Supporting Information for the paper "A Versatile Stereocontrolled Approach to Chiral Tetrahydrofuran and Tetrahydropyran Derivatives via Sequential Asymmetric Horner-Wadsworth-Emmons and Palladium-Catalyzed Ring Closure Reactions"

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General. All solvents were distilled prior to use. Ether and tetrahydrofuran were distilled from sodium/benzophenone ketyl. Dichloromethane, pentane and triethylamine were distilled from calcium hydride. All reactions were carried out in oven dried glassware unless water was used as the reaction medium. Commercial reagents were generally used as received unless otherwise noted. Potassium hexamethyldisilazide (KHMDS) was purchased as a stock solution (0.5 M in toluene), and titrated according to the method of Ireland and Meissner.[1] 18-Crown-6 was recrystallized from anhydrous acetonitrile and dried under vacuum. Cooling to temperatures below –78 °C was effected by an immersion cooler. TLC analyses were performed on Merck aluminum-backed F254 silica gel plates, using UV light and phosphomolybdic acid for visualization. Drying of organic extracts was generally performed with $MgSO_4$. Flash chromatography was performed as described by Still and coworkers[2] using either Merck silica gel 60 (230-400 mesh) or Amicon Matrex 60Å silica gel (35-70 μm). NMR spectra were recorded in $CDCl_3$ unless otherwise indicated, using $CHCl_3$ (δ 7.26 ppm) and $CDCl_3$ (δ 77.0 ppm) as internal references for ^1H and ^{13}C, respectively. IR spectra were recorded neat on thin films using AgCl or KBr plates. Combustion analyses were performed either at the Research Institute for Pharmacy and Biochemistry, Prague, Czech Republic, or at the Microanalysis Laboratory, Institute of Physical Chemistry, University of Vienna, Austria. HRMS analyses were performed at the Department of Chemistry and Biochemistry, University of Notre Dame, Indiana, USA or at the Department of Chemistry, Copenhagen University, Copenhagen, Denmark.

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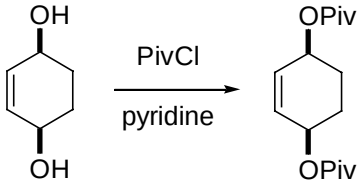
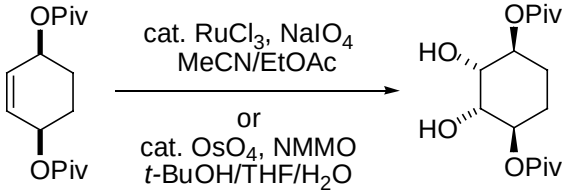
(1) Ireland, R. E.; Meissner, R. S. *J. Org. Chem.* **1991**, *56*, 4566.

(2) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.



25 **26**

Bis-Pivaloyl Ester 26. To a solution of diol **25**[3] (1.01 g, 8.85 mmol, 86:14 mixture of *cis*- and *trans*-isomers) and 4-(dimethylamino)pyridine (1.08 g, 8.85 mmol) in 30 mL of dry pyridine, pivaloyl chloride (5.5 mL, 44.25 mmol) was added**.** The reaction mixture was refluxed for 3 h, diluted with 1 N HCl, and extracted with EtOAc**.** Drying, concentration, and purification by flash chromatography (2%-6% EtOAc in hexanes) afforded 1.484 g (59%) of *cis*-ester **26** and 1.01 g (40%) of a mixture of *cis*- and *trans*-isomers (ca. 1.4:1). **26**: (R_f = 0.45 hexanes/EtOAc 9/1). ^{1}H NMR (250 MHz) δ 5.84 (app d, *J* = 1.4 Hz, 2H), 5.20-5.13 (m, 2H), 1.94-1.68 (m, 4H), 1.18 (s, 18 H); ^{13}C NMR (62.9 MHz) δ 178.0, 130.2, 67.0, 38.6, 27.0, 24.8; IR 2972, 1728, 1480, 1279, 1156, 1035, 1019 cm^{-1}.



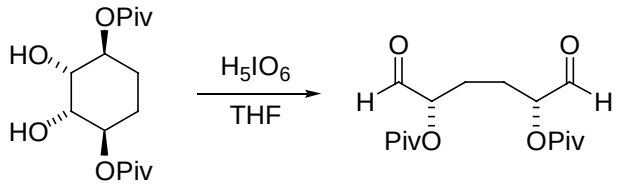
26 **27**

Diol 27. In our hands, the procedure described by Shing and Tam[4] has given the best results with this substrate. A solution of alkene **26** (447 mg, 1.584 mmol) in CH_3CN (26 mL) was cooled to 0 °C**.** A solution of $RuCl_3$·hydrate (38 mg, ca. 0.17 mmol) and $NaIO_4$ (818 mg, 3.75 mmol) in 5 mL of H_2O was then added to the alkene solution**.** The reaction mixture was stirred vigorously for 5 min and quenched with 20% aq $Na_2S_2O_3$ (5 mL)**.** The aqueous phase was separated and extracted with EtOAc**.** Drying, filtration and concentration followed by flash chromatography (25% EtOAc in hexanes) afforded 473 mg (94%) of diol **27** as a colorless oil which slowly solidified. **27**: (R_f = 0.2 hexanes/EtOAc 3/1).^{1}H NMR (250 MHz) δ 5.00 (br s, 2H), 3.84 (app dd, *J* = 8.2, 2.4 Hz, 2H), 3.20 (br s, 2H), 1.97-1.82 (m, 2H), 1.73-1.56 (m, 2H), 1.20 (s, 18H); ^{13}C NMR (62.9 MHz) δ 178.5, 72.0, 71.5, 38.8, 27.1, 23.7; IR 3481, 2974, 1732, 1481, 1283, 1156, 734 cm^{-1}**.** Anal. Calcd for $C_{16}H_{28}O_6$: C, 60.74; H, 8.85**.** Found: C, 61.07; H, 8.87.

Alternative procedure: To a solution of pivaloyl ester **26** (397 mg, 1.407 mmol) and *N*-methyl morpholine *N*-oxide (165 mg, 1.407 mmol) in a mixture of THF, *t*-butanol and H_2O (16 mL, 8 mL and 4 mL respectively), 540 μL of a 2.5 wt.-% solution of OsO_4 in *t*- butanol (0.042 mmol) was added**.** The reaction mixture was stirred for 60 h at 55 °C and then quenched by the addition of $Na_2S_2O_3$ (5 mL, 20% aq solution)**.** Dilution with brine followed by extraction (EtOAc), drying and concentration afforded 425 mg of a colorless oil**.** Purification by flash chromatography (4%-40% EtOAc in hexanes) afforded 65 mg (16%) of unreacted alkene **26** and 340 mg (76%) of diol **27** as a colorless oil which slowly solidified.

(3) Bäckvall, J.-E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619.

(4) Shing, T. K. M.; Tam, E. K. W. *Tetrahedron Lett.* **1999**, *40*, 2179.

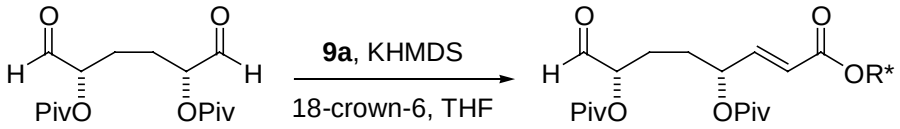


27 **8**

Dialdehyde 8. To a solution of diol **27** (127 mg, 0.402 mmol) in THF (8 mL) a solution of H_5IO_6 (91.6 mg, 0.402 mmol) in THF (8 mL) was added at 0 ˚C**.** After 80 min at room temperature, 5 mL phosphate buffer (pH 7) and 10 mL of brine was added**.** The solution was extracted with EtOAc, dried and concentrated**.** The residue was dissolved in $CHCl_3$ (2 mL) and filtered through a plug of cotton, giving 126 mg (99%) of **8** as a white crystalline compound**.** Due to its limited stability, the dialdehyde was generally used in HWE reactions without further purification. **8**: ^{1}H NMR (200 MHz) δ 9.47 (d, *J* = 0.7 Hz, 2H), 5.03-4.87 (m, 2H), 2.04-1.74 (m, 4H), 1.26 (s, 18H); ^{13}C NMR (50.3 MHz) δ 197.8, 177.9, 77.1, 38.8, 27.0, 24.2; IR 3466, 2974, 1732, 1481, 1282, 1151 cm^{-1}**.**

General Procedure for the Asymmetric Horner-Wadsworth-Emmons (HWE) Reactions. To a solution of the phosphonate (**9a** or **9b**, 1.1 equiv) and 18-crown-6 (5 equiv) in THF (0.04 M with respect to the phosphonate) at –85 °C under argon was added 1.0 equiv of KHMDS (0.5 M in toluene)**.** After 30 min the resulting greyish slurry was added by cannula to a precooled (-85 °C) solution of the dialdehyde (1.3 equiv)**.** The reaction mixture was stirred for 12-16 h at –85 °C and then quenched with phosphate buffer (pH 7)**.** After 5 min the reaction was slowly warmed to room temperature**.** Extractive workup (ethyl acetate), drying and concentration gave the crude condensation products**.**

Note: R* = (1*R*,2*S*,5*R*)-8-phenylmenthyl in all structures reported below**.**
General NMR data for the 8-phenylmenthyl unit: ^{1}H NMR (500 MHz) δ 7.3-7.2 (m, 4H) 7.15-7.05 (m, 1H), 2.0-0.8 (m, 9H), 1.29 ± 0.05 (s, 3H), 1.21 ± 0.05 (s, 3H), 0.87 (d, *J* = 6.5 Hz, 3H);); ^{13}C NMR (125 MHz) δ 151.7 (± 0.2), 128.0, (± 0.1), 125.4 (± 0.1), 125.1 (± 0.1), 74.5 (± 0.4), 50.3 (± 0.2), 41.7 (± 0.1), 39.7 (± 0.2), 34.5, 31.2 (± 0.1), 28.1 (± 0.2), 26.5 (± 0.1), 24.7 (± 0.2), 21.6.

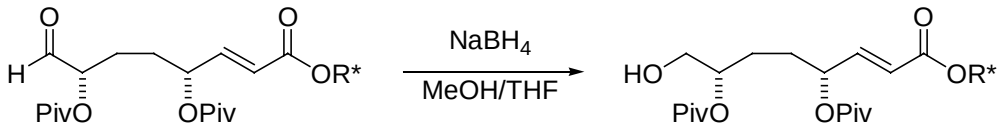


8 **10**

(***E***)**-Alkene 10.** Prepared in 55% yield from **8** and **9a**, (*E*):(*Z*) ≥ 98:2, diastereomeric ratio = 98:2. **10:** (R_f = 0.56 hexanes/EtOAc 3/1).^{1}H NMR (250 MHz, selected data) δ 9.47 (d, *J* = 0.6 Hz, 1H), 7.28-7.16 (m, 4H), 7.13-7.03 (m, 1H), 6.45 (dd, *J* = 15.7, 5.1 Hz, 1H, C*H*=CHC(O) in major diastereomer), 6.16 (dd, *J* = 16.0, 4.3 Hz, 1H, C*H*=CHC(O) in minor diastereomer), 5.38 (dd, *J* = 15.7, 1.6 Hz, 1H), 5.34-5.26 (m, 1H), 4.98-4.90 (m, 1H), 4.85 (ddd [app td], *J* = 10.7, 4.3 Hz, 1H), 1.27 (s, 9H), 1.21 (s, 9H), 0.86 (d, *J* = 6.5, 3H); ^{13}C NMR (62.9 MHz, some signals in the aliphatic region overlap) δ 197.8, 177.9, 177.1, 164.9, 151.4, 143.6, 127.8, 125.3, 124.9, 122.4, 77.2, 74.6, 70.9, 50.3, 41.6, 39.6, 38.9, 38.8, 34.5, 31.2, 29.0, 27.7, 27.1, 26.5, 25.1, 24.1, 21.7; IR 2960, 2928, 1732, 1480, 1280, 1152, 733 cm^{-1}. Anal. Calcd for $C_{34}H_{50}O_7$: C, 71.55; H, 8.83. Found: C, 71.50; H, 8.89.

General Procedure for Reduction of the Products from the Asymmetric HWE Reactions. *Method a:* To a solution of the HWE product in a 1:1 mixture of THF/MeOH (0.015 M with respect to the aldehyde), $NaBH_4$ (2-3 equiv) was added**.** After stirring for 1.5 h at 0 °C the reaction mixture was diluted with brine, extracted with ethyl acetate, dried and filtered to give the crude reduction product which was purified by flash chromatography (20% EtOAc in hexanes)**.**

Method b: Alternatively, if $LiBH_4$ was used instead of $NaBH_4$, the secondary alcohol **16** was isolated as the main product from **14** (see below).

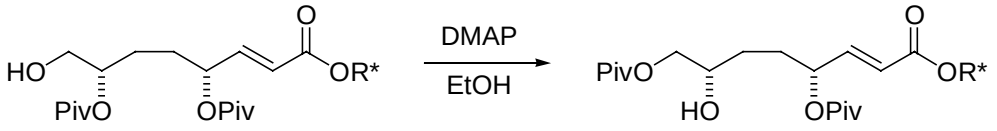


10 **11**

Primary Alcohol 11. Prepared from **10** in 85% yield. **11**: (R_f = 0.28 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.27-7.17 (m, 4H), 7.14-7.04 (m, 1H), 6.49 (dd, *J* = 15.7, 5.1 Hz, 1H), 5.39 (dd, *J* = 15.7, 1.6 Hz, 1H), 5.34-5.25 (m, 1H), 4.91-4.80 (m, 1H), 4.85 (ddd [app td], *J* = 10.6, 4.3 Hz, 1H), 3.69 (dd, *J* = 11.9, 4.0 Hz, 1H), 3.61 (dd, *J* = 11.9, 5.8 Hz, 1H), 1.21 (s, 18H), 0.86 (d, *J* = 6.5, 3H); ^{13}C NMR (62.9 MHz, some signals in the aliphatic region overlap) δ 178.6, 177.2, 165.1, 151.3, 144.1, 127.9, 125.4, 125.0, 122.1, 74.65, 74.56, 71.3, 64.7, 50.4, 41.6, 39.7, 38.9, 34.5, 31.2, 29.5, 27.4, 27.1, 26.6, 25.9, 25.5, 21.7; IR 3504, 2958, 2928, 1731, 1480, 1281, 1157, 1032 cm^{-1}**.**

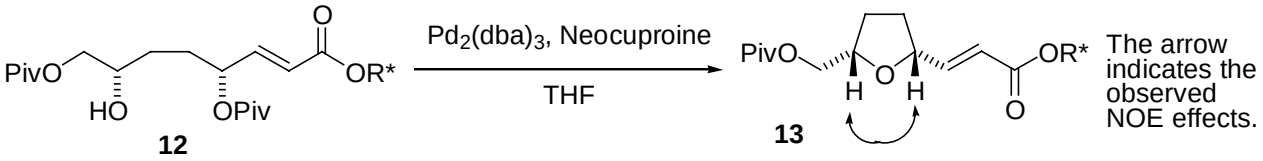
General Procedure for Pivaloyl Group Migration. A few different reagents (imidazole, DMAP and Et_3N) were tested for their ability to promote pivaloyl group migration. All of these reagents gave a mixture of the desired migration product (**12**, **16**, **20** or **23**) and the starting isomeric primary alcohol (**11**, **15**, **19** or **22**, respectively), which in all cases could be separated and recycled. After one such recycling, the overall yield of the desired secondary alcohol was generally ca 70%.

To a solution of the primary alcohol in EtOH (ca. 0.03M) was added 4-(dimethyl)aminopyridine (1 equiv). After refluxing for 15 h, the ethanol was evaporated and the mixture of secondary and primary alcohols was separated by flash chromatography (20% EtOAc in hexanes).

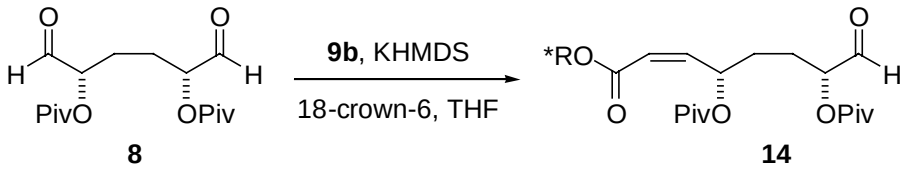


11 **12**

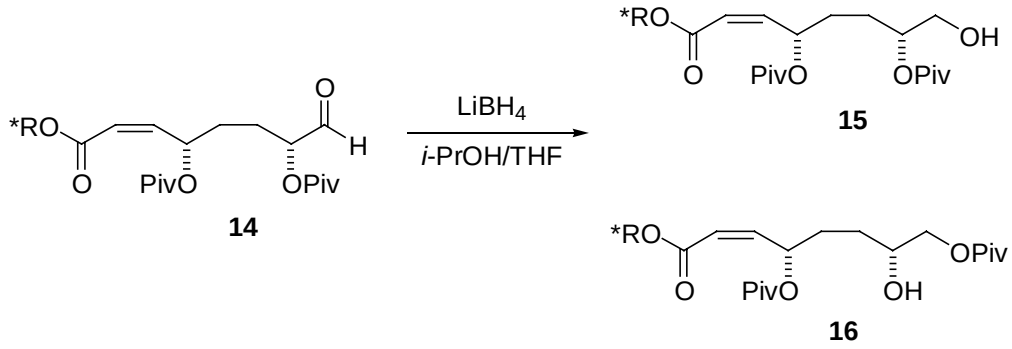
Secondary Alcohol 12. Prepared from **11**; 52% of secondary alcohol **12** and 38% of a 1:2.5 mixture of secondary and primary alcohols (**12** and **11**, respectively) was obtained**. 12**: (R_f = 0.33 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.28-7.18 (m, 4H), 7.15-7.06 (m, 1H), 6.52 (dd, *J* = 15.7, 5.1 Hz, 1H), 5.41 (dd, *J* = 15.7, 1.6 Hz, 1H), 5.37-5.28 (m, 1H), 4.86 (ddd [app td], *J* = 10.7, 4.4 Hz, 1H), 4.12 (dd, *J* = 11.3, 3.4 Hz, 1H), 3.97 (dd, *J* = 11.3, 6.8 Hz, 1H), 3.90-3.78 (m, 1H), 1.22 (s, 9H), 1.21 (s, 9H), 0.86 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (62.9 MHz) δ 178.7, 177.4, 165.1, 151.4, 144.4, 127.9, 125.4, 125.4, 122.1, 74.7, 71.7, 69.8, 68.4, 50.4, 41.7, 39.7, 38.9, 34.5, 31.3, 29.9, 29.7, 28.6, 27.4, 27.19, 27.15, 26.6, 25.5, 21.8; IR 3522, 2958, 2926, 1732, 1282, 1155 cm^{-1}; $[\alpha]_{546}$ +9.8 (c = 1.5, $CHCl_3$).



***cis*-Tetrahydrofuran derivative 13.** Neocuproine hemihydrate (1.3 mg, 0.006 mmol) and $Pd_2(dba)_3$•$CHCl_3$ (1.5 mg, 0.0015 mmol) were dissolved in 1 mL THF and the solution added via syringe to a solution of alkene **12** (8.5 mg, 0.015 mmol) in 2 mL of THF. After stirring 45 min at room temperature, 1 mL 2% aq HCl was added. Filtration through a plug of $MgSO_4$, concentration, and flash chromatograpy of the residue (7.5% EtOAc in hexanes) afforded 5.3 mg (76%) of **13** as a colorless oil. **13**: (R_f = 0.48 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.29-7.20 (m, 4H), 7.17-7.07 (m, 1H), 6.59 (dd, *J* = 15.6, 4.8 Hz, 1H), 5.52 (dd, *J* = 15.6, 1.6 Hz, 1H), 4.84 (ddd [app td], *J* = 10.7, 4.3 Hz, 1H), 4.44 (app br qd, *J* = 4.9, 1.6 Hz, 1H), 4.26-4.16 (m, 1H), 4.14 (dd, *J* = 11.5, 4.0 Hz, 1H), 4.06 (dd, *J* = 11.4, 5.2 Hz, 1H), 1.30 (s, 9H), 0.86 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (62.9 MHz, some signals in the aliphatic region overlap) δ 178.5, 165.7, 151.5, 147.3, 127.9, 125.4, 125.0, 120.9, 78.2, 77.2, 74.4, 66.0, 50.5, 41.7, 39.7, 38.8, 34.6, 31.3, 27.6, 27.2, 26.6, 25.7, 21.8; IR 2955, 1714, 1278, 1162 cm^{-1}; $[\alpha]_{546}$ -8.4 (c = 0.5, $CHCl_3$). HRMS (EI): calcd for $C_{29}H_{42}O_5$, 470.3032; found, 470.3050.

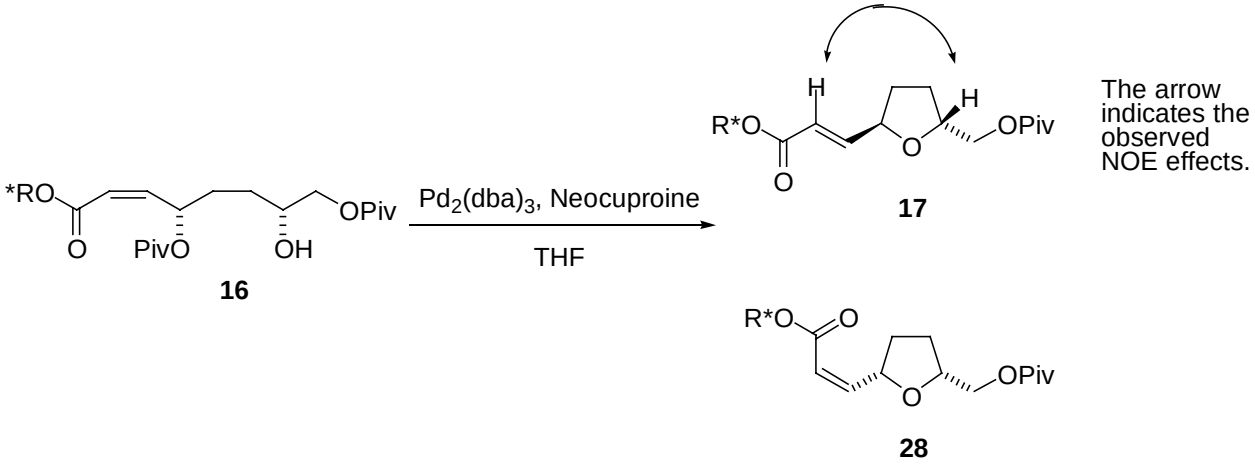


(*Z*)-Alkene 14. Prepared in 71% yield from **8** and **9b**, according to the general procedure (see above, preparation of **10**); (*Z*):(*E*) ≥ 98:2, diastereomeric ratio ≥ 98:2. **14**: (R_f = 0.56 hexanes/EtOAc 3/1).^{1}H NMR (250 MHz, selected data) δ 9.50 (d, *J* = 0.6 Hz, 1H), 7.27-7.17 (m, 4H), 7.14-7.04 (m, 1H), 6.07 (br q, *J* = 6 Hz, 1H), 5.81 (dd, *J* = 11.5, 7.6 Hz, 1H), 5.02 (dd, *J* = 11.5, 1.4 Hz, 1H), 5.03-4.95 (m, 1H), 4.79 (ddd [app td], *J* = 10.7, 4.4 Hz, 1H), 1.28 (s, 9H), 1.17 (s, 9H), 0.86 (d, *J* = 6.5, 3H); ^{13}C NMR (62.9 MHz) δ 197.9, 178.0, 177.5, 164.4, 151.6, 146.4, 127.8, 125.2, 124.9, 121.2, 77.5, 74.2, 70.9, 50.3, 41.6, 39.5, 38.7, 38.6, 34.4, 31.2, 29.4, 27.9, 27.1, 27.0, 26.4, 24.6, 24.5, 21.7; IR 2962, 2928, 1714, 1480, 1202, 1152 cm^{-1}**.** $[\alpha]_{546}$ +4.0 (c = 8.3, $CHCl_3$)**.** Anal. Calcd for $C_{34}H_{50}O_7$: C, 71.55; H, 8.83**.** Found: C, 71.55; H, 8.79**.**



Alcohols 16 and 15. The reduction of **14** with $LiBH_4$, according to the general procedure (see above, preparation of **11**), afforded 49% of secondary alcohol **16** (in which the pivaloyl group has migrated, and 38% of primary alcohol **15**, which were readily separated by flash chromatography (12% EtOAc in hexanes). **16**: (R_f = 0.4 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.28-7.18 (m, 4H), 7.16-7.06 (m, 1H), 6.15-6.03 (m,

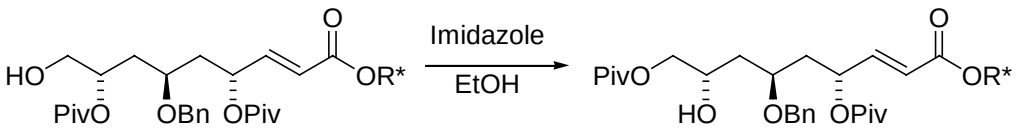
1H), 5.83 (dd, *J* = 11.5, 7.7 Hz, 1H), 5.05 (dd, *J* = 11.5, 1.3 Hz, 1H), 4.79 (ddd [app td], *J* = 10.7, 4.3 Hz, 1H), 4.15 (dd, *J* = 11.2, 3.3 Hz, 1H), 4.01 (dd, *J* = 11.2, 6.6 Hz, 1H), 3.97-3.86 (m, 1H), 1.23 (s, 9H), 1.17 (s, 9H), 0.86 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (62.9 MHz) δ 178.7, 177.7, 164.5, 151.6, 146.9, 127.9, 125.4, 124.9, 121.0, 74.4, 71.4, 70.0, 68.4, 50.4, 47.9, 41.6, 39.6, 38.9, 34.5, 31.3, 30.0, 29.0, 27.8, 27.2, 27.1, 26.5, 25.0, 21.1; IR 3528, 2960, 1732, 1715, 1283, 1202, 1155, 702 cm^{-1}; $[\alpha]_{546}$ -1.9 (c = 1.6, $CHCl_3$). **15**: (R_f = 0.27 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.25-7.17 (m, 4H), 7.14-7.05 (m, 1H), 6.10-6.00 (m, 1H), 5.81 (dd, *J* = 11.5, 7.6 Hz, 1H), 5.01 (dd, *J* = 11.5, 1.3 Hz, 1H), 4.97-4.87 (m, 1H), 4.79 (ddd [app td], *J* = 10.7, 4.3 Hz, 1H), 3.71 (br dd, *J* = 11.9, 3.2 Hz, 1H), 3.64 (br dd, *J* = 11.9, 6.5 Hz, 1H), 1.23 (s, 9H), 1.17 (s, 9H), 0.85 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (62.9 MHz) δ 178.9, 177.7, 164.4, 151.6, 146.9, 127.8, 125.3, 124.9, 120.9, 74.8, 74.2, 71.2, 64.8, 50.4, 41.6, 39.6, 38.9, 38.6, 34.4, 31.2, 29.7, 27.8, 27.1, 27.0, 26.45, 26.36, 24.8, 21.7; IR 3524, 2971, 1728, 1283, 1201, 1156 cm^{-1}.



***trans*-Tetrahydrofuran derivative 17.** Neocuproine hemihydrate (3.4 mg, 0.0155 mmol) and $Pd_2(dba)_3$•$CHCl_3$ (4 mg, 0.0039 mmol) were dissolved in 1 mL THF and the solution added via syringe to a solution of alkene **16** (22.1 mg, 0.0387 mmol) in 2 mL of THF. After heating to 65 °C for 1.5 h, an additional portion of 2 mg (0.002 mmol) of $(dba)_3Pd_2$•$CHCl_3$ was added. After another 1.5 h at 65 °C, the THF was evaporated and the crude product was purified by flash chromatography (5% EtOAc in hexanes) to give 14.3 mg (78%) of **17** as a colorless oil. In addition, ca. 10% of a compound tentatively assigned as the ring-closed (*Z*)-product **28** was isolated in a separate fraction, together with some dba ligand.[5] **17**: (R_f = 0.53 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.30-7.20 (m, 4H), 7.17-7.05 (m, 1H), 6.52 (dd, *J* = 15.6, 4.9 Hz, 1H), 5.49 (dd, *J* = 17.6, 1.6 Hz, 1H), 4.85 (ddd [app td], *J* = 10.7, 4.3 Hz, 1H), 4.52 (app br qd, *J* = 6.7, 1.6 Hz, 1H), 4.26 (br quintet, *J* = 5.8 Hz, 1H), 4.12 (dd, *J* = 11.5, 4.2 Hz, 1H), 4.05 (dd, *J* = 11.5, 5.4 Hz, 1H), 1.22 (s, 9H), 0.86 (d, *J* = 6.5 Hz, 1H); ^{13}C NMR (62.9 MHz, some signals in aliphatic region overlap) δ 178.4, 165.6, 151.5, 147.2, 127.9, 125.4, 125.0, 120.8, 78.0, 76.8, 74.5, 50.5, 41.6, 39.7, 38.8, 34.5, 31.5, 31.3, 29.7, 27.9, 27.3, 27.2, 26.6, 25.6; IR 2958, 2924, 1732, 1283, 1156, 700 cm^{-1}; $[\alpha]_{546}$ +17.4 (c = 0.7, $CHCl_3$). Anal. Calcd for $C_{29}H_{42}O_5$: C, 74.01; H, 8.99. Found: C, 73.76; H, 9.19. **28**: (R_f = 0.56 hexanes/EtOAc 3/1). ^{1}H NMR (500 MHz, selected data) δ 7.27-7.22 (m, 4H), 7.14-7.10 (m, 1H), 6.13 (dd, *J* = 11.5, 7 Hz, 1H), 5.23 (app br q, *J* = 7 Hz, 1H), 5.07 (dd, *J* = 12, 1.5 Hz, 1H), 4.77 (app td, *J* = 11, 4.5 Hz, 1H), 4.21-4.15 (m, 1H), 4.12 (dd, *J* = 11.5, 4 Hz, 1H), 4.07 (dd, *J* = 11.5, 5.5 Hz, 1H), 2.38-2.30 (m, 1H), 1.30 (s, 3H), 1.22 (s, 9H), 0.86 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz) δ 178.4, 170.0,

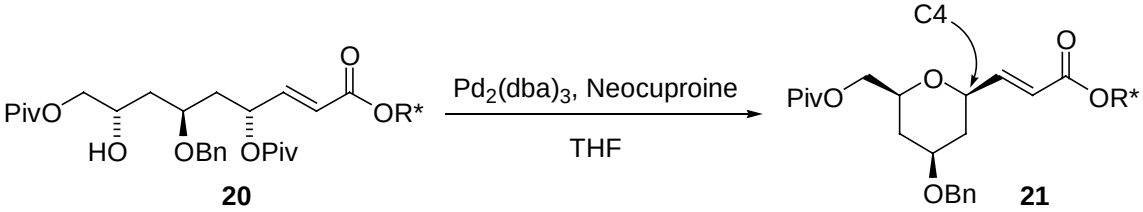
(5) Upon prolonged reaction time, an unidentified byproduct was formed. If the reaction was stopped as soon as only traces of starting material remain, the formation of this byproduct was suppressed.

151.4, 150.3, 127.9, 125.4, 125.0, 119.9, 77.2, 76.8, 72.3, 66.2, 50.1, 41.7, 39.7, 38.8, 34.5 ,31.8, 31.3, 28.2, 27.6, 27.2, 26.6, 25.3, 21.8; IR 2955, 2925, 1730, 1710, 1170, 1090 cm^{-1}.



19 **20**

Secondary Alcohol 20. Prepared from **19**[6] according to the general procedure[7] (see above, preparation of **12**); 59% of the secondary alcohol **20** and 28% of starting material **19** (R_f = 0.21 hexanes/EtOAc 3/1) was obtained. **20**: (R_f = 0.35 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.40-7.18 (m, 9H), 7.13-7.03 (m, 1H), 6.52 (dd, *J* = 15.8, 5.2 Hz, 1H), 5.58-5.47 (m, 1H), 5.42 (dd, *J* = 15.6, 1.5 Hz, 1H), 4.85 (ddd [app td], *J* = 10.7, 4.3 Hz, 1H), 4.57 (d, *J* = 10.7 Hz, 1H), 4.45 (d, *J* = 10.7 Hz, 1H), 4.17-3.93 (m, 3H), 3.83-3.68 (m, 1H), 1.23 (s, 9H), 1.22 (s, 9H), 0.86 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (62.9 MHz, some signals in the aliphatic region overlap) δ 178.5, 177.1, 165.1, 151.4, 144.8, 137.5, 128.6, 128.2, 128.0, 127.9, 125.4, 125.0, 121.8, 74.6, 73.2, 72.5, 69.1, 68.4, 66.9, 50.4, 41.6, 39.7, 39.4, 38.8, 37.0, 34.5, 31.2, 27.2, 26.6, 25.6, 21.8; IR 3508, 2960, 2930, 1731, 1281, 1153, 700 cm^{-1}; $[\alpha]_{546}$ +9.2 (c = 3.7, $CHCl_3$)**.**



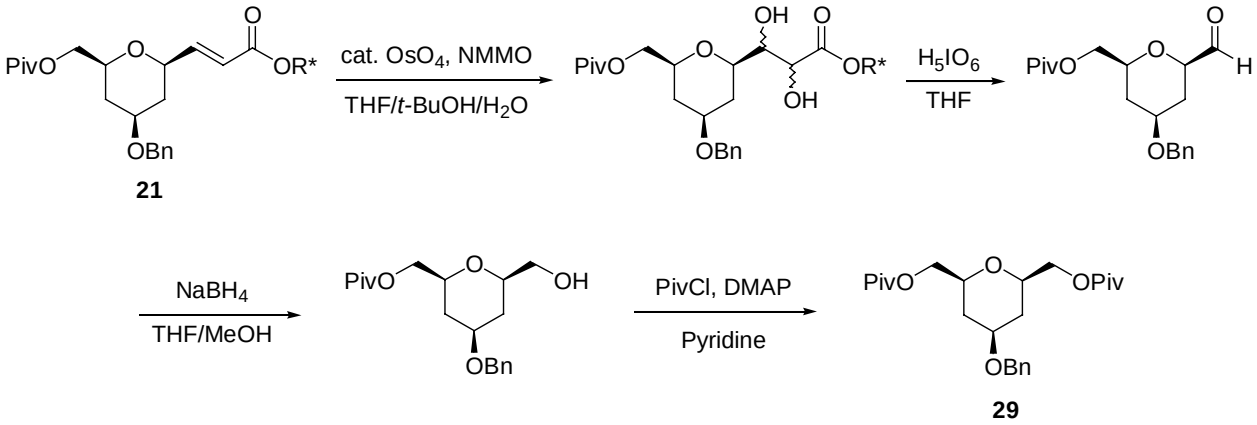
20 **21**

2,6-*cis*-Tetrahydropyran derivative 21. Neocuproine hemihydrate (0.9 mg, 0.0042 mmol) and $Pd_2(dba)_3$•$CHCl_3$ (1.1 mg, 0.001 mmol) were dissolved in 1 mL of dry THF and the solution added via syringe to a solution of alkene **20** (7.2 mg, 0.0104 mmol) in 1.5 mL of THF. After stirring for 50 min at room temperature, the THF was evaporated and the residue was purified by flash chromatograpy (7.5% EtOAc in hexanes) to give 4.9 mg (80%) of **21** as a colorless oil which slowly solidified. **21**: (R_f = 0.52 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.38-7.21 (m, 9H), 7.16-7.06 (m, 1H), 6.52 (dd, *J* = 15.7, 4.1 Hz, 1H), 5.54 (dd, *J* = 15.7, 1.8 Hz, 1H), 4.85 (ddd [app td], *J* = 10.7, 4.3 Hz, 1H), 4.60 (app s, 2H), 4.16 (dd, *J* = 11.5, 5.8 Hz, 1H), 4.10 (dd, *J* = 11.5, 4.5 Hz, 1H), 3.88 (dddd, *J* = 11.8, 4.0, 2.0, 2.0 Hz, 1H), 3.69-3.55 (m, 2H), 1.21 (s, 9H), 0.85 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (62.9 MHz) δ 178.4, 165.6, 151.4, 145.7, 138.2, 128.5, 127.9, 127.7, 127.5, 125.4, 125.0, 120.9, 74.5, 74.0, 73.6, 69.8, 66.4, 50.5, 41.6, 39.7, 38.8, 37.0, 34.5, 34.2, 31.2, 27.7, 27.1, 26.6, 25.8, 25.1, 21.8; IR 2951, 2922, 1726, 1710, 1283, 1176, 700 cm^{-1}; $[\alpha]_{546}$ +5.5 (c = 0.6, $CHCl_3$). Anal. Calcd for $C_{37}H_{49}O_6$: C, 75.35; H, 8.37. Found: C, 75.02; H, 8.75.

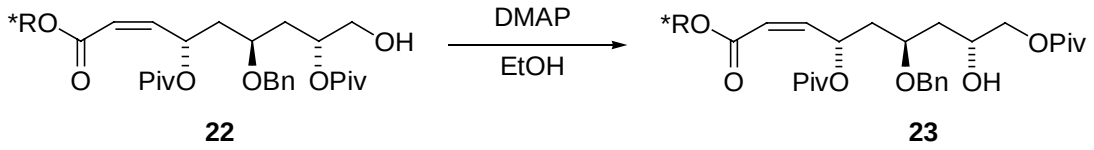
In order to prove the configuration at C-4 of compound **21**, it was converted to **29** in four straightforward steps.

(6) Tullis, J. S.; Vares, L.; Kann, N.; Norrby, P.-O.; Rein, T. *J. Org. Chem.* **1998**, *63*, 8284.

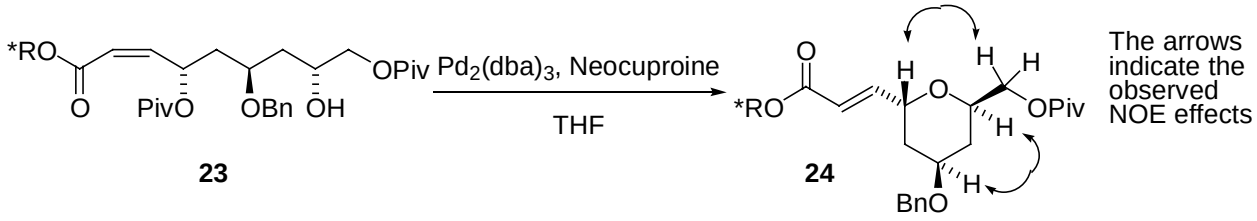
(7) Imidazole was used instead of DMAP.



According to ^{1}H and ^{13}C analysis, **29** is a *meso*-compound (and not pseudo-C_2-symmetric) which implies that the stereochemistry of **21** is the one shown. **29**: ^{1}H NMR (250 MHz) δ 7.37-7.27 (m, 5H), 4.58 (app s, 2H), 4.12 (dd, *J* = 11.6, 4.5 Hz, 2H), 4.06 (dd, *J* = 11.6, 5.8 Hz, 2H), 3.68-3.52 (m, 3H), 2.06 (br d, *J* = 4.6 Hz, 2H), 2.01 (br d, *J* = 4.5, 2H), 1.20 (s, 18H); ^{13}C NMR (62.9 MHz) δ 178.4, 138.2, 128.5, 127.7, 127.6, 73.9, 73.7, 69.8, 66.5, 38.8, 34.2, 27.2; IR 2963, 1731, 1285, 1148 cm^{-1}.



Secondary Alcohol 23. Prepared from **22**[6] according to the general procedure (see above, preparation of **12**); 48% of the secondary alcohol **23** and 42% of starting material **22** (R_f = 0.27 hexanes/EtOAc 3/1) was obtained. **23**: (R_f = 0.47 hexanes/EtOAc 3/1). NMR ^{1}H (500 MHz, selected data) δ 7.48-7.19 (m, 9H), 7.15-7.07 (m, 1H), 6.26-6.16 (m, 1H), 5.85 (dd, *J* = 11.6, 7.6 Hz, 1H), 5.04 (dd, *J* = 11.6, 1.5 Hz, 1H), 4.81 (td, *J* = 10.7, 4.3 Hz, 1H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.56 (d, *J* = 11.7, 1H), 4.14-4.00 (m, 3H), 3.87-3.80 (m, 1H), 0.86 (d, *J* = 6.4 Hz, 3H); ^{13}C (125 MHz, some signals overlap) δ 178.7, 177.5, 164.6, 151.7, 146.4, 133.3, 128.4, 128.3, 127.93, 127.89, 127.7, 125.4, 125.0, 121.2, 74.7, 74.5, 73.3, 71.6, 69.1, 65.7, 50.4, 41.5, 39.6, 38.7, 38.6, 37.9, 34.6, 31.4, 27.8, 27.2, 27.0, 26.6 24.9, 21.8; IR 3506, 2965, 1725, 1280, 1160, 700 cm^{-1}.



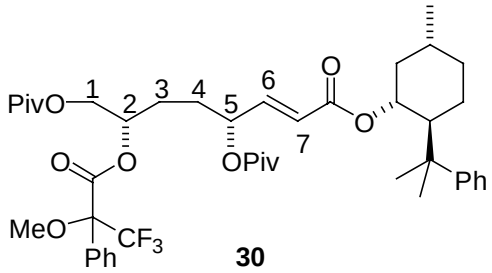
2,6-*trans*-Tetrahydropyran derivative 24. To a solution of **23** (50 mg, 0.072 mmol) in 5 mL of THF, neocuproine hemihydrate (6 mg, 0.028 mmol) and $Pd_2(dba)_3$•$CHCl_3$ (7.5 mg, 0.007 mmol) was added at 50 °C**.** After stirring for 30 min at 50 °C, an additional portion of 4 mg of $Pd_2(dba)_3$•$CHCl_3$ was added**.** After stirring for another 30 min at 50 °C, the reaction mixture was concentrated and purified by flash chromatography (10% EtOAc in hexanes) to give 25 mg (59%) of **24** as a colorless oil. **24**: (R_f = 0.61 hexanes/EtOAc 3/1). ^{1}H NMR (250 MHz, selected data) δ 7.41-7.06 (m, 10H), 6.54 (dd, *J* = 16.0, 3.4 Hz, 1H), 5.51 (dd, *J* = 16.0, 2.3 Hz, 1H), 4.87 (ddd [app td], *J* = 10.7, 4.4 Hz, 1H), 4.66 (app td, *J* = 7.9, 2.3 Hz, 1H), 4.57 (d, *J* = 11.2 Hz, 1H), 4.53 (d, *J* = 11.8 Hz, 1H),

4.23 (dd, *J* = 11.6, 7.1 Hz, 1H), 4.09 (dd, *J* = 11.6, 3.7 Hz, 1H), 3.82 (app ddd, *J* = 13.4, 6.8, 3.3 Hz, 1H), 3.82 (app ddd, *J* = 13.9, 9.2, 4.2 Hz, 1H), 1.23 (s, 9H), 0.87 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (50.3 MHz, some signals in the aliphatic region overlap) δ 178.3, 165.2, 151.3, 146.7, 138.3, 128.5, 127.9, 127.7, 127.5, 125.5, 125.0, 122.7, 74.6, 70.9, 70.4, 70.1, 69.1, 66.1, 50.6, 41.8, 39.8, 38.8, 34.7, 34.6, 33.4, 31.3, 27.2, 26.7, 25.9, 21.8; IR 2955, 2927, 1713, 1283, 1162, 1094, 700 cm^{-1}; $[\alpha]_{546}$ -35.7 (c = 0.8, $CHCl_3$). FAB-HRMS $(M + H)^+$: Calcd for $C_{37}H_{48}O_6$, 589.3529; Found, 589.3526.

Determination of Absolute Configuration for the Products from the Asymmetric Horner-Wadsworth-Emmons Reactions

The absolute configurations of compounds **12** and **16** were assigned on the basis of NMR analyses of the corresponding Mosher ester derivatives **30** and **31**.[8]

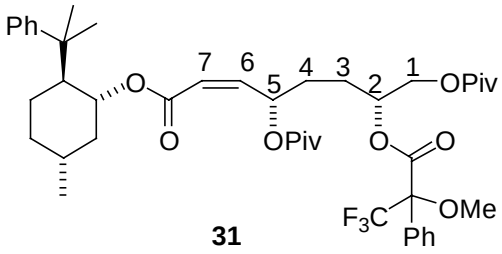
^{1}H NMR data (250 MHz) for MTPA-esters **30**[9] derived from **12**:



30

	(*S*)-30	**(*R*)-30**	$\Delta\delta = \delta$**(*S*)** $- \delta$**(*R*)**	
Proton	δ (ppm)	δ (ppm)	Δδ (ppm)	Δδ (Hz)
1a	4.367	4.286	+0.081	+20.3
1b	4.055	4.033	+0.022	+5.5
5	5.204	5.280	-0.076	-19.0
6	6.384	6.446	-0.062	-15.5
7	5.344	5.388	-0.044	-11.0

^{1}H NMR data (250 MHz) for MTPA-esters **31**[9] derived from **16**:



31

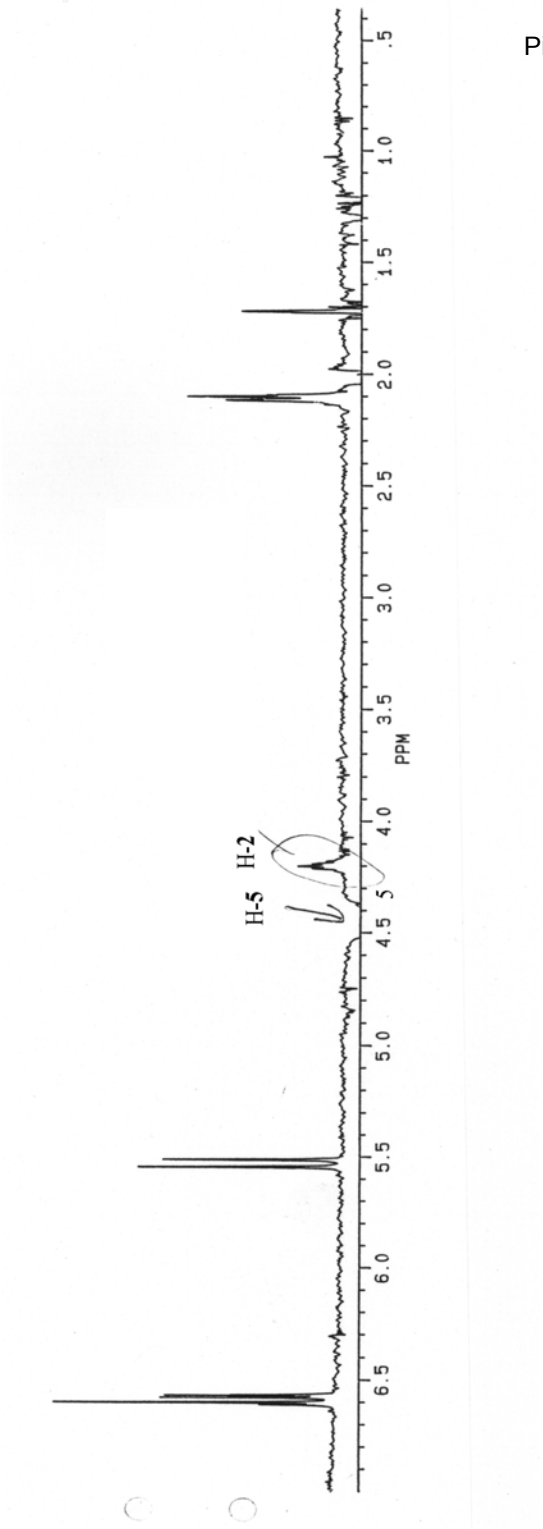
	(*S*)-31	**(*R*)-31**	$\Delta\delta = \delta$**(*S*)** $- \delta$**(*R*)**	
Proton	δ (ppm)	δ (ppm)	Δδ (ppm)	Δδ (Hz)
1a	4.333	4.417	-0.084	-21.0
1b	4.083	4.111	-0.028	-7.0
5	6.053	6.026	+0.027	+6.8
6	5.784	5.709	+0.075	+18.8
7	5.034	5.015	0.019	+4.8

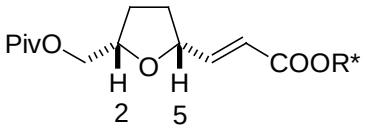
(8) For a description of this method, see: (a) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092. See also: (b) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(9) The notations (*S*) and (*R*) refer to the stereocenter of the Mosher acid unit.

Copies of NOE NMR spectra for compounds 13, 17 and 24 which were used for relative configuration assignments.

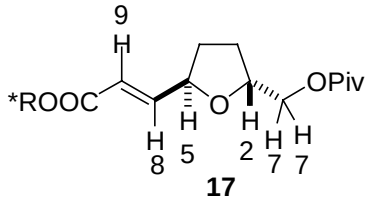
Compound **13**. The positive NOE between H-2 and H-5 support the indicated cis-configuration.



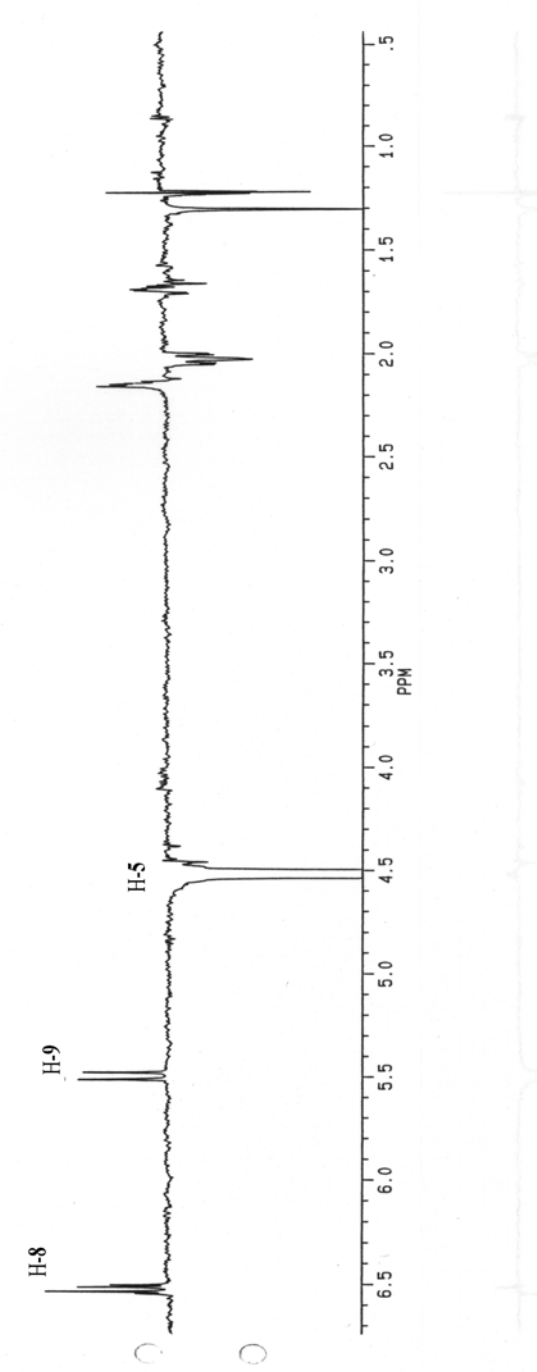


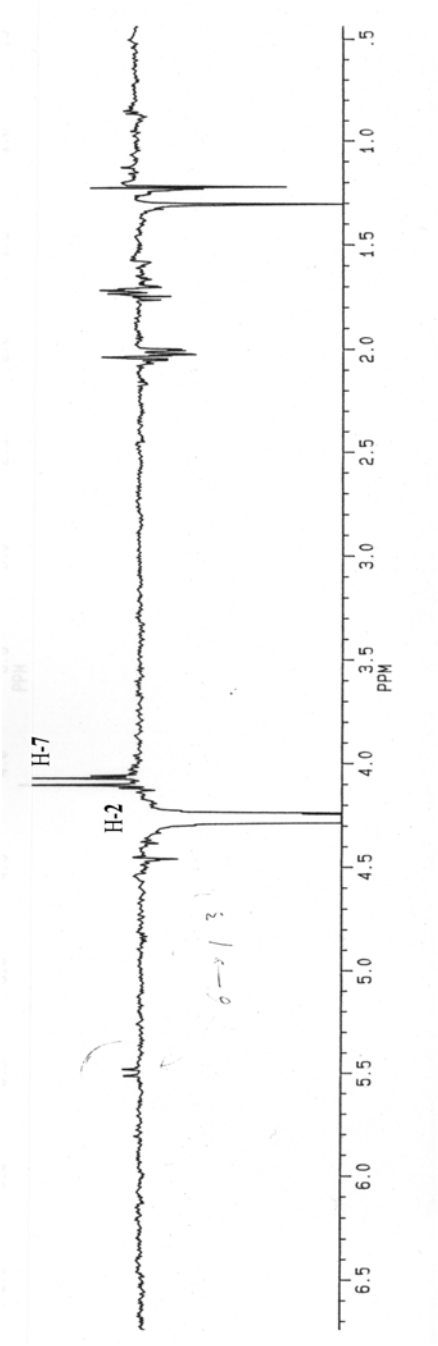
13

Compound **17**. The lack of NOE between H-2 and H-5 support the indicated trans-configuration.



17





Compound **24**. : The positive NOE between H-2 and H-4, and the lack of NOE between H-6 and H-2 or H-4, support the indicated relative configuration.