Supramolecular PhanePhos-analogous Ligands through Hydrogen Bonding for Asymmetric Hydrogenation

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Supplementary Material

(19 pages)

I General

The following starting materials were purchased and used without further purification: (*R*) and (S)-BINOL (Novartis), methyl 2-*N*-acetamido acrylate (**3**, Aldrich), dimethyl itaconate (**5**) and $[Rh(cod)_2]BF_4$ (BASF). 2-Z-Acetylamino-3-phenyl acrylic acid methylester (**4**)[1] was prepared according to literature procedures.

All reactions were carried out in dried glassware under an atmosphere of argon (argon 5.0 from Sauerstoffwerk Friedrichshafen GmbH). Air and moisture sensitive liquids and solutions were transferred *via* syringe. All reagents were commercially available unless otherwise noted. All solvents were dried and distilled by standard procedures. Organic solutions were concentrated under reduced pressure by rotary evaporation. Chromatographic purification of products was accomplished using flash chromatography on a Merck silica gel Si 60® (200-400 mesh).

Nuclear magnetic resonance spectra were acquired on a Varian Mercury 300 spectrometer (300 MHz, 121 MHz and 75 MHz for ^1H, ^{31}P and ^{13}C respectively), on a Bruker Avance 400 (400 MHz, 162 MHz and 100 MHz for ^1H, ^{31}P and ^{13}C respectively) and on a Bruker Avance 500 (500 MHz, 202 MHz and 125 MHz for ^1H, ^{31}P and ^{13}C respectively) and are referenced according to residual protio solvent signals [$CDCl_3$: 7.26 ppm (^1H), 77.10 ppm (^{13}C)]. Data for ^1H-NMR are reported as follows: chemical shift (δ in ppm), multiplicity (s, singlet; br, broad signal; d, doublet; t, triplet; q, quartet; m, multiplet; m_c, symmetrical multiplet), coupling constant (Hz), integration, assignment (if possible). Data for ^{13}C-NMR are reported in terms of chemical shift (δ in ppm), multiplicity (if not a singlet), coupling constant (Hz), assignment (if possible).

High-resolution mass spectra and ESI mass spectra were obtained on a Finnigan MAT 95 instrument and a Finnigan LCQ Advantage respectively. Elementary analysis was performed on an Elementar Vario (Fa. Elementar Analysensysteme GmbH).

The enantiomeric excess (*ee*) of the products was determined by chiral GC (hydrogenation product of **3**: Hydrodex-β-TBDAc; hydrogenation product of **5**: GT-A, trifluoroacetyl-γ-cyclodextrin) and chiral HPLC (hydrogenation product of **14**: *Chiralpak* AD). Optical rotations were measured on a Perkin-Elmer 241 polarimeter.

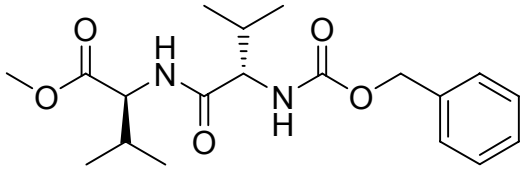
List of abbreviations:

Ala	alanine
cod	1,5-cyclooctadiene
DCC	dicyclohexylcarbodiimide
DIC	diisopropylcarbodiimide
DMAP	dimethylaminopyridine
m-DPPBA	***m****eta*-(**d**i**p**henyl**p**hosphanyl)-**b**enzoic **a**cid
EE	ethylester, ethyl acetate
HOBt	1-hydroxybenzotriazole
t-Leu	*tert*.-leucine
Moc	methoxycarbonyl
NEt_3	triethylamine
PE	petrolether (bp. 40-65°C)
THF	tetrahydrofuran
Val	valine
Z	benzyloxycarbonyl

II Experimental procedures and characterizations of ligands

1 Preparation of dipeptides

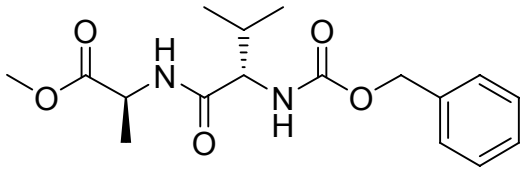
Z-L-Valyl-L-valine methylester (6):



(364.44)

Was prepared according to literature procedures.[2]

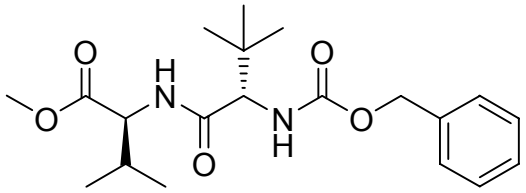
Z-L-Valyl-L-alanine methylester (7):



(336.39)

Was prepared according to literature procedures.[3]

Z-L-*tert*-Leucyl-L-valine methylester (8):

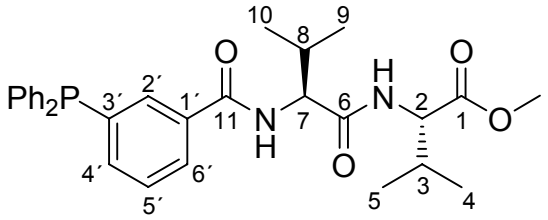


(378.46)

Was prepared according to literature procedures.[4]

2 Synthesis of peptidyl phosphine ligands

(+)-(3-Diphenylphosphanyl)-benzoyl-L-valyl-L-valine methylester (1a):



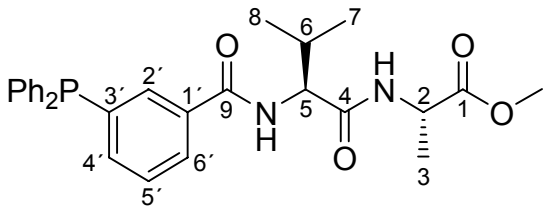
(518.59)

To a solution of Z–L-Val–L-Val–OMe (**6**) (1.782 g, 4.890 mmol) in dry MeOH (20 ml) was added Pd-C (10%, 20 mg, Fluka), and the suspension was stirred under H_2 (1 atm) at room temperature for 15 h. The reaction mixture was filtered through Celite and the solvent removed *in vacuo* to yield the free amine H–L-Val–L-Val–OMe as viscous oil (1.13 g, 4.89 mmol, quant.). The amine was dissolved in dry CH_2Cl_2 (25 ml), and *meta*-diphenylphosphanyl-benzoic acid (1.648 g, 5.379 mmol, 1.1 eq), DMAP (0.598 g, 4.89 mmol, 1.0 eq.) and DCC (1.112 g, 5.379 mmol, 1.1 eq.) (or DIC) were added at room temperature. The resulting white, chalky solution was stirred at room temperature for further 19 h. The mixture was filtered through a 2-cm pad of Celite (wetted with CH_2Cl_2), and the filter cake was washed with some CH_2Cl_2. After concentration *in vacuo*, the residue was chromatographed on silica gel (PE/EE, 2:1) to afford the dipeptide ligand **1a** as a glass foam (2.368 g, 93%, R_f 0.23); Mp. 172°C (PE/EE); $[\alpha]_D^{20}$ +5.50° (*c* 0.945, $CHCl_3$).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.87 (d, *J* = 6.9 Hz, 3H, CH_3), 0.88 (d, *J* = 6.9 Hz, 3H, CH_3), 0.96 (d, *J* = 7.8 Hz, 3H, CH_3), 0.98 (d, *J* = 7.0 Hz, 3H, CH_3), 2.09-2.23 (m, *J* = 6.8 Hz, 2H, 3-H, 8-H), 3.74 (s, 3H, OCH_3), 4.47-4.53 (m, *J* = 8.5, 8.2 Hz, 2H, 2-H, 7-H), 6.56 (d, *J* = 8.7 Hz, 1H, 2-NH), 6.71 (d, *J* = 8.7 Hz, 1H, 7-NH), 7.26-7.42 (m, 12H, ArH), 7.72 (d, *J* = 7.6 Hz, 1H, 2′-H), 7.77 (m_c, 1H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 17.8, 18.3, 19.0, 19.2 (C_4, C_5, C_9, C_{10}), 31.1, 31.4 (C_3, C_8), 52.2 (OCH_3), 57.4, 58.9 (C_2, C_7), 127.6 ($C_{6'}$), 128.7 (d, $J_{C,P}$ = 7.2 Hz, 2ArC_{meta}), 128.8 (d, $J_{C,P}$ = 7.2 Hz, 2ArC_{meta}), 128.9 (d, $J_{C,P}$ = 5.5 Hz, $C_{5'}$), 129.1 (ArC_{para}), 129.1 (ArC_{para}), 132.3 (d, $J_{C,P}$ = 23.3 Hz, $C_{2'}$), 133.8 (d, $J_{C,P}$ = 19.6 Hz, 2ArC_{ortho}), 133.9 (d, $J_{C,P}$ = 19.9 Hz, 2ArC_{ortho}), 134.5 (d, $J_{C,P}$ = 6.9 Hz, $C_{1'}$), 136.5 (d, $J_{C,P}$ = 10.9 Hz, ArC_{ipso}), 136.6 (d, $J_{C,P}$ = 10.9 Hz, ArC_{ipso}), 136.8 (d, $J_{C,P}$ = 15.8 Hz, $C_{4'}$), 138.6 (d, $J_{C,P}$ = 13.8 Hz, $C_{3'}$), 167.3 (C_1), 171.2,

172.1 (C_6, C_{11}); ^{31}P-NMR (162 MHz, $CDCl_3$): δ = –5.26 (s); Anal. calcd. for $C_{30}H_{35}N_2O_4P$: C, 69.48; H, 6.80; N, 5.40. Found: C, 69.44; H, 7.06; N, 5.53.

(+)-(3-Diphenylphosphanyl)-benzoyl-L-valyl-L-alanine methylester (1b):



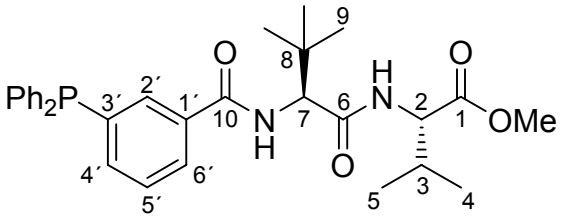
(490.53)

To a solution of Z–L-Val–L-Ala–OMe (**7**) (0.700 g, 2.08 mmol) in dry MeOH (9.5 ml) and DCM (3 ml) was added Pd-C (10%, 37 mg, Fluka), and the suspension was stirred under H_2 (1 atm) at room temperature for 17 h. The reaction mixture was filtered through Celite and the solvent removed *in vacuo* to yield the free amine H–L-Val–L-Ala–OMe as viscous oil (quant.). The amine was dissolved in dry CH_2Cl_2 (10 ml), and *meta*-diphenylphosphanyl-benzoic acid (0.624 g, 2.04 mmol, 1.0 eq.), DMAP (0.249 g, 2.04 mmol, 1.0 eq.) and DIC (0.257 g, 2.04 mmol, 1.0 eq.) were added at room temperature. The reaction mixture was stirred at room temperature for further 24 h. After concentration *in vacuo*, the residue was chromatographed on silica gel (PE/EE, 1:1) to afford the dipeptide ligand **1b** as a glass foam (0.640 g, 64%, R_f 0.31); Mp. 75°C (PE/EE); $[\alpha]_D^{20}$ +5.12° (*c* 1.270, $CHCl_3$).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.97 (d, *J* = 6.9 Hz, 3H, 7-H_3 or 8-H_3), 1.00 (d, *J* = 6.7 Hz, 3H, 7-H_3 or 8-H_3), 1.38 (d, *J* = 7.2 Hz, 3H, 3-H_3), 2.16 (m_c, *J* = 6.7 Hz, 1H, 6-H), 3.75 (s, 3H, OCH_3), 4.47 (dd, *J* = 8.5, 6.6 Hz, 1H, 5-H), 4.70 (dq, *J* = 7.3, 7.2 Hz, 1H, 2-H), 6.52 (d, *J* = 7.3 Hz, 1H, 2-NH), 6.68 (d, *J* = 8.5 Hz, 1H, 5-NH), 7.26-7.43 (m, 12H, ArH), 7.70-7.80 (m, 2H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 18.1, 18.2, 19.2 (C_3, C_7, C_8), 31.7 (C_6), 48.2 (C_2), 52.5 (OCH_3), 58.7 (C_5), 127.6 ($C_{6'}$), 128.7 (d, $J_{C,P}$ = 6.9 Hz, 4ArC_{meta}), 128.9 (d, $J_{C,P}$ = 5.8 Hz, $C_{5'}$), 129.1 (2ArC_{para}), 132.3 (d, $J_{C,P}$ = 23.9 Hz, $C_{2'}$), 133.8 (d, $J_{C,P}$ = 19.9 Hz, 2ArC_{ortho}), 133.9 (d, $J_{C,P}$ = 19.9 Hz, 2ArC_{ortho}), 134.5 (d, $J_{C,P}$ = 7.2 Hz, $C_{1'}$), 136.5 (2d, $J_{C,P}$ = 10.7 Hz, 2ArC_{ipso}), 136.8 (d, $J_{C,P}$ = 15.8 Hz, $C_{4'}$), 138.7 (d, $J_{C,P}$ = 13.5 Hz, $C_{3'}$), 167.3 (C_1), 170.7, 173.1 (C_4, C_9); ^{31}P-NMR (162 MHz, $CDCl_3$): δ = –5.26 (s); Anal. calcd. for $C_{28}H_{31}N_2O_4P$: C, 68.56; H, 6.37; N, 5.71.

Found: C, 68.43; H, 6.62; N, 5.97.

(+)-(3-Diphenylphosphanyl)-benzoyl-L-*tert*-leucyl-L-valine methylester (1c):



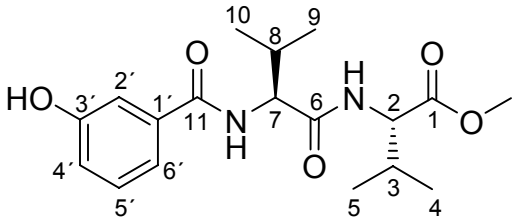
(532.61)

To a solution of Z–L-*t*-Leu–L-Val–OMe (**8**) (0.240 g, 0.634 mmol) in dry MeOH (3 ml) was added Pd-C (10%, 20 mg, Fluka), and the suspension was stirred under H_2 (1 atm) at room temperature for 15 h. The reaction mixture was filtered through Celite and the solvent removed *in vacuo* to yield the free amine H–L-*t*-Leu–L-Val–OMe as viscous oil (quant.). The amine was dissolved in dry CH_2Cl_2 (3 ml), and *meta*-diphenylphosphanyl-benzoic acid (0.194 g, 0.634 mmol, 1.0 eq.), DMAP (78 mg, 0.63 mmol, 1.0 eq.) and DIC (80 mg, 0.63 mmol, 1.0 eq.) were added at room temperature. The reaction mixture was stirred at room temperature for further 16 h. After concentration *in vacuo*, the residue was chromatographed on silica gel (PE/EE, 5:1→0:1) to afford the dipeptide ligand **1c** as a glass foam (0.274 g, 81%, R_f 0.39 with 2:1); Mp. 82°C (PE/EE); $[\alpha]_D^{20}$ +30.94° (*c* 0.640, $CHCl_3$).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.9 Hz, 3H, 4-H_3 or 5-H_3), 0.90 (d, *J* = 6.9 Hz, 3H, 5-H_3 or 4-H_3), 1.45 (s, 9H, *t*-Bu), 2.15 (m_c, *J* = 8.4, 4.8 Hz, 1H, 3-H), 3.75 (s, 3H, OCH_3), 4.45 (d, *J* = 9.2 Hz, 1H, 7-H), 4.50 (dd, *J* = 8.4, 4.8 Hz, 1H, 2-H), 6.16 (d, *J* = 8.5 Hz, 1H, 2-NH), 6.67 (d, *J* = 9.1 Hz, 1H, 7-NH), 7.26-7.38 (m, 11H, ArH), 7.42 (m_c, 1H, ArH), 7.66 (d, *J* = 7.0 Hz, 1H, ArH), 7.77 (m_c, 1H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 17.9, 19.0 (C_4, C_5), 26.7 ($3C_9$), 31.2 (C_3), 35.3 (C_8), 52.2 (OCH_3), 57.4 (C_2), 61.0 (C_7), 127.6 ($C_{6'}$), 128.8 (d, $J_{C,P}$ = 7.2 Hz, $4ArC_{meta}$), 128.9 (d, $J_{C,P}$ = 6.0 Hz, $C_{5'}$), 129.1 ($2ArC_{para}$), 132.1 (d, $J_{C,P}$ = 21.9 Hz, $C_{2'}$), 133.9 (2d, $J_{C,P}$ = 19.9 Hz, $4ArC_{ortho}$), 134.2 (d, $J_{C,P}$ = 6.9 Hz, $C_{1'}$), 136.6 (2d, $J_{C,P}$ = 10.7 Hz, $2ArC_{ipso}$), 136.8 (d, $J_{C,P}$ = 17.0 Hz, $C_{4'}$), 138.7 (d, $J_{C,P}$ = 13.5 Hz, $C_{3'}$), 167.2 (C_1), 170.5, 172.1 (C_6, C_{10}); ^{31}P-NMR (162 MHz, $CDCl_3$): δ = –5.29 (s); Anal. calcd. for $C_{31}H_{37}N_2O_4P$: C, 69.91; H, 7.00; N, 5.26. Found: C, 69.72; H, 7.19; N, 5.23.

3 Synthesis of phosphite ligands

(–)-3-Hydroxybenzoyl-L-valyl-L-valine methylester (9):

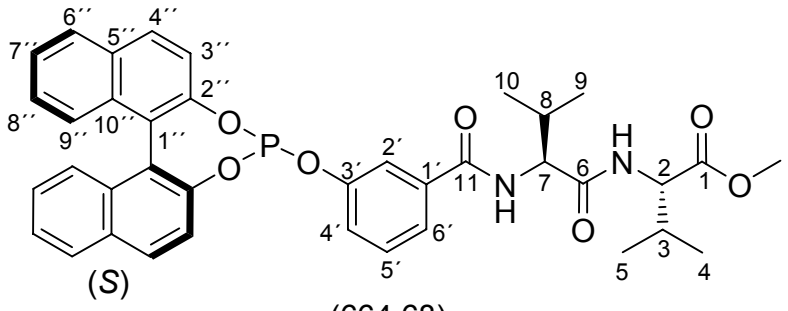


(350.41)

To a solution of Z–L-Val–L-Val–OMe (**6**) (2.000 g, 5.488 mmol) in dry MeOH (30 ml) was added Pd-C (10%, 51 mg, Fluka), and the suspension was stirred under H_2 (1 atm) at room temperature for 20 h. The reaction mixture was filtered through Celite and the solvent removed *in vacuo* to yield the free amine H–L-Val–L-Val–OMe as viscous oil (1.26 g, 5.48 mmol, quant.). The amine was dissolved in dry CH_2Cl_2 (3 ml), and 3-hydroxy benzoic acid (0.760 g, 5.488 mmol, 1.0 eq.), DMAP (67 mg, 0.55 mmol, 0.1 eq.), HOBt (0.740 g, 5.488 mmol, 1.0 eq.) and DIC (0.690 g, 5.488 mmol, 1.0 eq.) were added at room temperature. The resulting pale yellow, reaction mixture was stirred at room temperature for further 44 h. The mixture was filtered through a 2-cm pad of Celite (wetted with CH_2Cl_2), and the filter cake was washed with some DCM. After concentration *in vacuo*, the residue was chromatographed twice on silica gel (PE/EE, 2:1→1:1) to afford the dipeptide ligand **9** as a white solid (1.62 g, 84%, R_f 0.44 with 1:3); Mp. 85°C (CH_2Cl_2); $[\alpha]_D^{20}$ −18.86° (*c* 1.400, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.6 Hz, 3H, CH_3), 0.92 (d, *J* = 6.0 Hz, 3H, CH_3), 0.99 (d, *J* = 6.6 Hz, 3H, CH_3), 1.01 (d, *J* = 6.6 Hz, 3H, CH_3), 2.08-2.28 (m, 2H, 3-H, 8-H), 3.79 (s, 3H, OCH_3), 4.63 (dd, *J* = 8.8, 5.0 Hz, 1H, 2-H), 4.79 (dd, *J* = 8.5, 8.2 Hz, 1H, 7-H), 7.02 (ddd, *J* = 7.9, 1.3, 1.3 Hz, 1H, 4´-H),* 7.23 (dd, *J* = 9.5, 7.9 Hz, 1H, 5´-H), 7.30 (d, *J* = 8.9 Hz, 1H, 7-NH), 7.31 (overlapped d, *J* = 7.6 Hz, 1H, 6´-H),* 7.47 (d, *J* = 8.7 Hz, 1H, 2-NH), 7.67 (s, 1H, 2´-H), 8.55 (s, 1H, OH); For * assignment interchangeable; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 17.9, 18.7, 19.0, 19.2 (C_4, C_5, C_9, C_{10}), 31.2 (C_3), 32.0 (C_8), 52.4 (OCH_3), 57.5, 59.1 (C_2, C_7), 114.8 ($C_{2'}$), 118.5, 119.3 ($C_{4'}$, $C_{6'}$), 129.9 ($C_{5'}$), 134.6 ($C_{1'}$), 157.1 ($C_{3'}$), 167.4 (C_1), 172.4, 172.5 (C_6, C_{11}); Anal. calcd. for $C_{18}H_{26}N_2O_5$: C, 61.70; H, 7.48; N, 7.99. Found: C, 61.66; H, 7.54; N, 7.89.

(+)-(3,5-Dioxa-4-phospha-cyclohepta[2,1-*a*;3,4-*a*´]dinaphthalen-4-yl)-3-oxybenzoyl-L-valyl-L-valine methylester (2a):

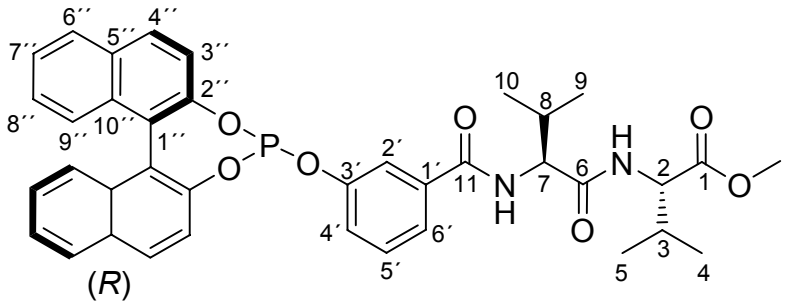


A warm solution (~60°C) of (*S*)-2,2´-binaphthol (0.430 g, 1.50 mmol, 1.0 eq.) in dry toluene (16 ml) was added in 5 min to a cooled solution (−78°C) of PCl_3 (0.222 g, 1.62 mmol, 1.08 eq.) and NEt_3 (0.310 g, 3.06 mmol, 2.04 eq.) in dry toluene (3 ml). The reaction mixture was stirred for 2 h at −60°C, warmed to room temperature and stirred for 1 h at this temperature. The white, chalky solution was treated with NEt_3 (0.165 g, 1.63 mmol, 1.09 eq.) and alcohol **9** (0.509 g, 1.46 mmol, 0.97 eq.) at −40°C. After stirring 23 h at room temperature, the reaction mixture was filtered through a 2-cm pad of Celite, and the filter cake was washed with dry toluene (24 ml). Concentration *in vacuo* (ventilated with argon!) afforded without further purification the peptidyl phosphite **2a** as a pale yellow foam (1.126 g, quant.); Mp. 104-106°C (toluene); $[\alpha]_D^{20}$ +102.26° (*c* 0.665, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.7 Hz, 3H, CH_3), 0.93 (d, *J* = 6.6 Hz, 3H, CH_3), 1.04 (d, *J* = 6.7 Hz, 3H, CH_3), 1.05 (d, *J* = 6.5 Hz, 3H, CH_3), 2.12-2.30 (m, 2H, 3-H, 8-H), 3.76 (s, 3H, OCH_3), 4.57 (dd, *J* = 8.5, 4.8 Hz, 1H, 2-H), 4.62 (dd, *J* = 8.4, 8.1 Hz, 1H, 7-H), 6.70 (d, *J* = 8.4 Hz, 1H, 2-NH), 6.92 (d, *J* = 8.4 Hz, 1H, 7-NH), 7.14-7.21 (m_c, 1H, ArH), 7.22-7.34 (m, 3H, 4´-H, ArH), 7.35-7.49 (m, 5H, 5´-H, ArH), 7.62 (d, *J* = 8.6 Hz, 2H, 6´-H, ArH), 7.66 (s, 1H, 2´-H), 7.88-7.98 (m, 3H, ArH), 8.01 (d, *J* = 8.8 Hz, 1H, ArH); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 17.9, 19.0 (C_4, C_5), 18.4, 19.2 (C_9, C_{10}), 31.2 (C_3), 31.7 (C_8), 52.2 (OCH_3), 57.4 (C_2), 59.0 (C_7), 119.6 (d, $J_{C,P}$ = 7.5 Hz, $C_{2'}$), 121.6, 121.7 ($2C_{3''}$), 122.8 ($C_{6'}$), 122.9 (d, $J_{C,P}$ = 2.3 Hz, $C_{1''}$), 123.7 (d, $J_{C,P}$ = 8.1 Hz, $C_{4'}$), 124.4 (d, $J_{C,P}$ = 5.2 Hz, $C_{1''}$), 125.2, 125.4 ($2C_{9''}$), 126.4, 126.5 ($2C_{8''}$), 127.0, 127.1 ($2C_{7''}$), 128.4, 128.5 ($2C_{6''}$), 130.1 ($C_{5'}$), 130.7 ($2C_{4''}$), 131.4, 131.8 ($2C_{10''}$), 132.6

(d, $J_{C,P}$ = 1.4 Hz, $C_{5''}$),* 132.9 (d, $J_{C,P}$ = 1.7 Hz, $C_{5''}$),* 136.1 ($C_{1'}$), 146.9 (d, $J_{C,P}$ = 2.3 Hz, $C_{2''}$),* 147.5 (d, $J_{C,P}$ = 4.6 Hz, $C_{2''}$),* 152.1 (d, $J_{C,P}$ = 8.1 Hz, $C_{3'}$), 166.6 (C_1), 171.2, 172.2 (C_6, C_{11}); For * assignment interchangeable; ^{31}P-NMR (121 MHz, $CDCl_3$): δ = +144.45 (s); HRMS (EI-MS *m/z*) calcd. for $C_{38}H_{37}N_2O_7P$ (M^+) 664.2338, found 664.2341.

(–)-(3,5-Dioxa-4-phospha-cyclohepta[2,1-*a*;3,4-*a*´]dinaphthalen-4-yl)-3-oxybenzoyl-L-valyl-L-valine methylester (2b):



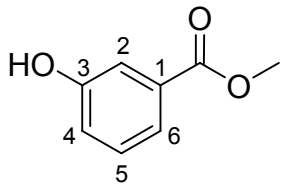
(664.68)

A solution of (*R*)-2,2´-binaphthol (0.354 g, 1.24 mmol, 1.0 eq.) in dry THF (6 ml) was added in 10 min to a cooled solution (–4°C) of PCl_3 (0.171 g, 1.24 mmol, 1.0 eq.) and NEt_3 (0.259 g, 2.56 mmol, 2.06 eq.) in dry THF (2.5 ml). The cooling bath was removed after 10 min and the reaction mixture was stirred for 1.5 h at room temperature. The white, chalky solution was then treated with NEt_3 (0.129 g, 1.27 mmol, 1.02 eq.) and alcohol **9** (0.421 g, 1.20 mmol, 0.97 eq.) at –5°C. After diluting with THF (3 ml) and stirring 18 h at room temperature, the reaction mixture was concentrated in vacuo. The residue was treated with dry toluene (10 ml), and the resulting suspension filtered through a 2-cm pad of Celite. The filter cake was washed with dry toluene (15 ml), and concentration *in vacuo* (ventilate with argon!) afforded without further purification the peptidyl phosphite **2b** as a pale yellow foam (0.841 g, quant., contains traces of $HCl{\cdot}NEt_3$); Mp. 115°C (toluene); $[\alpha]_D^{20}$ –113.62° (*c* 0.690, $CHCl_3$).

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.9 Hz, 3H, 4-H_3),* 0.93 (d, *J* = 6.9 Hz, 3H, 5-H_3),* 1.02 (d, *J* = 6.6 Hz, 3H, 9-H_3),** 1.03 (d, *J* = 6.6 Hz, 3H, 10-H_3),** 2.15-2.26 (m, 2H, 3-H, 8-H), 3.76 (s, 3H, OCH_3), 4.59 (dd, *J* = 8.6, 4.9 Hz, 1H, 2-H), 4.63 (dd, *J* = 8.5, 6.6 Hz, 1H, 7-H), 6.71 (d, *J* = 8.5 Hz, 1H, 2-NH), 6.91 (d, *J* = 8.8 Hz, 1H, 7-NH), 7.16-7.19 (m, 1H, ArH), 7.24-7.34 (m, 3H, 4´-H, ArH), 7.36-7.48 (m, 5H, 5´-H, ArH), 7.57 (ddd, *J* = 7.6, 1.3, 1.3 Hz, 1H, 6´-

H), 7.58 (d, J = 8.8 Hz, 1H, ArH), 7.66 (s, 1H, 2′-H), 7.92 (d, J = 8.8 Hz, 1H, ArH), 7.94 (d, J = 8.8 Hz, 1H, ArH), 7.95 (d, J = 8.2 Hz, 1H, ArH), 8.01 (d, J = 8.8 Hz, 1H, ArH); For * and ** assignment interchangeable; ^{13}C-NMR (126 MHz, $CDCl_3$): δ = 17.9, 19.0 (C_4, C_5), 18.4, 19.2 (C_9, C_{10}), 31.2 (C_3), 31.8 (C_8), 52.4 (OCH_3), 57.3 (C_2), 58.9 (C_7), 119.5 (d, $J_{C,P}$ = 7.5 Hz, $C_{2'}$), 121.6, 121.7 ($2C_{3''}$), 122.8 ($C_{6'}$), 122.9 (d, $J_{C,P}$ = 3.2 Hz, $C_{1''}$), 123.7 (d, $J_{C,P}$ = 8.6 Hz, $C_{4'}$), 124.4 (d, $J_{C,P}$ = 4.3 Hz, $C_{1''}$), 125.2, 125.4 ($2C_{9''}$), 126.4, 126.5 ($2C_{8''}$), 127.0, 127.1 ($2C_{7''}$), 128.4, 128.5 ($2C_{6''}$), 130.2 ($C_{5'}$), 130.7 ($2C_{4''}$), 131.4, 131.8 ($2C_{10''}$), 132.6, 132.8 ($2C_{5''}$), 136.0 ($C_{1'}$), 146.9 (d, $J_{C,P}$ = 2.2 Hz, $C_{2''}$), 147.4 (d, $J_{C,P}$ = 5.4 Hz, $C_{2''}$), 152.1 (d, $J_{C,P}$ = 8.6 Hz, $C_{3'}$), 166.6 (C_1), 171.2, 172.3 (C_6, C_{11}); ^{31}P-NMR (121 MHz, $CDCl_3$): δ = +144.65 (s); ESI-MS (5.0 kV): m/z = 664.8 (100%) $[M]^+$; HRMS (EI-MS m/z) calcd. for $C_{38}H_{37}N_2O_7P$ (M^+) 664.233841, found 664.235696.

3-Hydroxybenzoic acid methylester (10):[5]



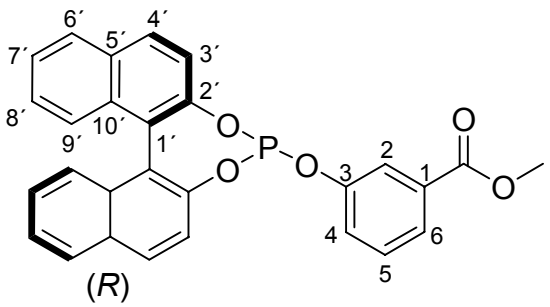
(152.15)

3-Hydroxybenzoic acid (6.90 g, 0.05 mol) was converted to the methyl ester by stirring in dry MeOH (150 mL) containing concentrated H_2SO_4 (3 ml) for 5 h at room temperature. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (3 x 100 ml). The combined ethereal extracts were washed with H_2O (100 ml), aq. $NaHCO_3$ (10%, 200 ml), and brine (100 ml), dried ($MgSO_4$), and concentrated to yield a colourless oil. After few minutes the oil crystallized and yielded the ester **10** as a white solid (7.55 g, 99%, R_f 0.64 with PE/EE 1:1); Mp. 67°C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.89 (s, 3H, OCH_3), 7.09 (dd, J = 8.1, 2.4 Hz, 1H, 4-H), 7.26 (m_c, 1H, 5-H), 7.41 (bs, 1H, OH), 7.56 (d, J = 7.6 Hz, 1H, 6-H), 7.61 (s, 1H, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 52.5 (OCH_3), 116.4 (C_2), 120.6 (C_4), 121.7 (C_6), 129.7 (C_5), 131.0 (C_1),

156.2 (C_3), 167.4 (C=O); HRMS (EI-MS *m/z*) calcd. for $C_8H_8O_3$ (M^+) 152.0473, found 152.0476; Anal. calcd. for $C_8H_8O_3$: C, 63.15; H, 5.30. Found: C, 63.17; H, 5.24.

(−)-(3,5-Dioxa-4-phospha-cyclohepta[2,1-*a*;3,4-*a*´]dinaphthalen-4-yl)-3-oxy-benzoic acid methylester (2c):



(*R*)

(466.42)

A solution of (*R*)-2,2´-binaphthol (0.400 g, 1.40 mmol, 1.0 eq.) in dry THF (5 ml) was added in 30 min to a cooled solution (−3°C) of PCl_3 (0.192 g, 1.40 mmol, 1.0 eq.) and NEt_3 (0.290 g, 2.87 mmol, 2.05 eq.) in dry THF (3 ml). The cooling bath was then removed and the reaction mixture was stirred for 2.5 h at room temperature. The white, chalky solution was cooled (−3°C) and then treated with NEt_3 (0.150 g, 1.48 mmol, 1.06 eq.) and alcohol **10** (0.212 g, 1.39 mmol, 0.99 eq.). After diluting with THF (4 ml) and stirring 24 h at room temperature, the reaction mixture was concentrated in vacuo (ventilated with argon!). The residue was treated with dry Et_2O (6 ml), and the resulting suspension filtered under argon through a 2-cm pad of Celite. The filter cake was washed with dry Et_2O (2 x 7 ml), and concentration *in vacuo* (ventilate with argon!) afforded without further purification the phosphite **2c** as a glass foam (0.841 g, quant.); Mp. 55°C; $[\alpha]_D^{20}$ −182.8° (*c* 1.000, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3H, OCH_3), 7.25-7.33 (m, 3H, ArH), 7.35-7.50 (m, 6H, ArH), 7.58 (d, *J* = 8.8 Hz, 1H, ArH), 7.83 (m_c, 2H, ArH), 7.91 (d, *J* = 8.7 Hz, 2H, ArH), 7.95 (d, *J* = 8.4 Hz, 1H, ArH), 8.02 (d, *J* = 8.8 Hz, 1H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 52.4 (OCH_3), 121.5 (d, $J_{C,P}$ = 8.4 Hz, C_2), 121.6, 121.7 ($2C_{3''}$), 121.7 (C_6), 122.0 (ArC), 122.9 (d, $J_{C,P}$ = 2.9 Hz, $C_{1''}$), 124.4 (d, $J_{C,P}$ = 5.2 Hz, C_4), 125.1 (d, $J_{C,P}$ = 5.2 Hz, ArC), 125.2, 125.4 ($2C_{9''}$), 125.6 (d, $J_{C,P}$ = 1.2 Hz, ArC), 126.4, 126.5 ($2C_{8''}$), 127.1, 127.2 ($2C_{7''}$), 128.4, 128.5 ($2C_{6''}$), 129.8 (ArC), 129.9 (C_5), 130.1, 130.7 ($2C_{4''}$), 131.4 ($C_{10''}$), 131.8 (d, $J_{C,P}$ = 0.9 Hz, $C_{10''}$), 132.0

(ArC), 132.7 (d, $J_{C,P}$ = 1.4 Hz, $C_{5''}$),* 133.0 (d, $J_{C,P}$ = 1.4 Hz, $C_{5''}$),* 147.0 (C_1), 147.6 (d, $J_{C,P}$ = 4.9 Hz, $2C_{2''}$),* 152.0 (d, $J_{C,P}$ = 7.2 Hz, C_3), 166.4 (C_1); For * assignment interchangeable; ^{31}P-NMR (121 MHz, $CDCl_3$): δ = +143.88 (s); HRMS (EI-MS *m/z*) calcd. for $C_{28}H_{19}O_5P$ (M^+) 466.0970, found 466.0966; Anal. calcd. for $C_{28}H_{19}O_5P$: C, 72.10; H, 4.11. Found: C, 72.10; H, 4.32.

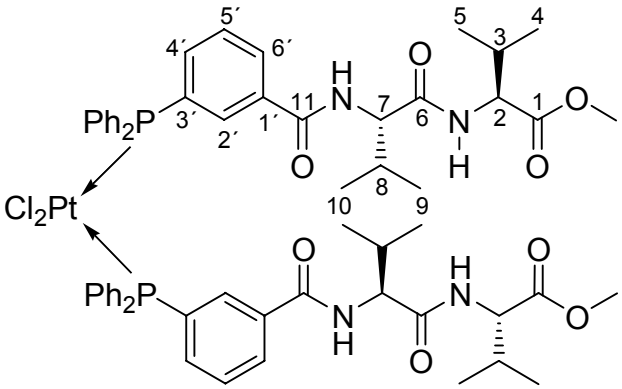
III Homodimeric complexes

1 General procedure for the generation of platinum and rhodium complexes

cis-[Cl_2Pt(cod)] (11.2 mg, 30.0 µmol, 1.0 eq.) or [$Rh(cod)_2BF_4$] (12.2 mg, 30.0 µmol, 1.0 eq.) and the appropriate ligand **1** or **2** (60.0 µmol, 2.0 eq.) were dissolved in degassed $CDCl_3$ (0.8 ml) at room temperature and analyzed via NMR and ESI-MS.

For other characterization experiments, an appropriate amount of the complex was dissolved in CH_2Cl_2 and stirred for 10 min at room temperature. The solvent was removed *in vacuo* and the residue was washed with *n*-pentane. The remaining white solid was dried *in vacuo*.

1.1 *cis*-[Cl_2Pt(1a·1a)]



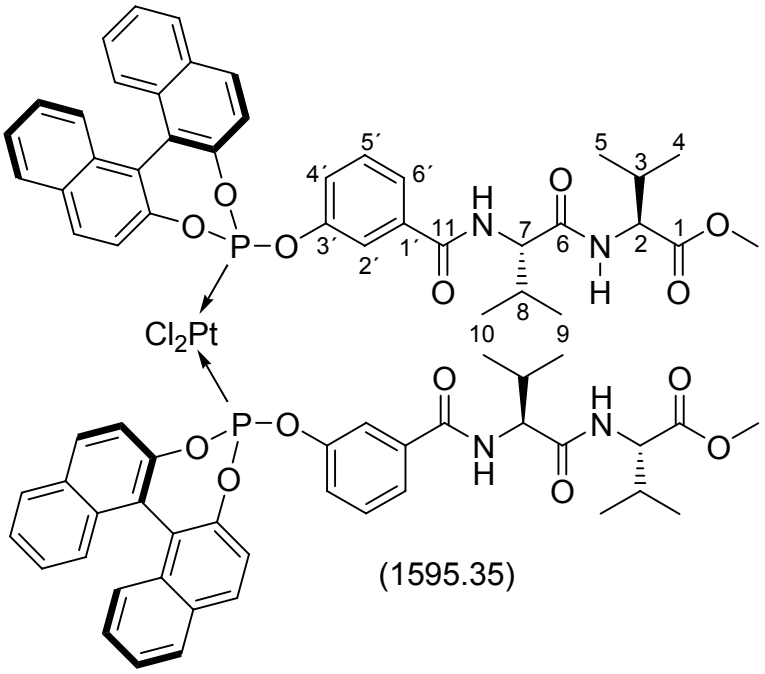
(1303.15)

Following the general procedure the title compound was obtained from *cis*-[Cl_2Pt(cod)] (11.3 mg, 30.0 µmol) and C-dipeptide ligand **1a** (31.6 mg, 60.9 µmol, 2.0 eq.) in $CDCl_3$ (0.8 ml).

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 6.9 Hz, 3H, 4-H_3 or 5-H_3), 0.96 (d, *J* = 6.9 Hz, 3H,

4-H_3 or 5-H_3), 1.00 (d, J = 6.8 Hz, 3H, 9-H_3 or 10-H_3), 1.02 (d, J = 6.8 Hz, 3H, 9-H_3 or 10-H_3), 2.15-2.25 (m, J = 6.8, 6.6, 5.4 Hz, 2H, 3-H, 8-H), 3.75 (s, 3H, OCH_3), 4.24 (dd, J = 8.5, 8.3 Hz, 1H, 7-H), 4.56 (dd, J = 8.7, 5.1 Hz, 1H, 2-H), 6.71 (d, J = 8.3 Hz, 1H, 2-NH), 6.99 (dd, J = 7.5, 7.5 Hz, 1H, 5′-H), 7.22 (dd, J = 7.2, 7.1 Hz, 2H, ArH_{meta}), 7.28 (dd, J = 7.4, 7.1 Hz, 2H, ArH_{meta}), 7.34-7.42 (m, 2H, ArH_{para}), 7.45 (dd, J = 9.2, 8.8 Hz, 1H, 4′-H), 7.54 (d, J = 7.8 Hz, 1H, 6′-H), 7.58-7.66 (m, 3H, 2′-H, ArH_{ortho}), 7.69 (dd, J = 11.4, 7.8 Hz, 2H, ArH_{ortho}), 8.14 (d, J = 6.9 Hz, 1H, 7-NH); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 18.0, 19.0 (C_4, C_5), 19.6, 19.7 (C_9, C_{10}), 30.2, 31.2 (C_3, C_8), 52.2 (OCH_3), 57.5 (C_2), 61.1 (C_7), 127.5 (2d, $J_{C,P}$ = 6.0, 5.2 Hz, $C_{5'}$), 128.0 (m, $J_{C,P}$ = 11.5 Hz, 4ArC), 128.5 ($C_{6'}$), 131.3 (ArC_{para}), 131.5 (ArC_{para}), 133.3 (2d, $J_{C,P}$ = 5.1, 4.9 Hz, $C_{2'}$), 133.6 (m, ArC), 135.6 (3d, $J_{C,P}$ = 22.1, 21.5, 21.5 Hz, $4ArC_{ortho}$), 136.2 ($C_{4'}$), 165.8 (C_1), 172.0, 172.7 (C_2, C_6); ^{31}P-NMR (121 MHz, $CDCl_3$): δ = 14.79 (d, $^1J_{P,Pt}$ = 3658.7 Hz); MS (ESI, 5 kV, calcd. for $C_{60}H_{70}Cl_2N_4O_8P_2Pt$): *m/z* (%) = 1267.2 (100) $[M-Cl]^+$.

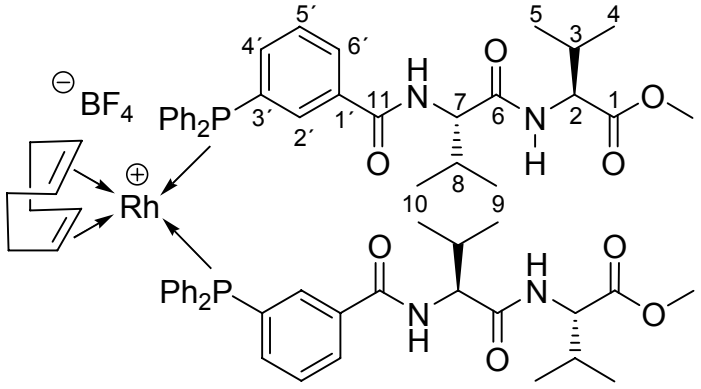
1.2 *cis*-[Cl_2Pt(2b·2b)]



Following the general procedure the title compound was obtained from *cis*-[Cl_2Pt(cod)] (9.9 mg, 26.5 µmol) and phosphite ligand **2b** (35.2 mg, 52.7 µmol, 2.0 eq.).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 7.0 Hz, 3H, 4-H_3 or 5-H_3), 0.92 (d, *J* = 6.8 Hz, 3H, 4-H_3 or 5-H_3), 1.05 (d, *J* = 6.7 Hz, 3H, 9-H_3 or 10-H_3), 1.06 (d, *J* = 6.7 Hz, 3H, 9-H_3 or 10-H_3), 2.18 (m_c, 1H, 3-H), 2.26 (m_c, *J* = 6.8 Hz, 1H, 8-H), 3.69 (s, 3H, OCH_3), 4.54-4.61 (m, 2H, 2-H, 7-H), 6.84 (d, *J* = 8.2 Hz, 1H, 2-NH), 6.86 (d, *J* = 7.6 Hz, 1H, 7-NH), 7.25-7.56 (m, 9H, ArH), 7.67 (d, *J* = 8.6 Hz, 2H, ArH), 7.91 (s, 2H, ArH), 7.98 (d, *J* = 8.2 Hz, 1H, ArH), 8.14 (d, *J* = 9.1 Hz, 2H, ArH); ^{31}P-NMR (162 MHz, $CDCl_3$): δ = 89.36 (d, $^1J_{P,Pt}$ = 5734.9 Hz); MS (ESI, 5 kV, calcd. for $C_{76}H_{74}Cl_2N_4O_{14}P_2Pt$): *m/z* (%) = 1611.4 (93) (oxidized product), 1594.8 (100) $[M+H]^+$, 1522.1 (95) $[M-Cl-Cl]^+$.

1.3 [(cod)Rh(1a·1a)BF_4]



(1335.06)

Following the general procedure the title compound was obtained from $[Rh(cod)_2BF_4]$ (10.0 mg, 24.6 µmol) and C-dipeptide ligand **1a** (25.5 mg, 49.3 µmol, 2.0 eq.) in $CDCl_3$ (0.7 ml).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.93 (2d, *J* = 7.3 Hz, 6H, 4-H_3, 5-H_3), 1.06 (d, *J* = 6.5 Hz, 3H, 9-H_3 or 10-H_3), 1.07 (d, *J* = 6.5 Hz, 3H, 9-H_3 or 10-H_3), 2.22 (m_c, 1H, 3-H), 2.29 (m_c, 1H, 8-H), 3.69 (s, 3H, OCH_3), 4.43 (dd, *J* = 8.2, 8.1 Hz, 1H, 7-H), 4.54 (dd, *J* = 8.5, 5.3 Hz, 1H, 2-H), 7.05 (d, *J* = 7.6 Hz, 1H, 2-NH), 7.15-7.70 (m, 12H, ArH), 7.80 (d, *J* = 7.3 Hz, 1H, ArH), 8.04 (d, *J* = 6.7 Hz, 1H, 7-NH), 8.30 (bs, 1H, ArH); ^{31}P-NMR (121 MHz, $CDCl_3$): δ = 27.28 (d, $^1J_{P,Rh}$ = 144.8 Hz); MS (ESI, 5 kV, calcd. for $C_{68}H_{82}BF_4N_4O_8P_2Rh$): *m/z* (%) = 1262.7 (41) $[M_{Oxide}-Cl]^+$, 1246.8 (100) $[M-Cl]^+$.

2 X-ray crystal structure analysis of *cis*-[Cl_2Pt(**1b**·**1b**)]

X-ray crystal structure analysis: Suitable single crystals for X-ray crystal-structure analysis were obtained from slow evaporation of a solution in ethyl acetate/CH_2Cl_2 (98:2). The crystal of *cis*-[Cl_2Pt(**1b**·**1b**)] was submitted for X-ray data collection on a Rigaku R-AXIS SPIDER image plate diffractometer using graphite monochromated $Mo_{K\alpha}$ radiation at 100 K. Structure solution was carried out by SHELXS-97,[6] refinement against F^2 with SHELXL-97.[7] Crystallographic data of *cis*-[Cl_2Pt(**1b**·**1b**)] have been deposited to the Cambridge Crystallographic Data Centre. CCDC-661682 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam. ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

There are two symmetry independent complex molecules in the asymmetric unit (see red and blue complex in the following picture). The structure exhibits disorder.

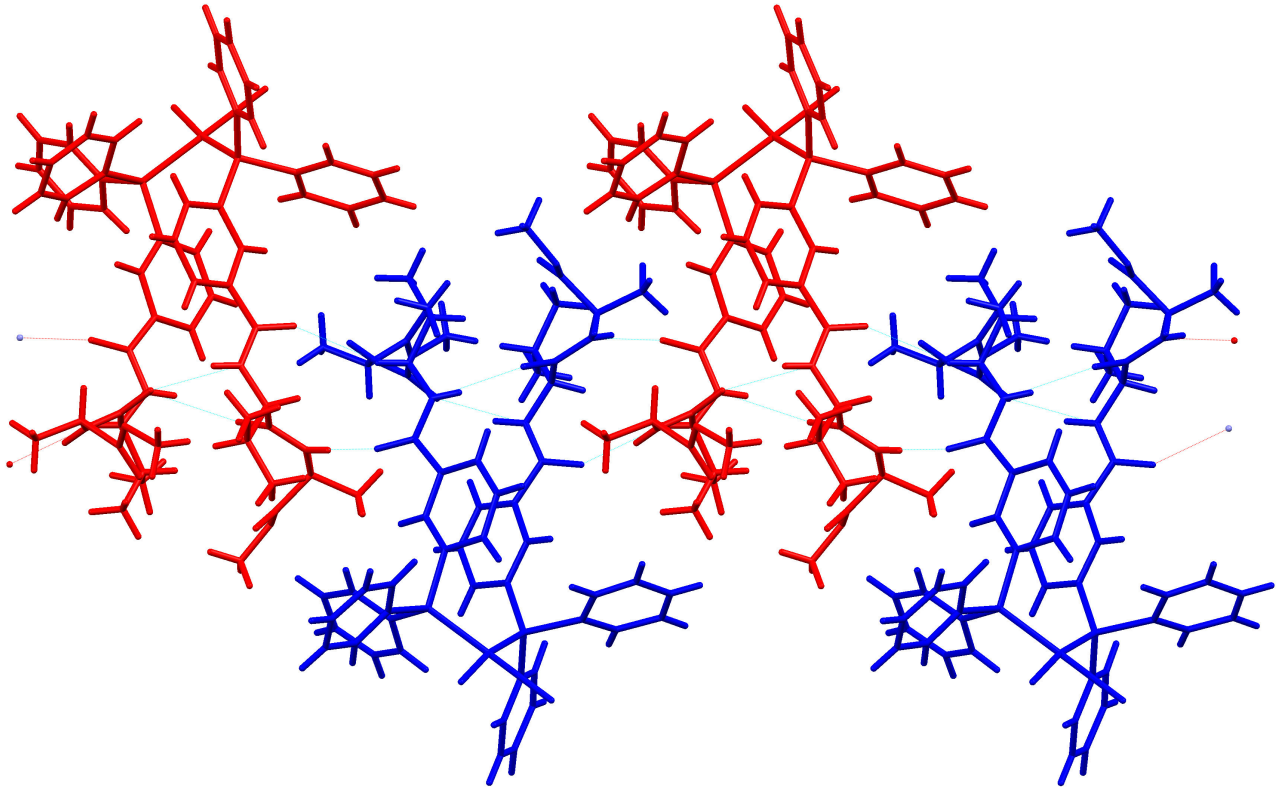


Figure: The homodimeric platinum complex *cis*-[Cl_2Pt(**1b**·**1b**)] forms self-assembled infinite chains of alternating transoid nature through intercomplex hydrogen bonding.

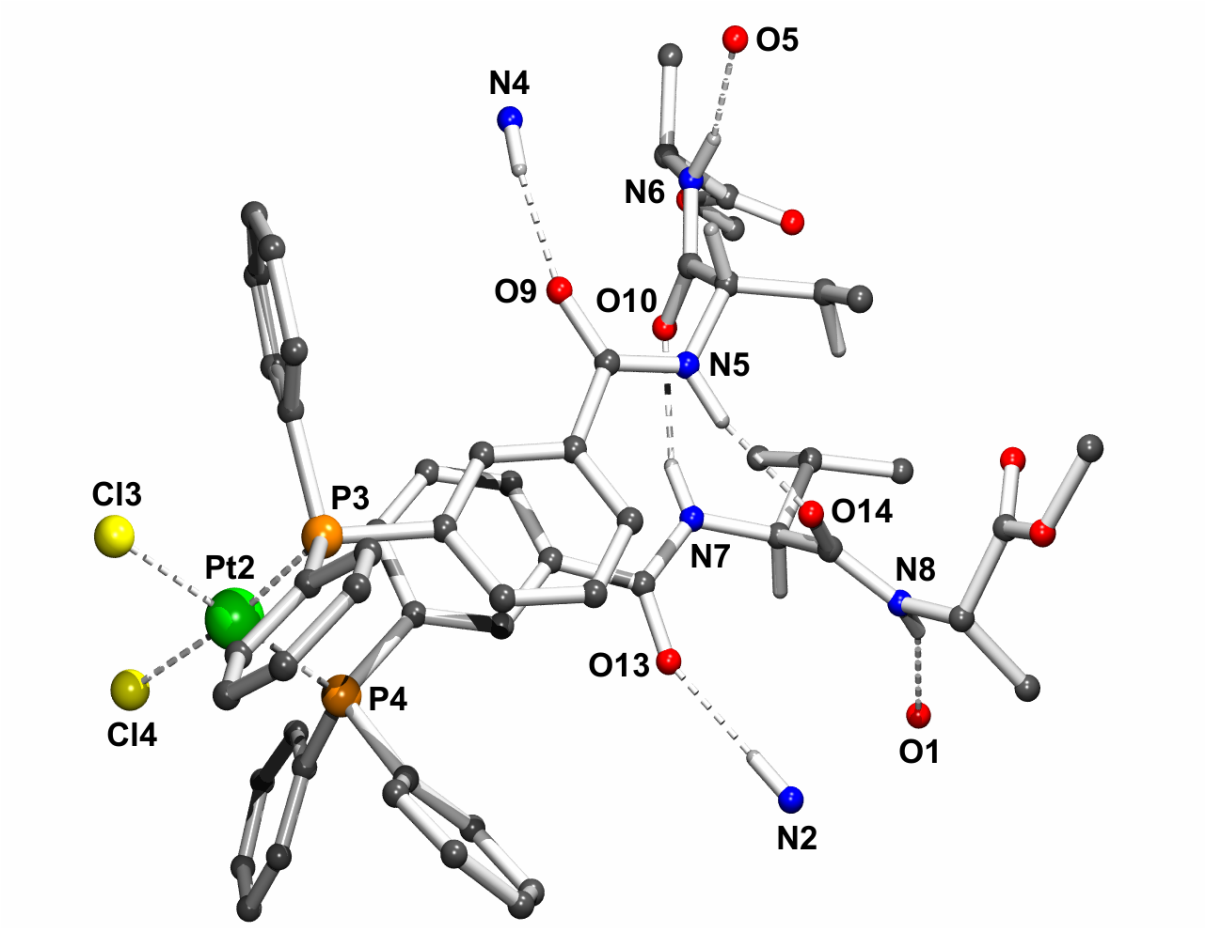


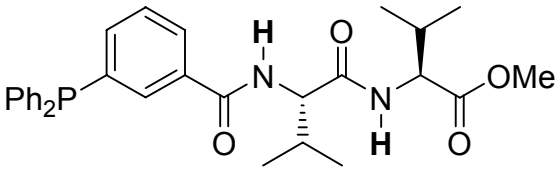
Figure: PLATON plot of *cis*-[Cl_2Pt(**1b**·**1b**)] in the solid-state at 100K. This picture represents one of both independent complexes in the asymmetric unit.

Specified hydrogen bonds (with esds except fixed and riding H):

D–H	H···A	D···A	<(DHA)		
0.86	2.03	2.856(9)	159	N4–H···O9	(intercomplex)
0.86	1.99	2.836(9)	168	N8–H···O1	(intercomplex)
0.90	1.99	2.872(9)	166	N2–H···O13	(intercomplex)
0.86	2.11	2.926(8)	159	N5–H···O14	(intramolecular)
0.83	2.10	2.913(9)	167	N7–H···O10	(intramolecular)
0.86	2.08	2.903(8)	159	N3–H···O2	(intramolecular)
0.96	1.98	2.920(9)	164	N1–H···O6	(intramolecular)
0.86	2.03	2.890(9)	177	N6–H···O5	(intercomplex)

3 ^{1}H-NMR analysis and solution structure

Table: Comparison of relevant ^{1}H-NMR proton shifts and coupling constants of free ligand and of the homodimeric Pt^{II} complex of representative ligand **1a** in $CDCl_3$.[a]

entry	species		
1	free ligand	6.71 (8.7)	6.56 (8.7)
2	Pt-complex	8.14 (6.9)	6.71 (8.3)

[a] Chemical shifts in ppm, and corresponding coupling constants in parenthesis in Hz.

The sharp signals in proton NMR and the changes in the coupling constants reveal the formation of a folded species upon complexation in solution. The significant downfield shift one amide N–H proton from 6.71 to 8.14 ppm is indicative of strong H-bonding.[x]

IV General procedure for asymmetric hydrogenation

$[Rh(cod)_2]BF_4$ (2.0 mg, 4.9 µmol, 1.0 mol%), ligand **1** or **2** (11.8 µmol, 2.4 mol%) were dissolved in dry degassed solvent (5 ml, CH_2Cl_2 or MeOH) and stirred under argon at room temperature for 10 min. Subsequently, the appropriate substrate (**3**-**5**, 0.5 mmol, 1 eq.) was added in one portion. For hydrogenation at atmospheric pressure, the reaction vessel was equipped with a septum, and hydrogen gas was bubbled via canula (hydrogen balloon) through the reaction mixture for 2-3 min. After short saturation, the canula was removed from the solution and the yellow reaction mixture was vigorously stirred under an atmosphere of hydrogen (hydrogen balloon) at room temperature.
Conversion was determined by ^{1}H-NMR.

Hydrogenation of acetamidoacrylate **3**:
Enantiomeric excess was determined by chiral GC analysis using a Hydrodex-β-TBDAc

column, 25 m × 0.25 mm, 120°C.

t_R [(*R*)-enantiomer] = 14.0 min.

t_R [(*S*)-enantiomer] = 20.3 min.

Hydrogenation of methyl-α-acetylamino cinnamate **4**:

Enantiomeric excess was determined by chiral HPLC analysis using a *Chiralpak*-AD column, 25 cm × 4.6 mm, *n*-heptane/*i*-propanol 90:10, 254 nm.

t_R [(*R*)-enantiomer] = 15.0 min.

t_R [(*S*)-enantiomer] = 19.5 min.

Hydrogenation of dimethylitaconate **5**:

Enantiomeric excess was determined by chiral GC analysis using a G-TA, Trifluoroacetyl-γ-cyclodextrin column, 30 m × 0.5 mm, 75°C.

t_R [(*S*)-enantiomer] = 32.2 min.

t_R [(*R*)-enantiomer] = 35.2 min.

V Literature

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[4] Miyazawa, T.; Takashima, K.; Yamada, T.; Kuwata, S.; Watanabe, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 341-342.

[5] Winkle, M. R.; Ronald, R. C. *J. Org. Chem.* **1982**, *47*, 2101-2108.

[6] a) G. M. Sheldrick, *SHELXS97, Program for the solution of crystal structures*, Univ. of Göttingen, Germany, **1997**; b) G. M. Sheldrick, *SHELXS97, Program for the refinement of crystal structures*, Univ. of Göttingen, Germany, **1997**.

[7] G. M. Sheldrick, *SHELXTL, The complete software package for single crystal structure determination*, release 5.10, Bruker AXS, Inc., Madison, **1997**.