Rhodium/Diene-Catalyzed Asymmetric 1,4-Addition of Arylboronic Acids to α,β-Unsaturated Weinreb Amides

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Supplementary Information

I. General

All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen or in a glove box under argon.

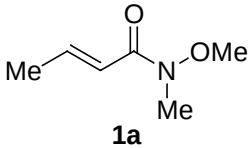
1,4-Dioxane and THF were distilled over benzophenone ketyl under nitrogen. Chloroform and dichloromethane were distilled over CaH_2 under nitrogen. Methanol was distilled over Mg turnings under nitrogen.

N,*O*-dimethylhydroxylamine hydrochloride (Aldrich), pyridine (Wako Chemicals), benzylamine (Wako Chemicals), acetaldehyde (Wako Chemicals), 1,1'-carbonyldiimidazole (Aldrich), ethylene glycol (Nacalai Tesque), crotonoyl chloride (TCI), *trans*-2-hexenoic acid (TCI), oxalyl chloride (TCI), *trans*-4-methyl-2-pentenoic acid (TCI), 4-methoxycinnamic acid (TCI), phenylboronic acid (TCI), *p*-toluenesulfonic acid (Nacalai Tesque; monohydrate), and diisobutylaluminum hydride (Kanto Chemicals; 1.0 M solution in hexane) were used as received. Other arylboronic acids were synthesized from the corresponding aryl bromides with $B(OMe)_3$ (Wako Chemicals). $[RhCl(C_2H_4)_2]_2$,[1] (*R*,*R*)-**3a**,[2] and (*S*,*S*)-**3b**[2] were prepared following the literature procedures.

All other chemicals and solvents were purchased from Aldrich, Wako Chemicals, TCI, or Kanto Chemicals and used as received.

[1] R. Cramer, *Inorg. Synth.*, 1974, **15**, 16.
[2] N. Tokunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani, T. Hayashi, *J. Am. Chem. Soc.*, 2004, **126**, 13584.

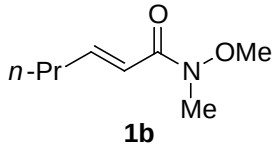
II. Synthesis of Substrates



1a

N,*O*-Dimethylhydroxylamine hydrochloride (600 mg, 6.15 mmol) and pyridine (840 μL, 10.4 mmol) were added to a solution of crotonoyl chloride (316 μL, 3.30 mmol) in chloroform (30 mL) at 0 °C. The resulting mixture was stirred for 2.5 h at room temperature and the reaction was quenched with water. After extraction with Et_2O, the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with hexane / Et_2O = 2 / 3 to afford amide **1a** (CAS 121712-52-5) as a colorless oil (258 mg, 2.00 mmol; 61% yield).

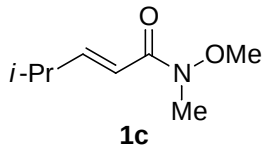
^{1}H NMR ($CDCl_3$): δ 6.99 (dq, $^3J_{HH}$ = 15.3 and 6.9 Hz, 1H), 6.42 (dq, $^3J_{HH}$ = 15.4 Hz and $^4J_{HH}$ = 1.6 Hz, 1H), 3.70 (s, 3H), 3.24 (s, 3H), 1.91 (dd, $^3J_{HH}$ = 6.9 Hz and $^4J_{HH}$ = 1.7 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 167.0, 142.8, 120.2, 61.6, 32.3, 18.1.



1b

(CAS 201996-70-5) This was synthesized from *trans*-2-hexenoyl chloride [prepared by treating *trans*-2-hexenoic acid with oxalyl chloride in Et_2O] following the procedure for compound **1a**. Colorless oil. 86% yield.

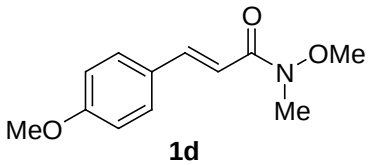
^{1}H NMR ($CDCl_3$): δ 6.98 (dt, $^3J_{HH}$ = 15.5 and 6.9 Hz, 1H), 6.40 (d, $^3J_{HH}$ = 15.5 Hz, 1H), 3.70 (s, 3H), 3.24 (s, 3H), 2.22 (qd, $^3J_{HH}$ = 7.2 Hz and $^4J_{HH}$ = 1.5 Hz, 2H), 1.55-1.47 (m, 2H), 0.94 (t, $^3J_{HH}$ = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 166.9, 147.4, 118.7, 61.4, 34.3, 32.2, 21.4, 13.5.



1c

(CAS 170969-86-5) This was synthesized from *trans*-4-methyl-2-pentenoyl chloride [prepared by treating *trans*-4-methyl-2-pentenoic acid with oxalyl chloride in Et_2O] following the procedure for compound **1a**. Pale yellow oil. 94% yield.

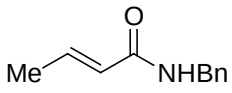
^{1}H NMR ($CDCl_3$): δ 6.90 (dd, $^3J_{HH}$ = 15.5 and 6.8 Hz, 1H), 6.29 (dd, $^3J_{HH}$ = 15.5 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 3.65 (s, 3H), 3.19 (s, 3H), 2.44 (d of septet of d, $^3J_{HH}$ = 6.9 and 6.6 Hz and $^4J_{HH}$ = 1.4 Hz, 1H), 1.03 (d, $^3J_{HH}$ = 6.7 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 167.2, 153.9, 115.8, 61.5, 32.3, 31.1, 21.4.



1d

(CAS 243665-13-6) This was synthesized from 4-methoxycinnamoyl chloride [prepared by treating 4-methoxycinnamic acid with oxalyl chloride in Et_2O] following the procedure for compound **1a**. Pale yellow solid. 95% yield.

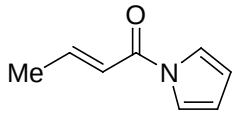
^{1}H NMR ($CDCl_3$): δ 7.67 (d, $^3J_{HH}$ = 15.7 Hz, 1H), 7.49 (d, $^3J_{HH}$ = 8.8 Hz, 2H), 6.88 (d, $^3J_{HH}$ = 16.0 Hz, 1H), 6.87 (d, $^3J_{HH}$ = 8.6 Hz, 2H), 3.79 (s, 3H), 3.73 (s, 3H), 3.27 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 167.2, 160.9, 142.9, 129.5, 127.8, 114.1, 113.2, 61.7, 55.2, 32.4.



1i

Benzylamine (1.09 mL, 9.98 mmol) was added dropwisely to a solution of crotonoyl chloride (479 μL, 5.00 mmol) in dichloromethane (30 mL) at 0 °C. The reaction mixture was stirred for 1 h at room temperature and quenched with water. After extraction with dichloromethane, the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with hexane / Et_2O = 1 / 3 to afford the amide (CAS 89232-30-4) as a white solid (753 mg, 4.30 mmol; 86% yield).

^{1}H NMR ($CDCl_3$): δ 7.30-7.22 (m, 5H), 6.80 (dq, $^3J_{HH}$ = 15.1 and 7.1 Hz, 1H), 6.32 (bs, 1H), 5.84 (d, $^3J_{HH}$ = 15.2 Hz, 1H), 4.43 (d, $^3J_{HH}$ = 5.7 Hz, 2H), 1.80 (d, $^3J_{HH}$ = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 165.9, 139.9, 138.4, 128.5, 127.6, 127.2, 124.9, 43.3, 17.6.



1j

(CAS 497147-42-9) This was synthesized using acetaldehyde instead of benzaldehyde following the literature procedure for the synthesis of *trans*-3-phenyl-1-pyrrol-1-yl-2-propen-1-one.[3] Pale yellow solid. 10% overall yield from 1,1'-carbonyldiimidazole.

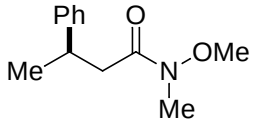
^{1}H NMR ($CDCl_3$): δ 7.38-7.36 (m, 2H), 7.27 (dq, $^3J_{HH}$ = 15.0 and 6.9 Hz, 1H), 6.58 (dq, $^3J_{HH}$ = 15.1 Hz and $^4J_{HH}$ = 1.7 Hz, 1H), 6.32-6.30 (m, 2H), 2.01 (dd, $^3J_{HH}$ = 7.0 Hz and $^4J_{HH}$ = 1.7 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 162.6, 147.8, 120.9, 119.1, 113.1, 18.5.

[3] S. Matsunaga, T. Kinoshita, S. Okada, S. Harada, M. Shibasaki, *J. Am. Chem. Soc.*, 2004, **126**, 7559.

III. 1,4-Addition Reactions

General Procedure for Table 1 and Equations 2–4.

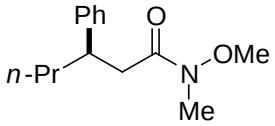
A solution of $[RhCl(C_2H_4)_2]_2$ (1.2 mg, 6.2 μmol Rh) and ligand (6.6 μmol) in 1,4-dioxane (0.5 mL) was stirred for 10 min at room temperature. KOH (0.1 mL, 0.10 mmol; 1.0 M aqueous) was then added to it, and the resulting solution was stirred for 5 min at room temperature. $ArB(OH)_2$ (0.60 mmol) and α,β-unsaturated amide (0.20 mmol) were then added to this with additional 1,4-dioxane (0.5 mL). The resulting mixture was stirred for 20 h at 50 °C, and was then passed through a pad of silica gel with EtOAc. The solvent was removed under vacuum and the residue was purified by silica gel PTLC with Et_2O / hexane to afford the desired 1,4-adduct.



(*R*)-**2a**

Table 1, Entry 1. (CAS 214759-91-8) Pale yellow oil. 92% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 98 : 2, flow = 0.75 mL / min. Retention times: 15.1 min [(*S*)-enantiomer], 17.8 min [(*R*)-enantiomer]. 90% ee. $[\alpha]^{20}_D$ +2.9 (*c* 1.13, $CHCl_3$). The absolute configuration was determined by converting it to the corresponding methyl ketone (see Procedure for Scheme 1(a) below).

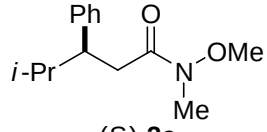
^{1}H NMR ($CDCl_3$): δ 7.31-7.24 (m, 4H), 7.21-7.17 (m, 1H), 3.60 (s, 3H), 3.41-3.34 (m, 1H), 3.14 (s, 3H), 2.74 (dd, $^2J_{HH}$ = 15.3 Hz and $^3J_{HH}$ = 6.0 Hz, 1H), 2.64 (dd, $^2J_{HH}$ = 15.3 Hz and $^3J_{HH}$ = 8.3 Hz, 1H), 1.32 (d, $^3J_{HH}$ = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 173.1, 146.5, 128.4, 126.9, 126.2, 61.1, 40.3, 35.8, 32.1, 21.6.



(*R*)-**2b**

Table 1, Entry 2. Pale yellow oil. 86% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL / min. Retention times: 16.5 min [(*S*)-enantiomer], 19.3 min [(*R*)-enantiomer]. 87% ee. $[\alpha]^{20}_D$ +2.7 (*c* 1.13, $CHCl_3$). The absolute configuration was assigned by analogy with compound **2a**.

^{1}H NMR ($CDCl_3$): δ 7.29-7.26 (m, 2H), 7.22-7.20 (m, 2H), 7.19-7.16 (m, 1H), 3.55 (s, 3H), 3.24-3.18 (m, 1H), 3.10 (s, 3H), 2.76-2.65 (m, 2H), 1.71-1.56 (m, 2H), 1.24-1.12 (m, 2H), 0.85 (t, $^3J_{HH}$ = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 173.2, 144.9, 128.3, 127.6, 126.1, 61.1, 41.3, 39.2, 38.3, 32.0, 20.6, 14.0. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99. Found: C, 71.50; H, 8.92.

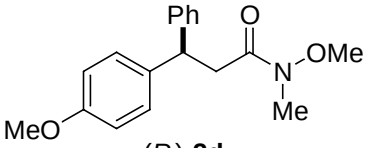


(*S*)-**2c**

Table 1, Entry 3. (CAS 350854-35-2) Pale yellow oil. 74% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL / min. Retention times: 16.3 min [(*R*)-enantiomer], 21.2 min [(*S*)-enantiomer].

86% ee. $[\alpha]^{20}_D$ +1.3 (*c* 0.79, $CHCl_3$). The absolute configuration was assigned by analogy with compound **2a**.

^{1}H NMR ($CDCl_3$): δ 7.27-7.24 (m, 2H), 7.19-7.14 (m, 3H), 3.56 (s, 3H), 3.05 (s, 3H), 3.03-2.99 (m, 1H), 2.83-2.76 (m, 2H), 1.94-1.87 (m, 1H), 0.97 (d, $^3J_{HH}$ = 6.7 Hz, 3H), 0.76 (d, $^3J_{HH}$ = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 173.6, 143.7, 128.5, 128.1, 126.2, 61.3, 48.2, 35.7, 33.0, 32.2, 20.9, 20.5.



(*R*)-**2d**

Table 1, Entry 4. White solid. 91% yield. $[\alpha]^{20}_D$ –4.1 (*c* 1.32, $CHCl_3$). The absolute configuration was determined by converting it to the corresponding methyl ketone (see below).

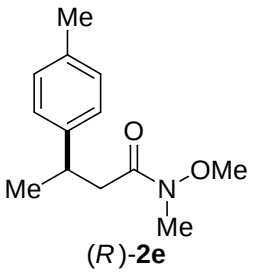
^{1}H NMR ($CDCl_3$): δ 7.28-7.23 (m, 4H), 7.18-7.14 (m, 3H), 6.83-6.80 (m, 2H), 4.64 (t, $^3J_{HH}$ = 7.8 Hz, 1H), 3.75 (s, 3H), 3.55 (s, 3H), 3.20-3.12 (m, 2H), 3.09 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 172.5, 158.0, 144.5, 136.3, 128.8, 128.4, 127.7, 126.2, 113.8, 61.2, 55.1, 45.5, 38.0, 32.1. Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07. Found: C, 71.97; H, 7.00.

For ee analysis, 1,4-adduct **2d** was converted to the corresponding methyl ketone (CAS 76217-07-7):

Methylmagnesium iodide (230 μL, 0.21 mmol; 0.93 M in Et_2O) was added to a solution of 1,4-adduct **2d** (34.9 mg, 0.12 mmol) in THF (1.0 mL) at –78 °C, and the resulting mixture was stirred for 1 h at 0 °C. After addition of water (50 μL), this was passed through a pad of silica gel with EtOAc, and the solvent was removed under vacuum. The residue was purified by silica gel PTLC with Et_2O / hexane = 1 / 7 to afford the methyl ketone as a white solid (22.2 mg, 87 μmol; 75% yield).

The ee of this ketone was determined on a Daicel Chiralcel OD-H column with hexane : 2-propanol = 80 : 20, flow = 0.7 mL / min. Retention times: 10.4 min [(*S*)-enantiomer], 12.2 min [(*R*)-enantiomer]. 80% ee. $[\alpha]^{20}_D$ +0.5 (*c* 1.56, $CHCl_3$). The absolute configuration was determined by comparison of the optical rotation with that reported in the literature.[4]

^{1}H NMR ($CDCl_3$): δ 7.28-7.25 (m, 2H), 7.21-7.11 (m, 5H), 6.82-6.79 (m, 2H), 4.53 (t, $^3J_{HH}$ = 7.7 Hz, 1H), 3.75 (s, 3H), 3.14 (d, $^3J_{HH}$ = 7.6 Hz, 2H), 2.06 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 206.9, 158.1, 144.2, 135.9, 128.6, 128.5, 127.6, 126.3, 113.9, 55.2, 49.9, 45.3, 30.6.



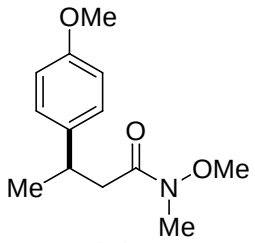
(*R*)-**2e**

Table 1, Entry 5. Pale yellow oil. 83% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL / min. Retention times: 20.5 min [(*S*)-enantiomer], 27.2 min [(*R*)-enantiomer]. 89% ee. $[\alpha]^{20}_D$

[4] C. Defieber, J.-F. Paquin, S. Serna, E. M. Carreira, *Org. Lett.*, 2004, **6**, 3873.

+3.6 (*c* 0.87, $CHCl_3$). The absolute configuration was assigned by analogy with compound **2a**.

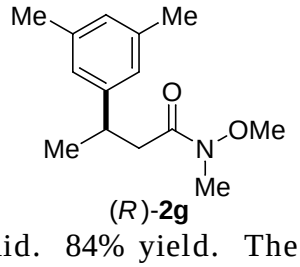
^{1}H NMR ($CDCl_3$): δ 7.16 (d, $^3J_{HH}$ = 8.0 Hz, 2H), 7.11 (d, $^3J_{HH}$ = 8.2 Hz, 2H), 3.59 (s, 3H), 3.40-3.31 (m, 1H), 3.14 (s, 3H), 2.72 (dd, $^2J_{HH}$ = 15.1 Hz and $^3J_{HH}$ = 5.7 Hz, 1H), 2.64 (dd, $^2J_{HH}$ = 14.8 Hz and $^3J_{HH}$ = 7.7 Hz, 1H), 2.32 (s, 3H), 1.30 (d, $^3J_{HH}$ = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 173.2, 143.5, 135.6, 129.1, 126.7, 61.1, 40.4, 35.3, 32.0, 21.7, 20.9. Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65. Found: C, 70.80; H, 8.79.



(*R*)-**2f**

Table 1, Entry 6. Pale yellow oil. 93% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL/min. Retention times: 21.9 min [(*S*)-enantiomer], 27.9 min [(*R*)-enantiomer]. 87% ee. $[\alpha]^{20}_D$ +3.3 (*c* 1.16, $CHCl_3$). The absolute configuration was assigned by analogy with compound **2a**.

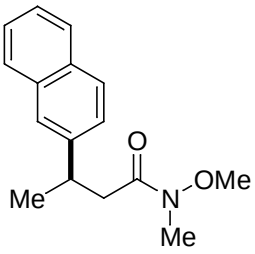
^{1}H NMR ($CDCl_3$): δ 7.18 (d, $^3J_{HH}$ = 8.8 Hz, 2H), 6.84 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 3.78 (s, 3H), 3.58 (s, 3H), 3.37-3.30 (m, 1H), 3.13 (s, 3H), 2.71 (dd, $^2J_{HH}$ = 15.4 Hz and $^3J_{HH}$ = 5.5 Hz, 1H), 2.61 (dd, $^2J_{HH}$ = 15.4 Hz and $^3J_{HH}$ = 7.9 Hz, 1H), 1.29 (d, $^3J_{HH}$ = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 173.3, 158.0, 138.7, 127.8, 113.8, 61.2, 55.2, 40.6, 35.0, 32.1, 21.9. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07. Found: C, 66.09; H, 7.99.



(*R*)-**2g**

Table 1, Entry 7. White solid. 84% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL/min. Retention times: 14.8 min [(*S*)-enantiomer], 15.8 min [(*R*)-enantiomer]. 92% ee. $[\alpha]^{20}_D$ +1.9 (*c* 1.21, $CHCl_3$). The absolute configuration was assigned by analogy with compound **2a**.

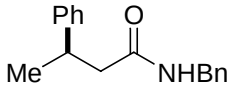
^{1}H NMR ($CDCl_3$): δ 6.86 (s, 2H), 6.82 (s, 1H), 3.59 (s, 3H), 3.32-3.25 (m, 1H), 3.14 (s, 3H), 2.70 (dd, $^2J_{HH}$ = 15.9 Hz and $^3J_{HH}$ = 6.1 Hz, 1H), 2.62 (dd, $^2J_{HH}$ = 15.5 Hz and $^3J_{HH}$ = 8.3 Hz, 1H), 2.28 (s, 6H), 1.28 (d, $^3J_{HH}$ = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 173.2, 146.6, 137.8, 127.8, 124.6, 61.1, 40.3, 35.6, 32.1, 21.6, 21.3. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99. Found: C, 71.54; H, 9.10.



(*R*)-**2h**

Table 1, Entry 8. Pale yellow oil. 90% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL / min. Retention times: 19.5 min [(*S*)-enantiomer], 25.1 min [(*R*)-enantiomer]. 86% ee. $[\alpha]^{20}_{D}$ +7.3 (*c* 1.01, $CHCl_3$). The absolute configuration was assigned by analogy with compound **2a**.

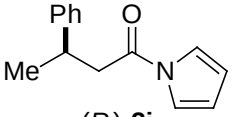
^{1}H NMR ($CDCl_3$): δ 7.83-7.79 (m, 3H), 7.71 (s, 1H), 7.48-7.41 (m, 3H), 3.59 (s, 3H), 3.60-3.54 (m, 1H), 3.15 (s, 3H), 2.87 (dd, $^2J_{HH}$ = 14.9 Hz and $^3J_{HH}$ = 5.6 Hz, 1H), 2.75 (dd, $^2J_{HH}$ = 15.3 Hz and $^3J_{HH}$ = 8.3 Hz, 1H), 1.43 (d, $^3J_{HH}$ = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 173.0, 143.9, 133.5, 132.2, 128.0, 127.6, 127.5, 125.8, 125.7, 125.2, 124.9, 61.1, 40.2, 35.9, 32.1, 21.7. Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44. Found: C, 74.67; H, 7.45.



(*R*)-**2i**

Equation 3. (CAS 535946-25-9; 338461-66-8 for (*R*)) White solid. 92% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 80 : 20, flow = 0.7 mL / min. Retention times: 6.9 min [(*S*)-enantiomer], 7.8 min [(*R*)-enantiomer]. 92% ee. $[\alpha]^{20}_{D}$ –9.2 (*c* 0.67, $CHCl_3$). The absolute configuration was determined by comparison of the optical rotation with that reported in the literature.[5]

^{1}H NMR ($CDCl_3$): δ 7.30-7.19 (m, 8H), 7.03-7.00 (m, 2H), 5.66 (bs, 1H), 4.35 (dd, $^2J_{HH}$ = 14.8 Hz and $^3J_{HH}$ = 6.0 Hz, 1H), 4.26 (dd, $^2J_{HH}$ = 14.7 Hz and $^3J_{HH}$ = 5.5 Hz, 1H), 3.35-3.28 (m, 1H), 2.45 (d, $^3J_{HH}$ = 7.4 Hz, 2H), 1.31 (d, $^3J_{HH}$ = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 171.4, 145.7, 138.1, 128.6, 128.5, 127.5, 127.3, 126.8, 126.4, 45.8, 43.4, 37.0, 21.8.



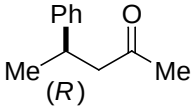
(*R*)-**2j**

Equation 4. Yellow oil. 92% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL / min. Retention times: 13.9 min [(*S*)-enantiomer], 15.6 min [(*R*)-enantiomer]. 85% ee. $[\alpha]^{20}_{D}$ +12.5 (*c* 0.82, $CHCl_3$). The absolute configuration was assigned by analogy with equation 3.

^{1}H NMR ($CDCl_3$): δ 7.32-7.19 (m, 7H), 6.26 (t, $^3J_{HH}$ = 2.6 Hz, 2H), 3.52-3.45 (m, 1H), 3.12 (dd, $^2J_{HH}$ = 16.1 Hz and $^3J_{HH}$ = 6.1 Hz, 1H), 3.02 (dd, $^2J_{HH}$ = 16.1 Hz and $^3J_{HH}$ = 8.1 Hz, 1H), 1.38 (d, $^3J_{HH}$ = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 169.2, 145.5, 128.6, 126.7, 126.6, 119.0, 113.1, 43.0, 35.9, 21.7. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.73; H, 7.25.

[5] S, Sakuma, N. Miyaura, *J. Org. Chem.*, 2001, **66**, 8944.

Procedure for Scheme 1 (a).

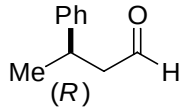


Methylmagnesium iodide (430 μL, 0.40 mmol; 0.93 M solution in Et_2O) was added to a solution of **2a** (41.5 mg, 0.20 mmol; 90% ee) in THF (2.0 mL) at –78 °C, and the resulting mixture was stirred for 1 h at room temperature. After quenching with HCl (0.10 mL; 10% aqueous), the mixture was directly passed through a pad of silica gel with Et_2O, and the solvent was removed under vacuum to afford the desired methyl ketone (CAS 17913-10-9; 67110-72-9 for (*R*)) as a colorless oil (30.5 mg, 0.19 mmol; 94% yield).

The ee was determined on a Daicel Chiralcel OJ-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL / min. Retention times: 23.5 min [(*S*)-enantiomer], 24.9 min [(*R*)-enantiomer]. 90% ee. $[\alpha]^{20}_D$ –41.5 (*c* 1.10, $CHCl_3$). The absolute configuration was determined by comparison of the optical rotation with that reported in the literature.[6]

^{1}H NMR ($CDCl_3$): δ 7.30-7.27 (m, 2H), 7.21-7.17 (m, 3H), 3.34-3.27 (m, 1H), 2.75 (dd, $^2J_{HH}$ = 16.2 Hz and $^3J_{HH}$ = 6.6 Hz, 1H), 2.65 (dd, $^2J_{HH}$ = 16.2 Hz and $^3J_{HH}$ = 7.9 Hz, 1H), 2.06 (s, 3H), 1.26 (d, $^3J_{HH}$ = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 207.9, 146.3, 128.7, 126.9, 126.4, 52.1, 35.6, 30.7, 22.1.

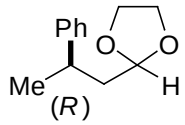
Procedure for Scheme 1 (b).



Diisobutylaluminum hydride (300 μL, 0.30 mmol; 1.0 M solution in hexane) was added to a solution of **2a** (41.5 mg, 0.20 mmol; 90% ee) in THF (2.0 mL) at –78 °C, and the resulting mixture was stirred for 30 min at –78 °C. After quenching with HCl (0.10 mL; 10% aqueous), the mixture was directly passed through a pad of silica gel with Et_2O, and the solvent was removed under vacuum. The residue was chromatographed on silica gel with hexane / Et_2O = 7 / 1 to afford the desired aldehyde (CAS 16251-77-7; 42307-58-9 for (*R*)) as a colorless oil (22.3 mg, 0.15 mmol; 75% yield). $[\alpha]^{20}_D$ –33.2 (*c* 0.74, $CHCl_3$). The absolute configuration was assigned by analogy with the methyl ketone.

^{1}H NMR ($CDCl_3$): δ 9.71 (t, $^3J_{HH}$ = 1.8 Hz, 1H), 7.32-7.28 (m, 2H), 7.23-7.18 (m, 3H), 3.39-3.32 (m, 1H), 2.74 (ddd, $^2J_{HH}$ = 16.6 Hz and $^3J_{HH}$ = 6.8 and 1.7 Hz, 1H), 2.65 (ddd, $^2J_{HH}$ = 16.6 Hz and $^3J_{HH}$ = 7.7 and 2.2 Hz, 1H), 1.32 (d, $^3J_{HH}$ = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 201.9, 145.6, 128.8, 126.9, 126.7, 51.9, 34.5, 22.3.

For ee analysis, the aldehyde was converted to the corresponding ethylene glycol acetal (CAS 38739-78-5):



A mixture of the aldehyde (16.2 mg, 0.11 mmol), ethylene glycol (23 μL, 0.41 mmol), and *p*-toluenesulfonic acid (1.5 mg, 7.9 μmol; monohydrate) in benzene (25 mL) was refluxed for 10 h with a Dean-Stark trap. After removal of the solvent under vacuum, the residue was chromatographed on silica gel with Et_2O / hexane = 1 / 10 to afford the acetal as a colorless oil (16.8 mg, 87 μmol; 80% yield).

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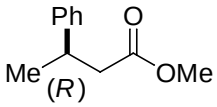
[6] L. F. Tietze, B. Weigand, L. Völkel, C. Wulff, C. Bittner, *Chem. Eur. J.*, 2001, **7**, 161.

The ee of this acetal was determined on a Daicel Chiralcel OJ-H column with hexane : 2-propanol = 98 : 2, flow = 0.7 mL/min. Retention times: 23.5 min [(*R*)-enantiomer], 31.3 min [(*S*)-enantiomer]. 90% ee. $[\alpha]^{20}_{D}$ –40.8 (*c* 0.78, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ 7.30-7.27 (m, 2H), 7.23-7.17 (m, 3H), 4.68 (dd, $^3J_{HH}$ = 6.5 and 4.0 Hz, 1H), 3.97-3.91 (m, 2H), 3.83-3.75 (m, 2H), 3.01-2.94 (m, 1H), 2.01 (ddd, $^2J_{HH}$ = 13.7 Hz and $^3J_{HH}$ = 8.4 and 4.0 Hz, 1H), 1.86 (dt, $^2J_{HH}$ = 13.8 Hz and $^3J_{HH}$ = 6.4 Hz, 1H), 1.29 (d, $^3J_{HH}$ = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 146.9, 128.6, 127.1, 126.2, 103.5, 64.9, 64.8, 42.2, 36.2, 22.9.

Procedure for Scheme 1 (c).



H_2SO_4 (0.20 mL; concentrated) was added to a solution of **2a** (41.5 mg, 0.20 mmol; 90% ee) in methanol (1.0 mL) at room temperature, and the resulting solution was refluxed for 2.5 h. The mixture was poured into $NaHCO_3$ (aqueous) and extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum to afford the desired methyl ester (CAS 3461-39-0; 1472-07-7 for (*R*)) as a pale yellow oil (31.9 mg, 0.18 mmol; 89% yield). The ee was determined on a Daicel Chiralcel OB-H column with hexane : 2-propanol = 98 : 2, flow = 1.0 mL/min. Retention times: 9.0 min [(*R*)-enantiomer], 10.6 min [(*S*)-enantiomer]. 90% ee. $[\alpha]^{20}_{D}$ –28.5 (*c* 1.18, $CHCl_3$). The absolute configuration was assigned by analogy with the methyl ketone.

^{1}H NMR ($CDCl_3$): δ 7.31-7.27 (m, 2H), 7.24-7.18 (m, 3H), 3.62 (s, 3H), 3.31-3.24 (m, 1H), 2.62 (dd, $^2J_{HH}$ = 15.1 Hz and $^3J_{HH}$ = 7.0 Hz, 1H), 2.54 (dd, $^2J_{HH}$ = 15.1 Hz and $^3J_{HH}$ = 8.2 Hz, 1H), 1.30 (d, $^3J_{HH}$ = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 172.8, 145.7, 128.5, 126.7, 126.4, 51.5, 42.8, 36.4, 21.8.