Wittig rearrangement of crotyl furfuryl ethers using (−)-sparteine as a chiral ligand.

Initially, (*Z*)-crotyl furfuryl ether **15**[2] was studied and the results are shown in Table 2. The reactions were carried out by treatment of **15** with butyllithium (1.3 equiv.) and (−)-sparteine (1.5 equiv.) at −78°C except entry 3. The enantioselectivities were influenced by the solvent used. In Et_2O, low enantioselectivity (27% ee) was observed (entry 2), while no enantioselectivity was found in THF (entry 1). Generally, non-polar solvents, such as hexane and toluene, gave better results (entries 4–6 and 10). As for the base employed, both *n*- and *sec*-butyllithiums showed almost the same enantioselectivities (entries 2–10), whereas *tert*-butyllithium resulted in poor enantioselectivity (entry 12). The best result was obtained by treatment with *n*-butyllithium and (−)-sparteine in toluene at −90°C to afford *syn*-isomer **16**,[12] $[\alpha]_D^{26}$ −9.5 ($CHCl_3$), in 43% ee with 98% de (entry 11).

Table 2
Enantioselective Wittig rearrangement of (*Z*)-crotyl 2-furfuryl ether **15**[a]



15 **16**

Entry	Solvent	Base	*syn*/*anti*[b]	Ee (%)[c]	Yield (%)
1	THF	*sec*-BuLi	96/4	0	15
2	Et_2O	*sec*-BuLi	98/2	27	35
3	Et_2O	*sec*-BuLi[d]	98/2	27	34
4	Pentane	*sec*-BuLi	99/1	28	36
5	Hexane	*sec*-BuLi	99/1	35	43
6	Toluene	*sec*-BuLi	99/1	38	33
7	Toluene[e]	*sec*-BuLi	99/1	39	41
8	Et_2O	*n*-BuLi	99/1	36	40
9	Hexane	*n*-BuLi	99/1	34	31
10	Toluene	*n*-BuLi	99/1	42	37
11	Toluene[e]	*n*-BuLi	99/1	43	25
12	Et_2O	*tert*-BuLi	97/3	7	Trace

[a] All reactions were carried out using butyllithium (1.3 equiv.) and (−)-sparteine (1.5 equiv.) at −78°C unless otherwise noted.

[b] The *syn*/*anti* ratio was determined by ^1H NMR spectroscopy.

[c] The ee of the *syn*-product **16** was determined by HPLC analysis using Chiralcel OD.

[d] The reaction was carried out using *sec*-butyllithium (3.0 equiv.) and (−)-sparteine (3.5 equiv.).

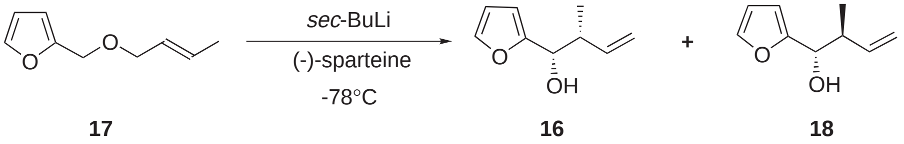
[e] The reaction was carried out at −90°C.

Next, we examined the enantioselective rearrangement of (*E*)-crotyl furfuryl ether **17**,[2] as shown in Table 3. The same reaction conditions as above were used. In THF, the rearrangement provided *anti*-isomer **18**[12] as the major product (entry 1), while *syn*-isomer **16** was the major product in Et_2O and hexane (entries 2 and 5). Unfortunately, the ee's of both **16** and **18** obtained in THF were found to be zero. In Et_2O and hexane, the ee of the major isomer **16** was 25–28% ee (entries 2–5). Both the enantio- and diastereoselectivities in the rearrangement of (*E*)-**17** were slightly lower than those of the product from the rearrangement of (*Z*)-**15**.

In order to determine the absolute configuration of *syn*-**16**, (1*R*,2*S*)-1-(2-furyl)-2-methyl-3-butene **23** was prepared from the known hydroxy ester **19**,[3d] as shown in Scheme 4. Silylation of the hydroxyl moiety in **19** with *tert*-butyldimethylsilyl trifluoromethanesulfonate gave ether **20**, which was reduced to the aldehyde **21** in 75% yield from **19**. Wittig olefination of **21** afforded **22** (84%), which was desilylated to give *syn*-homoallyl alcohol **23**, $[\alpha]_D^{26}$ +20.4 ($CHCl_3$), with 94% ee in 87% yield. Thus, the absolute configuration of *syn*-**16** obtained by the [2,3] Wittig rearrangement was unambiguously determined to be (1*S*,2*R*).

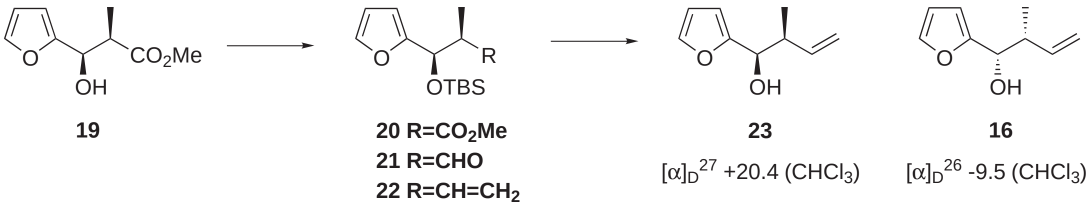
In summary, we have shown the asymmetric [2,3] Wittig rearrangement of crotyl furfuryl ethers in diastereo- and enantioselective fashions. Complete chirality transfer has been accomplished in the rearrangement of both (2*S*,3*Z*)- and (2*S*,3*E*)-3-penten-2-yl furfuryl ethers leading to the corresponding *syn*- and *anti*-homoallyl alcohols, respectively. This asymmetric transmission should be applicable to natural product synthesis.

Table 3
Enantioselective Wittig rearrangement of (*E*)-crotyl 2-furfuryl ether **17**



Entry	Solvent	*sec*-BuLi/(−)-sparteine (equiv.)	*syn*/*anti*[a]	Ee (%)[b]	Yield (%)
1	THF	1.3/1.5	30/70	0[c]	13
2	Et_2O	1.3/1.5	92/8	28	28
3	Et_2O	3.0/3.5	90/10	28	36
4	Et_2O	3.0/1.5	89/11	25	41
5	Hexane	1.3/1.5	92/8	27	35

[a] The *syn*/*anti* ratio was determined by ^{1}H NMR spectroscopy.
[b] The ee of the *syn*-product **16** was determined by HPLC analysis using Chiralcel OD.
[c] The ee of the *anti*-product **18** was determined by HPLC analysis using Chiralcel OD.



Scheme 4. Enantioselective synthesis of (1*R*,2*S*)-1-(2-furyl)-2-methyl-3-butene **23**

3. Experimental

3.1. General

IR spectra were obtained using a JASCO FT/IR-200 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained on JEOL LAMBDA-270 (^{1}H NMR: 270 MHz; ^{13}C NMR: 67.8 MHz) instruments for solutions in $CDCl_3$, and chemical shifts are reported on the δ scale from internal TMS. Mass spectra were measured with a JEOL JMS-D300 spectrometer. Optical rotations were taken with a JASCO DIP-360 polarimeter. CD spectra were recorded in acetonitrile on a JASCO J-600 spectropolarimeter. Elemental analyses were performed on a Yanaco-MT5 instrument.

3.2. Preparation of (2S,3Z)-3-penten-2-yl furfuryl ether **3**

To a stirred solution of furfuryl chloride[5] (2.70 g, 23.2 mmol) and (2*S*,3*Z*)-3-penten-2-ol[4] (1.17 g, 13.6 mmol) in dimethylformamide (80 mL) was added sodium hydride (60% dispersion in mineral oil, 1.20 g, 30.0 mmol) at 0°C. The reaction mixture was stirred at room temperature for 10 h. The reaction mixture was quenched with water and the aqueous solution was extracted three times with Et_2O. The organic layer was washed with brine and dried over Na_2SO_4.

Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using hexane and Et_2O (99/1) as eluent to give furfuryl ether **3** (1.16 g, 51%) as a colorless oil. Bp 120°C (20 mmHg); $[\alpha]_D^{23}$ −50.6 (*c* 1.12, $CHCl_3$); ^1H NMR: δ 1.22 (3H, d, $J=6.3$ Hz, 1-CH_3), 1.66 (3H, dd, $J=1.8$, 6.9 Hz, 5-CH_3), 4.30–4.40 (1H, m, 2-CH), 4.31 and 4.47 (each 1H, each d, $J=12.6$ Hz, CH_2O), 5.30–5.40 (1H, m, 3-CH), 5.60–5.70 (1H, m, 4-CH), 6.27 (1H, dd, $J=0.8$, 3.1 Hz, 3′-CH), 6.32 (1H, dd, $J=1.8$, 3.1 Hz, 4′-CH), 7.39 (1H, dd, $J=0.8$, 1.8 Hz, 5′-CH); ^{13}C NMR: δ 13.2, 21.2, 61.7, 69.7, 108.8, 110.1, 126.8, 132.5, 142.6, 152.3; MS (EI): 166 (M^+); HRMS (EI) calcd for $C_{10}H_{14}O_2$: 166.0994; found: 166.1023. Anal. calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.96; H, 8.56. HPLC analysis using a Chiralcel OJ column showed it to be 87% ee [*i*-PrOH/hexane (5/95), flow rate 1.0 mL/min, $t_R(R)$ 5.48 min and $t_R(S)$ 6.24 min].

*3.3. Preparation of (2*S*,3*E*)-3-penten-2-yl furfuryl ether* ***9***

The etherification was performed as described above from furfuryl chloride and (2*S*,3*E*)-3-penten-2-ol[4b,7] to give ether **9** (55%) as a colorless oil. Bp 103°C (17 mmHg); $[\alpha]_D^{26}$ −66.8 (*c* 1.04, $CHCl_3$); ^1H NMR: δ 1.24 (3H, d, $J=6.3$ Hz, 1-CH_3), 1.73 (3H, dd, $J=1.5$, 6.3 Hz, 5-CH_3), 3.89 (1H, quintet, $J=6.3$ Hz, 2-CH), 4.31 and 4.46 (each 1H, each d, $J=12.7$ Hz, CH_2O), 5.40 (1H, ddd, $J=1.2$, 6.3, 15.2 Hz, 3-CH), 5.66 (1H, dq, $J=6.3$, 15.2 Hz, 4-CH), 6.27 (1H, d, $J=3.1$ Hz, 3′-CH), 6.32 (1H, dd, $J=1.8$, 3.1 Hz, 4′-CH), 7.39 (1H, d, $J=1.8$ Hz, 5′-CH); ^{13}C NMR: δ 17.4, 21.4, 61.5, 75.6, 108.5, 110.0, 127.9, 132.8, 142.3, 152.3; MS (EI): 166 (M^+); HRMS (EI) calcd for $C_{10}H_{14}O_2$: 166.0994; found: 166.0987. Anal. calcd for $C_{10}H_{14}O_2$: C, 72.05; H, 8.51. Found: C, 71.96; H, 8.56. HPLC analysis using a Chiralcel OJ column showed it to be 87% ee [*i*-PrOH/hexane (5/95), flow rate 1.0 mL/min, $t_R(R)$ 4.81 min and $t_R(S)$ 5.86 min].

3.4. Wittig rearrangement of furfuryl ether ***3***

To a stirred solution of ether **3** (200 mg, 1.20 mmol) in THF (10 mL) was added dropwise *tert*-butyllithium (1.51 M in pentane, 3.98 mL, 6.01 mmol) at −78°C under argon and stirring was continued at the same temperature for 2 h. The reaction mixture was quenched with water and the reaction mixture was allowed to warm to room temperature. Concentration of the solvent gave the aqueous layer, which was extracted three times with pentane and Et_2O (1/1). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using pentane and Et_2O (95/5) as eluent to give an inseparable mixture of diastereoisomers **4** and **5** (101.4 mg, 60% based on the recovery of the starting material **3**). The ^1H NMR spectrum of the mixture showed the ratio of **4** and **5** to be 93/7. Further purification of the diastereomers was carried out as follows.

To a stirred solution of the alcohols (101.4 mg, 0.61 mmol) and 2,6-lutidine (0.21 mL, 1.83 mmol) in CH_2Cl_2 (4 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.21 mL, 0.92 mmol) at 0°C and stirring was continued at the same temperature for 15 min. The reaction mixture was quenched with water and the aqueous solution was extracted three times with CH_2Cl_2. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using hexane as eluent to give a less polar product, (1*R*,2*S*,3*E*)-1-*tert*-butyldimethylsilyloxy-2-furyl-2-methyl-3-pentene **6** (67.2 mg, 39%) as a colorless oil. $[\alpha]_D^{25}$ +22.9 (*c* 0.69, $CHCl_3$); ^1H NMR: δ −0.14 and 0.02 (each 3H, each s, $Si(CH_3)_2$), 0.87 (9H, s, $C(CH_3)_3$), 1.00 (3H, d, $J=6.6$ Hz, 2-$CHC\underline{H}_3$), 1.59 (3H, d, $J=5.4$ Hz, 5-CH_3), 2.54 (1H, sextet, $J=6.6$ Hz, 2-CH), 4.44 (1H, d, $J=6.6$ Hz, 1-CH), 5.20–5.45

(2H, m, 3-CH, 4-H), 6.11 (1H, d, *J*=3.1 Hz, 3′-CH), 6.27 (1H, dd, *J*=1.8, 3.1 Hz, 4′-CH), 7.31 (1H, d, *J*=1.8 Hz, 5′-CH); ^{13}C NMR: δ −5.2, −5.0, 15.4, 18.0, 18.2, 25.8, 42.7, 73.0, 106.4, 109.8, 124.9, 133.3, 140.9, 156.7; MS (CI): 281 (M+1); HRMS (CI) calcd for $C_{16}H_{28}O_2Si$+H: 281.1937; found: 281.1930. Further eluent gave a more polar product, (1*S*,2*S*,3*E*)-1-*tert*-butyldimethylsilyloxy-2-furyl-2-methyl-3-pentene **7** (9.8 mg, 6%) as a colorless oil. ^{1}H NMR: δ −0.15 and 0.00 (each 3H, each s, Si(CH$_3$)$_2$), 0.83 (9H, s, C(CH$_3$)$_3$), 0.84 (3H, d, *J*=6.6 Hz, 2-CHC$\underline{\text{H}}_3$), 1.64 (3H, d, *J*=4.8 Hz, 5-CH$_3$), 2.53 (1H, sextet, *J*=6.8 Hz, 2-CH), 4.37 (1H, d, *J*=6.8 Hz, 1-CH), 5.30–5.50 (2H, m, 3-CH, 4-H), 6.12 (1H, d, *J*=3.1 Hz, 3′-CH), 6.28 (1H, dd, *J*=1.8, 3.1 Hz, 4′-CH), 7.32 (1H, d, *J*=1.8 Hz, 5′-CH); ^{13}C NMR: δ −5.2, −5.0, 16.4, 18.0, 18.2, 25.7, 43.2, 73.0, 106.6, 109.8, 125.1, 133.7, 141.0, 156.6; MS (CI): 281 (M+1); HRMS (CI) calcd for $C_{16}H_{28}O_2Si$+H: 281.1937; found: 281.1918.

To a stirred solution of the major silyl ether **6** (67.2 mg, 0.24 mmol) in THF (1 mL) was added tetrabutylammonium fluoride (1 M in THF, 0.72 mL, 0.72 mmol) at room temperature and stirring was continued at the same temperature for 1 h. After dilution with water and the aqueous solution was extracted three times with pentane and Et$_2$O (1/1). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using pentane and Et$_2$O (9/1) as eluent to give (1*R*,2*S*,3*E*)-1-(2-furyl)-2-methyl-3-penten-1-ol **4** (35.8 mg, 90%) as a colorless oil. $[\alpha]_D^{24}$ +14.0 (*c* 1.32, CHCl$_3$); IR: 3400 cm^{-1}; ^{1}H NMR: δ 1.01 (3H, d, *J*=6.8 Hz, 2-CHC$\underline{\text{H}}_3$), 1.67 (3H, dd, *J*=0.7, 6.2 Hz, 5-CH$_3$), 2.64 (1H, sextet, *J*=6.8 Hz, 2-CH), 4.54 (1H, br s, 1-CH), 5.35 (1H, ddd, *J*=1.3, 6.8, 15.3 Hz, 3-CH), 5.54 (1H, dq, *J*=6.2, 15.3 Hz, 4-CH), 6.21 (1H, dd, *J*=0.8, 3.1 Hz, 3′-CH), 6.32 (1H, dd, *J*=1.6, 3.1 Hz, 4′-CH), 7.36 (1H, dd, *J*=0.8, 1.6 Hz, 5′-CH); ^{13}C NMR: δ 15.6, 18.0, 42.1, 71.5, 106.7, 110.0, 126.8, 132.1, 141.5, 155.5; MS (EI): 166 (M$^+$); HRMS (CI) calcd for $C_{10}H_{14}O_2$+H: 167.1072; found: 167.1050. HPLC analysis using a Chiralcel AS column showed it to be 87% ee [*i*-PrOH/hexane (2/98), flow rate 1.0 mL/min, t_R(1*R*,2*S*) 7.40 min and t_R(1*S*,2*R*) 7.92 min].

Desilylation of the minor silyl ether **7** (9.8 mg, 0.03 mmol) was performed as described above to give (1*S*,2*S*,3*E*)-1-(2-furyl)-2-methyl-3-penten-1-ol **5** (5.2 mg, 89%) as a colorless oil. $[\alpha]_D^{24}$ −28.3 (*c* 0.14, CHCl$_3$); IR: 3410 cm^{-1}; ^{1}H NMR: δ 0.81 (3H, d, *J*=7.3 Hz, 2-CHC$\underline{\text{H}}_3$), 1.64 (3H, dd, *J*=1.5, 6.3 Hz, 5-CH$_3$), 2.00–2.30 (1H, br s, OH), 2.55 (1H, sextet, *J*=7.5 Hz, 2-CH), 4.25 (1H, d, *J*=7.5 Hz, 1-CH), 5.29 (1H, ddd, *J*=1.5, 7.5, 15.2 Hz, 3-CH), 5.56 (1H, ddq, *J*=0.8, 6.3, 15.2 Hz, 4-CH), 6.17 (1H, dd, *J*=0.8, 2.9 Hz, 3′-CH), 6.24 (1H, dd, *J*=1.8, 2.9 Hz, 4′-CH), 7.36 (1H, dd, *J*=0.8, 1.8 Hz, 5′-CH); ^{13}C NMR: δ 16.8, 18.1, 42.8, 71.4, 107.2, 110.0, 128.2, 132.6, 141.9, 155.0; MS (EI): 166 (M$^+$); HRMS (EI) calcd for $C_{10}H_{14}O_2$: 166.0994; found: 166.0978. HPLC analysis using a Chiralcel OJ column showed it to be 45% ee [*i*-PrOH/hexane (5/95), flow rate 1.0 mL/min, t_R(1*R*,2*R*) 9.14 min and t_R(1*S*,2*S*) 10.70 min].

*3.5. Wittig rearrangement of furfuryl ether **9***

The rearrangement was performed as described above by treatment of ether **9** (205 mg, 1.23 mmol) with *tert*-butyllithium (1.51 M in pentane, 4.1 mL, 6.19 mmol) in THF (10 mL) at −78°C to give an inseparable mixture of diastereoisomers **10** and **11** (107 mg, 69% based on the recovery of the starting material **9**). The ^{1}H NMR spectrum of the mixture showed the ratio of **10** and **11** to be 61/39.

Silylation of the diastereomers **10** and **11** (107 mg, 0.64 mmol) gave a more polar product, (1*R*,2*R*,3*E*)-1-*tert*-butyldimethylsilyloxy-2-furyl-2-methyl-3-pentene **12** (65 mg, 36%), and a less polar product, (1*S*,2*R*,3*E*)-1-*tert*-butyldimethylsilyloxy-2-furyl-2-methyl-3-pentene **13** (9.3 mg, 5%), which were desilylated by tetrabutylammonium fluoride to afford **10** (30.9 mg, 80%) and **11** (4.7 mg, 85%), respectively.

*3.5.1. (1*R*,2*R*,3*E*)-1-(2-Furyl)-2-methyl-3-penten-1-ol* ***10***

Colorless oil; $[\alpha]_D^{24}$ +54.8 (*c* 0.62, $CHCl_3$). HPLC analysis using a Chiralcel OJ column showed it to be 87% ee [*i*-PrOH/hexane (5/95), flow rate 1.0 mL/min, t_R(1*R*,2*R*) 9.14 min and t_R(1*S*,2*S*) 10.70 min].

*3.5.2. (1*S*,2*R*)-1-(2-Furyl)-2-methyl-3-penten-1-ol* ***11***

Colorless oil; $[\alpha]_D^{24}$ +2.22 (*c* 0.48, $CHCl_3$). The enantiomeric excess of **11** could not be determined by HPLC analysis owing to an inseparable mixture of geometrical isomers ($E/Z=78/22$).

*3.6. Preparation of (1*R*,2*S*,3*E*)-1-benzoyloxy-1-(2-furyl)-2-methylpent-3-en-1-ol* ***8***

A mixture of alcohol **4** (5.5 mg, 0.03 mmol), a catalytic amount of *N*,*N*-dimethylaminopyridine, and benzoyl chloride (7 mg, 0.05 mmol) in pyridine (0.5 mL) was stirred at room temperature for 10 h. The reaction mixture was diluted with water and the aqueous solution was extracted three times with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using hexane and AcOEt (95/5) as eluent to give benzoate **8** (8.2 mg, 92%) as a colorless oil. $[\alpha]_D^{26}$ +46.2 (*c* 0.16, $CHCl_3$); IR: 1720 cm^{-1}; ^1H NMR: δ 1.13 (3H, d, $J=7.0$ Hz, 2-$CH\underline{H}_3$), 1.61 (3H, d, $J=6.1$ Hz, 5-CH_3), 2.97 (1H, sextet, $J=7.0$ Hz, 2-CH), 5.35 (1H, ddq, $J=1.1$, 7.0, 15.3 Hz, 3-CH), 5.50 (1H, dq, $J=6.1$, 15.3 Hz, 4-CH), 5.89 (1H, d, $J=7.0$ Hz, 1-CH), 6.30–6.40 (2H, m, 3′-CH, 4′-CH), 7.35–7.60 (4H, m, 5′-CH, *o*-CH, *p*-CH), 8.00–8.10 (2H, m, *m*-CH); ^{13}C NMR: δ 16.5, 18.0, 39.8, 72.9, 108.9, 110.0, 126.5, 128.3, 129.7, 130.2, 131.3, 133.0, 142.1, 152.0, 165.7; MS (EI): 270 (M^+); HRMS (CI) calcd for $C_{17}H_{18}O_3$+H: 271.1334; found: 271.1331.

*3.7. Preparation of (1*R*,2*R*,3*E*)-1-benzoyloxy-1-(2-furyl)-2-methylpent-3-en-1-ol* ***14***

Esterification was performed as described above by treatment of alcohol **10** (5.5 mg, 0.03 mmol), a catalytic amount of *N*,*N*-dimethylaminopyridine, and benzoyl chloride (7 mg, 0.05 mmol) in pyridine (0.5 mL) to afford benzoate **14** (8.7 mg, 97%) as a colorless oil. $[\alpha]_D^{24}$ +52.9 (*c* 0.29, $CHCl_3$); IR: 1720 cm^{-1}; ^1H NMR: δ 0.98 (3H, d, $J=7.6$ Hz, 2-$CH\underline{H}_3$), 1.60 (3H, d, $J=6.3$ Hz, 5-CH_3), 2.96 (1H, sextet, $J=7.6$ Hz, 2-CH), 5.40 (1H, ddq, $J=1.3$, 7.6, 15.3 Hz, 3-CH), 5.57 (1H, dq, $J=6.3$, 15.3 Hz, 4-CH), 5.86 (1H, d, $J=7.6$ Hz, 1-CH), 6.30–6.40 (2H, m, 3′-CH, 4′-CH), 7.35–7.60 (4H, m, 5′-CH, *o*-CH, *p*-CH), 8.00–8.10 (2H, m, *m*-CH); ^{13}C NMR: δ 16.8, 17.9, 40.4, 72.7, 109.2, 110.1, 126.7, 128.3, 129.6, 130.3, 132.0, 132.9, 142.3, 151.9, 165.7; MS (EI): 270 (M^+); HRMS (EI) calcd for $C_{17}H_{18}O_3$: 270.1256; found: 270.1269.

3.8. A general method for asymmetric Wittig rearrangement of crotyl furfuryl ethers ***15*** *and* ***17***

To a stirred solution of crotyl furfuryl ether (100 mg, 0.66 mmol) and (−)-sparteine (0.23 mL, 1.00 mmol) in solvent (7 mL) was added dropwise *sec*-butyllithium (1.03 M in cyclohexane, 0.83 mL, 0.85 mmol) at −78°C under argon and stirring was continued at the same temperature for

2 h. The reaction mixture was quenched with water and the reaction mixture was allowed to warm to room temperature. Concentration of the solvent gave the aqueous layer, which was extracted three times with pentane and Et_2O (1/1). The organic layer was washed with 5% phosphoric acid and then brine, and dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using pentane and Et_2O (90/10) as eluent to give an inseparable mixture of diastereoisomers. The ratio of *syn*- and *anti*-isomers **16** and **18** was determined by ^1H NMR spectroscopy. The enantiomeric excess of *syn*-1-(2-furyl)-2-methyl-3-buten-1-ol **16** was determined by HPLC analysis using a Chiralcel OD column [*i*-PrOH/hexane (5/95), flow rate 1.0 mL/min, $t_R(1S,2R)$ 6.86 min and $t_R(1R,2S)$ 7.33 min] and the results are shown in Tables 2 and 3. The enantiomeric excess of *anti*-1-(2-furyl)-2-methyl-3-buten-1-ol **18** was determined using a Chiralcel OD column [*i*-PrOH/hexane (5/95), flow rate 1.0 mL/min, t_R 6.96 min and t_R 8.08 min].

3.8.1. syn*-1-(2-Furyl)-2-methyl-3-buten-1-ol **16** (Table 2, entry 11)*

$[\alpha]_D^{26}$ −9.5 (*c* 0.49, $CHCl_3$); IR: 3400 cm^{-1}; ^1H NMR: δ 1.07 (3H, d, J=6.8 Hz, 2-$CHC\underline{H}_3$), 2.00–2.20 (1H, br s, OH), 2.71 (1H, sextet, J=6.8 Hz, 2-CH), 4.56 (1H, d, J=6.8 Hz, 1-CH), 5.07 (1H, dd, J=1.0, 10.2 Hz, 4-$C\underline{H}H$), 5.10 (1H, dd, J=1.0, 17.1 Hz, 4-$CH\underline{H}$), 5.75 (1H, ddd, J=6.8, 10.2, 17.1 Hz, 3-CH), 6.23 (1H, dd, J=0.8, 3.1 Hz, 3′-CH), 6.32 (1H, dd, J=1.7, 3.1 Hz, 4′-CH), 7.36 (1H, dd, J=0.8, 1.7 Hz, 5′-CH); ^{13}C NMR: δ 15.0, 42.8, 71.2, 106.7, 109.9, 115.5, 139.7, 141.5, 155.4; MS (EI): 152 (M^+); HRMS (EI) calcd for $C_9H_{12}O_2$: 152.0836; found: 152.0822. The ^1H and ^{13}C NMR spectra were in good accordance with those reported.[12]

3.8.2. anti*-1-(2-Furyl)-2-methyl-3-buten-1-ol **18** (Table 3, entry 1)*

$[\alpha]_D^{28}$ 0 (*c* 0.21, $CHCl_3$); IR: 3400 cm^{-1}; ^1H NMR: δ 0.96 (3H, d, J=6.7 Hz, 2-$CHC\underline{H}_3$), 2.00–2.20 (1H, br s, OH), 2.71 (1H, d sextet, J=1.2, 6.8 Hz, 2-CH), 4.42 (1H, d, J=6.7 Hz, 1-CH), 5.18 (1H, dd, J=1.2, 10.4 Hz, 4-$C\underline{H}H$), 5.21 (1H, dd, J=1.2, 17.7 Hz, 4-$CH\underline{H}$), 5.81 (1H, ddd, J=6.7, 10.4, 17.7 Hz, 3-CH), 6.27 (1H, d, J=3.1 Hz, 3′-CH), 6.34 (1H, dd, J=1.8, 3.1 Hz, 4′-CH), 7.38 (1H, d, J=1.8 Hz, 5′-CH); ^{13}C NMR: δ 16.2, 43.6, 71.4, 106.7, 107.3, 110.1, 117.0, 140.0, 142.0, 155.0; MS (EI): 134 (M^+–H_2O); HRMS (EI) calcd for $C_9H_{10}O$: 134.0732; found: 134.0732. The ^1H and ^{13}C NMR spectra were in good accordance with those reported.[12]

*3.9. Preparation of methyl (2*R*,3*R*)-3-(*tert*-butyldimethylsilyloxy)-3-(2-furyl)-2-methylpropionate **20***

To a stirred suspension of the known alcohol **19**[3d] (423 mg, 2.52 mmol) and imidazole (856 mg, 12.6 mmol) in dimethylformamide (20 mL) was added *tert*-butyldimethylsilyl chloride (1.54 g, 10.2 mmol) at 0°C. The reaction mixture was stirred at room temperature for 10 h. The reaction mixture was then quenched with water and the aqueous solution was extracted three times with hexane and Et_2O (1/1). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using hexane and AcOEt (95/5) as eluent to give silyl ether **20** (710 mg, 100%) as a colorless oil. $[\alpha]_D^{26}$ +29.7 (*c* 1.01, $CHCl_3$); IR: 1740 cm^{-1}; ^1H NMR: δ −0.12 and 0.01 (each 3H, each s, $Si(CH_3)_2$), 0.85 (9H, s, $C(CH_3)_3$), 1.14 (3H, d, J=6.9 Hz, 2-$CHC\underline{H}_3$), 2.88 (1H, quintet, J=6.9 Hz, 2-CH), 3.60 (3H, s, OCH_3), 5.02 (1H, d, J=6.9 Hz, 3-CH), 6.18 (1H, d, J=3.3 Hz, 3′-CH), 6.27 (1H, dd, J=1.9, 3.3 Hz, 4′-CH), 7.32 (1H, d, J=1.9 Hz, 5′-CH); ^{13}C NMR: δ −5.6, −5.1, 11.7, 18.0, 25.6, 45.9, 51.5, 69.7, 106.6, 110.0, 141.4, 155.2, 174.3.

*3.10. Preparation of (2*R*,3*R*)-3-(*tert*-butyldimethylsilyloxy)-3-(2-furyl)-2-methylpropanal* ***21***

*3.10.1. From methyl (2*R*,3*R*)-3-(*tert*-butyldimethylsilyloxy)-3-(2-furyl)-2-methylpropionate* ***19***

To a stirred solution of the ester **20** (784 mg, 2.78 mmol) in CH_2Cl_2 (40 mL) was added dropwise diisobutylaluminum hydride (0.95 M in hexane, 5.3 mL, 4.77 mmol) at −78°C under argon and stirring was continued at the same temperature for 2 h. The reaction mixture was quenched with methanol and was then allowed to warm to room temperature. Saturated aqueous potassium sodium tartrate solution was added and the reaction mixture was stirred vigorously for 30 min. The insoluble material was filtered through Celite and the filtrate was extracted three times with CH_2Cl_2. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a mixture of the corresponding aldehyde and alcohol, which was used for the next reaction without further purification.

To a stirred solution of the above mixture (587 mg) in CH_2Cl_2 (15 mL) was added Dess–Martin periodinane (1.66 g, 3.91 mmol) at room temperature. The reaction mixture was stirred at room temperature for 1 h. After dilution with Et_2O, the resulting suspension was filtered and the filtrate was washed with 2% NaOH solution and brine and then dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using hexane and AcOEt (98/2) as eluent to give aldehyde **21** (556 mg, 75% from the ester) as a colorless oil. $[\alpha]_D^{29}$ +29.6 (*c* 1.06, $CHCl_3$); IR: 1725 cm^{-1}; ^1H NMR: δ −0.13 and 0.02 (each 3H, each s, $Si(CH_3)_2$), 0.94 (9H, s, $C(CH_3)_3$), 1.04 (3H, d, $J=7.1$ Hz, 2-$CH\underline{H}_3$), 2.74 (1H, d quintet, $J=1.0$, 7.1 Hz, 2-CH), 5.06 (1H, d, $J=4.9$ Hz, 3-CH), 6.19 (1H, d, $J=3.3$ Hz, 3′-CH), 6.28 (1H, dd, $J=1.0$, 3.3 Hz, 4′-CH), 7.31 (1H, d, $J=1.8$ Hz, 5′-CH), 9.49 (1H, d, $J=1.0$ Hz, 1-CH); ^{13}C NMR: δ −5.4, −5.1, 8.8, 18.0, 25.6, 52.1, 68.6, 107.5, 110.0, 141.8, 154.4, 203.6; MS (CI): 253 (M+1); HRMS (CI) calcd for $C_{14}H_{24}O_3Si$+H: 253.1624; found: 253.1595.

*3.10.2. From (1*R*,2*S*,3*E*)-1-*tert*-butyldimethylsilyloxy-2-furyl-2-methyl-3-pentene* ***6***

To a stirred solution of alkene **6** (113 mg, 0.40 mmol) and pyridine (0.10 mL, 1.24 mmol) in *tert*-butyl alcohol (3 mL) were added aqueous sodium periodate (0.5 M, 2.4 mL, 1.20 mmol) and a catalytic amount of osmium tetroxide at room temperature. The reaction mixture was stirred at room temperature for 30 min. After dilution with AcOEt, the organic layer was washed with saturated aqueous sodium thiosulfate solution and brine and then dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using hexane and Et_2O (99/1) as eluent to give aldehyde **21** (31 mg, 29%). $[\alpha]_D^{24}$ +25.9 (*c* 0.11, $CHCl_3$). The ^1H and ^{13}C NMR spectra of this aldehyde were identical with those above.

*3.11. Preparation of (1*R*,2*S*)-1-(*tert*-butyldimethylsilyloxy)-1-(2-furyl)-2-methyl-3-butene* ***22***

To a stirred solution of methylenetriphenylphosphorane, prepared from methyltriphenylphosphonium bromide (160 mg, 0.45 mmol) and *n*-butyllithium (1.59 M in hexane, 0.28 mL, 0.45 mmol) in THF (2 mL), was added a solution of aldehyde **21** (100 mg, 0.37 mmol) in THF (1 mL) at 0°C under argon and stirring was continued at room temperature for 1 h. The reaction mixture was quenched with water and the aqueous solution was extracted three times with pentane. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using pentane as eluent to give alkene **22** (83 mg, 84%) as a colorless oil. $[\alpha]_D^{28}$ +42.0 (*c* 1.02, $CHCl_3$); ^1H NMR: δ −0.13 and 0.03 (each 3H, each s, $Si(CH_3)_2$), 0.87 (9H, s, $C(CH_3)_3$), 1.05 (3H, d, $J=6.7$ Hz, 2-$CH\underline{H}_3$), 2.62

(1H, sextet, $J=6.7$ Hz, 2-CH), 4.48 (1H, d, $J=6.7$ Hz, 1-CH), 4.94 (1H, dd, $J=1.0$, 10.3 Hz, 4-C$\underline{H}$H), 4.97 (1H, dd, $J=1.0$, 17.3 Hz, 4-CH$\underline{H}$), 5.71 (1H, ddd, $J=6.7$, 10.3, 17.3 Hz, 3-CH), 6.14 (1H, dd, $J=0.8$, 3.1 Hz, 3′-CH), 6.28 (1H, dd, $J=1.7$, 3.1 Hz, 4′-CH), 7.32 (1H, dd, $J=0.8$, 1.7 Hz, 5′-CH); ^{13}C NMR: δ −5.2, −5.0, 15.1, 18.2, 25.8, 43.9, 72.7, 106.7, 109.8, 114.5, 140.5, 141.0, 156.3; MS (FAB) calcd for $C_{15}H_{26}O_2Si–CH_3$: 251.1468; found: 251.1462.

*3.12. Preparation of (1*R*,2*S*)-1-(2-furyl)-2-methyl-3-buten-1-ol* **23**

To a stirred solution of silyl ether **22** (67 mg, 0.25 mmol) in THF (2 mL) was added tetrabutylammonium fluoride (1 M in THF, 0.37 mL, 0.37 mmol) at room temperature and stirring was continued at the same temperature for 1 h. After dilution with water, the aqueous solution was extracted three times with pentane and Et_2O (1/1). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave an oil, which was purified by silica gel chromatography using pentane and Et_2O (9/1) as eluent to give alcohol **23** (33 mg, 87%) as a colorless oil. $[\alpha]_D^{27}$ +20.4 (*c* 1.98, $CHCl_3$). The ^{1}H and ^{13}C NMR spectra were in good accordance with those reported.[12] HPLC analysis using a Chiralcel OD column showed it to be 94% ee [*i*-PrOH/hexane (5/95), flow rate 1.0 mL/min, $t_R(1S,2R)$ 6.86 min and $t_R(1R,2S)$ 7.33 min].

Acknowledgements

This work was supported by a Grant-in-Aid for the Scientific Research (C) from the Ministry of Education, Science, Sports and Culture, Japan.

References

1. For recent reviews, see: (a) Marshall, J. A. In Trost, B. M.; Fleming, I., Eds.; *Comprehensive Organic Synthesis*; Pergamon: New York, 1991; Vol. 3, pp. 975–1014; (b) Brückner, R. In Trost, B. M.; Fleming, I., Eds.; *Comprehensive Organic Synthesis*; Pergamon: New York, 1991; Vol. 6, pp. 873–908; (c) Nakai, T.; Mikami, K. *Org. React*. **1994**, *46*, 105–209; (d) Nakai, T.; Tomooka, K. *Pure Appl. Chem*. **1997**, *69*, 595–600.
2. Tsubuki, M.; Kamata, T.; Okita, H.; Arai, M.; Shigihara, A.; Honda, T. *Chem. Commun*. **1999**, 2263–2264.
3. (a) DeShong, P.; Ramesh, S.; Perez, J. J. *J. Org. Chem*. **1983**, *48*, 2117–2118; (b) Martin, S. F.; Gluchowski, C.; Campbell, C. L.; Chapman, R. C. *J. Org. Chem*. **1984**, *49*, 2512–2513; (c) Ziegler, F. E.; Wester, R. T. *Tetrahedron Lett*. **1984**, *25*, 617–620; (d) Martin, S. F.; Guinn, D. E. *J. Org. Chem*. **1987**, *52*, 5588–5593; (e) Akita, H.; Koshiji, H.; Furuichi, A.; Horikoshi, K.; Oishi, T. *Chem. Pharm. Bull*. **1984**, *32*, 1242–1243; (f) Akita, H.; Furuichi, A.; Koshiji, H.; Horikoshi, K.; Oishi, T. *Chem. Pharm. Bull*. **1984**, *32*, 1333–1341; (g) Kusakabe, M.; Sato, F. *J. Org. Chem*. **1989**, *54*, 3486–3487.
4. (a) Sayo, N.; Azuma, K.; Mikami, K.; Nakai, T. *Tetrahedron Lett*. **1984**, *25*, 565–568; (b) McKew, J. C.; Kurth, M. J. *J. Org. Chem*. **1993**, *58*, 4589–4595.
5. Kirner, W. R. *J. Am. Chem. Soc*. **1928**, *50*, 1955–1961.
6. Baldwin, J. E.; Patrick, J. E. *J. Am. Chem. Soc*. **1971**, *93*, 3556–3558.
7. (a) McKee, B. H.; Kalantar, T. H.; Sharpless, K. B. *J. Org. Chem*. **1991**, *56*, 6966–6968; (b) Liu, L.; Lin, G. *Prog. Nat. Sci*. **1991**, 173–174.
8. Gawronski, J.; Radocki, D.; Jurczak, J.; Pakulski, Z.; Raczko, J.; Ramza, J.; Zamojski, A. *J. Org. Chem*. **1990**, *55*, 1118–1120.
9. (a) Marshall, J. A.; Lebreton, J. *J. Am. Chem. Soc*. **1988**, *110*, 2925–2931; (b) Fujimoto, K.; Nakai, T. *Tetrahedron Lett*. **1994**, *35*, 5019–5022; (c) Kang, J.; Cho, W. O.; Cho, H. G.; Oh, H. J. *Bull. Korean Chem. Soc*.

1994, *15*, 732–739; (d) Manabe, S. *Chem. Commun.* **1997**, 737–738; (e) Tomooka, K.; Komine, N.; Nakai, T. *Tetrahedron Lett.* **1998**, *39*, 5513–5516; (f) Gibson, S. E.; Ham, P.; Jefferson, G. R. *Chem. Commun.* **1998**, 123–124; (g) Kawasaki, T.; Kimachi, T. *Synlett* **1998**, 1429–1431.

10. Beak, P.; Basu, A.; Gallagher, D. J.; Park, Y. S.; Thayumanavan, S. *Acc. Chem. Res.* **1996**, *29*, 552–560.
11. Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2282–2316.
12. Racemates of both *syn*- and *anti*-isomers **16** and **18** are known, see: (a) Wutz, P. G. M.; Callen, G. R. *Synth. Commun.* **1986**, *16*, 1833–1837; (b) Jones, P.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 186–195.