

Supporting Information

Cofactor-Controlled Chirality of Tropoisomeric Ligand

Laure Theveau,⁺ Rosalba Bellini,⁺ Paweł Dydio,[§] Zoltan Szabo,⁺ Angela van der Werf,^{+,§} Robin Afshin Sander,⁺ Joost N. H. Reek,^{*,§} and Christina Moberg^{*,+}

⁺KTH Royal Institute of Technology, Department of Chemistry, Organic Chemistry, SE 10044
Stockholm, Sweden

[§]van't Hoff Institute for Molecular Sciences, University of Amsterdam, Science Park 904, 1098
XH, Amsterdam, The Netherlands

Contents

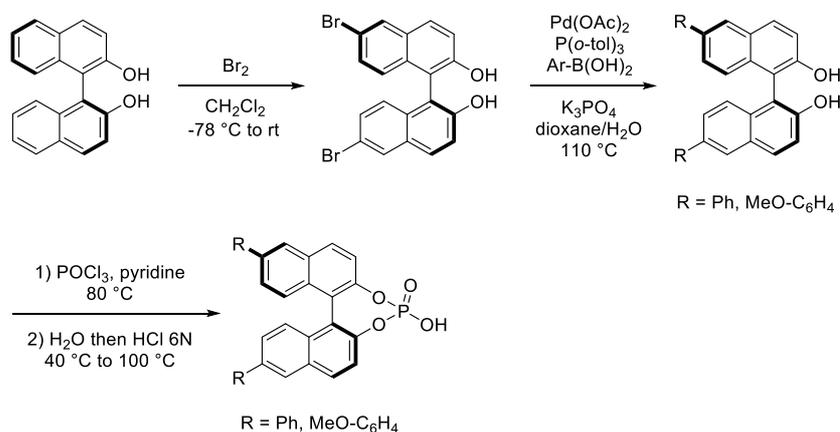
1. General information	S2
2. Synthetic procedures	S2
- Synthesis of chiral BINOL-based phosphates	S2
3. Allylic alkylations	S5
4. Screening of cofactors for the asymmetric allylic alkylation	S10
5. NMR study	S14
- Variable temperature NMR experiments of ligand 1	S14
- Binding study of chiral cofactor anions in the DIM pocket of ligand 1	S15
- Preparation of palladium(0)/olefin complexes of PPh ₃ -ligand 13 with acetate as the cofactor	S18
- Preparation of palladium(0)/olefin complexes of ligand 1 with various cofactors	S19
6. Stereochemistry of olefin complexes with co-factor ligands	S36
7. NMR spectra	S37

1. General information

All commercially available reagents were used as received, except otherwise specified. Chiral carboxylic or phosphoric acid-derived cofactors were obtained from chemical suppliers or synthesized according to previously reported procedures.¹ *rac*-(*E*)-1,3-Diphenylallyl methyl carbonate and *rac*-cyclohex-2-en-1-yl methyl carbonate were synthesized according to previously reported procedures.² Dry CH₂Cl₂, THF, toluene, and hexane were taken from a glass-contour solvent dispensing system. CD₂Cl₂ was dried over 3 Å molecular sieves before use. Et₃N, DIPEA, and benzylamine were distilled from potassium hydroxide under nitrogen. Dimethyl malonate was distilled under reduced pressure. Column chromatography was performed using silica gel 40–63 μm (230–400 mesh). TLC was performed using TLC silica gel 60 F254 and products revealed by UV irradiation (λ = 254 nm). ¹H NMR, ¹³C NMR, and ³¹P NMR spectra were recorded at room temperature at 400 or 500 MHz, 100 MHz, and 162 MHz or 202 MHz, respectively. Low temperature ¹H NMR and ³¹P NMR spectra were recorded at 400 MHz and 162 MHz, respectively. Chemical shifts (δ) are given in ppm relative to the residual solvent peak. Splitting patterns are indicated as follows: br: broad; s: singlet; d: doublet; t: triplet; dd: doublet of doublet; m: multiplet. Yields were determined by ¹H NMR using 1-methoxynaphthalene as internal standard and enantiomeric excesses were measured by HPLC using a UV detector and a chiral column, Daicel Chiralpak IC (0.46 cm × 25 cm) or Daicel Chiralcel OD-H (0.46 cm × 25 cm), or by GC using a FID detector and a chiral column, CYCLOSIL B (30 m × 0.25 mm × 0.25 μm).

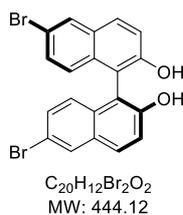
2. Synthetic procedures

- Synthesis of chiral BINOL-based phosphates



¹ (a) Dydio, P.; Rubay, C.; Gadzikwa, T.; Lutz, M.; Reek, J. N. H. *J. Am. Chem. Soc.* **2011**, *133*, 17176–17179. (b) Bartoszek, M.; Beller, M.; Deutsch, J.; Klawonn, M.; Köckritz, A.; Nemati, N.; Pews-Davtyan, A. *Tetrahedron* **2008**, *64*, 1316–1322.

² (a) Hayashi, T.; Yamamoto, A.; Ito, Y.; Nishioka, E.; Miura, H.; Yanagi, K. *J. Am. Chem. Soc.* **1989**, *111*, 6301–6311. (b) Gais, H.-J.; Jagusch, T.; Spalthoff, N.; Gerhards, F.; Frank, M.; Raabe, G. *Chem.-Eur. J.* **2003**, *9*, 4202–4221.

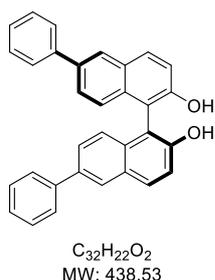


(S)-6,6'-Dibromo-1,1'-binaphthalene-2,2'-diol³

(S)-1,1'-Bi-2-naphthol (1 g, 3.5 mmol, 1 equiv) was dissolved in CH_2Cl_2 (20 mL) and cooled to $-78\text{ }^\circ C$. Br_2 (486 μL , 9.45 mmol, 2.7 equiv) was diluted with CH_2Cl_2 (4 mL) and then added dropwise. The reaction mixture was stirred 2 h at $-78\text{ }^\circ C$ then allowed to gradually reach room temperature and stirred for an additional 2 h. The excess of bromine was quenched with a saturated solution of Na_2SO_3 , the two phases were separated, the organic phase was washed with water and brine, then dried over Na_2SO_4 and the solvent evaporated. The solid residue was re-precipitated from CH_2Cl_2 /hexane affording the product as a light beige solid (1.2 g, 77% yield). Analytical data are consistent with those reported in the literature.

1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, 2H, J = 2.1 Hz), 7.90 (d, 2H, J = 8.9 Hz), 7.40 (d, 2H, J = 9.2 Hz), 7.37 (dd, 2H, J = 9.2 Hz, J = 2.1 Hz), 6.96 (d, 2H, J = 8.9 Hz), 5.00 (s, OH).

General procedure for arylation of (S)-6,6'-dibromo-1,1'-binaphthalene-2,2'-diol by Suzuki-Miyaura cross-coupling. In an oven-dried screw-capped sealed tube (10 mL) were placed (S)-6,6'-dibromo-1,1'-binaphthalene-2,2'-diol (1 equiv), $Pd(OAc)_2$ (5 mol %), $P(o\text{-tol})_3$ (10 mol %), potassium phosphate (2.5 equiv), and arylboronic acid (2.5 equiv). 1,4-Dioxane and H_2O (3:1) were added (the total volume corresponded to 1.2 mL per 0.35 mmol of 6,6'-dibromo-1,1'-binaphthalene-2,2'-diol), the vial was sealed, and the mixture was heated in an oil bath at $100\text{ }^\circ C$ for 24 h. After cooling, the phases were separated and the aqueous phase was extracted three times with CH_2Cl_2 . The combined organic phases were washed with saturated aqueous NH_4Cl solution, dried over Na_2SO_4 and the solvent evaporated. The product was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate as eluent (9:1).



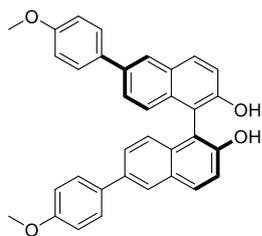
(S)-6,6'-Diphenyl-1,1'-binaphthalene-2,2'-diol

The general procedure was followed using phenylboronic acid (122 mg, 1 mmol). The product was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate (9:1) as eluent. A beige solid was obtained by precipitation from CH_2Cl_2 /hexane (127 mg, 73% yield). Analytical data are consistent with those reported in the literature.⁴

1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, 2H, J = 1.6 Hz), 8.06 (d, 2H, J = 8.8 Hz), 7.68 (d, 4H, J = 7.2 Hz), 7.60 (dd, 2H, J = 8.6 Hz, J = 1.6 Hz), 7.49–7.43 (m, 6H), 7.36 (t, 2H, J = 7.2 Hz), 7.28 (d, 2H, J = 8.6 Hz), 5.10 (s, OH).

³ Andrushko, V.; Schwinn, D.; Tzschucke, C. C.; Michalek, F.; Horn, J.; Mössner, C.; Bannwarth, W. *Helv. Chim. Acta* **2005**, *88*, 936–949.

⁴ Kumaraswamy, G.; Sastry, M. N. V.; Jena, N.; Kumar, K. R.; Vairamani, M. *Tetrahedron: Asymmetry* **2003**, *14*, 3797–3803.



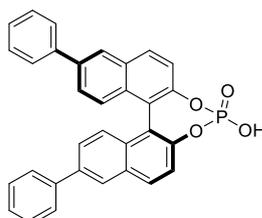
C₃₄H₂₆O₄
MW: 498.58

(S)-6,6'-Bis(4-methoxyphenyl)-1,1'-binaphthalene-2,2'-diol

The general procedure was followed using 4-methoxyphenylboronic acid (133 mg, 0.875 mmol). The product was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate (9:1) as eluent affording the product as a beige solid (138 mg, 77% yield).

$[\alpha]_D^{25} +158.4$ (*c* 0.98, CH₂Cl₂). mp 142–157 °C (dec.). IR 3514, 3403, 2954, 2834, 1607, 1517, 1500, 1286, 1177, 819 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 8.05 (d, 2H, *J* = 1.6 Hz), 8.03 (d, 2H, *J* = 9.2 Hz), 7.61 (d, 4H, *J* = 8.7 Hz), 7.56 (dd, 2H, *J* = 8.7 Hz, *J* = 1.6 Hz), 7.42 (d, 2H, *J* = 9.2 Hz), 7.25 (d, 2H, *J* = 8.7 Hz), 7.00 (d, 4H, *J* = 8.7 Hz), 5.08 (s, OH), 3.86 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ = 159.4 (2C), 152.8 (2C), 136.8 (2C), 133.5 (2C), 132.4 (2C), 131.8 (2C), 130.0 (2C), 128.4 (4C), 127.2 (2C), 125.8 (2C), 124.9 (2C), 118.3 (2C), 114.5 (4C), 110.9 (2C), 55.5 (2C).

General procedure for the synthesis of (S)-6,6'-diaryl-1,1'-binaphthalene-2,2'-diyl-hydrogen phosphate.^{1b} To a solution of (S)-6,6'-disubstituted-1,1'-binaphthalene-2,2'-diol (1 equiv, 0.5 M) in dry pyridine was added dropwise, at room temperature, a solution of distilled phosphorus oxychloride (2 equiv, 2 M) in dry pyridine. The mixture was stirred at 80 °C overnight then cooled to 40 °C before H₂O (55 equiv) and, after 10 min, 6 N HCl (23 equiv) were added dropwise. The resulting mixture was heated for 5 min at 100 °C and then cooled to 0 °C. 6 N HCl (1–2 mL) was added and the solid obtained was filtered off. The isolated solid was re-precipitated from EtOH/6 N HCl, washed with water and finally re-precipitated from CH₂Cl₂/hexane. The solid obtained was dried over P₂O₅ under vacuum at 70 °C for one night.

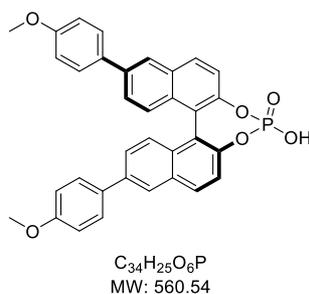


C₃₂H₂₁O₄P
MW: 500.49

(S)-6,6'-Bisphenyl-1,1'-binaphthyl-2,2'-diyl-hydrogen phosphate (7b)

The general procedure was followed using (S)-6,6'-diphenyl-1,1'-binaphthalene-2,2'-diol (100 mg, 0.23 mmol). The product was obtained as an off-white solid (71 mg, 61% yield).

$[\alpha]_D^{26} +321.2$ (*c* 0.34, CH₂Cl₂). mp 225–248 °C (dec.). IR 3062, 3027, 2924, 2854, 1594, 1491, 1228, 1212, 1023, 952, 893 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 8.43 (d, 2H, *J* = 1.6 Hz), 8.25 (d, 2H, *J* = 8.8 Hz), 7.84 (d, 4H, *J* = 7.7 Hz), 7.77 (dd, 2H, *J* = 9.2 Hz, *J* = 1.6 Hz), 7.58 (d, 2H, *J* = 9.2 Hz), 7.54–7.50 (m, 4H), 7.43–7.38 (m, 4H), 3.92 (br, OH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 148.0 (2C), 147.9 (2C), 139.3 (2C), 136.8 (2C), 131.4 (2C), 131.3 (2C), 130.9 (2C), 129.0 (4C), 127.7 (2C), 126.8 (4C), 125.9 (2C), 121.9 (2C), 121.0 (4C). ³¹P NMR (162 MHz, DMSO-*d*₆): δ = 2.88. HRMS (ESI-Orbitrap) *m/z*: [M + H]⁺ calcd for C₃₂H₂₂O₄P 501.1250, found 501.1231.



(S)-6,6'-Bis(4-methoxyphenyl)-1,1'-binaphthyl-2,2'-diyl-hydrogenphosphate (7c)

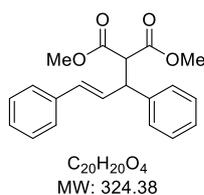
The general procedure was followed using (S)-6,6'-bis(4-methoxyphenyl)-1,1'-binaphthalene-2,2'-diol (192 mg, 0.39 mmol). The product was obtained as a beige solid (138 mg, 64% yield).

$[\alpha]_D^{26} +253.2$ (*c* 1, CH₂Cl₂). mp 229–242 °C (dec.). IR 3033, 2933, 2834, 1608, 1518, 1498, 1242, 1179, 1025, 953, 819 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 8.35 (s, 2H), 8.22 (d, 2H, *J* = 8.9 Hz), 7.77 (d, 4H, *J* = 8.6 Hz), 7.72 (dd, 2H, *J* = 8.9 Hz, *J* = 1.6 Hz), 7.56 (d, 2H, *J* = 8.9 Hz), 7.34 (d, 2H, *J* = 8.9 Hz), 7.06 (d, 4H, *J* = 8.6 Hz), 3.81 (s, 6H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 159.1 (2C), 147.8, 147.7, 136.4 (2C), 131.5 (4C), 131.0 (2C), 130.5 (2C), 127.9 (4C), 126.8 (2C), 125.6 (2C), 124.9 (2C), 121.8 (2C), 121.0 (2C), 114.5 (4C), 55.2 (2C). ³¹P NMR (162 MHz, DMSO-*d*₆): δ = 3.20. HRMS (ESI-Orbitrap) *m/z*: [M + H]⁺ calcd for C₃₄H₂₆O₆P 561.1462, found 561.1445.

3. Allylic alkylations

General procedure for asymmetric allylic substitution using the flexible cofactor-based ligand 1

[Pd(allyl)Cl]₂ (0.0014 mmol, 0.5 mg, 5 mol %), ligand **1** (0.0031 mmol, 4.2 mg, 5.5 mol %), chiral cofactor (0.0495 mmol, 0.9 equiv), and distilled DIPEA (0.0371 mmol, 7 μ L, 0.7 equiv) were dissolved in dry and degassed CH₂Cl₂ or THF (0.3 mL) under N₂ (glovebox) and the solution was stirred for 5 min at room temperature. A solution of the appropriate allylic carbonate (0.055 mmol, 1 equiv) in dry and degassed THF (0.3 mL) was then added to the catalyst solution. The appropriate nucleophile (3 equiv), dissolved in dry and degassed THF (0.4 mL), was added in one portion or dropwise (100 μ L/h) to the catalyst/substrate mixture at room temperature under N₂ atmosphere. After completion of the reaction, 1-methoxynaphthalene (internal standard, 0.055 mmol, 8 μ L, 1 equiv) was added and the reaction mixture was transferred to a separation funnel. CH₂Cl₂ and saturated aqueous NH₄Cl solution were added and the two phases were separated. The aqueous phase was extracted twice with Et₂O and then the combined organic phases were dried over MgSO₄ and the solvent evaporated. The product was analysed by ¹H NMR and chiral HPLC or GC.

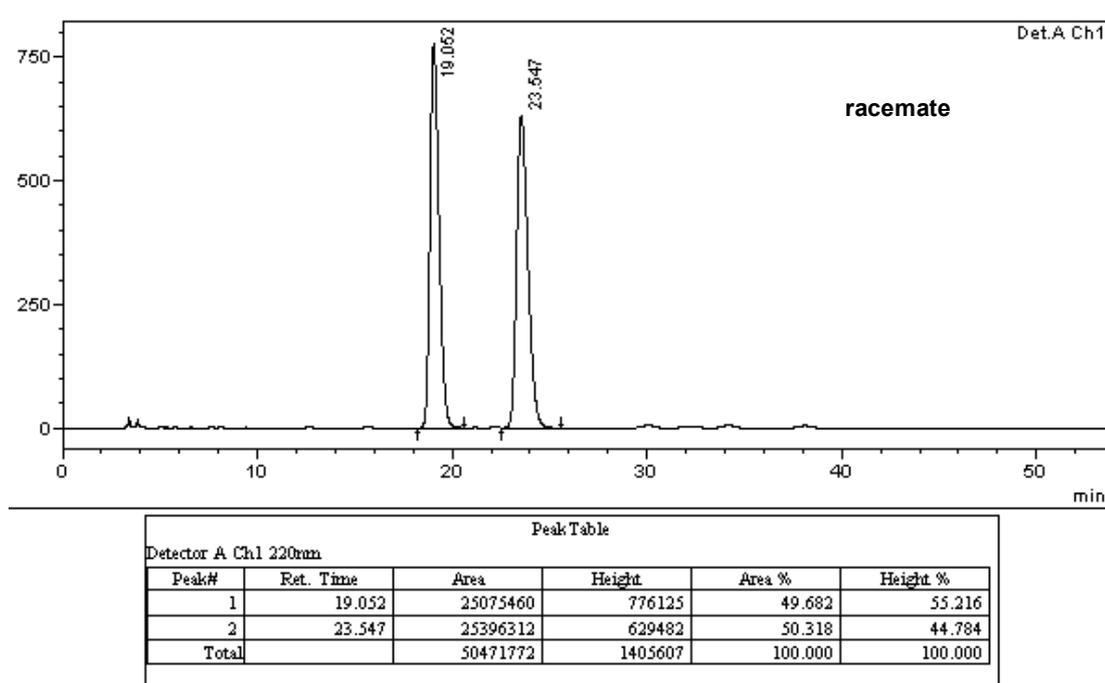


(S)-Dimethyl (E)-2-(1,3-diphenylallyl)malonate (5)

The general procedure was followed using (S)-2-hydroxy-3-methylbutyric acid (5.8 mg) in THF, (E)-1,3-diphenylallyl methyl carbonate (14.8 mg), and dimethyl malonate (23 μ L, 0.2 mmol, 3.6 equiv)/NaH 60% in mineral oil (6.7 mg, 0.167 mmol, 3 equiv) as the nucleophile which was added dropwise to the catalyst/substrate mixture during 4 h. The reaction mixture was stirred for another 0.5 h before the

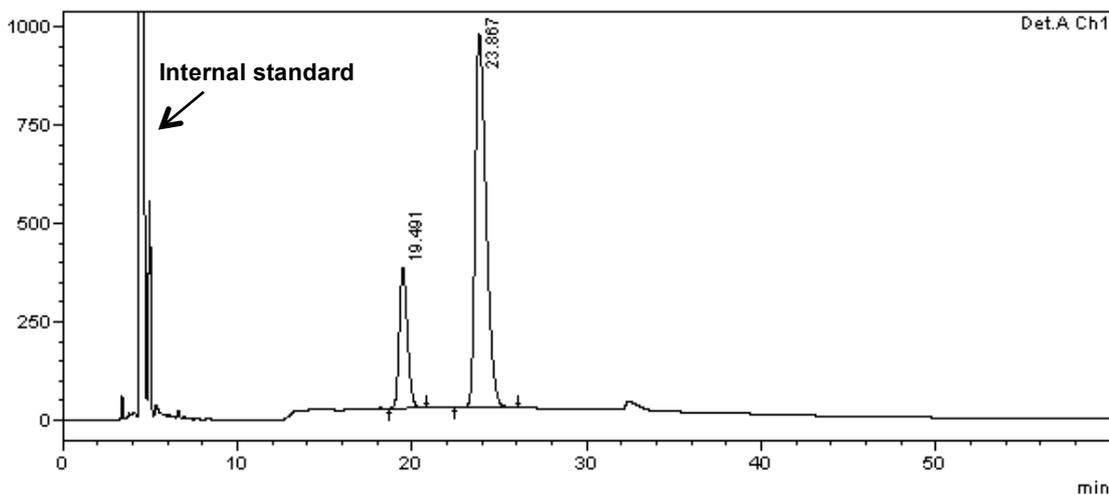
reaction was quenched. Compound **x** was obtained in 97% yield (determined by ^1H NMR using 1-methoxynaphthalene as internal standard) with 57% ee.

^1H NMR (400 MHz, CDCl_3): δ = 7.33–7.19 (m, 10H), 6.48 (d, 1H, J = 15.8 Hz), 6.32 (dd, 1H, J = 15.8 Hz, J = 8.4 Hz), 4.26 (dd, 1H, J = 10.8 Hz, J = 8.7 Hz), 3.95 (d, 1H, J = 10.8 Hz), 3.70 (s, 3H), 3.52 (s, 3H).⁵ HPLC (Daicel Chiralcel OD-H, hexanes/2-propanol 99:1, 0.5 mL/min, detection at 220 nm): t_R (minor) 24.9 min (*R*), t_R (major) 26.5 min (*S*). HPLC (Daicel Chiralpak IC, hexane/2-propanol 99:1, 1 mL/min, detection at 220 nm): t_R (minor) 19.5 min (*R*), t_R (major) 23.9 min (*S*). The absolute configuration was determined by comparison of the retention times of the enantiomers with literature data.⁶

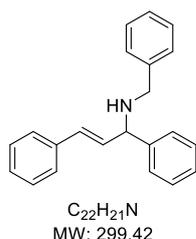


⁵ Coll, M.; Pàmies, O.; Diéguez, M. *Org. Lett.* **2014**, *16*, 1892–1895.

⁶ Nemoto, T.; Masuda, T.; Matsumoto, T.; Hamada, Y. *J. Org. Chem.* **2005**, *70*, 7172–7178.



PeakTable					
Detector A Ch1 220nm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.491	11414814	354757	21.739	27.170
2	23.867	41092620	950915	78.261	72.830
Total		52507434	1305671	100.000	100.000

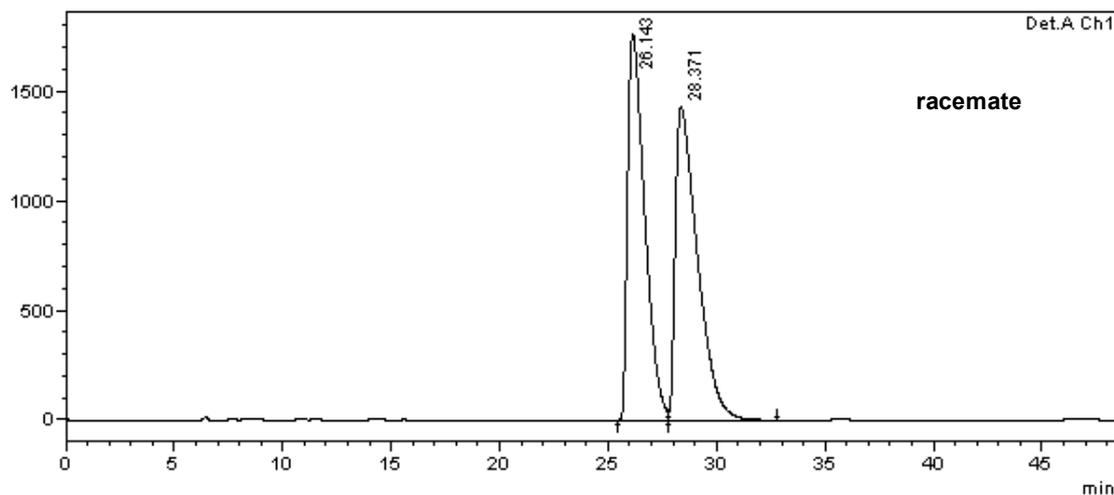


(*E*)-*N*-Benzyl-1,3-diphenylprop-2-en-1-amine (10)

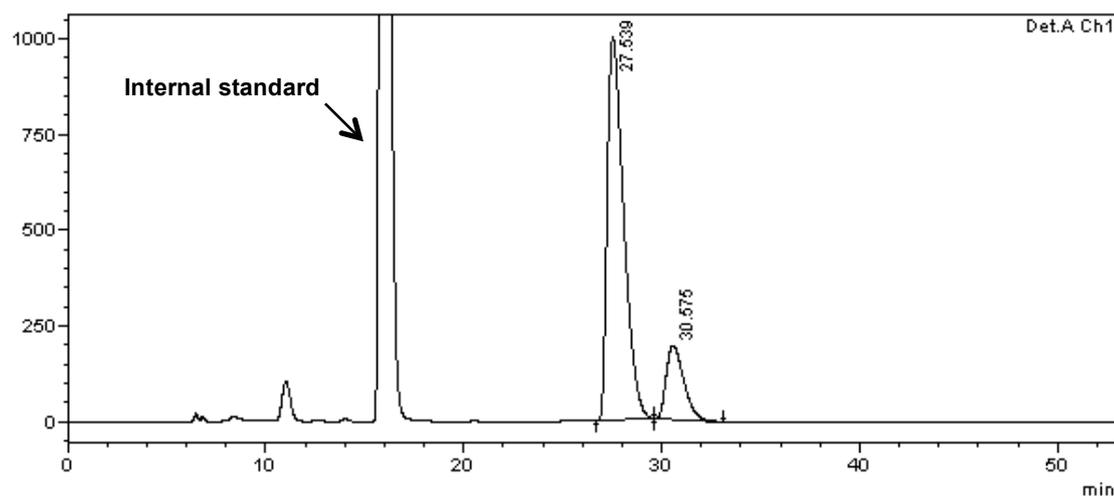
The general procedure was followed using (*S*)-2-hydroxy-3-methylbutyric acid (5.8 mg) in THF, (*E*)-1,3-diphenylallyl methyl carbonate (14.8 mg), and benzylamine (18 μ L, 0.167 mmol, 3 equiv) as the nucleophile which was added in one portion to the catalyst/substrate mixture. The reaction mixture was stirred for 0.5 h before the reaction was quenched. Compound **x** was obtained in 85% yield (determined by 1H NMR using 1-methoxynaphtalene as internal standard) with 65% ee.

1H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.18 (m, 15H), 6.58 (d, 1H, J = 16.5 Hz), 6.32 (dd, 1H, J = 16.5 Hz, J = 7.2 Hz), 4.40 (d, 1H, J = 7.2 Hz), 3.79 (d, 2H, J = 4 Hz).⁷ HPLC (Daicel Chiralcel OD-H, hexanes/2-propanol 99.7:0.3, 0.5 mL/min, detection at 220 nm): t_R (major) 27.5 min (*R*), t_R (minor) 30.6 min (*S*). The absolute configuration was determined by comparison of the retention times of the enantiomers with literature data.⁵

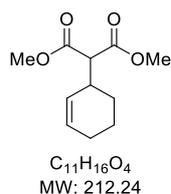
⁷ Fukuzawa, S.-i.; Yamamoto, M.; Hosaka, M.; Kikuchi, S. *Eur. J. Org. Chem.* **2007**, 5540–5545.



PeakTable					
Detector A Ch1 220nm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.143	97054252	1763072	48.753	55.238
2	28.371	102018786	1428699	51.247	44.762
Total		199073038	3191771	100.000	100.000



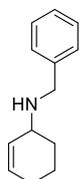
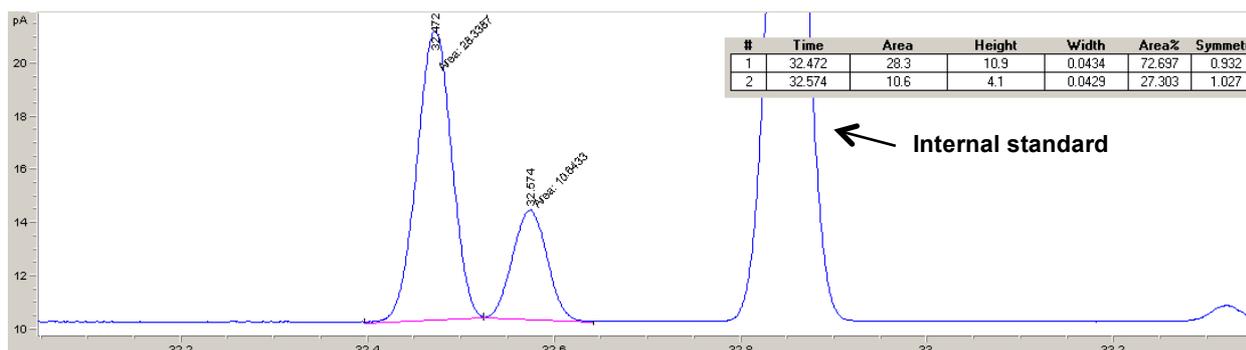
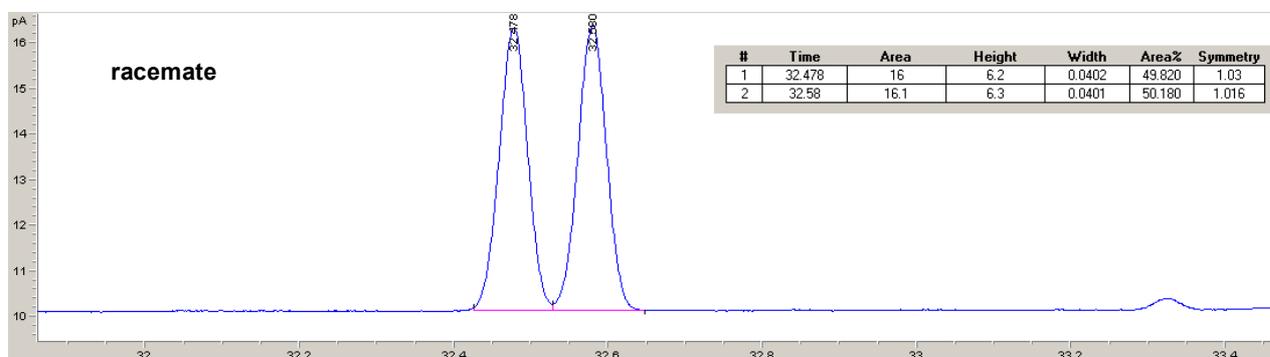
PeakTable					
Detector A Ch1 220nm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.539	57877125	1000844	82.740	83.798
2	30.575	12073103	193511	17.260	16.202
Total		69950229	1194355	100.000	100.000



Dimethyl 2-(cyclohex-2-en-1-yl)malonate (9)

The general procedure was followed using (*R*)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (17.2 mg) in CH_2Cl_2 , cyclohex-2-en-1-yl methyl carbonate (8.6 mg), and dimethyl malonate (23 μ L, 0.2 mmol, 3.6 equiv)/NaH 60% in mineral oil (6.7 mg, 0.167 mmol, 3 equiv) as the nucleophile which was added dropwise to the catalyst/substrate mixture during 4 h. The reaction mixture was stirred for another 0.5 h before the reaction was quenched. Compound **x** was obtained in 73% yield (determined by 1H NMR using 1-methoxynaphthalene as internal standard) with 43% ee.

^1H NMR (400 MHz, CDCl_3): δ = 5.80–5.76 (m, 1H), 5.45–5.51 (m, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.28 (d, 1H, J = 9.5 Hz), 2.94–2.87 (m, 1H), 2.00–1.97 (m, 2H), 1.81–1.67 (m, 2H), 1.61–1.51 (m, 1H), 1.40–1.33 (m, 1H).⁸ GC (CYCLOSIL-B): t_R (major) 32.5 min (*R*), t_R (minor) 32.6 min (*S*). The absolute configuration was determined by comparison of the optical rotation of the scalemic mixture obtained with literature data.⁸

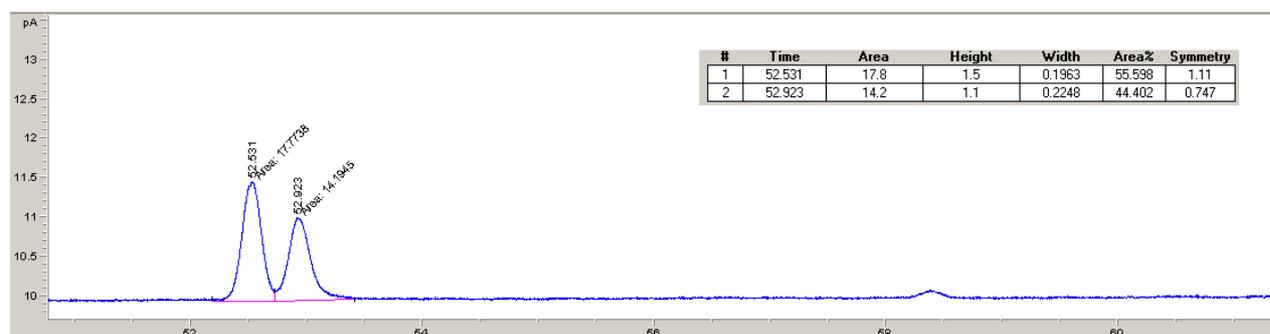
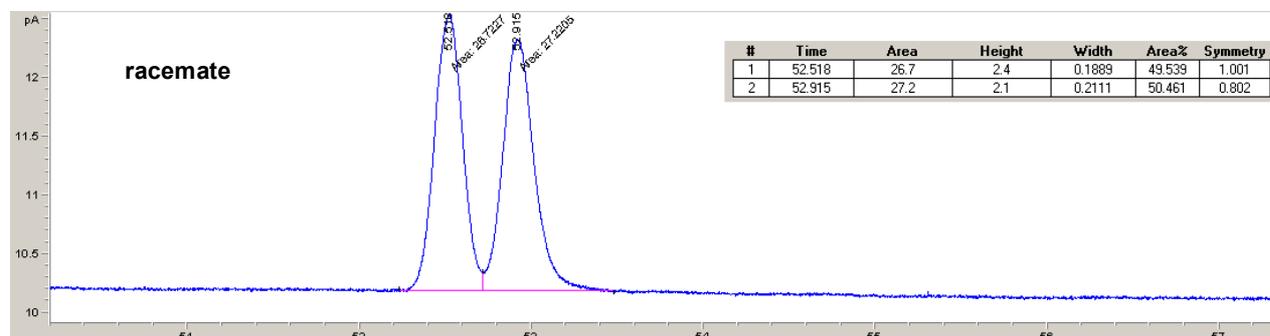


***N*-Benzylcyclohex-2-en-1-amine (11)**

The general procedure was followed using (*R*)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (17.2 mg) in CH_2Cl_2 , cyclohex-2-en-1-yl methyl carbonate (8.6 mg), and benzylamine (18 μL , 0.167 mmol, 3 equiv) as the nucleophile which was added dropwise to the catalyst/substrate mixture during 4 h. The reaction mixture was stirred for another 0.5 h before the reaction was quenched. Compound **x** was obtained in 85% yield (determined by ^1H NMR using 1-methoxynaphthalene as internal standard) with 11% ee.

⁸ Bergner, Eike J.; Helmchen, G. *Eur. J. Org. Chem.* **2000**, 419–423.

^1H NMR (400 MHz, CDCl_3): δ = 7.37–7.22 (m, 5H), 5.80–5.72 (m, 2H), 3.85 (m, 2H), 3.24 (m, 1H), 2.02–1.88 (m, 3H), 1.78–1.74 (m, 1H), 1.57–1.49 (m, 2H).⁹ GC/FID (CYCLOSIL-B): t_{R} (major) 52.5 min (*S*), t_{R} (minor) 52.9 min (*R*). The absolute configuration was determined by comparison of the optical rotation of the scalemic mixture obtained with literature data.⁹



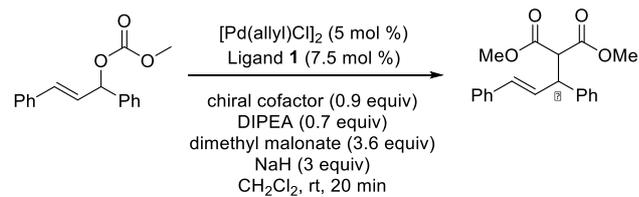
Control experiment using ligand 12

The general procedure was followed using the silver salt of chiral cofactor **7a** in place of the phosphate and DIPEA, and ligand **12** in place of ligand **1**.

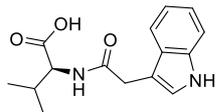
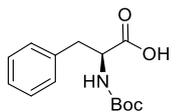
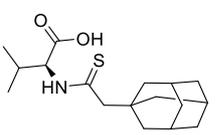
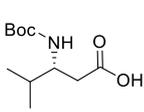
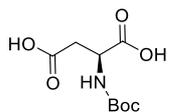
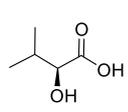
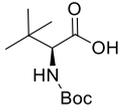
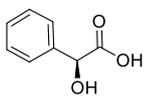
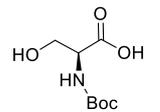
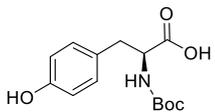
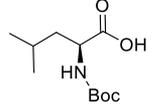
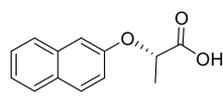
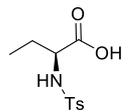
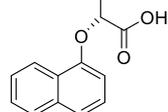
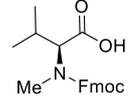
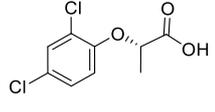
4. Screening of cofactors for the asymmetric allylic alkylation

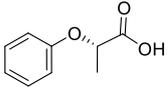
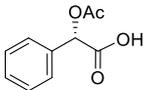
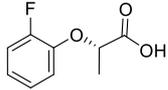
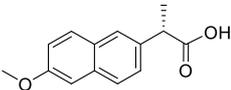
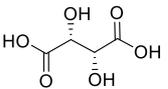
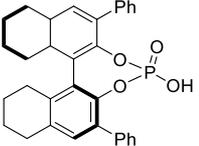
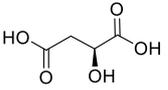
Screening of cofactors was performed using a modified procedure for the asymmetric allylic substitution. The reaction was run in CH_2Cl_2 and the catalyst/allylic substrate solution was added in one portion to the nucleophile solution at room temperature. Full conversions were observed within 20 min in all experiments (except for entry 5).

⁹ Evans, D. A.; Campos, K. R.; Tedrow, J. S.; Michael, F. E.; Gagné, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 7905–7920.



Entry	Chiral cofactor	ee %	Entry	Chiral cofactor	ee %
1		4	8		1
2		1	9		10 (<i>S</i>)
3		5 (<i>R</i>)	10		9 (<i>R</i>)
4		1	11		2
5		n.r.	12		3
6		1	13		2
7		2	14		8 (<i>R</i>)

Entry	Chiral cofactor	ee %	Entry	Chiral cofactor	ee %
15		3	23		2
16		0	24		21 (<i>R</i>)
17		2	25		34 (<i>S</i>)
18		5 (<i>S</i>)	26		10 (<i>R</i>)
19		1	27		1
20		2	28		6 (<i>S</i>)
21		1	29		5 (<i>R</i>)
22		9 (<i>R</i>)	30		9 (<i>R</i>)

Entry	Chiral cofactor	ee %	Entry	Chiral cofactor	ee %
31		8 (<i>R</i>)	35		8 (<i>R</i>)
32		11 (<i>R</i>)	36		10 (<i>S</i>)
33		1	37		0
34		1			

5. NMR study

- Variable temperature NMR experiments of ligand 1

In the glovebox, ligand **1** (13.4 mg, 0.01 mmol) was dissolved in dry and degassed CD_2Cl_2 (0.5 mL) and transferred to an NMR tube for ^1H and ^{31}P NMR analyses.

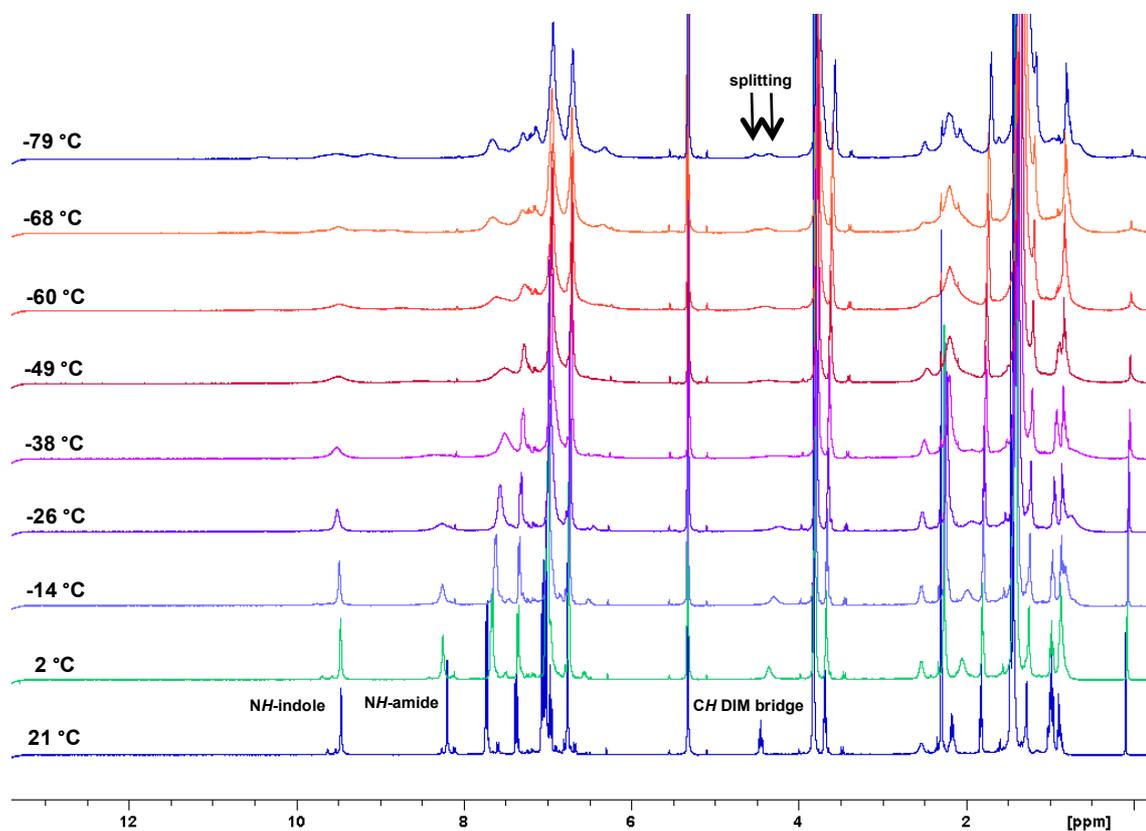


Figure S1. ^1H NMR spectra of ligand **1** at various temperatures in CD_2Cl_2 (400 MHz).

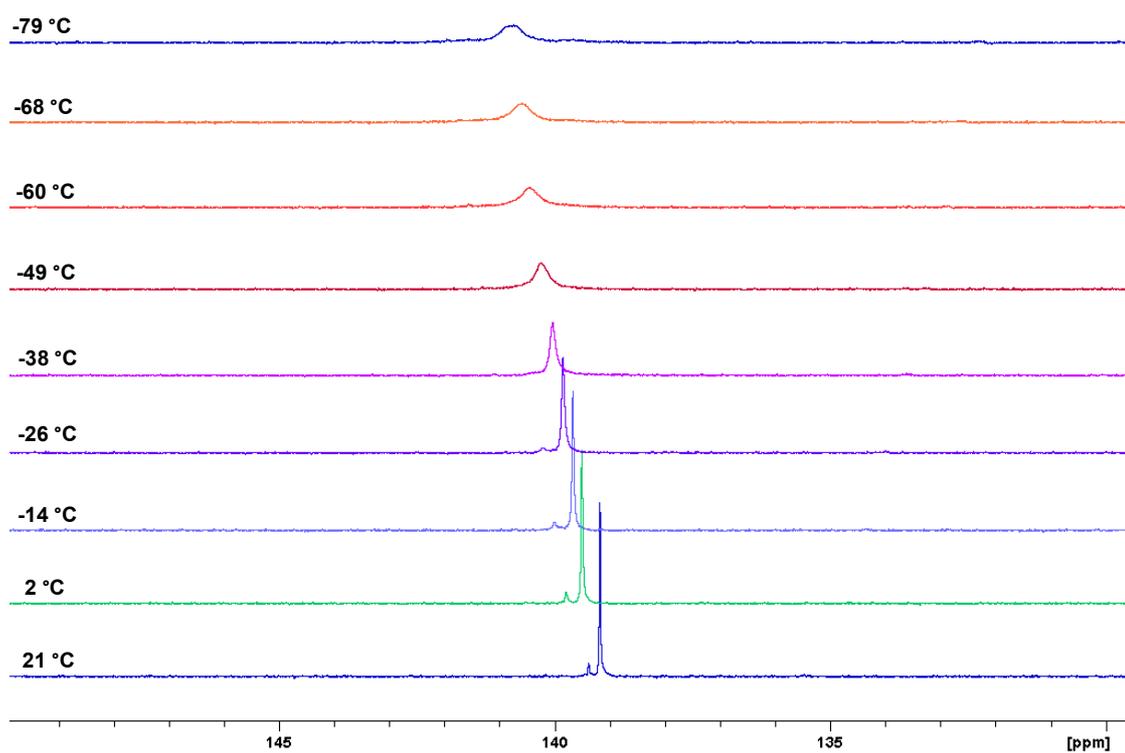


Figure S2. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of ligand **1** at various temperatures in CD_2Cl_2 (162 MHz).

- Binding study of chiral cofactor anions in the DIM pocket of ligand 1

In the glovebox, ligand **1** (6.7 mg, 0.005 mmol, 1 equiv) and a chiral cofactor (1.1 equiv) were mixed in dry and degassed CD_2Cl_2 (0.5 mL) and DIPEA (3 equiv) was added. The mixture was stirred for 30 min before being transferred to an NMR tube for ^1H and ^{31}P NMR analyses.

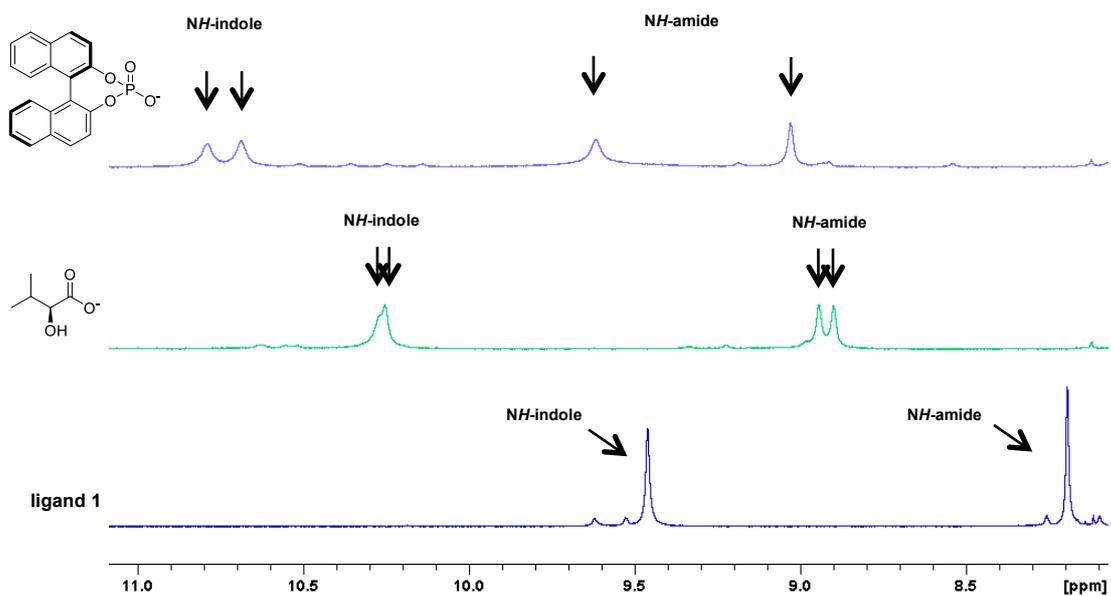


Figure S3. ^1H NMR (NH signals) spectra of ligand **1** in the presence of a chiral cofactor and DIPEA in CD_2Cl_2 (400 MHz).

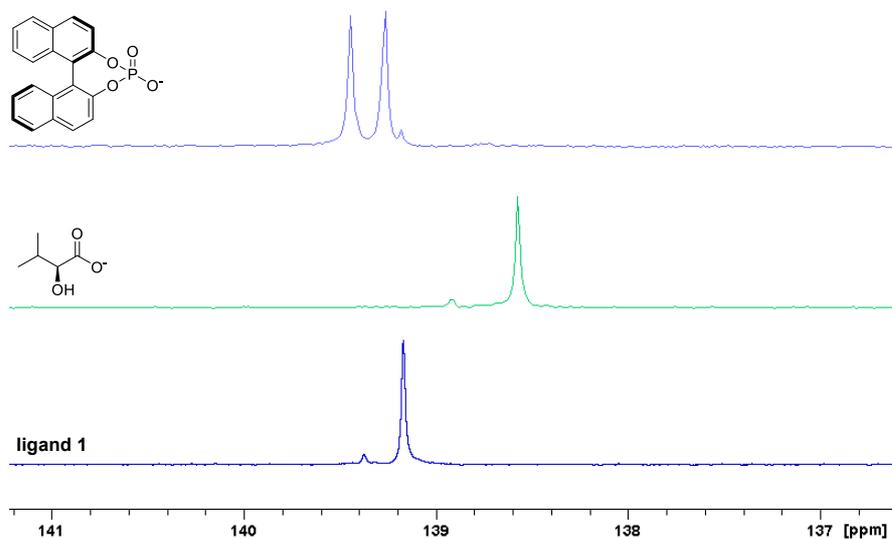


Figure S4. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of ligand **1** in the presence of a chiral cofactor and DIPEA in CD_2Cl_2 (162 MHz).

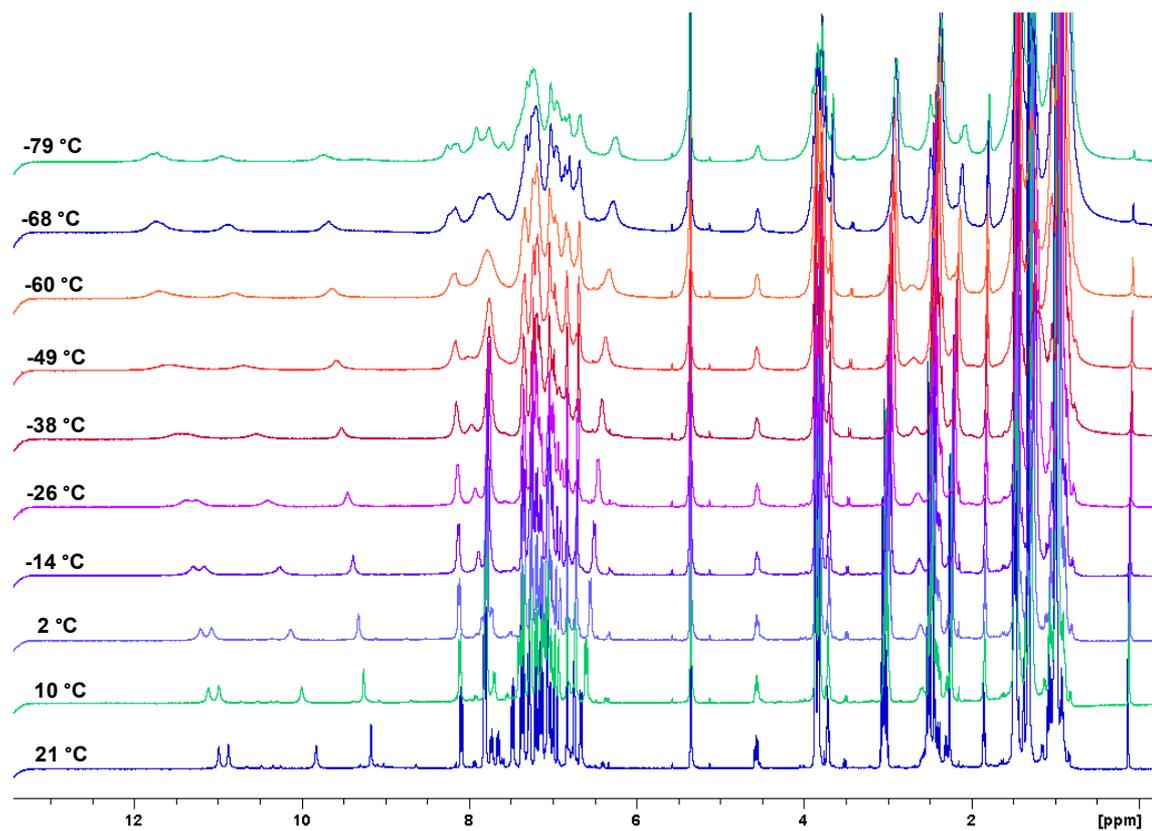


Figure S5. ¹H NMR spectra of ligand **1** in the presence of (*R*)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (**7a**) and DIPEA at various temperatures in CD₂Cl₂ (400 MHz). The general procedure was followed using 0.01 mmol of ligand **1**.

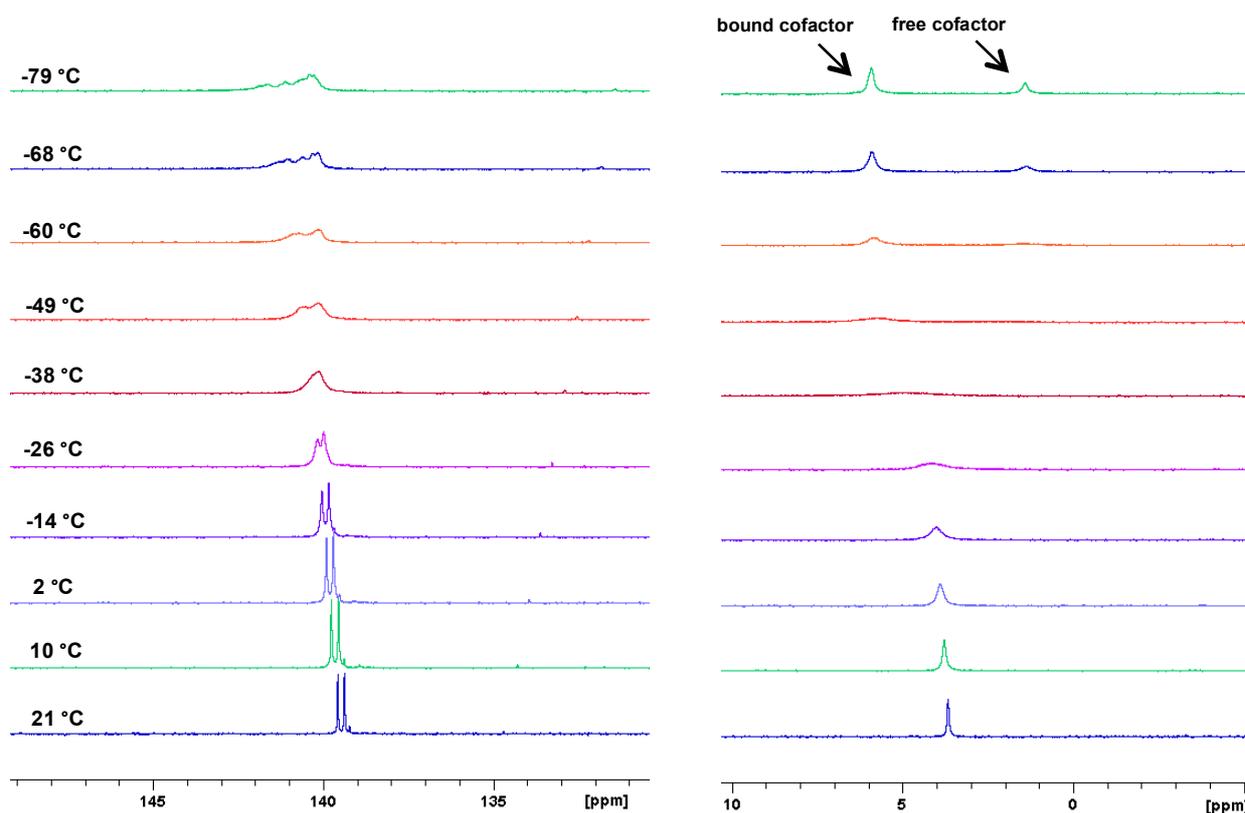


Figure S6. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of ligand **1** in the presence of (*R*)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (**7a**) and DIPEA at various temperatures in CD_2Cl_2 (162 MHz). The general procedure was followed using 0.01 mmol of ligand **1**.

- Preparation of palladium(0)/olefin complexes of PPh_3 -ligand **13 with acetate as the cofactor.**

Using Schlenk technique, PPh_3 ligand (9.1 mg, 0.01 mmol, 1 equiv), $\text{Pd}_2\text{dba}_3\cdot\text{CHCl}_3$ (5.2 mg, 0.005 mmol, 1 equiv), olefin (1.3–1.4 equiv), and acetic acid/DIPEA solution (1:1.5, 0.2 M) in CH_2Cl_2 (50 μL , 0.01 mmol, 1 equiv) were mixed in dry and degassed CD_2Cl_2 (0.5 mL). The mixture was stirred for 30 min before being transferred to an NMR tube for ^1H and ^{31}P NMR analyses.

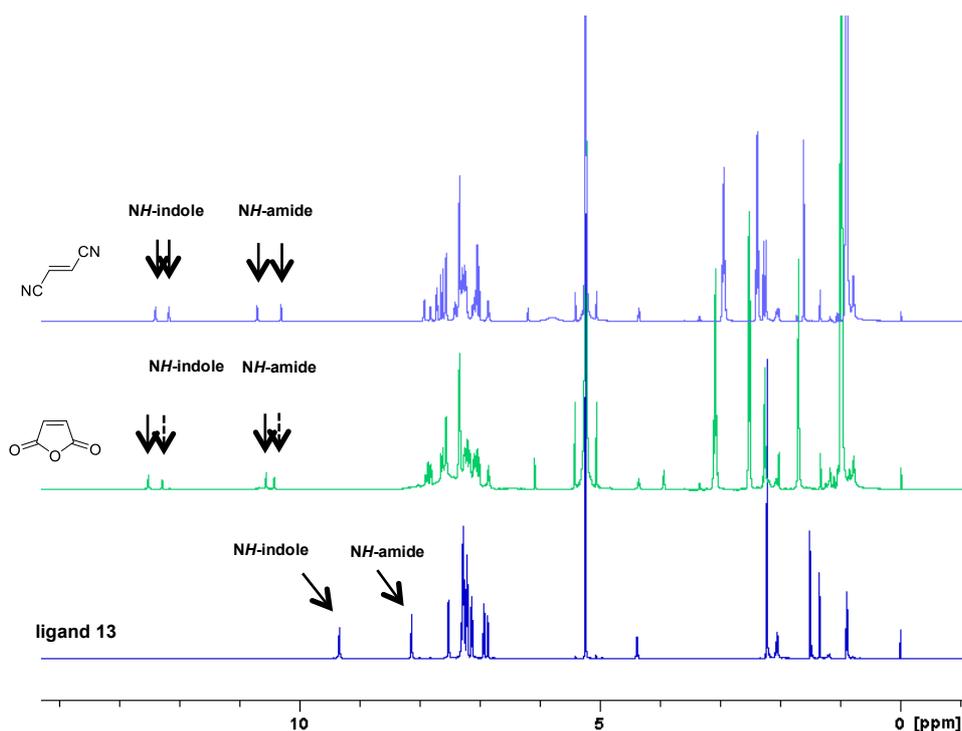


Figure S7. ^1H NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{13}]$ and $[\text{Pd}(\text{maleic anhydride})\mathbf{13}]$ complexes in the presence of acetic acid and DIPEA in CD_2Cl_2 (500 MHz).

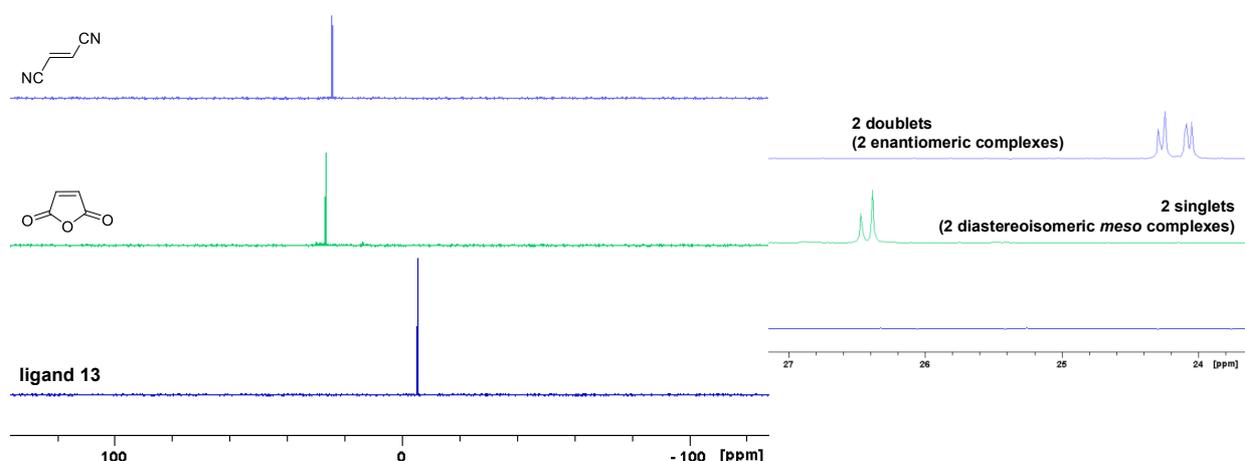


Figure S8. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{13}]$ and $[\text{Pd}(\text{maleic anhydride})\mathbf{13}]$ complexes in the presence of acetic acid and DIPEA in CD_2Cl_2 (202 MHz).

- Preparation of palladium(0)/olefin complexes of ligand 1 with various cofactors

In the glovebox or using Schlenk technique, ligand **1** (6.7 mg, 0.005 mmol, 1 equiv), $\text{Pd}_2\text{dba}_3\cdot\text{CHCl}_3$ (2.6 mg, 0.0025 mmol, 1 equiv), olefin (~7 equiv), and cofactor (1.1 equiv) were mixed in dry and degassed CD_2Cl_2 (0.5 mL) and DIPEA (3 equiv) was added (in a few cases DIPEA was added before the solubilisation of other compounds in the solvent). The mixture was stirred for 30 min before being transferred to an NMR tube for ^1H and ^{31}P NMR analyses.

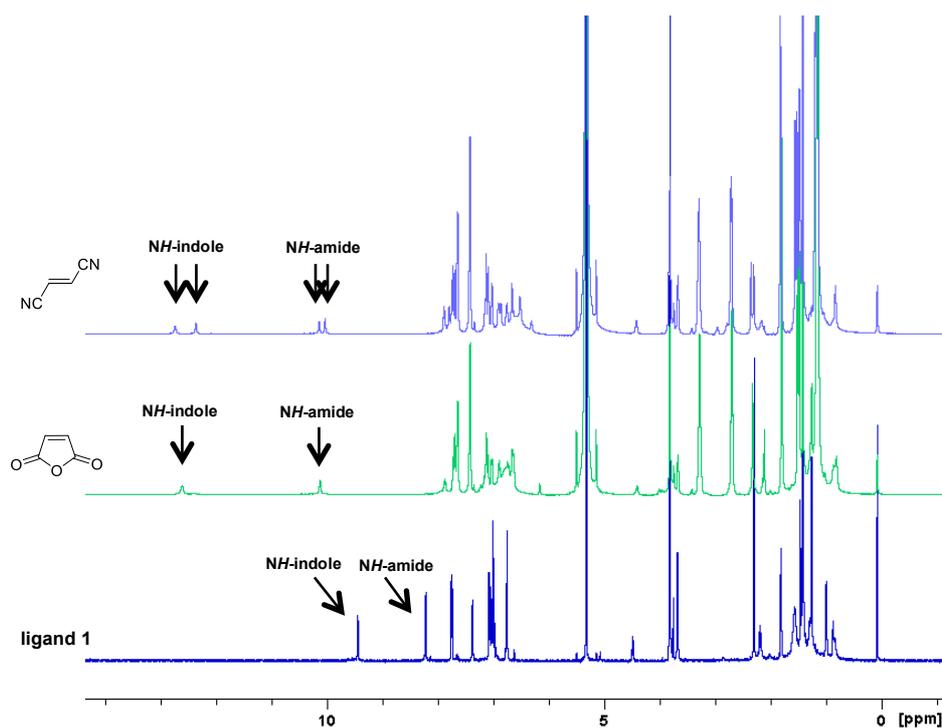


Figure S9. ^1H NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ and $[\text{Pd}(\text{maleic anhydride})\mathbf{1}]$ complexes in the presence of acetic acid and DIPEA in CD_2Cl_2 (500 MHz). The general procedure was followed using 0.01 mmol of ligand **1** and 1.1–1.2 equiv of olefin.

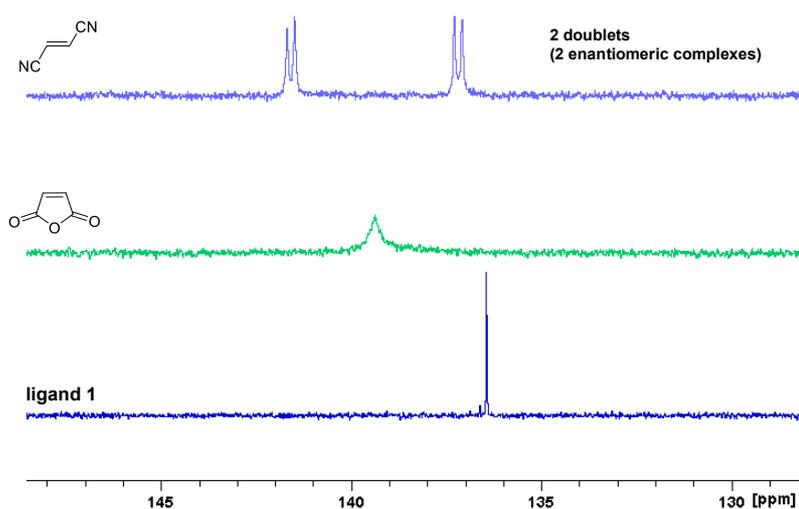


Figure S10. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ and $[\text{Pd}(\text{maleic anhydride})\mathbf{1}]$ complexes in the presence of acetic acid and DIPEA in CD_2Cl_2 (202 MHz). The general procedure was followed using 0.01 mmol of ligand **1** and 1.1–1.2 equiv of olefin.

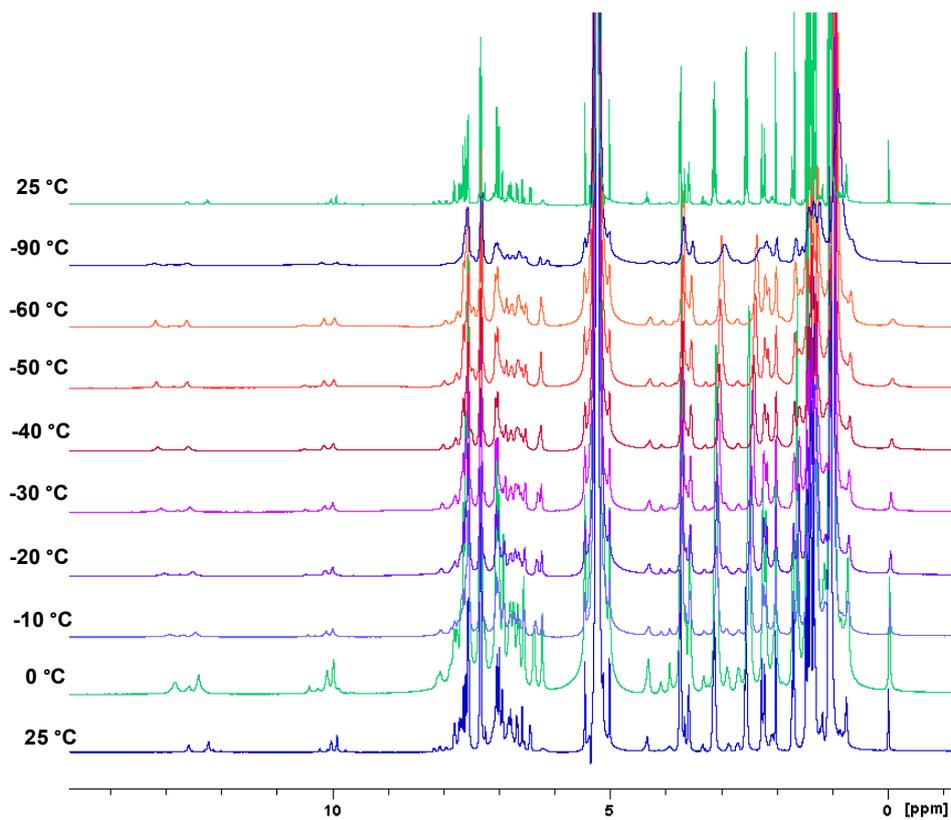


Figure S11. ¹H NMR spectra of the [Pd(fumaronitrile)1] complex in the presence of acetic acid and DIPEA at various temperatures in CD₂Cl₂ (400 MHz). The general procedure was followed using 0.015 mmol of ligand **1** and 1.1–1.2 equiv of olefin.

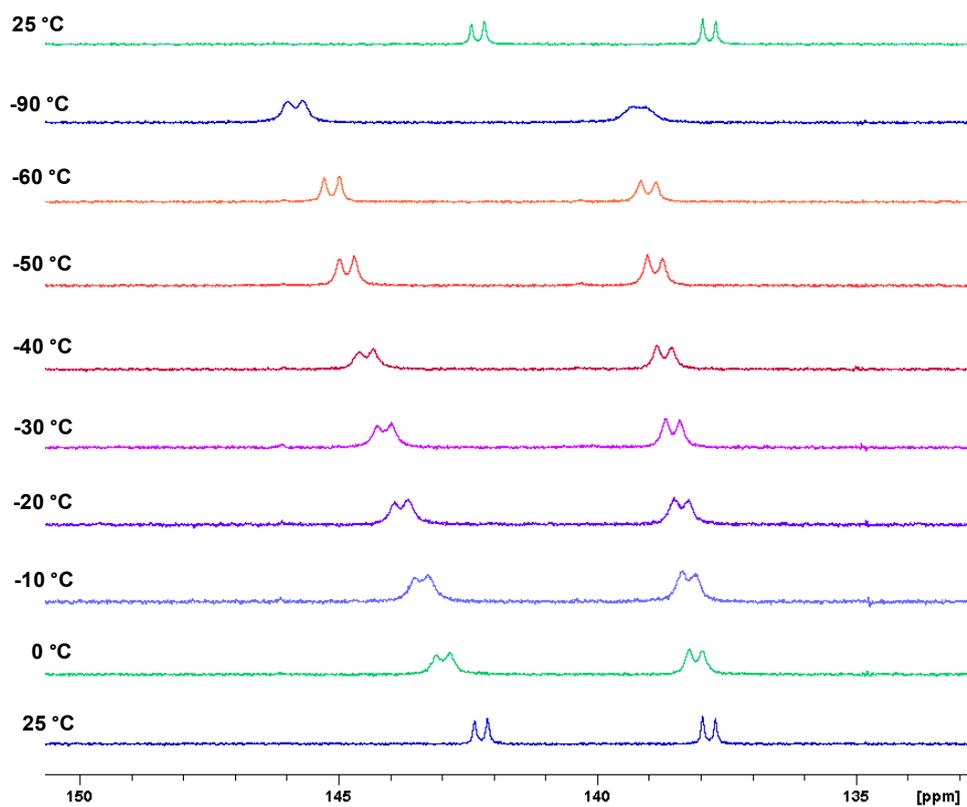


Figure S12. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the [Pd(fumaronitrile)1] complex in the presence of acetic acid and DIPEA at various temperatures in CD_2Cl_2 (162 MHz). The general procedure was followed using 0.015 mmol of ligand **1** and 1.1–1.2 equiv of olefin.

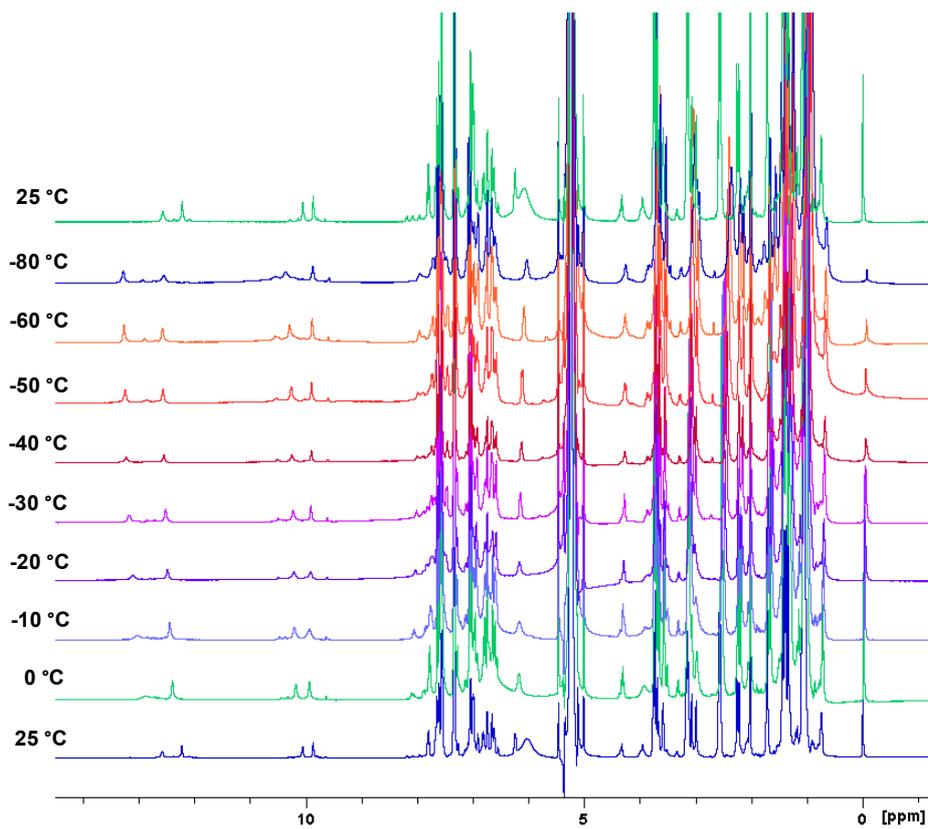


Figure S13. ¹H NMR spectra of the [Pd(dimethyl fumarate)1] complex in the presence of acetic acid and DIPEA at various temperatures in CD₂Cl₂ (400 MHz). The general procedure was followed using 0.015 mmol of ligand **1** and 1.1–1.2 equiv of olefin.

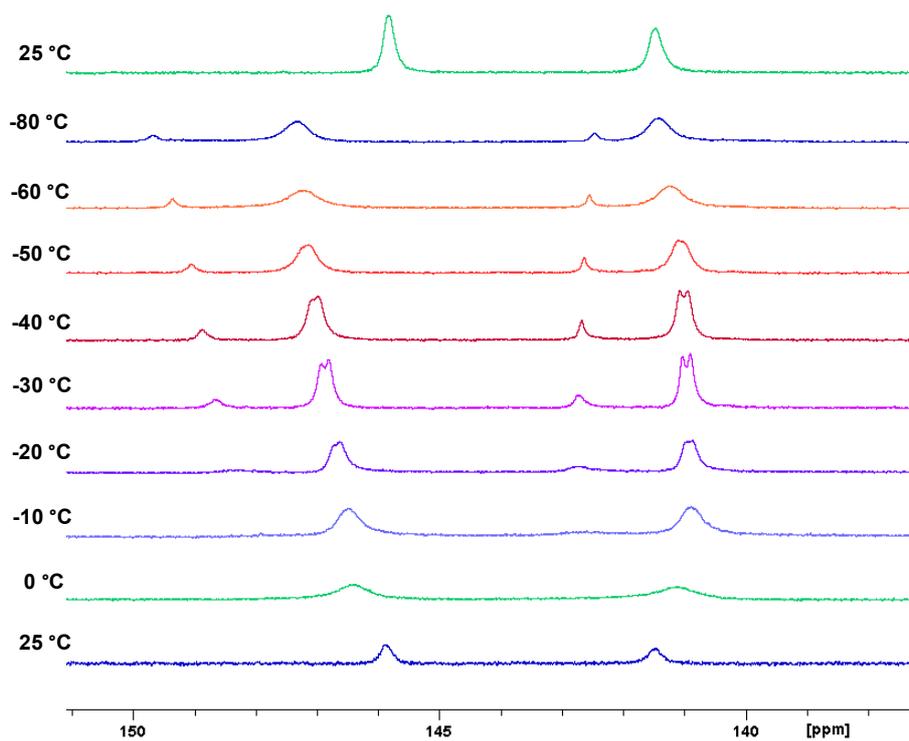


Figure S14. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the [Pd(dimethyl fumarate)**1**] complex in the presence of acetic acid and DIPEA at various temperatures in CD_2Cl_2 (162 MHz). The general procedure was followed using 0.015 mmol of ligand **1** and 1.1–1.2 equiv of olefin.

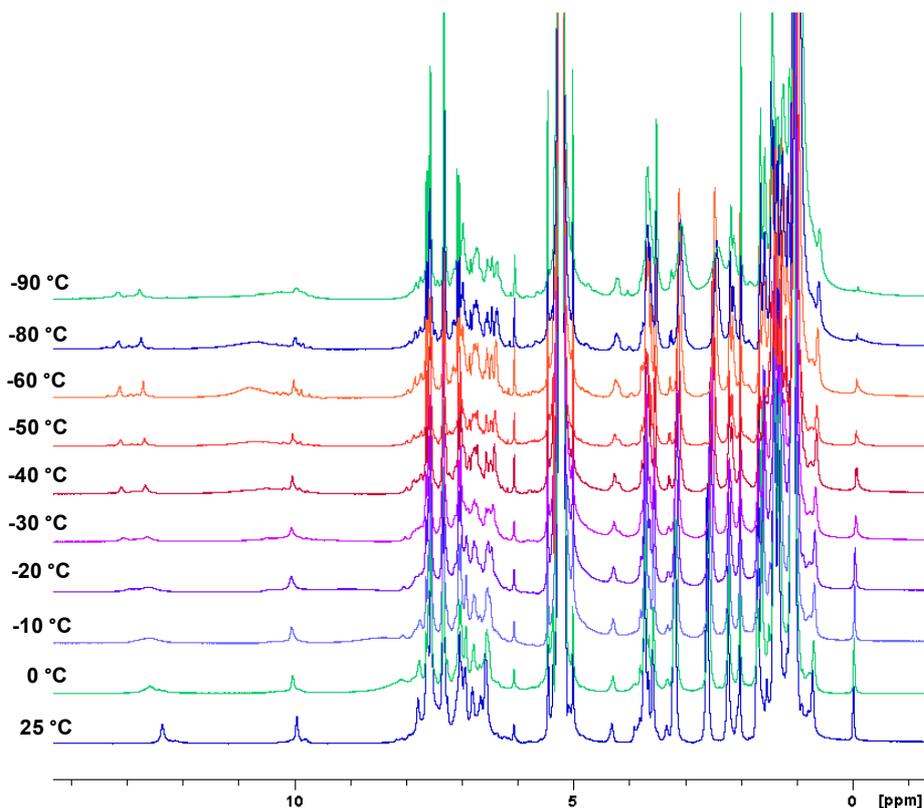


Figure S15. ^1H NMR spectra of the $[\text{Pd}(\text{maleic anhydride})\mathbf{1}]$ complex in the presence of acetic acid and DIPEA at various temperatures in CD_2Cl_2 (400 MHz). The general procedure was followed using 0.015 mmol of ligand **1** and 1.1–1.2 equiv of olefin.

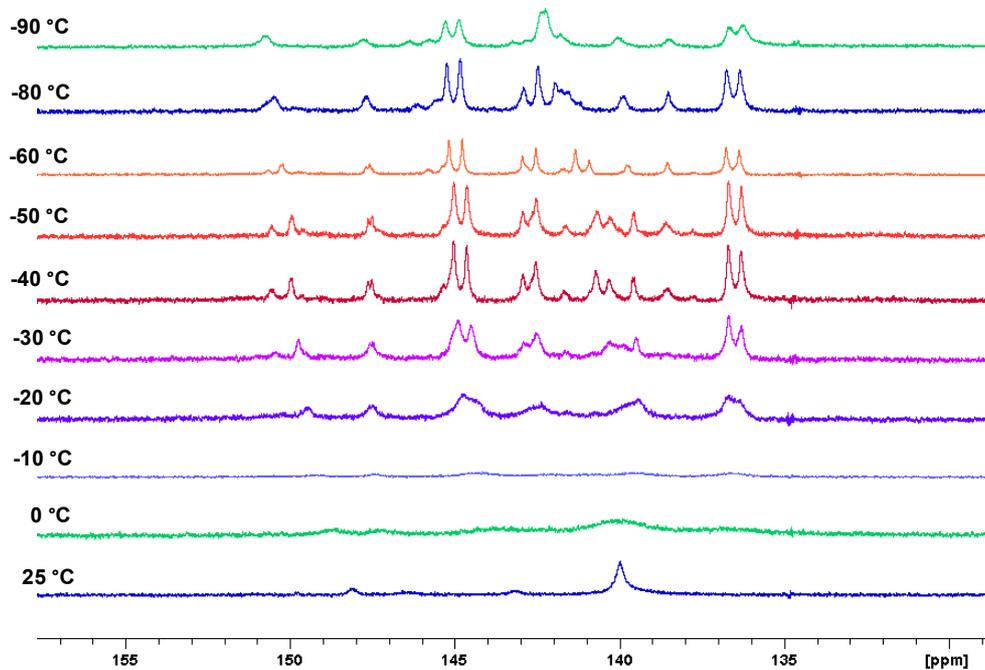


Figure S16. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{maleic anhydride})\mathbf{1}]$ complex in the presence of acetic acid and DIPEA at various temperatures in CD_2Cl_2 (162 MHz). The general procedure was followed using 0.015 mmol of ligand **1** and 1.1–1.2 equiv of olefin.

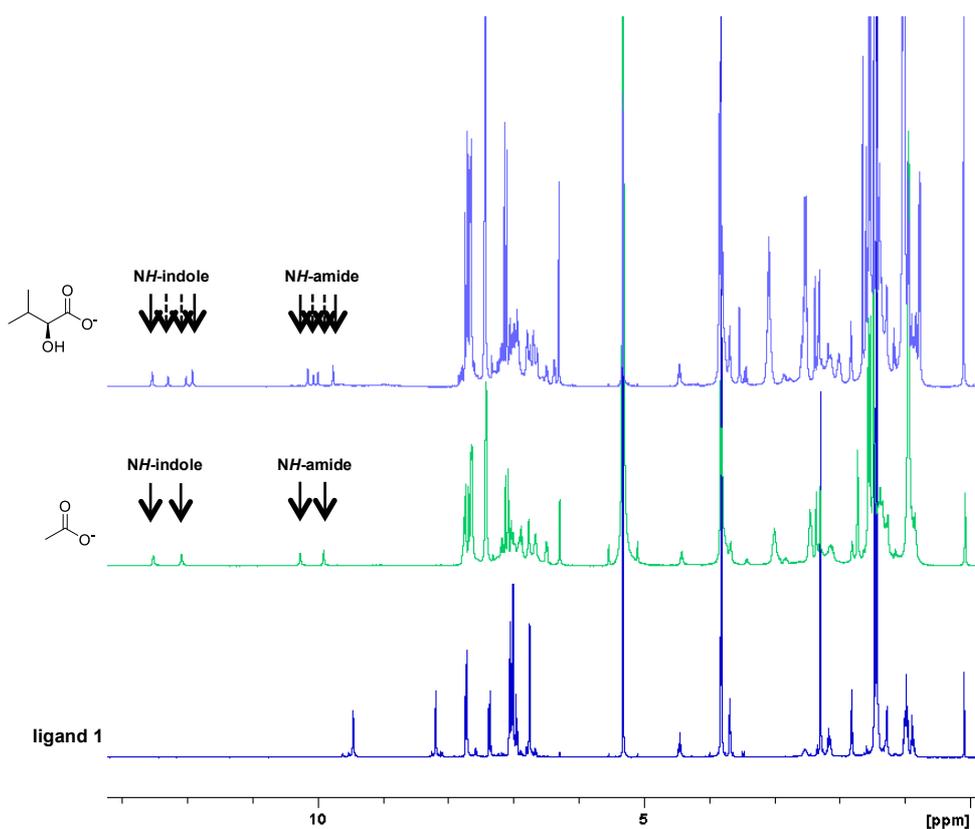


Figure S17. ¹H NMR spectra of the [Pd(fumaronitrile)1] complex in the presence of acetic acid or (*S*)-2-hydroxy-3-methylbutyric acid (**6**) and DIPEA in CD₂Cl₂ (400 MHz). For the preparation of sample containing (*S*)-2-hydroxy-3-methylbutyric acid, the general procedure was followed using 0.01 mmol of ligand **1**.

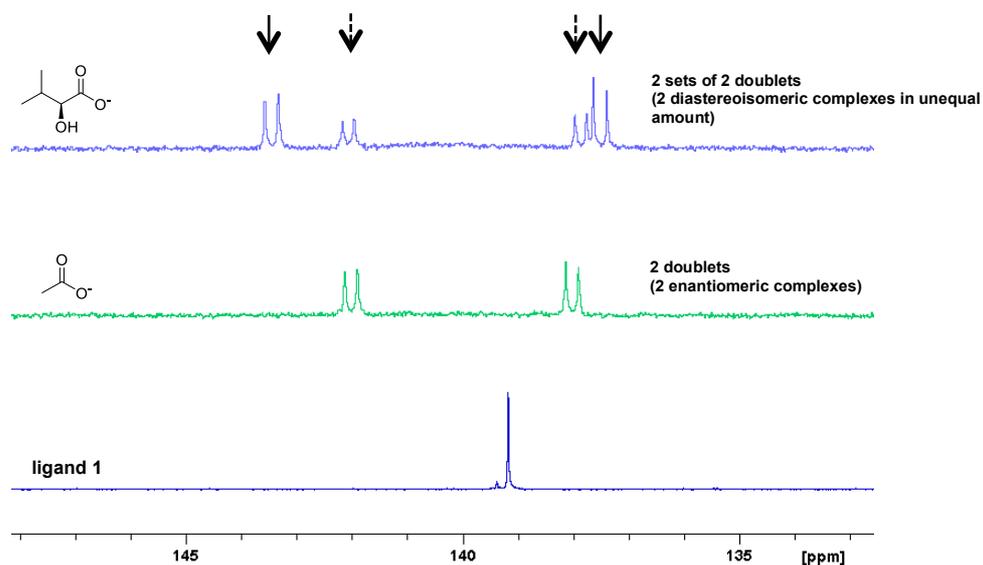


Figure S18. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of acetic acid or (*S*)-2-hydroxy-3-methylbutyric acid (**6**) and DIPEA in CD_2Cl_2 (162 MHz). For the preparation of sample containing (*S*)-2-hydroxy-3-methylbutyric acid, the general procedure was followed using 0.01 mmol of ligand **1**.

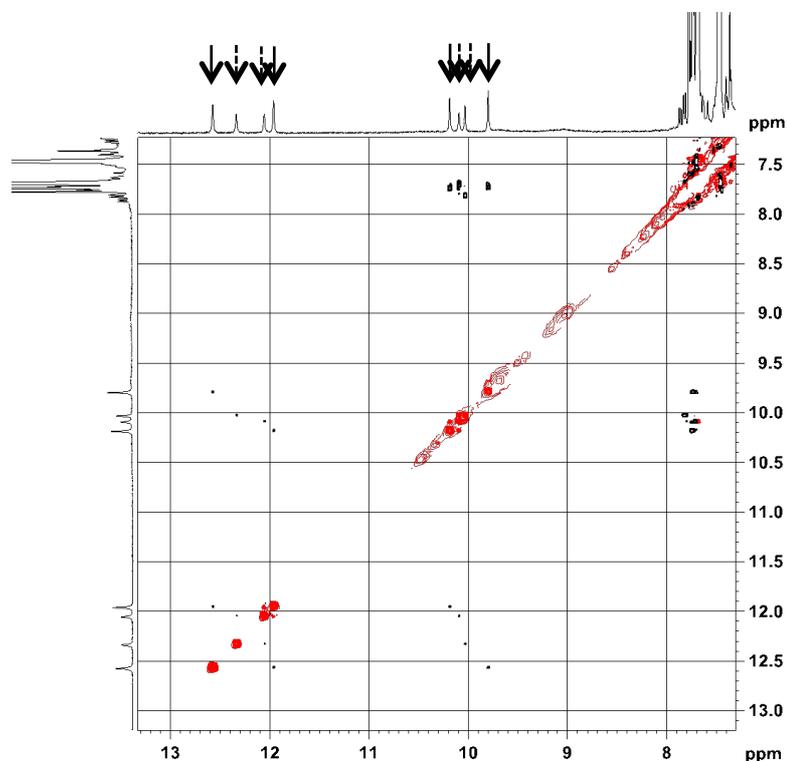


Figure S19. NOESY spectrum (*NH* signals) of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of (*S*)-2-hydroxy-3-methylbutyric acid (**6**) and DIPEA in CD_2Cl_2 (400 MHz). The general procedure was followed using 0.01 mmol of ligand **1**.

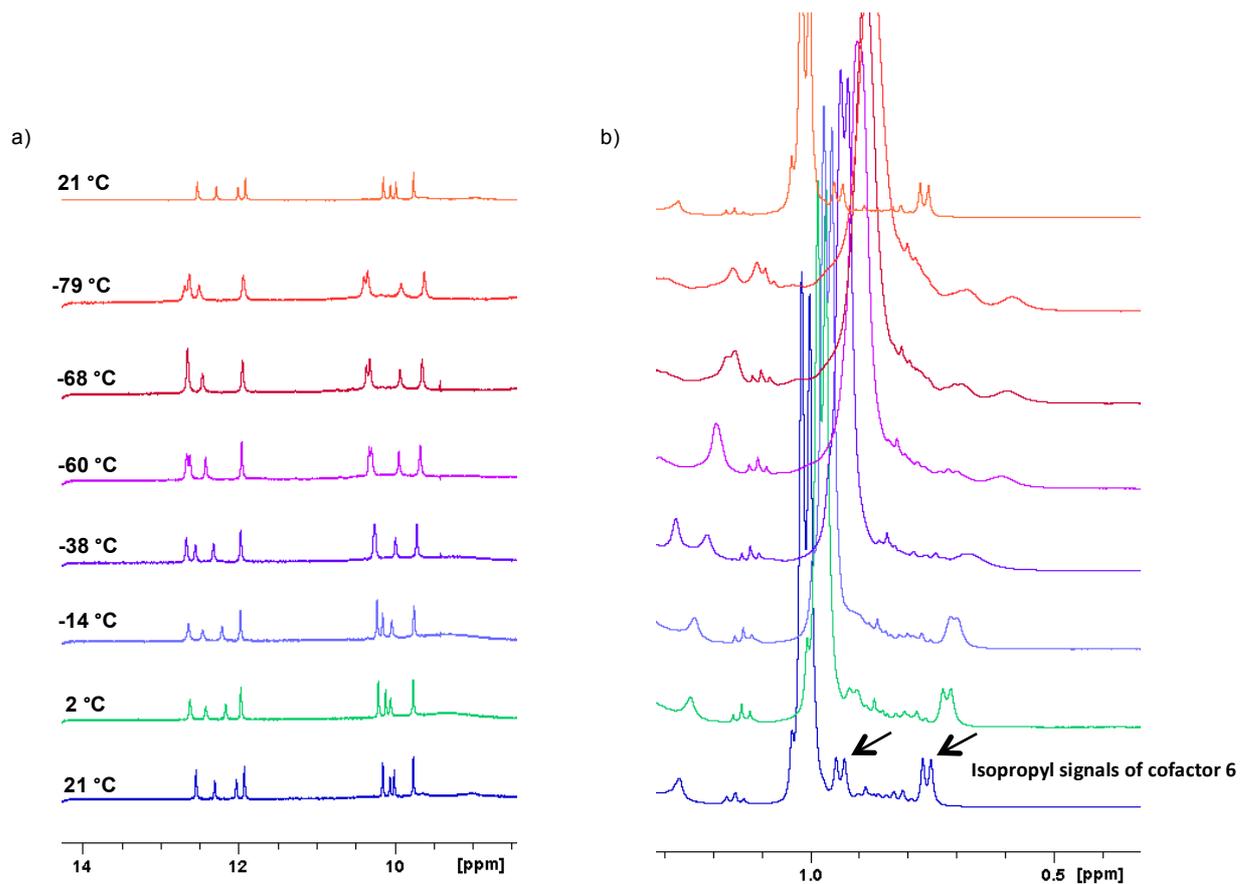


Figure S20. ^1H NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of (*S*)-2-hydroxy-3-methylbutyric acid (**6**) and DIPEA at various temperatures in CD_2Cl_2 (400 MHz). The general procedure was followed using 0.01 mmol of ligand **1**.

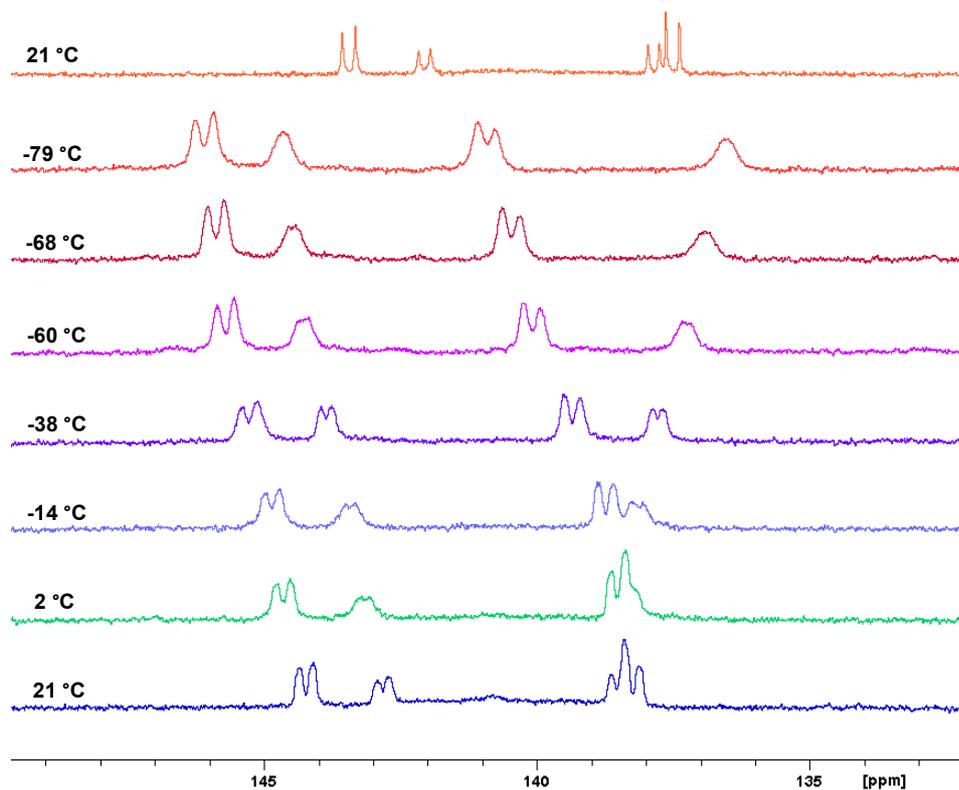


Figure S21. ^{31}P NMR spectra of the [Pd(fumaronitrile)1] complex in the presence of (*S*)-2-hydroxy-3-methylbutyric acid (6) and DIPEA at various temperatures in CD_2Cl_2 (162 MHz). The spectrum at the top was recorded with proton decoupling. The general procedure was followed using 0.01 mmol of ligand 1.

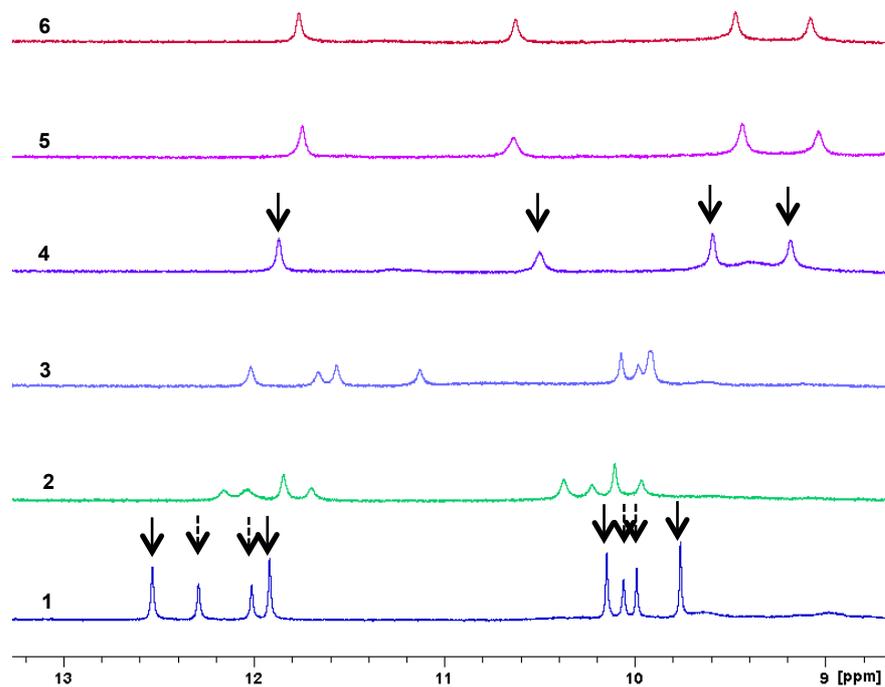
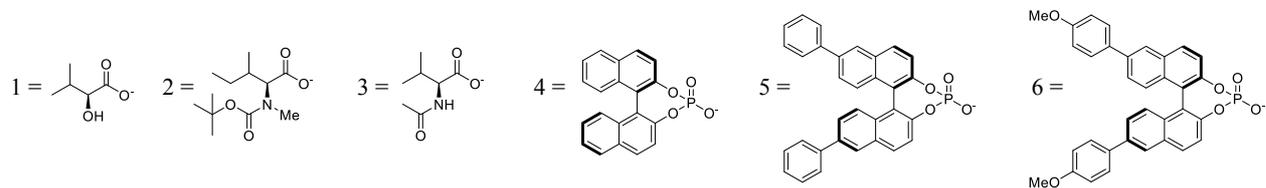


Figure S22. ^1H NMR spectra (NH signals) of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of chiral cofactors and DIPEA in CD_2Cl_2 (400 MHz). For the preparation of sample containing (*S*)-2-hydroxy-3-methylbutyric acid, the general procedure was followed using 0.01 mmol of ligand **1**.



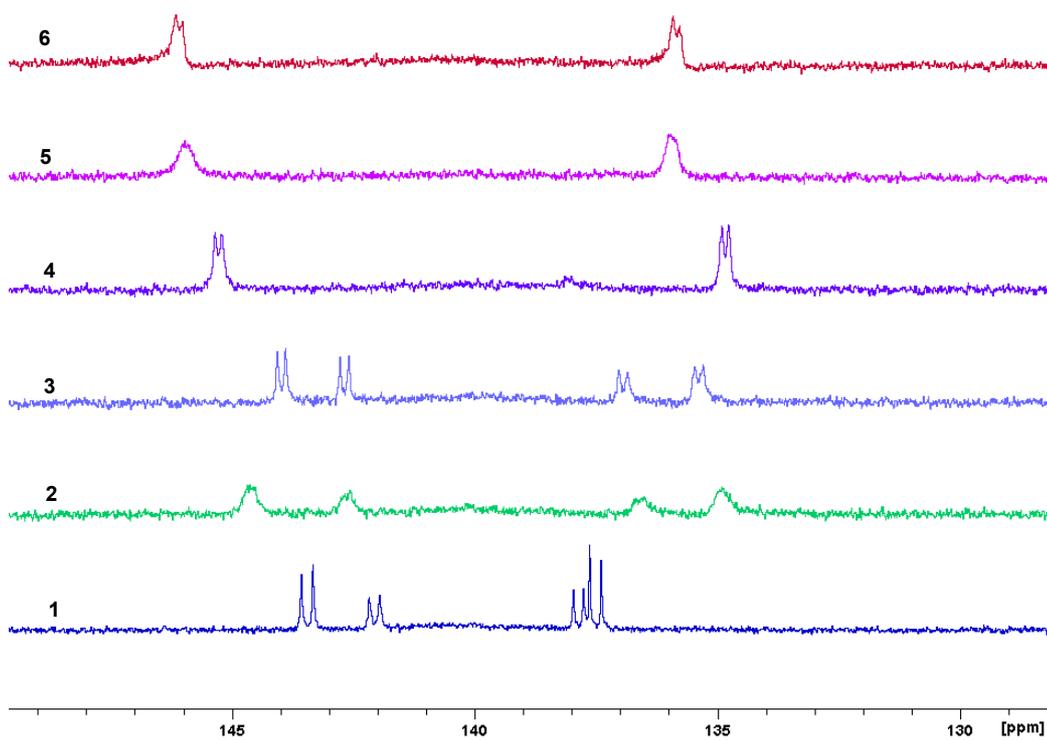
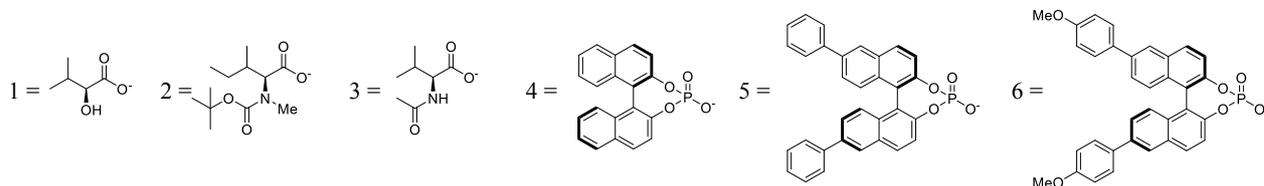


Figure S23. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of chiral cofactors and DIPEA in CD_2Cl_2 (162 MHz). For the preparation of sample containing (*S*)-2-hydroxy-3-methylbutyric acid, the general procedure was followed using 0.01 mmol of ligand **1**.



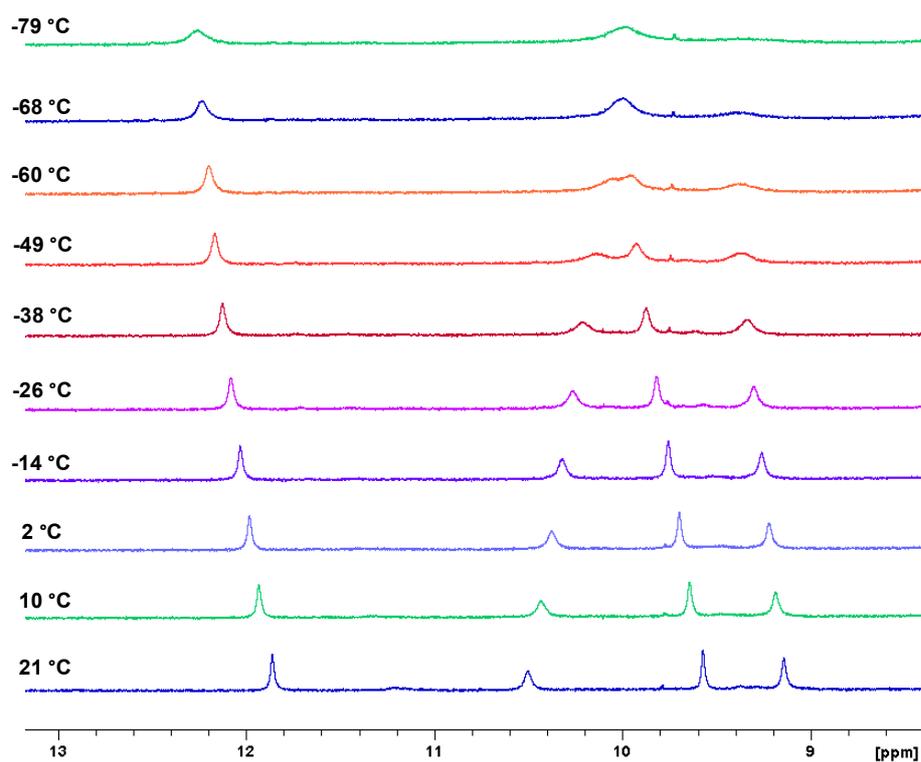
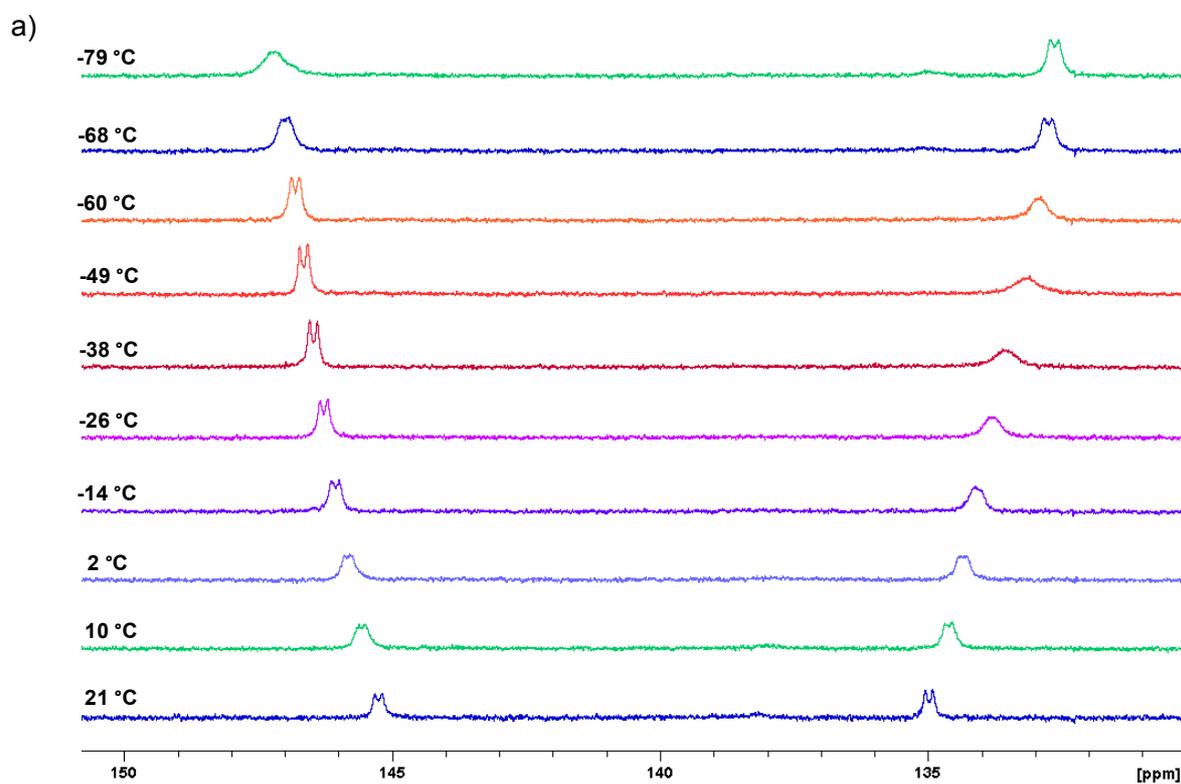


Figure S24. ^1H NMR spectra (NH signals) of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of (*R*)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (**7a**) and DIPEA at various temperatures in CD_2Cl_2 (400 MHz). The general procedure was followed using 0.01 mmol of ligand **1**.



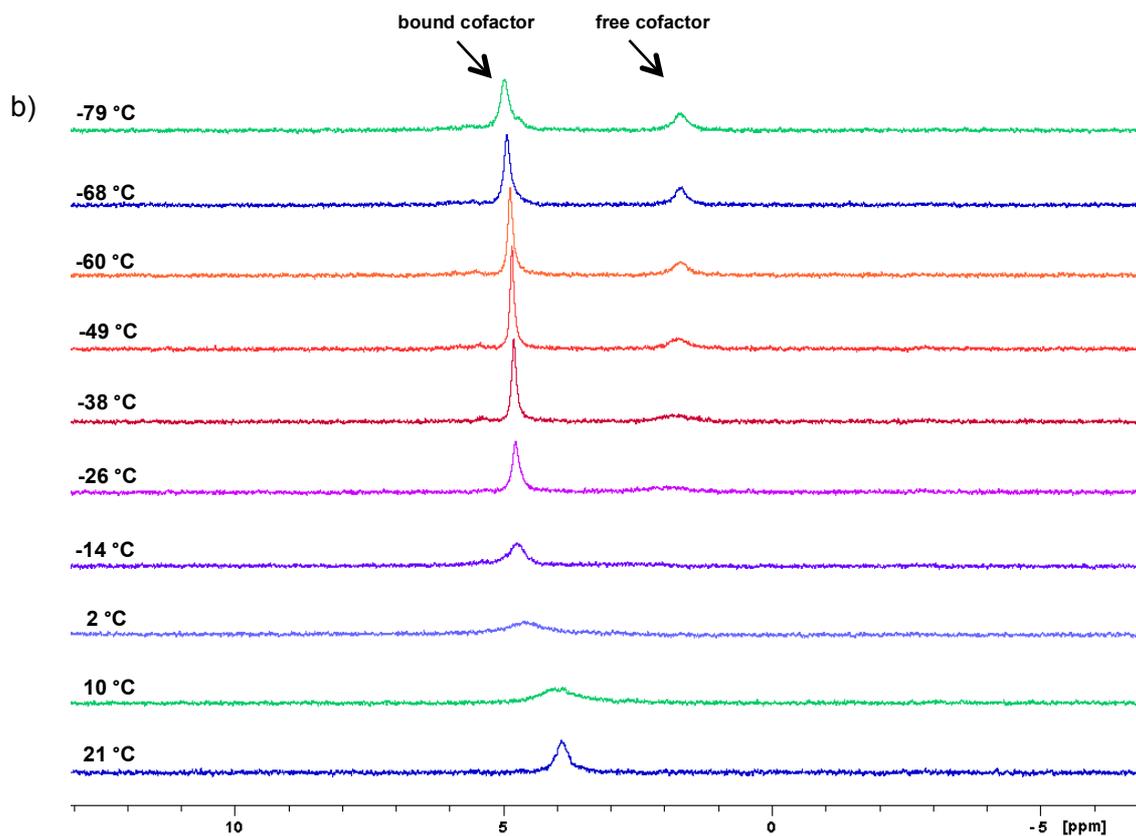


Figure S25. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of (*R*)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (**7a**) and DIPEA at various temperatures in CD_2Cl_2 (162 MHz). The general procedure was followed using 0.01 mmol of ligand **1**.

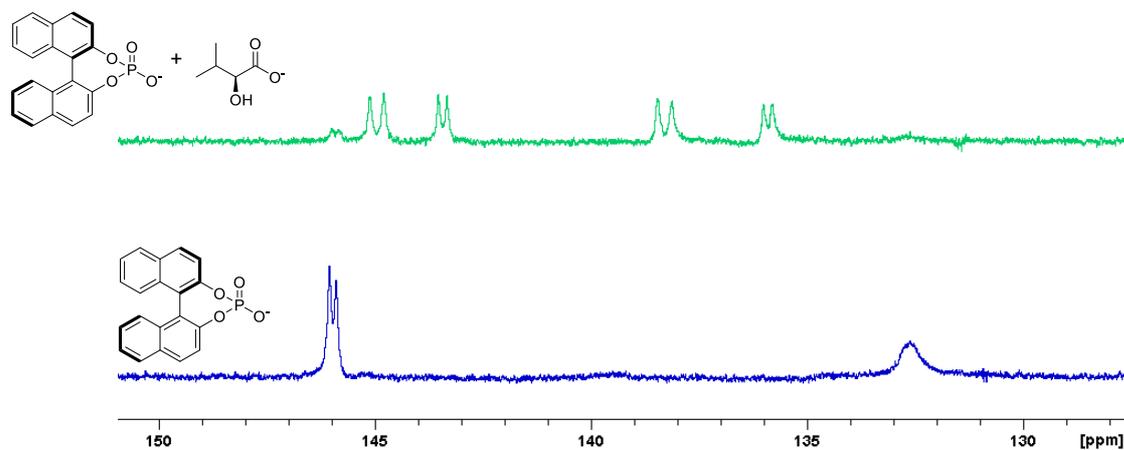


Figure S26. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of (*R*)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (**7a**), (*S*)-2-hydroxy-3-methylbutyric acid (**6**) and DIPEA at 223 K in CD_2Cl_2 (162 MHz). Displacement of the phosphate cofactor by the carboxylate cofactor was observed. The general procedure was followed using 0.01 mmol of ligand **1**.

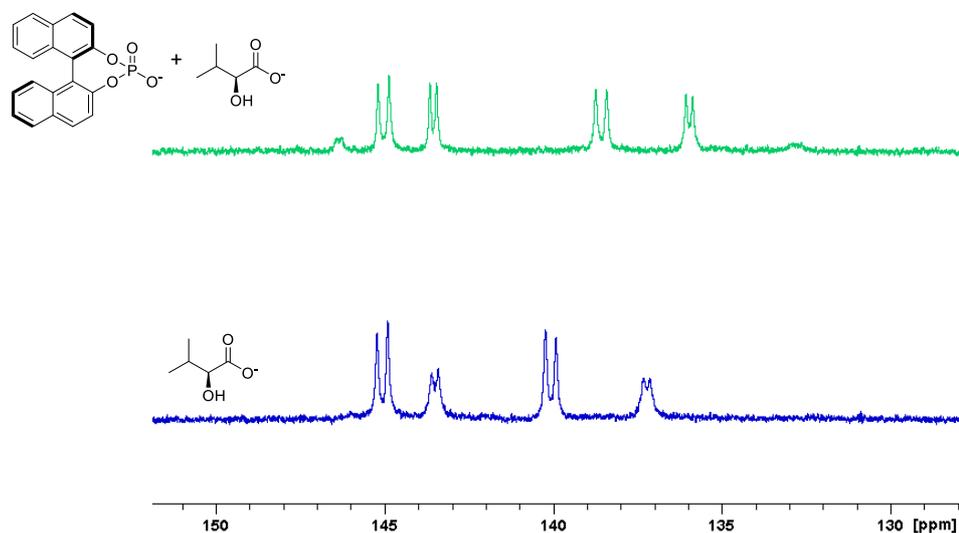


Figure S27. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{fumaronitrile})\mathbf{1}]$ complex in the presence of (*S*)-2-hydroxy-3-methylbutyric acid (**6**), (*R*)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (**7a**) and DIPEA at 223 K in CD_2Cl_2 (162 MHz). Only minor displacement of the carboxylate cofactor by the phosphate cofactor was observed. The general procedure was followed using 0.01 mmol of ligand **1**.

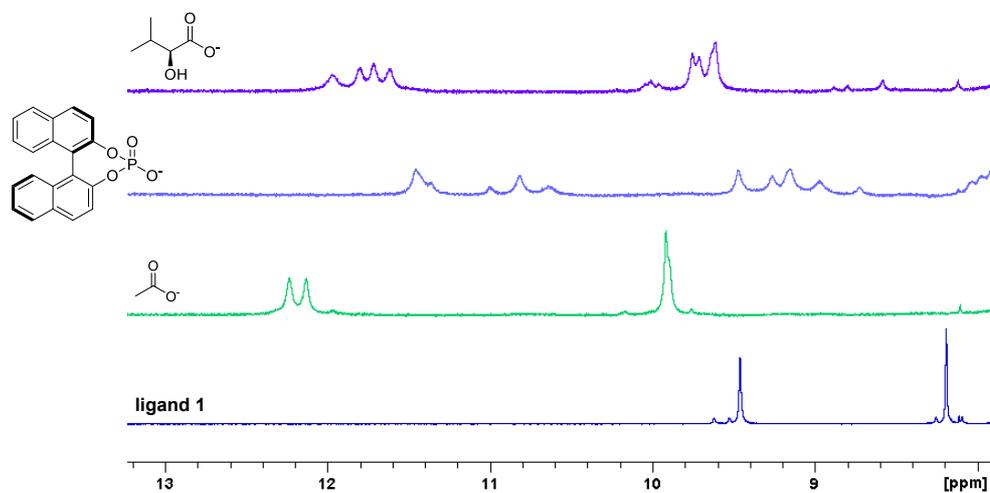


Figure S28. ^1H NMR spectra (NH signals) of the $[\text{Pd}(\text{diethyl maleate})\mathbf{1}]$ complex in the presence of cofactors and DIPEA in CD_2Cl_2 (400 MHz).

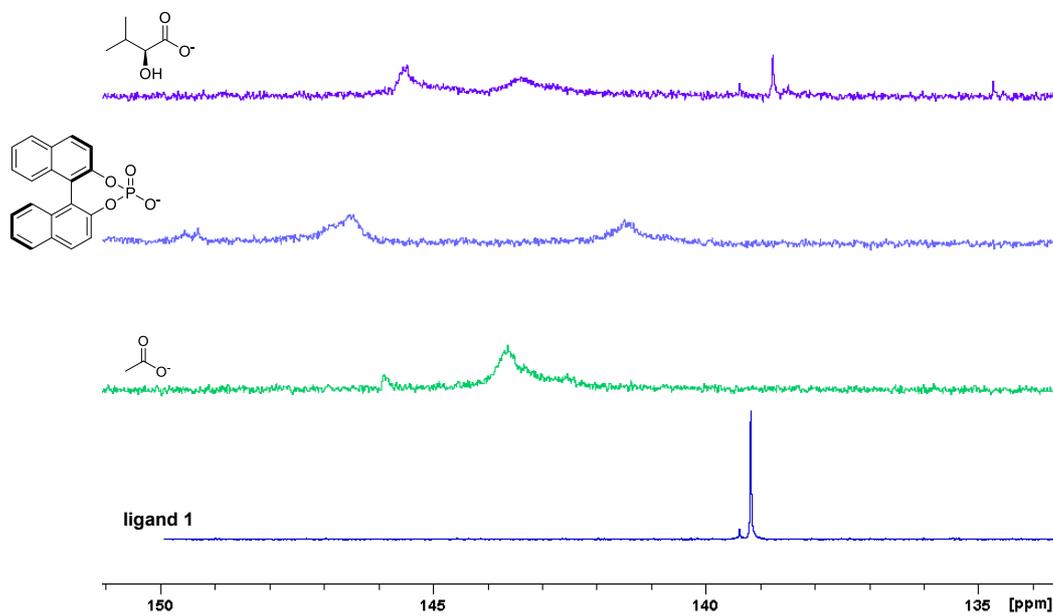
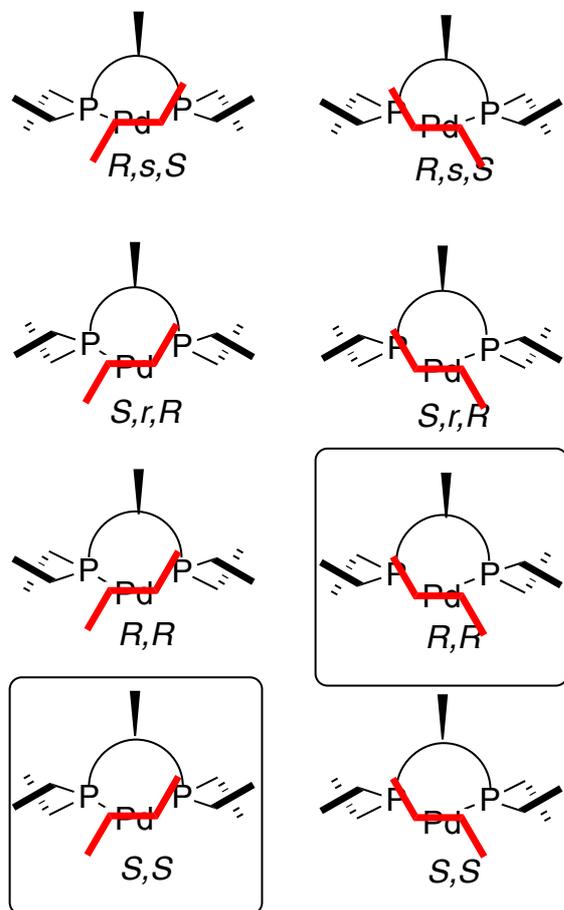


Figure S29. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of the $[\text{Pd}(\text{diethyl maleate})\mathbf{1}]$ complex in the presence of cofactors and DIPEA in CD_2Cl_2 (162 MHz).

6. Stereochemistry of olefin complexes with co-factor ligands

trans-olefin:



cis-olefin:

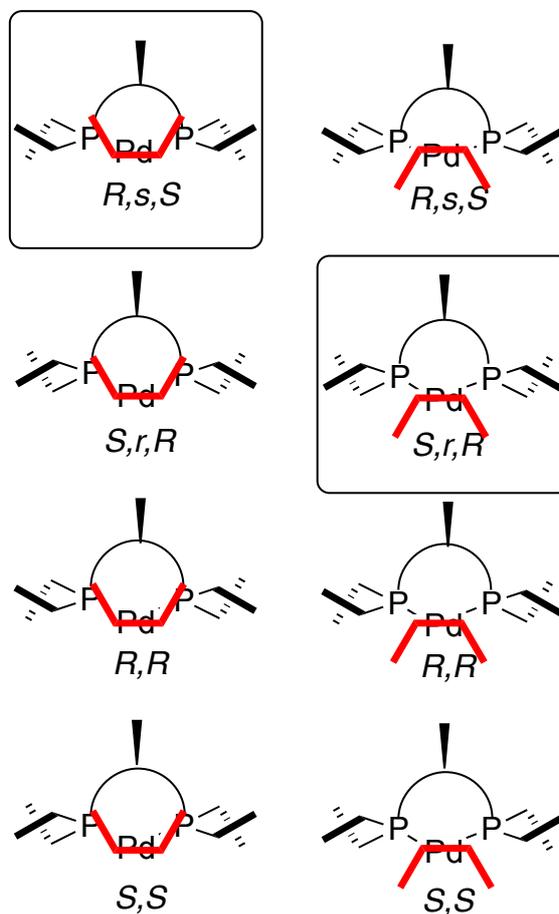
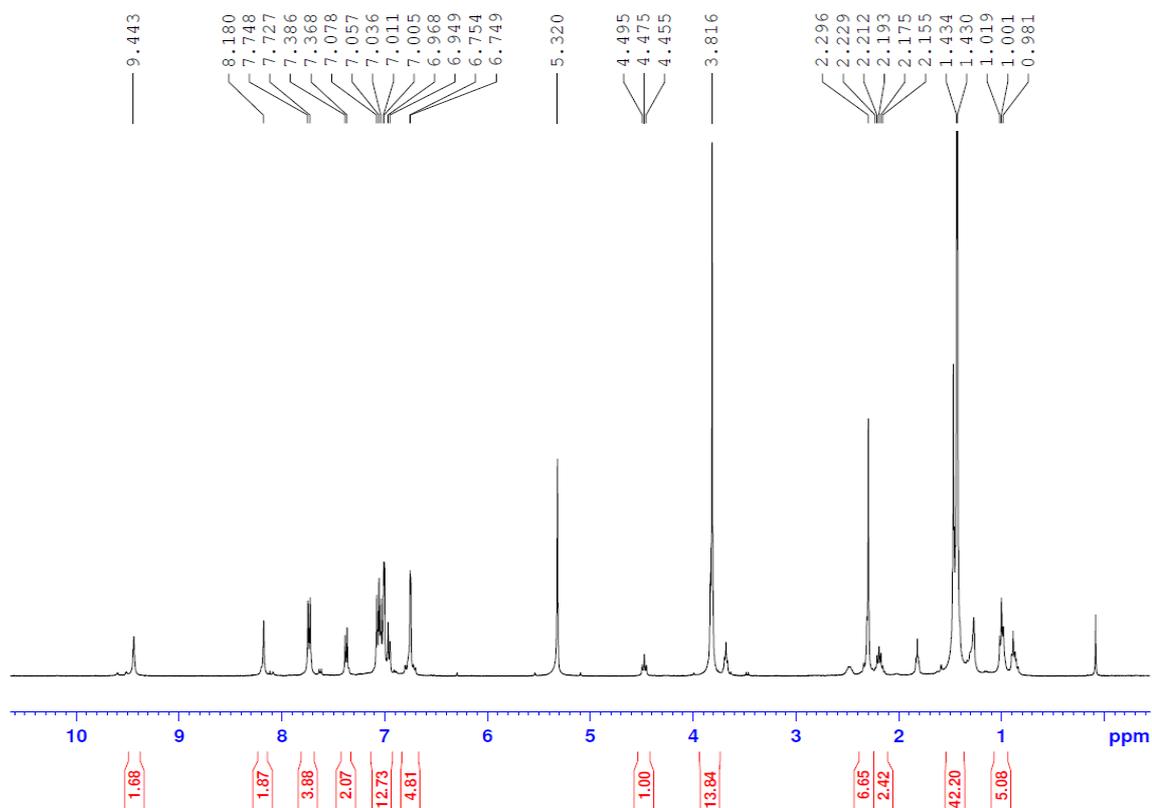
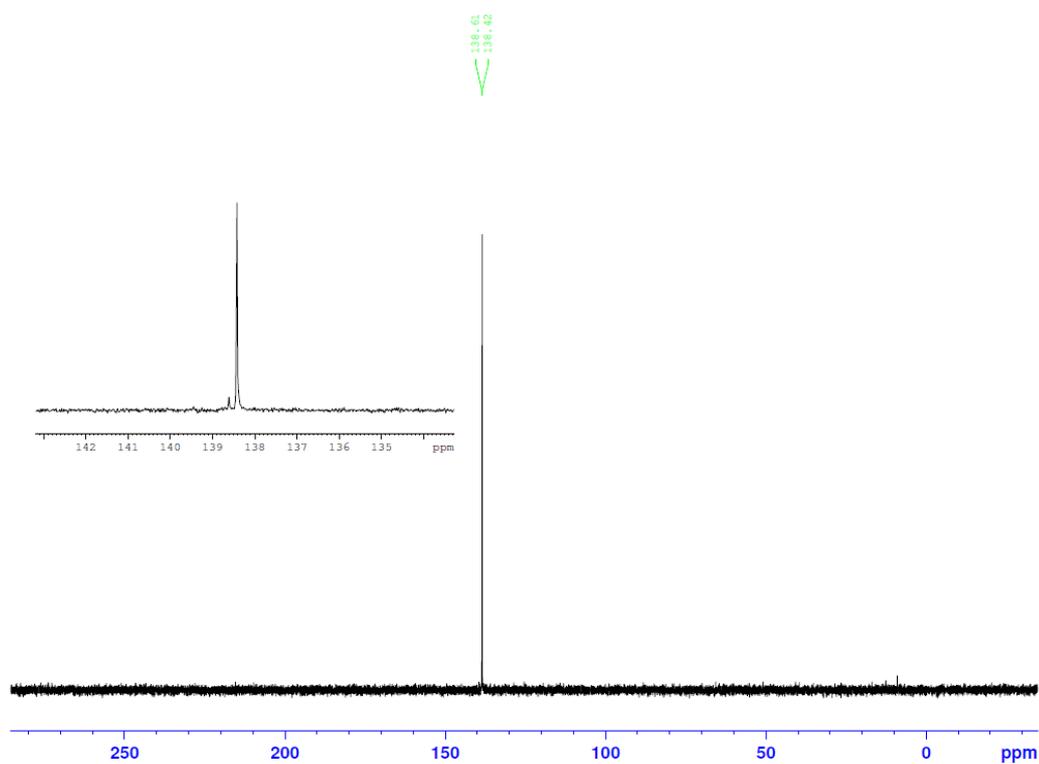


Figure S30. Complexes of ligand 1 with *trans* and *cis* olefins. Complexes in columns are interconvertible via flipping of the ligand whereas interconversion of ligands in rows require de-coordination – re-coordination. Favored complexes are in frames.

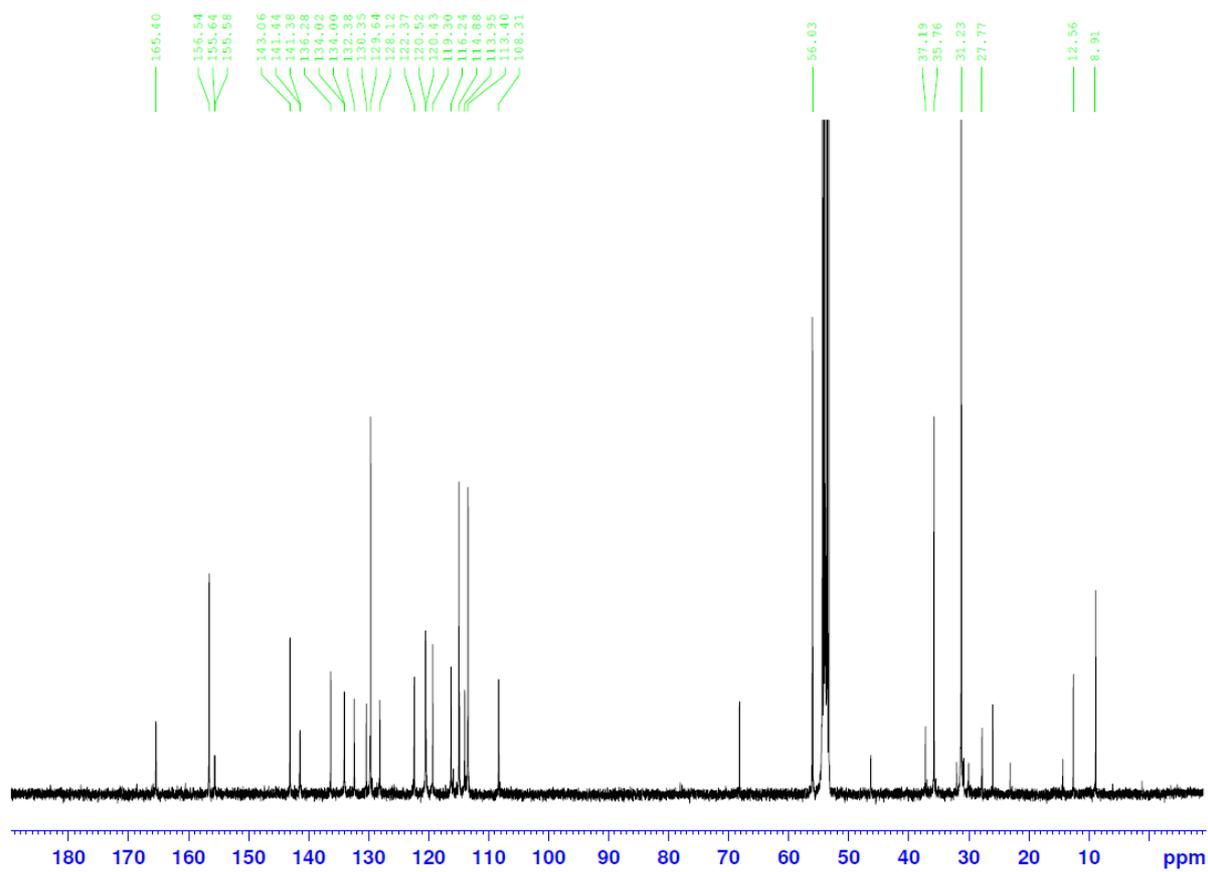
7. NMR spectra



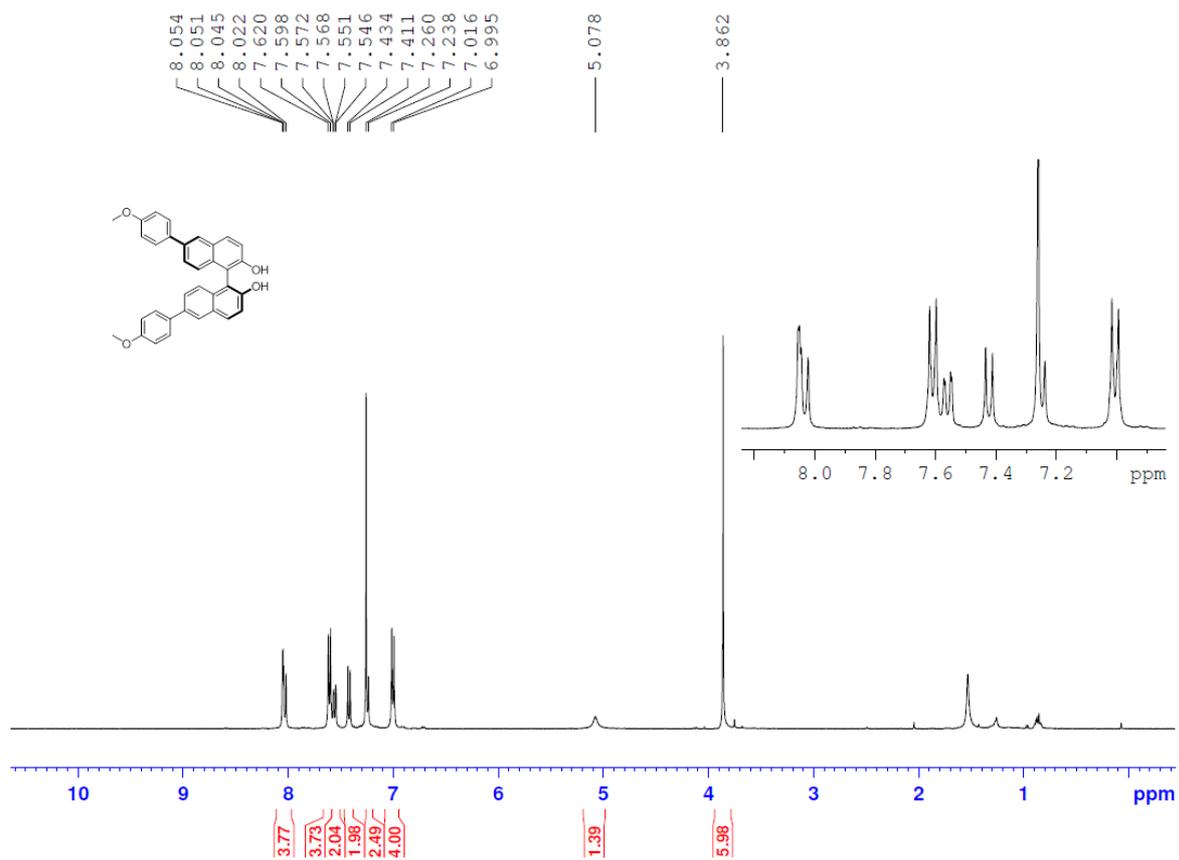
^1H NMR (400 MHz, CD_2Cl_2) spectrum of ligand **1**



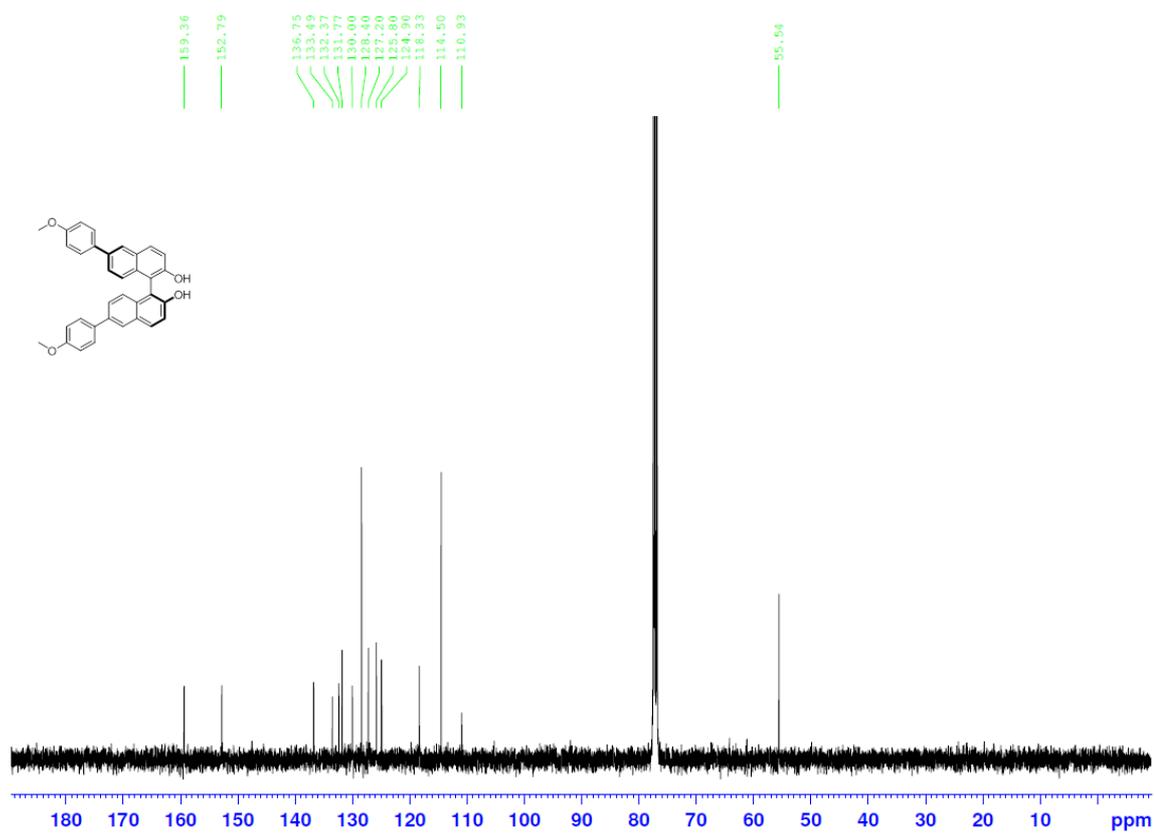
$^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, CD_2Cl_2) spectrum of ligand **1**



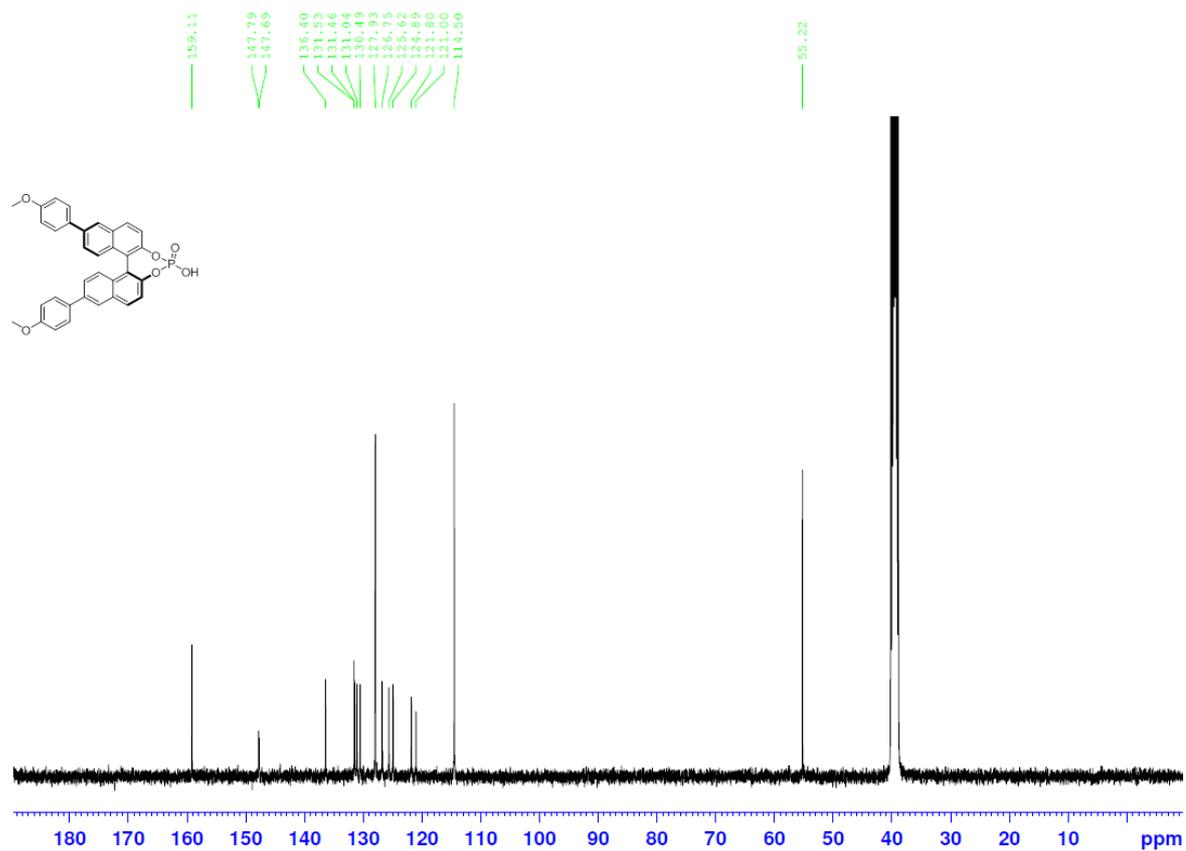
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CD_2Cl_2) spectrum of ligand **1**



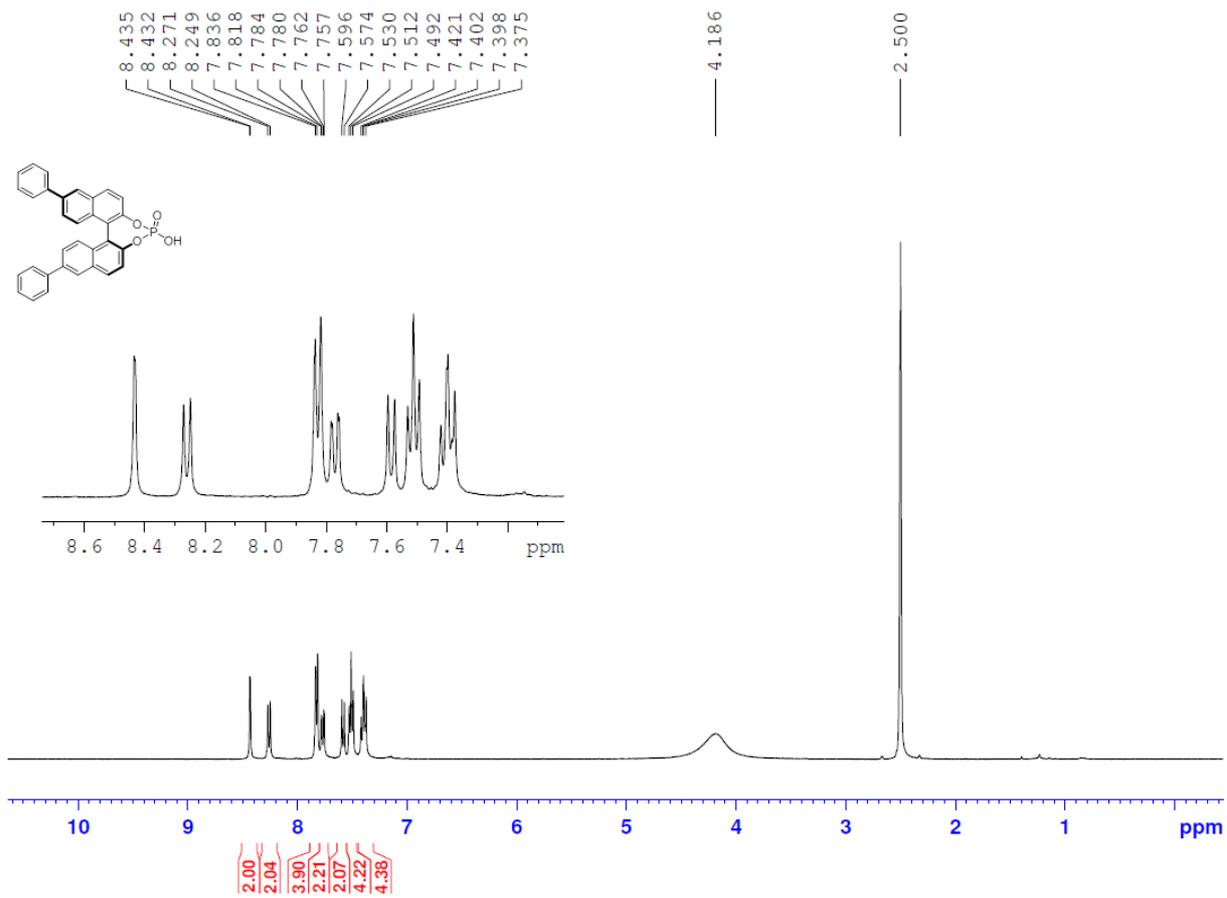
^1H NMR (400 MHz, CDCl_3) spectrum of *(S)*-6,6'-bis(4-methoxyphenyl)-1,1'-binaphthalene-2,2'-diol



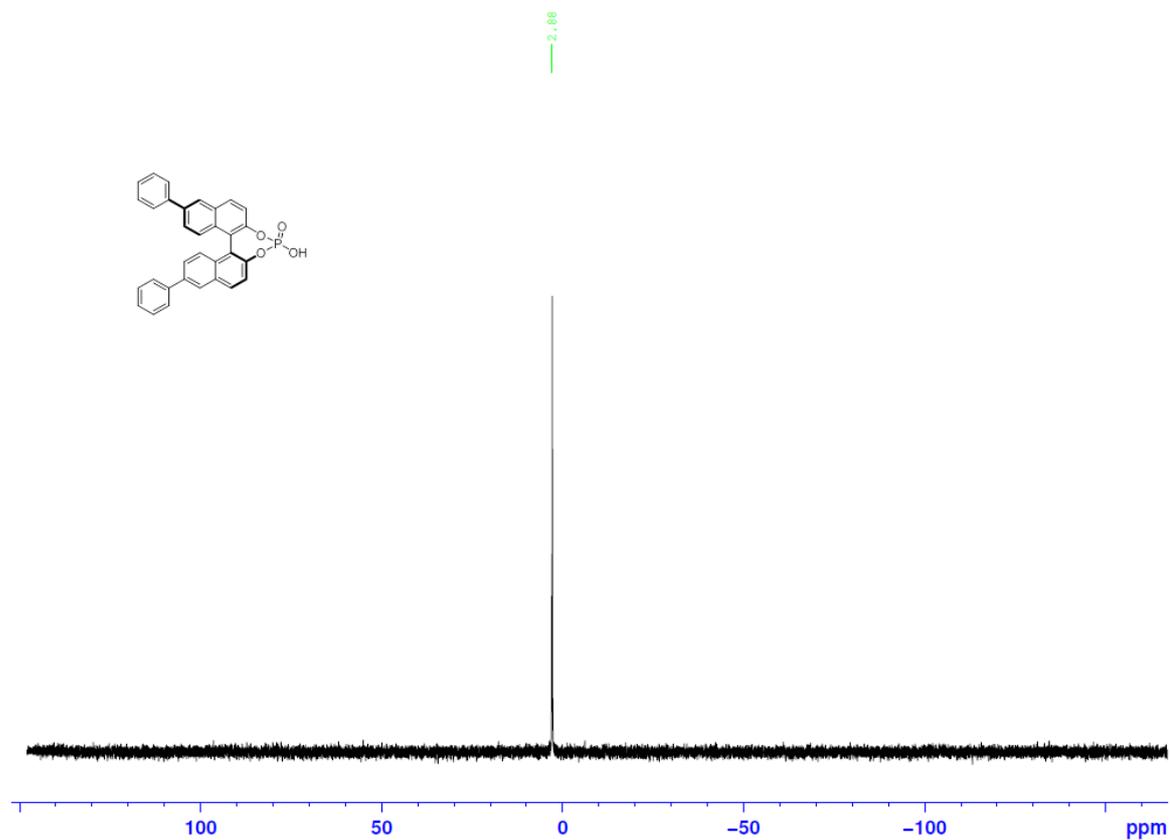
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) spectrum of *(S)*-6,6'-bis(4-methoxyphenyl)-1,1'-binaphthalene-2,2'-diol



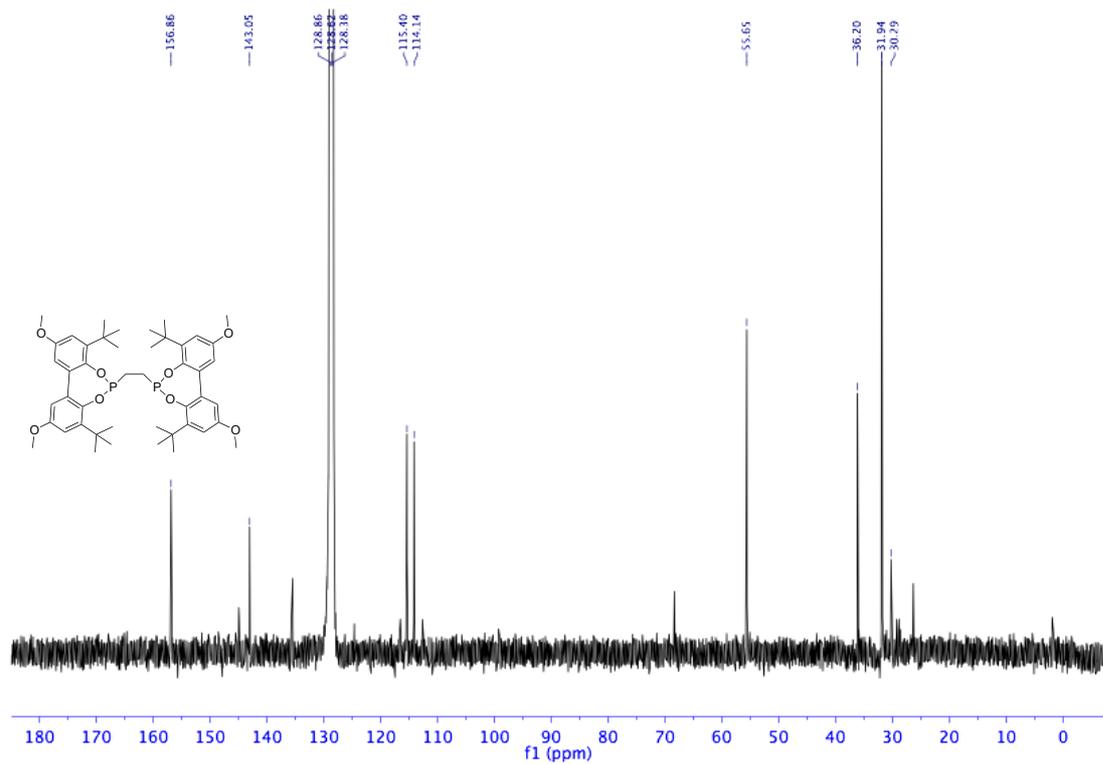
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of **7b**



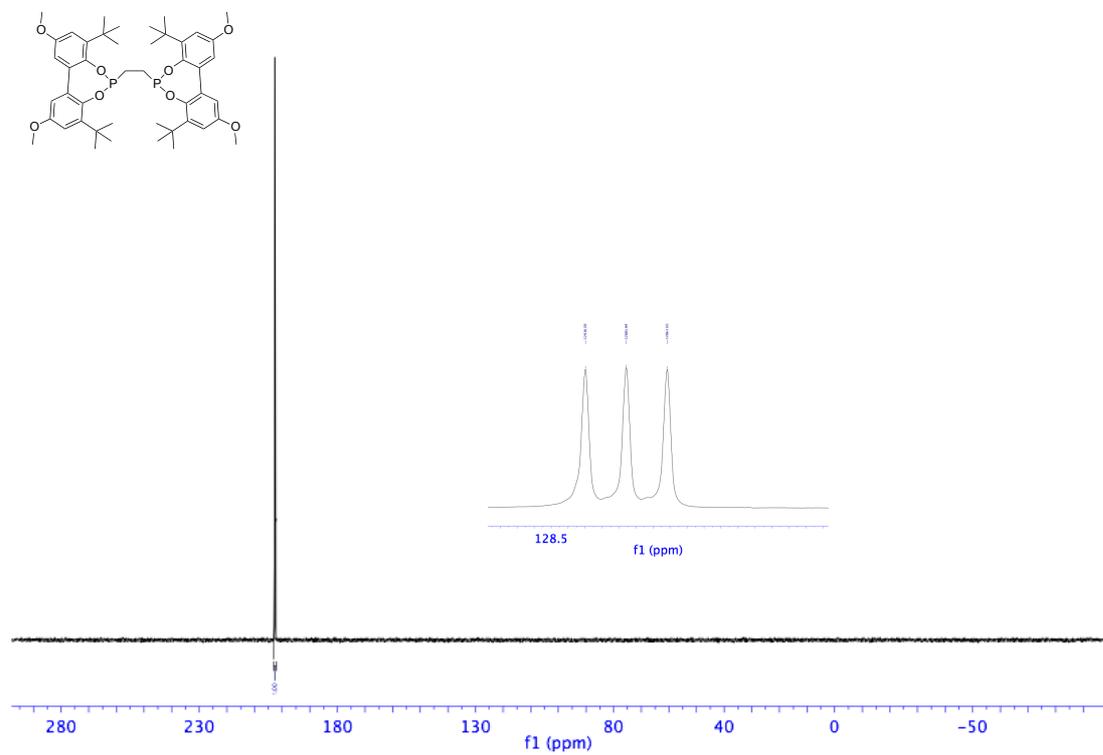
^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of **7b**



$^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, $\text{DMSO-}d_6$) spectrum of **7b**



$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, C_6D_6) spectrum of **12**



^{31}P NMR (162 MHz, C_6D_6) spectrum of **12**