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Supporting Information

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Trichloromethyl Ketones as Synthetically Versatile Donors: Application in Direct Catalytic Mannich-type Reaction and Stereoselective Synthesis of Azetidines

Hiroyuki Morimoto, Sean H. Wiedemann, Akitake Yamaguchi, Shinji Harada, Zhihua Chen, Shigeki Matsunaga*, and Masakatsu Shibasaki*

Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan.
Phone: +81-3-5841-4830
Fax: +81-3-5684-5206
Email: mshibasa@mol.f.u-tokyo.ac.jp; smatsuna@mol.f.u-tokyo.ac.jp

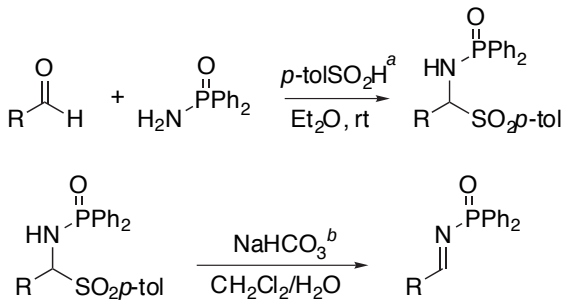
Experimental Section

General: Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on JEOL JNM-LA500 and JNM-ECX500 spectrometers, operating at 500 MHz for ^{1}H NMR and 125.65 MHz for ^{13}C NMR. Chemical shifts in $CDCl_3$ were reported in the scale relative to $CHCl_3$ (7.24 ppm for ^{1}H NMR) and $CDCl_3$ (77.0 ppm for ^{13}C NMR) as an internal reference. ESI mass spectra (for LRMS) were measured on a Waters ZQ4000 spectrometer. FAB mass spectra (for HRMS) were measured on a JEOL JMS-700 spectrometer. Column chromatography was performed with silica gel Merck 60 (230-400 mesh ASTM). Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise stated. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Single crystal X-ray analyses were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-Kα radiation. CCDC 295183-295185 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Preparation of *N*-Dpp imines: *N*-Dpp imines **2d**-**2j** (aryl and alkenyl imines) were prepared according to the literature method (W. B. Jennings, C. J. Lovely, *Tetrahedron* **1991**, *47*, 5561). *N*-Dpp imines **2k**-**2m** (enolizable imines) were prepared according to Charette's method with slight modification (A. Côté, A. A. Boezio, A. B. Charette, *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5405).

Preparation of *N*-Dpp imines 2k-2m

Sulfinic adducts were synthesized by Charette's method.[a] Aliphatic imines were generated by treatment of the sulfinic adducts with $NaHCO_3$ in CH_2Cl_2/H_2O, which are utilized for the preparation of aliphatic Ts-imine,[b] and used without purification.



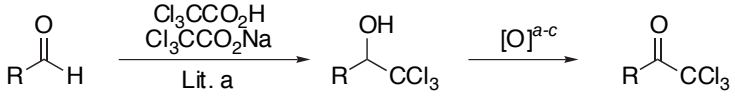
[a] A. Côté, A. A. Boezio, A. B. Charette, *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5405.
[b] F. Chemla, V. Hebbe, J.-F. Normant *Synthesis* **2000**, 75.

General procedure for preparation of *N*-Dpp imines 2k-2m

To a mixture of sulfinic adduct (0.2 mmol) in CH_2Cl_2 (4 mL) at room temperature was added freshly prepared sat. aq. $NaHCO_3$ (4 mL). The mixture was stirred for 2.5 h at 20 °C. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. After evaporation under reduced pressure, the residue was used for the Mannich-type reaction without purification.

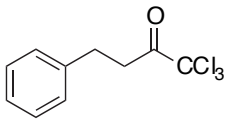
Preparation of trichloromethyl ketones: Trichloromethyl carbinols were prepared from the corresponding aldehydes according to literature method (E. J. Corey, J. O. Link, Y. Shao, *Tetrahedron Lett*. **1992**, *33*, 3435). Trichloromethyl ketones **1a**-**1d** were prepared from the corresponding carbinols according to literature method (M. Zhao, J. Li, Z. Song, R. Desmond, D. M. Tschaen, E. J. J. Grabowski, P. J. Reider, *Tetrahedron Lett*. **1998**, *39*,

5323; S. L. Huang, K. Omura, D. Swern, *J. Org. Chem.* **1976**, *41*, 3329) and distilled before use. Typical procedures for chromium-catalyzed oxidation and Swern oxidation were shown below.



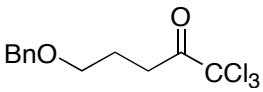
[a] E. J. Corey, J. O. Link, Y. Shao, *Tetrahedron Lett.* **1992**, *33*, 3435.
[b] M. Zhao, J. Li, Z. Song, R. Desmond, D. M. Tschaen, E. J. J. Grabowski, P. J. Reider, *Tetrahedron Lett.* **1998**, *39*, 5323
[c] S. L. Huang, K. Omura, D. Swern, *J. Org. Chem.* **1976**, *41*, 3329

1,1,1-Trichloro-4-phenylbutan-2-one (1c): (Cr-catalyzed oxidation)



To a stirred solution of 2-phenylethyl trichloromethyl carbinol (6.36 g, 25.0 mmol) in CH_3CN (containing 0.75 v/v % of H_2O, 125 mL) at 0 °C was added a solution of CrO_3 (250 mg, 2.5 mmol, 10 mol %) and H_5IO_6 (7.125 g, 31.25 mmol, 1.25 equiv) in CH_3CN (containing 0.75 v/v % of H_2O, 71.25 mL) over 5 min. The resulting mixture was stirred at room temperature for 1.5 h and quenched with an aqueous Na_2HPO_4 solution and extracted twice with ethyl acetate. The combined organic layers were washed with brine (twice), aqueous $NaHSO_3$ and brine, and dried over Na_2SO_4. After removing the solvent, the residue was purified by flash silica gel column chromatography to afford trichloromethyl ketone **1c** as a colorless liquid (5.47 g, 99.0 w/w %, 86% yield). The spectral data were matched with reported values (E. J. Corey, J. O. Link, Y. Shao, *Tetrahedron Lett.* **1992**, *33*, 3435).

5-Benzyloxy-1,1,1-trichloropentan-2-one (1d): (Swern oxidation)



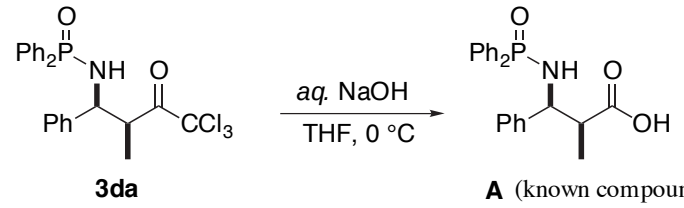
To a solution of DMSO (1.42 mL, 20.0 mmol, 2.0 equiv) in CH_2Cl_2 (10 mL) at –78 °C was added trifluoroacetic anhydride (2.09 mL, 15.0 mmol, 1.5 equiv) in CH_2Cl_2 (5 mL) over 5 min. The resulting mixture was stirred at –78 °C for 10 min and 3-(benzyloxy)propyl trichloromethyl carbinol (2.98 g, 10.0 mmol) in CH_2Cl_2 (10 mL) was added over 10 min. The mixture was stirred at –78 °C for 5 min, and warmed to room temperature for 1 h. *i*-Pr_2NEt (5.0 mL, 29 mmol) was added at 0 °C, and the mixture was stirred at room temperature for 1 h. After dilution with Et_2O, the organic layer was washed with 1M HCl, saturated aqueous $NaHCO_3$, H_2O and brine, and dried over

Na_2SO_4. After evaporation of the solvent, the crude mixture was purified by flash silica gel column chromatography to afford trichloromethyl ketone **1d** as pale yellow oil (2.06 g, 70% yield). Colorless oil after distillation; IR (neat) ν 2861, 1752, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.04 (tt, *J* = 5.8, 7.0 Hz, 2H), 3.13 (t, *J* = 7.0 Hz, 2H), 3.52 (t, *J* = 5.8 Hz, 2H), 4.49 (s, 2H), 7.25–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 24.9, 30.8, 68.5, 73.0, 96.3, 127.6, 127.6, 128.4, 138.1, 190.6; LRMS (ESI) *m/z* 317, 319, 321 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{12}H_{13}{}^{35}Cl_3CsO_2$ $[M+Cs]^+$: 426.9035, found: 426.9037.

General procedure of Mannich-type reaction for *N*-Dpp imines 2d-2j (Tables 1 and 2): MS 3Å (40 mg) in a test tube was dried under reduced pressure using a heat gun. After cooling to room temperature, argon gas was re-filled and a solution of lithium *p*-methoxyphenoxide (0.020 mmol, 10 mol %) in THF (0.33 mL) was added. The resulting suspension was cooled to –40 °C, and trichloromethyl ketone **1a** (53.8 μL, d 1.31, 0.40 mmol, 2.0 equiv) was added. The mixture was stirred at –40 °C for 5 min, then *N*-Dpp imine **2d** (61.1 mg, 0.20 mmol, 1.0 equiv) in CH_2Cl_2 (0.33 mL) was added. The resulting mixture was stirred for 3 h at –40 °C and quenched with *aq. sat.* NH_4Cl. The mixture was extracted twice with ethyl acetate, and the organic layers were washed with brine, dried over Na_2SO_4, filtered, and evaporated under reduced pressure. After determination of diastereomeric ratio of Mannich adduct by ^1H NMR analysis, the residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 2/1 to 1/2) to afford Mannich adducts **3da** (92.4 mg, 96% yield).

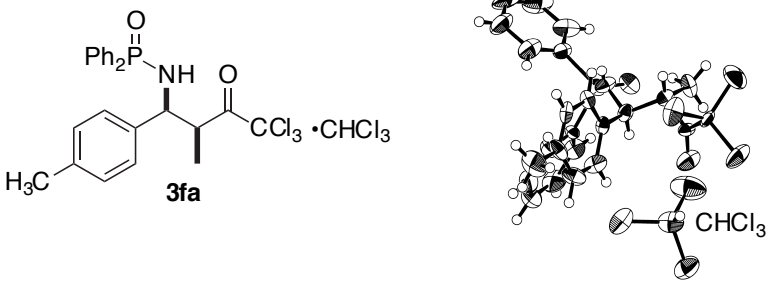
Determination of relative configuration of Mannich adducts: Relative configuration of **3da** was determined after conversion to carboxylic acid **A** (Scheme below). The chemical shifts of ^1H NMR spectrum was matched to reported values (A. B. McLaren, J. B. Sweeney, *Synlett* **2000**, 1625). Relative configuration of the Mannich adduct **3fa** was determined by X-ray crystallographic analysis (crystallization from $CHCl_3$/hexane; CCDC 295184). Relative configuration of the Mannich adduct **3la** was determined after conversion to Boc-protected β-amino acid methyl ester **B** (Scheme below). The chemical shifts of ^1H NMR spectrum was matched to reported values (D. Seebach, S. Abele, K. Gademann, G.

Guichard, T. Hintermann, B. Jaun, J. L. Matthews, J. V. Schreiber, *Helv. Chim. Acta* **1998**, *81*, 932). Relative configurations of other Mannich adducts were tentatively assigned by analogy.

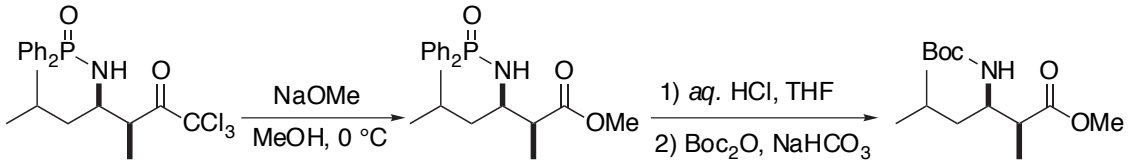


3da **A** (known compound)

A. B. McLaren, J. B. Sweeney, *Synlett* **2000**, 1625

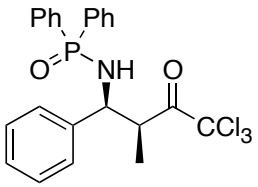


3fa



3la **4la** **B** (known compound)

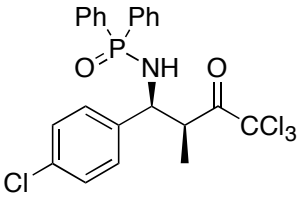
D. Seebach, S. Abele, K. Gademann, G. Guichard, T. Hintermann, B. Jaun, J. L. Matthews, J. V. Schreiber, *Helv. Chim. Acta* **1998**, *81*, 932



(±)-(3*S,4*S**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3-methyl-4-phenylbutan-2-one (3da):** colorless solid; IR (KBr) ν 3127, 1747, 1457, 1438, 1182, 1125, 1111, 1031 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.50 (d, *J* = 6.7 Hz, 3H), 3.51 (dd, *J* = 7.6, 10,8 Hz, 1H), 3.68 (qd, *J* = 6.7, 7.0 Hz, 1H), 4.56 (ddd, *J* = 7.0, 10.7, 10.8 Hz, 1H), 7.14 (brd, *J* = 6.7 Hz, 2H), 7.19–7.28 (m, 3H), 7.34 (ddd, *J* = 3.4, 7.3, 7.7 Hz, 2H), 7.39 (ddd, *J* = 3.1, 7.3, 7.7 Hz, 2H), 7.43–7.52 (m, 2H), 7.74 (dd, *J* = 7.3, 11.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ17.2, 47.3, 58.0, 96.2, 127.0, 127.6, 128.2 (d, $J_{C\text{-}P}$ = 13.0 Hz), 128.3, 128.4 (d, $J_{C\text{-}P}$ = 13.4 Hz), 131.7 (d, $J_{C\text{-}P}$ = 129.6 Hz), 131.8 (brd), 131.8 (brd), 131.9 (d, $J_{C\text{-}P}$ = 10.3 Hz), 132.4 (d, $J_{C\text{-}P}$ = 128.5 Hz), 132.6 (d, $J_{C\text{-}P}$ = 9.3 Hz), 141.2, 191.3; LRMS (ESI) *m/z* 502, 504, 506 $[M+Na]^+$;

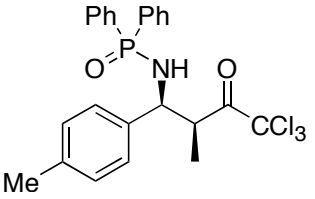
HRMS (FAB) *m/z* calcd. for $C_{23}H_{21}{}^{35}Cl_2{}^{37}Cl_1CsNO_2P$ $[M+Cs]^+$: 613.9400, found: 613.9402.

(±)-(3*S,4*S**)-1,1,1-Trichloro-4-(4-chlorophenyl)-4-[*N*-(diphenylphosphinoyl)amino]-3-methylbutan-2-one (3ea):**

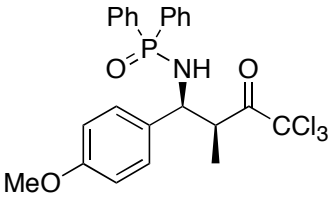


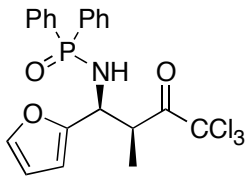
colorless solid; IR (KBr) ν 3176, 1746, 1594, 1492, 1438, 1182, 1125, 1109, 1092, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (d, *J* = 6.7 Hz, 3H), 3.50 (dd, *J* = 7.4, 10.4 Hz, 1H), 3.65 (qd, *J* = 6.7, 6.9 Hz, 1H), 4.54 (ddd, *J* = 6.9, 10.1, 10.4 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.37 (ddd, *J* = 3.4, 7.3, 7.8 Hz, 2H), 7.40 (ddd, *J* = 3.4, 7.6, 7.9 Hz, 2H), 7.48 (brt, *J* = 7.6 Hz, 1H), 7.48 (brt, *J* = 7.6 Hz, 1H), 7.73 (ddd, *J* = 1.2, 7.8, 11.9 Hz, 2H), 7.77 (ddd, *J* = 1.3, 7.9, 11.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 16.8, 47.0 (d, $J_{C\text{-}P}$ = 6.1 Hz), 57.4, 96.1, 128.4 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.5, 128.5, 128.6 (d, $J_{C\text{-}P}$ = 12.4 Hz), 131.6 (d, $J_{C\text{-}P}$ = 130.0 Hz), 131.9 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.0 (d, $J_{C\text{-}P}$ = 130.0 Hz), 132.0 (brd), 132.0 (brd), 132.5, (d, $J_{C\text{-}P}$ = 9.3 Hz), 133.5, 139.7, 191.1; LRMS (ESI) *m/z* 538, 536, 540 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{23}H_{20}{}^{35}Cl_4CsNO_2P$ $[M+Cs]^+$: 645.9040, found: 645.9037.

(±)-(3*S,4*S**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3-methyl-4-(4-methylphenyl)butan-2-one (3fa):**



colorless solid; IR (KBr) ν 3244, 1737, 1440, 1187, 1123, 1109, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (d, *J* = 6.9 Hz, 3H), 2.29 (s, 3H), 3.47 (dd, *J* = 7.4, 10.9 Hz, 1H), 3.66 (qd, *J* = 6.9, 7.0 Hz, 1H), 4.52 (ddd, *J* = 7.0, 10.7, 10.9 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 7.36 (ddd, *J* = 3.4, 7.5, 7.7 Hz, 2H), 7.38 (ddd, *J* = 3.4, 7.6, 8.0 Hz, 2H), 7.42–7.55 (m, 2H), 7.74 (dd, *J* = 7.5, 11.9 Hz, 2H), 7.79 (dd, *J* = 7.6, 12.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 16.9, 20.9, 47.2 (d, $J_{C\text{-}P}$ = 5.1 Hz), 57.8, 96.2, 126.9, 128.2 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.4 (d, $J_{C\text{-}P}$ = 12.3 Hz), 129.0, 131.7 (d, $J_{C\text{-}P}$ = 2.1 Hz), 131.8 (d, $J_{C\text{-}P}$ = 129.2 Hz), 131.8 (d, $J_{C\text{-}P}$ = 2.1 Hz), 131.9 (d, $J_{C\text{-}P}$ = 10.3 Hz), 132.4 (d, $J_{C\text{-}P}$ = 127.5 Hz), 132.6 (d, $J_{C\text{-}P}$ = 10.3 Hz), 137.2, 138.1, 191.3; LRMS (ESI) *m/z* 516, 518, 520 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{24}H_{23}{}^{35}Cl_3CsNO_2P$ $[M+Cs]^+$: 625.9586, found: 625.9581; CCDC 295184.

(±)-(3*S,4*S**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-4-(4-methoxyphenyl)-3-methylbutan-2-one (3ga):** 
colorless solid; IR (KBr) ν 3189, 1743, 1613, 1514, 1429, 1251, 1181, 1124, 1109, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (d, *J* = 6.9 Hz, 3H), 3.45 (dd, *J* = 7.7, 10.7 Hz, 1H), 3.64 (qd, *J* = 6.9, 7.2 Hz, 1H), 3.76 (s, 3H), 4.50 (ddd, *J* = 7.2, 10.4, 10.7 Hz, 2H), 6.77 (d, *J* = 8.9 Hz, 2H), 7.05 (d, *J* = 8.9 Hz, 2H), 7.36 (ddd, *J* = 3.4, 7.2, 8.0 Hz, 2H), 7.39 (ddd, *J* = 3.4, 7.6, 7.9 Hz, 2H), 7.46 (brt, *J* = 7.2 Hz, 1H), 7.46 (brt, *J* = 7.6 Hz, 1H), 7.74 (ddd, *J* = 1.6, 8.0, 12.2 Hz, 2H), 7.78 (ddd, *J* = 1.3, 7.9, 11.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 17.1, 47.4 (d, $J_{C\text{-}P}$ = 5.1 Hz), 55.2, 57.5, 96.3, 113.7, 128.2, 128.3 (d, $J_{C\text{-}P}$ = 13.4 Hz), 128.4 (d, $J_{C\text{-}P}$ = 12.3 Hz), 131.8 (d, $J_{C\text{-}P}$ = 2.0 Hz), 131.8 (d, $J_{C\text{-}P}$ = 129.6 Hz), 131.8 (d, $J_{C\text{-}P}$ = 2.0 Hz), 131.9 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.4 (d, $J_{C\text{-}P}$ = 130.6 Hz), 132.6 (d, $J_{C\text{-}P}$ = 10.3 Hz), 133.3, 159.0, 191.4; LRMS (ESI) *m/z* 532, 534, 536 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{24}H_{23}{}^{35}Cl_3CsNO_3P$ $[M+Cs]^+$: 641.9535, found: 641.9537.

(±)-(3*S,4*S**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-4-(2-furyl)-3-methylbutan-2-one (3ha):** 
colorless solid; IR (KBr) ν 3176, 1742, 1592, 1438, 1186, 1150, 1123, 1029 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56 (d, *J* = 6.8 Hz, 3H), 3.46 (dd, *J* = 8.9, 11.4 Hz, 1H), 3.82 (qd, *J* = 6.8, 8.3 Hz, 1H), 4.55 (ddd, *J* = 8.3, 10.1, 11.4 Hz, 1H), 6.01 (brd, *J* = 3.2 Hz, 1H), 6.21 (dd, *J* = 2.2, 3.2 Hz, 1H), 7.30 (dd, *J* = 0.7, 2.2 Hz, 1H), 7.39 (ddd, *J* = 3.4, 7.3, 7.7 Hz, 2H), 7.40 (ddd, *J* = 3.1, 7.4, 7.9 Hz, 2H), 7.48 (brt, *J* = 7.4 Hz, 1H), 7.48 (brt, *J* = 7.3 Hz, 1H), 7.75 (ddd, *J* = 1.3, 7.7, 12.2 Hz, 2H), 7.77 (ddd, *J* = 1.2, 7.9, 12.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 17.4, 45.6 (d, $J_{C\text{-}P}$ = 4.5 Hz), 52.3, 96.5, 108.1, 110.7, 128.4 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.6 (d, $J_{C\text{-}P}$ = 12.4 Hz), 131.6 (d, $J_{C\text{-}P}$ = 128.9 Hz), 131.8 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.0 (d, $J_{C\text{-}P}$ = 4.8 Hz), 132.0 (d, $J_{C\text{-}P}$ = 2.8 Hz), 132.2 (d, $J_{C\text{-}P}$ = 127.8 Hz), 132.4 (d, $J_{C\text{-}P}$ = 9.3 Hz), 141.6, 152.4, 191.1; LRMS (ESI) *m/z* 492, 494, 496 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{21}H_{19}{}^{35}Cl_3CsNO_3P$ $[M+Cs]^+$: 601.9222, found: 601.9218.

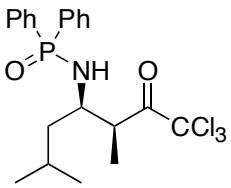
(±)-(3*S,4*S**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3-methyl-4-(2-**

thiophenyl)butan-2-one (3ia): colorless solid; IR (KBr) ν 3158, 1745, 1438, 1187, 1125 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.54 (d, *J* = 6.7 Hz, 3H), 3.43 (dd, *J* = 7.7, 11.0 Hz, 1H), 3.75 (qd, *J* = 6.7, 7.2 Hz, 1H), 4.81 (ddd, *J* = 7.2, 10.7, 11.0 Hz, 1H), 6.78 (brd, *J* = 3.4 Hz, 1H), 6.84 (dd, *J* = 3.4, 5.0 Hz, 1H), 7.18 (dd, *J* = 1.2, 5.0 Hz, 1H), 7.37 (ddd, *J* = 3.7, 7.7, 8.0 Hz, 2H), 7.41 (ddd, *J* = 3.1, 7.4, 7.8 Hz, 2H), 7.44–7.51 (m, 2H), 7.80 (ddd, *J* = 1.6, 8.0, 11.9 Hz, 2H), 7.85 (ddd, *J* = 1.6, 7.8, 12.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 16.9, 48.1 (d, $J_{C\text{-}P}$ = 5.1 Hz), 54.2, 96.2, 124.6, 126.0, 126.9, 128.4 (d, $J_{C\text{-}P}$ = 13.4 Hz), 128.6 (d, $J_{C\text{-}P}$ = 13.4 Hz), 131.4 (d, $J_{C\text{-}P}$ = 126.8 Hz), 131.9 (d, $J_{C\text{-}P}$ = 127.5 Hz), 132.0 (d, $J_{C\text{-}P}$ = 10.3 Hz), 132.0 (brd), 132.0 (brd), 132.6 (d, $J_{C\text{-}P}$ = 9.3 Hz), 145.3, 191.1; LRMS (ESI) *m/z* 508, 510, 512 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{21}H_{19}{}^{35}Cl_3CsNO_2PS$ $[M+Cs]^+$: 617.8994, found: 617.8988.

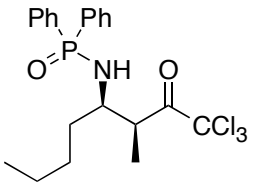
(±)-(3*S,4*R**,5*E*)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3-methyl-6-phenylhex-5-en-2-one (3ja):** colorless solid; IR (KBr) ν 3157, 1745, 1438, 1181, 1125, 1048, 974 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (d, *J* = 6.9 Hz, 3H), 3.23 (dd, *J* = 8.3, 9.0 Hz, 1H), 3.72 (qd, *J* = 6.7, 6.9 Hz, 1H), 4.10 (dddd, *J* = 6.7, 7.6, 9.0, 9.5 Hz, 1H), 6.17 (dd, *J* = 7.6, 15.9 Hz, 1H), 6.33 (d, *J* = 15.9 Hz, 1H), 7.18–7.30 (m, 5H), 7.40 (ddd, *J* = 3.4, 7.4, 7.8 Hz, 2H), 7.41 (ddd, *J* = 3.1, 8.3, 8.3 Hz, 2H), 7.44–7.52 (m, 2H), 7.79 (ddd, *J* = 1.2, 7.8, 11.9 Hz, 2H), 7.93 (ddd, *J* = 1.4, 8.3, 12.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 17.0, 45.8 (d, $J_{C\text{-}P}$ = 5.1 Hz), 57.3, 96.3, 126.6, 127.8, 128.0 (d, $J_{C\text{-}P}$ = 4.0 Hz), 128.4 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.4, 128.5 (d, $J_{C\text{-}P}$ = 12.4 Hz), 131.7 (d, $J_{C\text{-}P}$ = 9.4 Hz), 131.9 (d, $J_{C\text{-}P}$ = 3.1 Hz), 131.9 (d, $J_{C\text{-}P}$ = 4.1 Hz), 132.1 (d, $J_{C\text{-}P}$ = 128.5 Hz), 132.5 (d, $J_{C\text{-}P}$ = 127.5 Hz), 132.6, 132.7 (d, $J_{C\text{-}P}$ = 8.3 Hz), 136.2, 191.9; LRMS (ESI) *m/z* 528, 530, 532 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{25}H_{23}{}^{35}Cl_2{}^{37}Cl_1CsNO_2P$ $[M+Cs]^+$: 639.9557, found: 639.9553.

(±)-(3*S,4*R**)-1,1,1-Trichloro-4-cyclohexyl-4-[*N*-(diphenylphosphinoyl)amino]-3-methylbutan-2-one (3ka):** colorless solid; IR (KBr) ν 1032, 1077, 1108, 1122, 1189, 1252, 1437,

1448, 1509, 1543, 1560, 1655, 1741, 2853, 2915, 3056, 3187 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07-1.29 (m, 5H), 1.36-1.41 (m, 1H), 1.38 (d, *J* = 6.7 Hz, 3H), 1.48-1.79 (m, 4H), 1.99-2.03 (m, 1H), 2.79 (dd, *J* = 5.2, 12.0 Hz, 1H), 3.21-3.27 (m, 1H), 3.56-3.61 (m, 1H), 7.38-7.55 (m, 6H), 7.76 (dd, *J* = 8.0, 12.6 Hz, 2H), 8.08 (dd, *J* = 8.0, 12.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.6, 26.2, 26.2, 26.5, 28.9, 31.0, 41.7 (d, $J_{C\text{-}P}$ = 6.1 Hz), 42.9, 59.0, 96.4, 128.5 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.5 (d, $J_{C\text{-}P}$ = 12.4 Hz), 131.4 (d, $J_{C\text{-}P}$ = 131.6 Hz), 131.7 (d, $J_{C\text{-}P}$ = 3.1 Hz), 132.0 (d, $J_{C\text{-}P}$ = 3.1 Hz), 132.4 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.6 (d, $J_{C\text{-}P}$ = 130.6 Hz), 132.8 (d, $J_{C\text{-}P}$ = 9.3 Hz), 191.7; LRMS (ESI) *m/z* 508 $[M+Na]^+$; HRMS (FAB): *m/z* calcd. for $C_{23}H_{27}{}^{35}Cl_3CsNO_2P$ $[M+Cs]^+$: 617.9899, found: 617.9899.



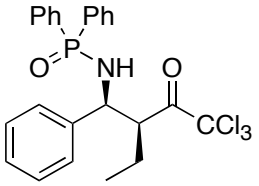
(±)-(3*S,4*R**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3,6-dimethylheptan-2-one (3la):** colorless solid; IR (KBr) ν 1034, 1121, 1139, 1189, 1251, 1310, 1369, 1437, 1459, 1560, 1655, 1743, 2872, 2914, 2936, 2962, 3057, 3211 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78 (d, *J* = 6.4 Hz, 3H), 0.80 (d, *J* = 6.4 Hz, 3H), 1.31 (d, *J* = 6.8 Hz, 3H), 1.40-1.47 (m, 1H), 1.70-1.80 (m, 2H), 2.95 (dd, *J* = 4.9, 11.0 Hz, 1H), 3.45-3.57 (m, 2H), 7.36-7.53 (m, 6H), 7.76 (dd, *J* = 7.3, 12.5 Hz, 2H), 8.04 (dd, *J* = 7.0, 11.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.4, 22.3, 22.6, 24.6, 42.4 (d, $J_{C\text{-}P}$ = 7.2 Hz), 45.6, 52.1, 96.4, 128.6 (d, $J_{C\text{-}P}$ = 11.3 Hz), 128.6 (d, $J_{C\text{-}P}$ = 11.3 Hz), 131.4 (d, $J_{C\text{-}P}$ = 128.5 Hz), 131.7 (d, $J_{C\text{-}P}$ = 3.1 Hz), 132.0 (d, $J_{C\text{-}P}$ = 2.1 Hz), 132.4 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.4 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.9 (d, $J_{C\text{-}P}$ = 129.5 Hz), 191.4; LRMS (ESI) *m/z* 482 $[M+Na]^+$; HRMS (FAB): *m/z* calcd. for $C_{21}H_{25}{}^{35}Cl_2{}^{37}ClCsNO_2P$ $[M+Cs]^+$: 593.9713, found: 593.9713.



(±)-(3*S,4*R**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3-methyloctan-2-one (3ma):** colorless solid; IR (KBr) ν 1031, 1063, 1123, 1186, 1247, 1376, 1438, 1459, 1560, 1655, 1719, 1742, 2872, 2928, 2959, 3060, 3187 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (t, *J* = 7.5 Hz, 3H), 1.19-1.27 (m, 3H), 1.30-1.39 (m, 1H), 1.32 (d, *J* = 6.9 Hz, 3H), 1.57-1.64 (m, 1H), 1.80-1.87 (m, 1H), 2.98 (dd, *J* = 5.2, 10.9 Hz, 1H), 3.42-3.49 (m, 1H), 3.55-3.60 (m, 1H), 7.37-7.53 (m, 6H), 7.76 (dd, *J* = 6.9, 12.6 Hz, 2H), 8.01 (dd, *J* = 6.9, 10.3 Hz, 2H); ^{13}C

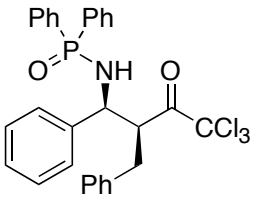
NMR ($CDCl_3$) δ 13.4, 13.9, 22.4, 28.2, 35.7, 41.9 (d, $J_{C\text{-}P}$ = 7.2 Hz), 54.0, 96.4, 128.6 (d, $J_{C\text{-}P}$ = 13.2 Hz), 128.6 (d, $J_{C\text{-}P}$ = 12.0 Hz), 131.5 (d, $J_{C\text{-}P}$ = 129.3 Hz), 131.8 (d, $J_{C\text{-}P}$ = 2.4 Hz), 132.0 (d, $J_{C\text{-}P}$ = 2.3 Hz), 132.3 (d, $J_{C\text{-}P}$ = 8.4 Hz), 132.3 (d, $J_{C\text{-}P}$ = 9.6 Hz), 132.9 (d, $J_{C\text{-}P}$ = 129.3 Hz), 191.6; LRMS (ESI) *m/z* 482 $[M+Na]^+$; HRMS (FAB): *m/z* calcd. for $C_{21}H_{25}{}^{35}Cl_2{}^{37}ClCsNO_2P$ $[M+Cs]^+$: 593.9713, found: 593.9717.

(±)-(*S)-1,1,1-Trichloro-3-{(*S**)-[*N*-(diphenylphosphinoyl)amino](phenyl)methyl}pentan-2-one (3db):**



0.60 mmol (3.0 equiv) of trichloromethyl ketone **1b** was used. colorless solid; IR (KBr) ν 3168, 1738, 1458, 1438, 1180, 1125, 1109 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (dd, *J* = 7.4, 7.4 Hz, 3H), 1.66 (qdd, *J* = 3.4, 7.4, 14.0 Hz, 1H), 1.98 (qdd, *J* = 7.4, 8.9, 14.0 Hz, 1H), 3.52 (dd, *J* = 7.0, 11.1 Hz, 1H), 3.61 (ddd, *J* = 3.4, 4.3, 8.9 Hz, 1H), 4.78 (ddd, *J* = 4.3, 9.2, 11.1 Hz, 1H), 7.18–7.32 (m, 5H), 7.35–7.43 (m, 4H), 7.45 (ttd, *J* = 1.5, 1.5, 7.1 Hz, 1H), 7.49 (ttd, *J* = 1.4, 1.5, 7.2 Hz, 1H), 7.71 (ddd, *J* = 1.5, 7.1, 12.2 Hz, 2H), 7.90 (ddd, *J* = 1.4, 7.2, 11.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 11.6, 20.8, 53.3 (d, $J_{C\text{-}P}$ = 6.1 Hz), 56.8, 96.5, 126.7, 127.6, 128.4 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.5, 128.6 (d, $J_{C\text{-}P}$ = 12.4 Hz), 131.5 (d, $J_{C\text{-}P}$ = 129.0 Hz), 131.8 (brd), 132.0 (brd), 132.1 (d, $J_{C\text{-}P}$ = 129.5 Hz), 132.1 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.5 (d, $J_{C\text{-}P}$ = 10.3 Hz), 141.0, 189.7; LRMS (ESI) *m/z* 516, 518, 520 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{24}H_{23}{}^{35}Cl_3CsNO_2P$ $[M+Cs]^+$: 625.9586, found: 625.9581.

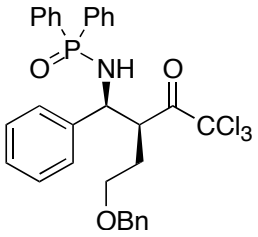
(±)-(3*S,4*S**)-3-Benzyl-1,1,1-trichloro-4-[*N*-(diphenylphosphinoyl)amino]-4-phenylbutan-2-one (3dc):**



Reaction was performed at –60 °C. colorless solid; IR (KBr) ν 3190, 1738, 1496, 1457, 1438, 1186, 1124, 1110, 1066 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.89 (dd, *J* = 3.3, 13.2 Hz, 1H), 3.06 (dd, *J* = 10.4, 13.2 Hz, 1H), 3.67 (dd, *J* = 6.9, 11.0 Hz, 1H), 3.90 (dddd, *J* = 1.3, 3.3, 4.4, 10.4 Hz, 1H), 4.92 (ddd, *J* = 4.4, 9.6, 11.0 Hz, 1H), 6.92 (dd, *J* = 1.7, 6.4 Hz, 2H), 7.07–7.15 (m, 3H), 7.24–7.31 (m, 1H), 7.31–7.39 (m, 6H), 7.40–7.48 (m, 3H), 7.48–7.54 (m, 1H), 7.70 (ddd, *J* = 1.4, 8.4, 12.2 Hz, 2H), 7.97 (ddd, *J* = 1.5, 8.4, 11.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 33.5, 54.9 (d, $J_{C\text{-}P}$ = 7.3 Hz), 57.5, 96.4,

126.7, 126.8, 127.8, 128.4, 128.5 (d, $J_{C\text{-}P}$ = 11.3 Hz), 128.6 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.6, 129.2, 131.2 (d, $J_{C\text{-}P}$ = 128.5 Hz), 131.8 (d, $J_{C\text{-}P}$ = 2.0 Hz), 132.0 (d, $J_{C\text{-}P}$ = 3.1 Hz), 132.2 (d, $J_{C\text{-}P}$ = 10.3 Hz), 132.2 (d, $J_{C\text{-}P}$ = 129.5 Hz), 132.5 (d, $J_{C\text{-}P}$ = 9.3 Hz), 137.5, 140.6, 189.0; LRMS (ESI) *m/z* 578, 580, 582, 579, 581 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{29}H_{25}{}^{35}Cl_3CsNO_2P$ $[M+Cs]^+$: 687.9743, found: 687.9744.

(±)-(*S)-5-(Beznyloxy)-1,1,1-trichloro-3-{(*S**)-[*N*-(diphenylphosphinoyl)amino](phenyl)methyl}pentan-2-one (3dd):**



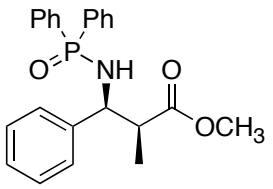
colorless foam; IR (KBr) ν 3177, 3060, 2861, 1740, 1456, 1438, 1180, 1124 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.08–2.17 (m, 1H), 2.28–2.36 (m, 1H), 3.43 (ddd, *J* = 4.3, 9.2, 9.6 Hz, 1H), 3.53 (ddd, *J* = 5.2, 5.2, 9.6 Hz, 1H), 3.79 (ddd, *J* = 4.0, 6.9, 7.0 Hz, 1H), 4.18 (dd, *J* = 6.4, 10.2 Hz, 1H), 4.29 (s, 2H), 4.73 (ddd, *J* = 6.9, 10.2, 10.4 Hz, 1H), 7.14–7.28 (m, 10H), 7.30 (ddd, *J* = 3.4, 7.7, 8.1 Hz, 2H), 7.36 (ddd, *J* = 3.1, 7.7, 7.9 Hz, 2H), 7.39–7.46 (m, 2H), 7.73 (ddd, *J* = 1.5, 8.1, 12.2 Hz, 2H), 7.77 (ddd, *J* = 1.5, 7.9, 12.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 29.4, 49.4 (d, $J_{C\text{-}P}$ = 6.1 Hz), 57.2, 67.4, 72.8, 96.3, 127.0, 127.5, 127.6, 127.6, 128.1 (d, $J_{C\text{-}P}$ = 13.4 Hz), 128.2, 128.3, 128.4 (d, $J_{C\text{-}P}$ = 12.4 Hz), 131.6 (d, $J_{C\text{-}P}$ = 3.8 Hz), 131.7 (d, $J_{C\text{-}P}$ = 3.8 Hz), 131.9 (d, $J_{C\text{-}P}$ = 129.5 Hz), 131.9 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.0 (d, $J_{C\text{-}P}$ = 128.6 Hz), 132.5 (d, $J_{C\text{-}P}$ = 10.4 Hz), 137.6, 141.2, 190.2; LRMS (ESI) *m/z* 622, 624, 626 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{31}H_{29}{}^{35}Cl_3CsNO_3P$ $[M+Cs]^+$: 732.0005, found: 732.0009.

<Transformation of the Mannich adducts>

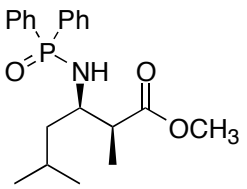
To ester 4: To a solution of Mannich adduct **3da** (7.21 mg, 0.015 mmol) in MeOH (50 μL) at 0 °C was added NaOMe (0.12 mL, 0.282 M in MeOH, 0.033 mmol) and the mixture was stirred for 15 min at room temperature. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution and extracted twice with ethyl acetate. The combined organic layers were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by flash silica gel column chromatography to afford ester **4da** (6.48 mg, quantitative yield).

Following the same procedure, Mannich adduct **3la** was successfully converted to the

corresponding ester **4la** in 94% yield.

(±)-Methyl (2*S,3*S**)-3-[*N*-(diphenylphosphinoyl)amino]-2-methyl-3-phenylpropionate (4da):** 

colorless foam; IR (KBr) ν 3180, 1734, 1455, 1437 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (d, J = 7.2 Hz, 3H), 3.06 (qd, J = 5.7, 7.2 Hz, 1H), 3.54 (s, 3H), 4.24 (dd, J = 7.6, 11.0 Hz, 1H), 4.36 (ddd, J = 5.7, 10.9, 11.0 Hz, 1H), 7.10 (dd, J = 1.6, 8.0 Hz, 2H), 7.20–7.30 (m, 3H), 7.27 (ddd, J = 3.1, 7.5, 8.0 Hz, 2H), 7.37–7.43 (m, 3H), 7.44–7.50 (m, 1H), 7.67 (ddd, J = 1.3, 8.3, 12.3 Hz, 2H), 7.78 (ddd, J = 1.2, 8.0, 11.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.6, 47.1 (d, $J_{C\text{-}P}$ = 3.3 Hz), 51.7, 57.6, 127.0, 127.4, 128.3 (d, $J_{C\text{-}P}$ = 12.6 Hz), 128.2, 128.5 (d, $J_{C\text{-}P}$ = 12.5 Hz), 131.7 (d, $J_{C\text{-}P}$ = 9.3 Hz), 131.8 (brd), 131.8 (d, $J_{C\text{-}P}$ = 155.8 Hz), 131.8 (brd), 132.9 (d, $J_{C\text{-}P}$ = 151.9 Hz), 132.6 (d, $J_{C\text{-}P}$ = 9.5 Hz), 140.8 (d, $J_{C\text{-}P}$ = 4.6 Hz), 174.3; LRMS (ESI) *m/z* 416 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{23}H_{24}CsNO_3P$ $[M+Cs]^+$:526.0548, found: 526.0543.

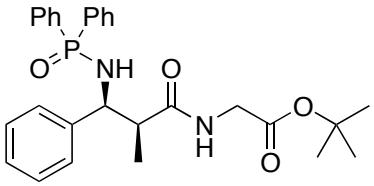
(±)-Methyl (2*S,3*R**)-3-[*N*-(diphenylphosphinoyl)amino]-2,5-dimethylhexanoate (4la):** 

colorless solid; IR (KBr) ν 1012, 1057, 1107, 1124, 1187, 1262, 1365, 1437, 1458, 1508, 1542, 1559, 1654, 1685, 1726, 2869, 2925, 2953, 3057, 3174 cm^{-1};^1H NMR ($CDCl_3$) δ 0.65 (d, J = 6.4 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H), 1.07 (d, J = 7.4 Hz, 3H), 1.20-1.25 (m, 1H), 1.41 (ddd, J = 5.2, 9.2, 14.1 Hz, 1H), 1.73-1.82 (m, 1H), 2.95 (dq, J = 3.4, 7.4 Hz, 1H), 3.21-3.28 (m, 1H), 3.38 (dd, J = 6.1, 11.3 Hz, 1H), 3.62 (s, 3H), 7.40-7.44 (m, 4H), 7.46-7.50 (m, 2H), 7.83-89 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 12.6, 21.7, 23.2, 24.4, 42.6 (d, $J_{C\text{-}P}$ = 5.1 Hz), 44.5 (d, $J_{C\text{-}P}$ = 3.1 Hz), 51.6, 52.0, 128.4 (d, $J_{C\text{-}P}$ = 12.3 Hz), 128.4 (d, $J_{C\text{-}P}$ = 12.4 Hz), 131.7 (d, $J_{C\text{-}P}$ = 3.1 Hz), 131.7 (d, $J_{C\text{-}P}$ = 3.1 Hz), 132.0 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.3 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.7 (d, $J_{C\text{-}P}$ = 131.6 Hz), 132.9 (d, $J_{C\text{-}P}$ = 144.4 Hz), 175.0; LRMS (ESI) *m/z* 396 $[M+Na]^+$; HRMS (FAB): *m/z* calcd. for $C_{21}H_{28}CsNO_3P$ $[M+Cs]^+$: 506.0861, found: 506.0862.

To amide 5: To a solution of Mannich adduct **3da** (10.0 mg, 0.0208 mmol) in THF (0.52

mL) at 0 °C was added NaOH (0.104 mL, 1.0 M in H_2O, 0.104 mmol) and the resulting partially heterogeneous solution was stirred for 20 min at 0 °C. The reaction mixture was quenched with an aqueous 1 M HCl solution (20 drops) and extracted with ethyl acetate (20 mL). The organic layer was washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude carboxylic acid was used without further purification.

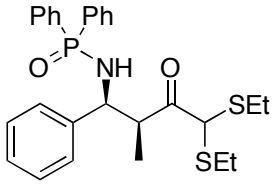
To a solution of the crude carboxylic acid (obtained above) in CH_2Cl_2 (0.22 mL, containing Et_3N (8.7 μL, 0.0624 mmol)) was added HOAt (3.12 mg, 0.0229 mmol) and GlyO^{t}Bu•HCl (3.84 mg, 0.0229 mmol), and the mixture was cooled to 0 °C. To this yellowish solution was added EDC•HCl (5.18 mg, 0.0270 mmol), and the mixture was stirred for 2 h at 0 °C and 12 h at room temperature. The resulting mixture was diluted with ethyl acetate and washed with aqueous citric acid solution (twice), aqueous saturated $NaHCO_3$ solution and brine, and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by flash silica gel column chromatography (AcOEt only) to afford amide **5da** (8.6 mg, 84% yield from the Mannich adduct **3da**).



(±)-(2*S,3*S**)-*N*-[(*tert*-Butoxycarbonyl)methyl]-3-[*N*-(diphenylphosphinoyl)amino]-2-methyl-3-phenylpropionamide (5da):** colorless solid; IR (KBr) ν 3253, 3061, 2979, 2931, 2221, 1746, 1653, 1551, 1438, 1367, 1156, 1111, 1072 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.82 (d, *J* = 6.9 Hz, 3H), 1.28 (s, 9H), 3.21 (qd, *J* = 6.9, 7.1 Hz, 1H), 3.52 (dd, *J* = 4.0, 17.7 Hz, 1H), 4.13 (ddd, *J* = 7.1, 7.3, 10.9 Hz, 1H), 4.34 (dd, *J* = 8.0, 17.7 Hz, 1H), 5.39 (dd, *J* = 3.1, 10.9 Hz, 1H), 7.14 (dd, *J* = 1.8, 6.7 Hz, 2H), 7.23–7.29 (m, 3H), 7.34 (ddd, *J* = 3.5, 7.2, 7.8 Hz, 2H), 7.37–7.43 (m, 1H), 7.43 (ddd, *J* = 3.4, 7.8, 8.0 Hz, 2H), 7.47–7.54 (m, 1H), 7.82 (ddd, *J* = 1.5, 7.8, 12.2 Hz, 2H), 7.85 (ddd, *J* = 1.4, 8.0, 12.1 Hz, 2H), 7.93 (dd, *J* = 4.0, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ14.1, 27.8, 42.1, 46.2, 59.8, 82.1, 127.5, 127.9, 128.0, 128.3 (d, $J_{C\text{-}P}$ = 12.3 Hz), 128.7 (d, $J_{C\text{-}P}$ = 12.3 Hz), 130.5 (d, $J_{C\text{-}P}$ = 129.6 Hz), 131.6 (d, $J_{C\text{-}P}$ = 9.3 Hz), 131.7 (brd), 132.1 (brd), 132.8 (d, $J_{C\text{-}P}$ = 9.3 Hz), 133.0 (d, $J_{C\text{-}P}$ = 127.5 Hz) 139.1 (d, $J_{C\text{-}P}$ =10.3 Hz), 170.5, 173.4; LRMS (ESI) *m/z* 515 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{28}H_{33}CsN_2O_4P$ $[M+Cs]^+$:625.1232, found: 625.1237.

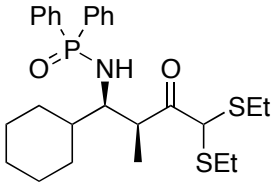
To dithiane 6: To a solution of Mannich adduct **3da** (7.21 mg, 0.015 mmol) in THF (50 μL) at 0 °C was added a mixture of LiSEt and EtSH in THF (prepared from EtSH (3.4 μL, 0.045 mmol) and *n*-BuLi (26.3 μL, 1.6 M in hexane, 0.042 mmol) in THF (100 μL) at 0 °C) and the resulting mixture was stirred at room temperature for 15 min. The mixture was quenched with a saturated aqueous NH_4Cl solution and extracted twice with ethyl acetate. The combined organic layers were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by flash silica gel column chromatography to afford dithiane **6da** (7.20 mg, 96% yield).

Following the same procedure, Mannich adduct **3ka** was successfully converted to the corresponding dithiane **6ka** (93% yield).

(±)-(3*S,4*S**)-4-[*N*-(diphenylphosphinoyl)amino]-1,1-bis(ethylsulfanyl)-3-methyl-4-phenylbutan-2-one (6da):** 

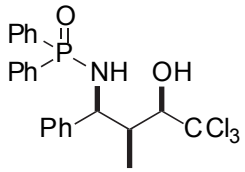
colorless foam; IR (KBr) ν 3409, 2926, 1701, 1438 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.94 (dd, *J* = 7.5, 7.5 Hz, 3H), 1.13 (dd, *J* = 7.5, 7.5 Hz, 3H), 1.33 (d, *J* = 7.0 Hz, 3H), 1.89 (qd, *J* = 7.5, 12.4 Hz, 1H), 2.27 (qd, *J* = 7.5, 12.4 Hz, 1H), 2.31 (qd, *J* = 7.5, 12.3 Hz, 1H), 2.47 (qd, *J* = 7.5, 12.3 Hz, 1H), 3.48 (qd, *J* = 7.0, 7.7 Hz, 1H), 3.51 (dd, *J* = 9.9, 11.1 Hz, 1H), 4.22 (s, 1H), 4.28 (ddd, *J* = 7.7, 10.4, 11.1 Hz, 1H), 7.09 (dd, *J* = 1.6, 7.5 Hz, 2H), 7.18–7.26 (m, 3H), 7.29 (ddd, *J* = 3.2, 7.8, 8.0 Hz, 2H), 7.38 (ddd, *J* = 3.4, 7.3, 7.8 Hz, 2H), 7.38–7.48 (m, 2H), 7.66 (ddd, *J* = 1.3, 8.0, 12.2 Hz, 2H), 7.74 (ddd, *J* = 1.4, 7.8, 11.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ13.8, 14.0, 15.7, 23.5, 23.7, 50.9 (d, $J_{C\text{-}P}$ = 3.6 Hz), 58.1, 58.5, 127.3, 127.5, 128.3 (d, $J_{C\text{-}P}$ = 13.4 Hz), 128.4, 128.5 (d, $J_{C\text{-}P}$ = 12.4 Hz), 131.6 (d, $J_{C\text{-}P}$ = 128.5 Hz), 131.8 (d, $J_{C\text{-}P}$ = 8.5 Hz), 131.8 (brd), 132.1 (brd) 132.8 (d, $J_{C\text{-}P}$ = 126.5 Hz), 132.6 (d, $J_{C\text{-}P}$ = 9.8 Hz), 141.5, 202.6; LRMS (ESI) *m/z* 498 $[M+H]^+$, 520 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{27}H_{32}CsNO_2PS_2$ $[M+Cs]^+$:630.0666, found: 630.0657.

(±)-(3*S,4*R**)-4-cyclohexyl-4-[*N*-(diphenylphosphinoyl)amino]-1,1-bis(ethylsulfanyl)-3-methylbutan-2-one (6ka):** colorless solid; IR (KBr) ν1020, 1109, 1122, 1190, 1263,



1376, 1438, 1449, 1508, 1542, 1560, 1592, 1637, 1655, 1690, 2851, 2926, 2964, 3055, 3201 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04-1.25 (m, 5H), 1.17 (t, J = 7.5 Hz, 3H), 1.20 (t, J = 7.5 Hz, 3H), 1.24 (d, J = 6.9 Hz, 3H) 1.29-1.41 (m, 3H), 1.69-1.76 (m, 3H), 2.41-2.48 (m, 2H), 2.56-2.64 (m, 2H), 2.81 (dd, J = 6.3, 11.5 Hz, 1H), 3.11-3.18 (m, 1H), 3.24-3.30 (m, 1H), 4.56 (s, 1H), 7.41-7.50 (m, 6H), 7.82-7.86 (m, 2H), 7.89-7.92 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.0, 15.0, 23.8, 24.0, 26.3, 26.3, 26.6, 28.0, 31.2, 42.0, 46.8, 57.9, 58.3, 128.4 (d, $J_{C\text{-}P}$ = 12.0 Hz), 128.5 (d, $J_{C\text{-}P}$ = 13.2 Hz), 131.7 (d, $J_{C\text{-}P}$ = 2.4 Hz), 131.8 (d, $J_{C\text{-}P}$ = 3.6 Hz), 132.4 (d, $J_{C\text{-}P}$ = 10.8 Hz), 132.4 (d, $J_{C\text{-}P}$ = 130.6 Hz), 132.5 (d, $J_{C\text{-}P}$ = 9.6 Hz), 132.7 (d, $J_{C\text{-}P}$ = 131.0 Hz), 203.6; LRMS (ESI) m/z 526 $[M+Na]^+$; HRMS (FAB): m/z calcd. for $C_{27}H_{38}CsNO_2PS_2$ $[M+Cs]^+$: 636.1136, found: 636.1132.

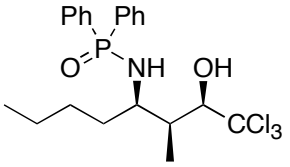
(±)-(2*R,3*S**,4*S**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3-methyl-4-phenylbutan-2-ol (7da):**



In a round-bottom flask, **3da** (150 mg, 0.312 mmol) was dissolved in 1.5 mL CH_2Cl_2 under Ar. The flask containing **3da** was cooled to –40 °C and then $LiAlH(OtBu)_3$ (119 mg, 0.468 mmol) in THF (1.5 mL) was added dropwise by syringe with stirring. After 5 h, the cooling bath was removed and, while still cold, the reaction was quenched by rapid addition of *conc*. *aq*. NH_4Cl (1.5 mL) with vigorous stirring. Ethyl acetate and water (4 mL each) were added to the resulting white suspension. The organic phase was removed and the aqueous phase was further extracted with ethyl acetate (2 x 2.5 mL). Combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give a yellow oil. ^1H NMR analysis of the crude material indicated >20:1 dr. Purification by column chromatography on silica (CH_2Cl_2/EtOAc 15:1 = 4:1) afforded **7da** as colorless foam (125 mg, 83%). IR (KBr) ν 3218 1439, 1160, 1124, 805, 697 cm^{-1}; ^1H NMR (500 MHz $CDCl_3$) δ 0.99 (d, J = 6.7 Hz, 3H), 2.77 (brdq, J = 6.7, 2.1 Hz, 1H), 3.55 (dd, J = 11.6, 5.2 Hz, 1H), 4.42 (ddd, J = 11.6, 11.6, 2.1 Hz, 1H), 4.58 (d, J = 6.6 Hz, 1H), 6.58 (d, J = 6.6 Hz, 1H), 7.6-7.3 (m, 11H), 7.73 (m, 2H), 7.92 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.4, 41.8, 61.5, 84.9, 103.7, 125.9, 127.2, 128.5, 128.7 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.8 (d, $J_{C\text{-}P}$ = 13.4 Hz), 129.5 (d, $J_{C\text{-}P}$ = 134.4

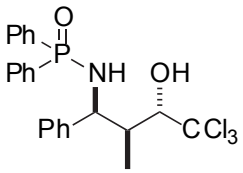
Hz), 131.6, (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.3 (d, $J_{C\text{-}P}$ = 130.2 Hz), 132.4 (d, $J_{C\text{-}P}$ = 2.1 Hz), 132.4 (d, $J_{C\text{-}P}$ = 3.1 Hz), 132.6 (d, $J_{C\text{-}P}$ = 9.3 Hz), 142.0; ^{31}P NMR (202 MHz, $CDCl_3$) δ 23.1; LRMS (ESI) *m/z* 504 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{23}H_{23}{}^{35}Cl_3CsNO_2P$ $[M+Cs]^+$: 613.9586, found: 613.9581.

(±)-(2*R,3*S**,4*R**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3-methyloctan-2-ol (7ma):**



Following the same procedure mentioned above, Mannich adduct **3ma** (40 mg, 0.0868 mmol) was reduced to the corresponding alcohol **7ma** as colorless foam (37.2 mg, 93% yield). ^{1}H NMR analysis of the crude material indicated 19:1 dr. IR (neat) ν 3204, 2931, 1438 cm^{-1}; ^{1}H NMR (500 MHz $CDCl_3$) δ0.87 (t, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 1.16–1.39 (m, 4H), 1.49–1.63 (m, 2H), 2.46 (brq, *J* = 7.0 Hz, 1H), 2.85 (dd, *J* = 6.8, 11.3 Hz, 1H), 2.96–3.05 (m, 1H), 4.19 (brd, *J* = 6.4 Hz, 1H), 6.73 (d, *J* = 6.4 Hz, 1H), 7.48 (ddd, *J* = 3.4, 7.4, 8.0 Hz, 2H), 7.51 (ddd, *J* = 3.4, 7.8, 8.6 Hz, 2H), 7.50–7.60 (m, 2H), 7.91 (ddd, *J* = 1.5, 7.8, 11.9 Hz, 2H), 7.95 (ddd, *J* = 1.5, 7.4, 11.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.2, 13.9, 22.3, 28.7, 36.1 (d, $J_{C\text{-}P}$ = 9.3 Hz), 38.0, 58.6 (d, $J_{C\text{-}P}$ = 2.1 Hz), 85.3, 103.9, 128.7 (d, $J_{C\text{-}P}$ = 12.3 Hz), 128.7 (d, $J_{C\text{-}P}$ = 12.3 Hz), 130.0 (d, $J_{C\text{-}P}$ = 132.6 Hz), 131.7 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.3 (d, $J_{C\text{-}P}$ = 122.4 Hz), 132.4 (d, $J_{C\text{-}P}$ = 2.0 Hz), 132.4 (d, $J_{C\text{-}P}$ = 2.0 Hz), 132.8 (d, $J_{C\text{-}P}$ = 9.3 Hz); LRMS (ESI) *m/z* 484 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{21}H_{27}{}^{35}Cl_2{}^{37}ClCsNO_2P$ $[M+Cs]^+$: 595.9870, found: 595.9871.

(±)-(2*S,3*S**,4*S**)-1,1,1-Trichloro-4-[*N*-(diphenylphosphinoyl)amino]-3-methyl-4-phenylbutan-2-ol (8da):**



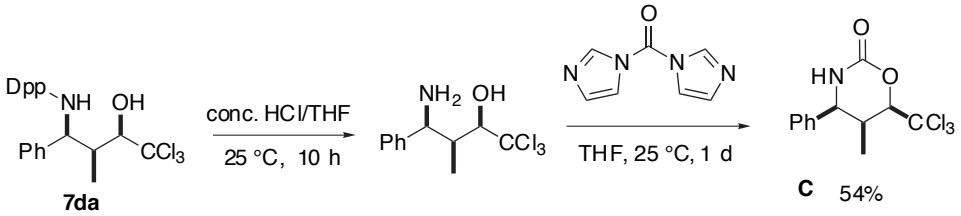
In an Ar atmosphere glovebox, $NaBH_4$ (126 mg, 3.33 mmol) was added to a round-bottom flask. After removal from the glovebox, the flask was filled with Ar and 4 mL dry Et_2O was added with stirring. To the resulting suspension was added 1.66 mL of $ZnCl_2$ (1 M in Et_2O, 1.66 mmol) by syringe. The suspension remained white after stirred at 25 °C for 24 h to afford $Zn(BH_4)_2$. To a second reaction tube was added **3da** (201 mg, 0.416 mmol). THF (2 mL) was added to the tube with stirring under Ar. The round-bottom flask containing $Zn(BH_4)_2$ was cooled to –78 °C

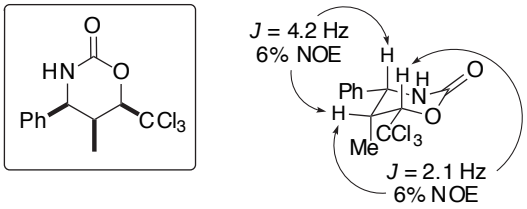
and **3da** (201 mg, 0.416 mmol) in THF solution was added to it dropwise by syringe. After rinsing the syringe and reaction tube with 0.5 mL additional THF, the combined reaction suspension was stirred for 2 h at –78 °C, and then 15 h at –45 °C. The cooling bath was then removed and, while still cold, the reaction was quenched by addition of *conc*. *aq*. NH_4Cl (3 mL). After 5 min of vigorous stirring EtOAc and water (3 mL each) were added to the resulting white suspension. The organic phase was removed and the aqueous phase further extracted with EtOAc (2 x 2.5 mL). Combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give colorless foam. ^{1}H NMR analysis of the crude material indicated 10:1 dr. Purification by silica gel column chromatography (CH_2Cl_2/EtOAc = 15:1 to 5:1) afforded **8da** as colorless foam (178 mg, 88%). IR (KBr) ν 3220 (b), 1439, 1182, 1124, 813, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (d, *J* = 7.0 Hz, 3H), 2.41 (ddq, *J* = 2.2, 7.0, 7.0 Hz, 1H), 3.48 (dd, *J* = 12.2, 8.5 Hz, 1H), 4.28 (dd, *J* = 7.0, 7.0 Hz, 1H), 5.10 (ddd, *J* = 12.2, 12.2, 2.2, 1H), 7.00 (d, 1H, *J* = 7.0 Hz), 7.2-7.3 (m, 5H), 7.3-7.4 (m, 3H), 7.5-7.6 (m, 3H), 7.6-7.7 (m, 2H), 7.9-8.0 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.1, 44.1, 55.1, 83.8, 103.8, 126.2, 126.9, 128.5, 128.5 (d, $J_{C\text{-}P}$ = 12.4 Hz), 128.9 (d, $J_{C\text{-}P}$ = 12.4 Hz), 129.9 (d, $J_{C\text{-}P}$ = 134.3 Hz), 131.5 (d, $J_{C\text{-}P}$ = 9.3 Hz), 132.1 (d, $J_{C\text{-}P}$ = 128.2 Hz), 132.2 (d, $J_{C\text{-}P}$ = 3.1 Hz), 132.5 (d, $J_{C\text{-}P}$ = 2.1 Hz), 132.6 (d, $J_{C\text{-}P}$ = 10.3 Hz), 142.5; ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.7; LRMS (ESI) *m/z* 504 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{23}H_{23}{}^{35}Cl_3CsNO_2P$ $[M+Cs]^+$: 613.9586, found: 613.9581.

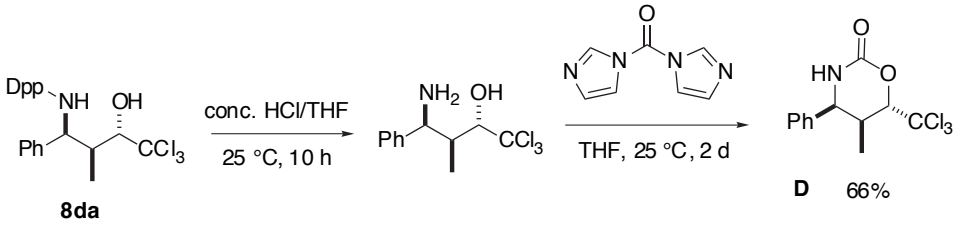
Determination of relative configuration of 7da and 8da

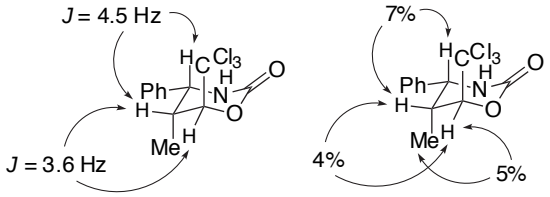
Relative configurations of **7da** and **8da** were determined by NOE and single crystal X-ray X-ray analysis after conversion into corresponding cyclic carbamates.

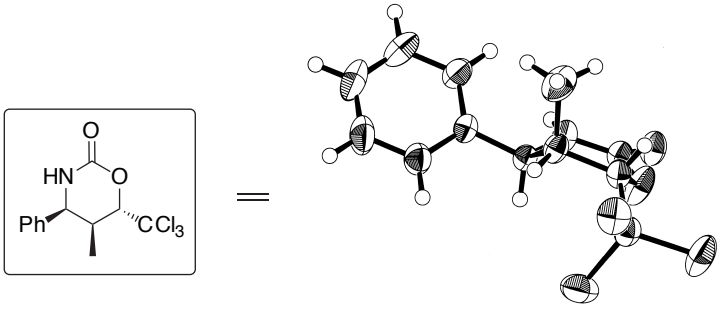
Determination of relative stereochemistry











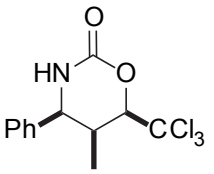
General method for the synthesis of cyclic carbamates

In a plastic-cap vial Dpp-protected aminoalcohol (50 mg, 0.104 mmol) was dissolved in THF (1.5 mL) and cooled to 0 °C. HCl (conc. aqueous, 1.5 mL) was added dropwise

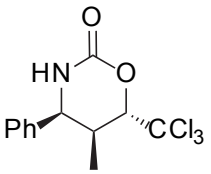
over 10 min. The reaction solution was warmed to 25 °C for 12 h, and then recooled to 0 °C. Na_2CO_3 (sat. aqueous) was carefully added to basify the solution. Following the addition of 1 mL EtOAc, the organic layer was removed. The aqueous phase was further extracted with EtOAc (2 x 2 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to a white solid. ^{1}H NMR of this crude material indicated complete cleavage of the diphenylphosphinoyl group.

The crude mixture of acid hydrolysis products was dissolved in THF (1 mL) and added to solid carbonyl diimidazole (20 mg, 0.123 mmol) under Ar with stirred. The reaction solution was further stirred at 25 °C for 1-2 d. Next, water (1 mL) was added and the solution was extracted with EtOAc (3 x 1.5 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated under vacuum to afford a colorless solid. Column chromatography on silica afforded cyclic carbamates as colorless crystalline solids.

(±)-(4*S,5*S**,6*R**)-5-Methyl-4-phenyl-6-(trichloromethyl)-1,3-oxazinan-2-one (C):** The reaction was carried out using **7da**, stirring for 1 d with CDI. Column chromatography, eluting with 1:1 hexanes/EtOAc, afforded **C** (18 mg, 54%) as a colorless solid. IR (KBr) 3254, 1721, 1457, 1385, 1170, 1110, 1016 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (d, 3H, *J* = 7.1 Hz, C*H*$_3$), 2.84 (m, 1H, H_3CC*H*), 4.91 (brd, 1H, *J* = 4.2 Hz, PhC*H*), 5.08 (d, 1H, *J* = 2.1 Hz, Cl_3CC*H*), 5.71 (brs, 1H, N*H*), 7.28 (m, 2H, Ar-*o*-*H*), 7.36 (m, 1H, Ar-*p*-*H*), 7.43 (m, 2H, Ar-*m*-*H*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.8, 34.7, 59.7, 87.8, 96.7, 126.3, 128.7, 129.1, 136.8, 151.9; LRMS (ESI) *m/z* 330 [M+Na]$^+$; HRMS (FAB) *m/z* calcd. for $C_{12}H_{12}{}^{35}Cl_3CsNO_2$ [M+Cs]$^+$: 439.8988, found: 439.8980.



(±)-(4*S,5*S**,6*S**)-5-Methyl-4-phenyl-6-(trichloromethyl)-1,3-oxazinan-2-one (D):** The reaction was carried out using **8da**, stirring for 2 d with CDI. Column chromatography, eluting with 3:1 to 1:1 hexanes/EtOAc, afforded **D** (21 mg, 66%) as a colorless solid. Slow crystallization by vapor diffusion of hexanes into a concentrated chloroform solution



gave **D** as colorless single-crystalline blocks. IR (KBr) ν 3245, 1735, 1457, 1402, 1319, 1126, 1030, 811, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.98 (d, 3H, *J* = 7.0 Hz, C*H*$_3$), 2.89 (m, 1H, H_3CCH), 4.62 (d, 1H, *J* = 3.3 Hz, Cl_3CCH), 5.06 (brd, 1H, *J* = 4.5 Hz, PhC*H*), 5.95 (brs, 1H, N*H*), 7.26 (m, 2H, Ar-*o*-*H*), 7.34 (m, 1H, Ar-*p*-*H*), 7.41 (m, 2H, Ar-*m*-*H*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9, 33.5, 55.4, 89.2, 99.0, 126.6, 128.5, 129.0, 137.2, 152.0; LRMS (ESI) *m/z* 330 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{12}H_{12}{}^{35}Cl_3CsNO_2$ $[M+Cs]^+$: 439.8988, found: 439.8980; CCDC 295185.

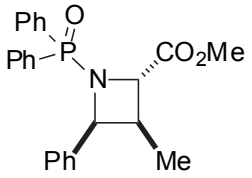
To azetidine 10da and 12da:

General method for the synthesis of azetidine-2-carboxylic acid methyl esters

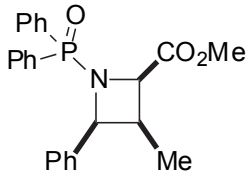
In a plastic-cap vial Dpp-protected aminoalcohol (50 mg, 0.104 mmol) was dissolved in DME (0.6 mL), and then NaOH (0.400 mL, 1.5 M aqueous) was added dropwise with stirring. The resulting cloudy emulsion became clear over 18h hours of stirring at 25 °C. Next, DME was removed under vacuum and 0.5 mL water was added. The resulting solution was acidified to pH 4 with citric acid (conc. aqueous). Precipitated organic products were dissolved by addition of EtOAc (1.5 mL). The organic phase was separated and the aqueous phase was further extracted with EtOAc (2x 1.5 mL). Combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to give a colorless oil.

The crude product mixture from azetidine-2-carboxylic acid formation was dissolved in MeOH (2.5 mL) in a plastic-cap vial fitted with a vent needle. After cooling the vial to 0 °C, trimethylsilyldiazomethane (2M in hexanes) was added dropwise with stirring until a yellow color persisted for ca. 5 min. The resulting reaction solution was concentrated under vacuum to give a yellow oil. Column chromatography on silica afforded azetidine-2-carboxylic acid methyl esters as colorless solids.

(±)-(2*S,3*S**,4*S**)-1-(Diphenylphosphinoyl)-3-methyl-4-phenylazetidine-2-carboxylic acid methyl ester (10da).** The reaction was carried out according to the general procedure using **7da**. Column chromatography, eluting with 1:1 → 0:1 hexanes/EtOAc,



afforded **10da** (31 mg, 72%) as a white solid. Slow crystallization by layering of pentane onto a concentrated ethyl acetate solution gave **10da** as colorless needles. IR (KBr) ν 1723, 1441, 1284, 1200, 1153, 1050, 704 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.80 (d, *J* = 7.3 Hz, 3H), 3.23 (m, 1H, H_3CCH), 3.38 (s, 3H, CO_2CH_3), 4.43 (dd, *J* = 5.8, 4.3 Hz, 1H, H_3CCH), 5.38 (dd, *J* = 8.8, 3.6 Hz, 1H, PhC*H*), 7.1-7.2 (m, 3H), 7.3-7.4 (m, 8H), 7.7-7.8 (m, 2H), 7.8-7.9 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 36.2 (d, J_{C-P} = 14.4 Hz), 51.8, 65.7 (d, J_{C-P} = 2.0 Hz), 67.7 (d, J_{C-P} = 2.0 Hz), 127.4, 127.6, 127.9 (d, J_{C-P} = 12.4 Hz), 128.0, 128.2 (d, J_{C-P} = 12.4 Hz), 130.3 (d, J_{C-P} = 129.2 Hz), 131.3 (d, J_{C-P} = 3.1 Hz), 131.5 (d, J_{C-P} = 129.2 Hz), 131.7 (d, J_{C-P} = 2.1 Hz), 132.1 (d, J_{C-P} = 10.3 Hz), 132.4 (d, J_{C-P} = 9.3 Hz), 137.5, 172.2; ^{31}P NMR (202 MHz, $CDCl_3$) δ 20.9; LRMS (ESI) *m/z* 428 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{24}H_{24}CsNO_3P$ $[M+Cs]^+$: 538.0548, found: 538.0553.

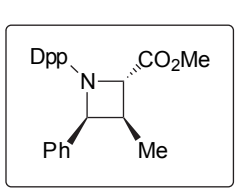


(±)-(2*R,3*S**,4*S**)-1-(Diphenylphosphinoyl)-3-methyl-4-phenylazetidine-2-carboxylic acid methyl ester (12da).** The reaction was carried out according to the general procedure using **8da**. Column chromatography, eluting with 60:35 to 30:65 hexanes/EtOAc containing 2% Et_3N, afforded **12da** (24 mg, 57%) as a colorless solid. Slow crystallization by layering of pentane onto a concentrated ethyl acetate solution gave **12da** as colorless blocks. IR (KBr) ν 1752, 1439, 1202, 1111, 1090, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.63 (d, *J* = 7.7 Hz, 3H, $HCCH_3$), 3.48 (m, 1H, H_3CCH), 3.58 (s, 3H, CO_2CH_3), 4.88 (dd, *J* = 13.7, 10.0 Hz, 1H, H_3CCH), 5.29 (dd, *J* = 14.1, 9.5 Hz, 1H, PhC*H*), 7.1-7.3 (m, 6H), 7.4-7.7 (m, 5H), 7.7-7.8 (m, 2H), 8.05-8.15 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.7, 33.2 (d, J_{C-P} = 13.4 Hz), 51.4, 58.7, 62.5 (d, J_{C-P} = 2.1 Hz), 127.3, 127.6, 127.7 (d, J_{C-P} = 13.4 Hz), 128.2 (d, J_{C-P} = 10 Hz), 128.2, 129.7 (d, J_{C-P} = 128.2 Hz), 130.1 (d, J_{C-P} = 127.0 Hz), 131.7 (d, J_{C-P} = 3.1 Hz), 132.1 (d, J_{C-P} = 3.1 Hz), 132.4 (d, J_{C-P} = 9.3 Hz), 132.9 (d, J_{C-P} = 9.3 Hz), 138.1, 171.1 (d, J_{C-P} = 5.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 25.9; LRMS (ESI) *m/z* 428 $[M+Na]^+$; HRMS (FAB) *m/z* calcd. for $C_{24}H_{24}CsNO_3P$ $[M+Cs]^+$: 538.0548, found: 538.0547; CCDC 295183.

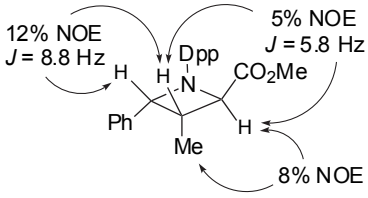
Stereochemistry of **10da** and **12da** was confirmed by NOE (for **10da** and **12da**) and single

crystal X-ray analysis (for **12da**; CCDC 295183).

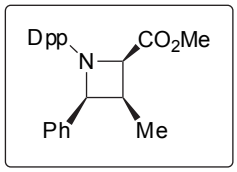
Azetidine NOE Measurements



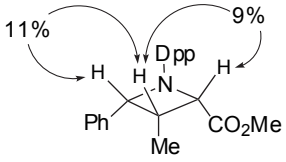
10da



Azetidine NOE Measurements



12da



12da =