Hydrogen Bonding as a Construction Element for Bidentate Donor Ligands in Homogenous Catalysis:

Regioselective Hydroformylation of Terminal Alkenes

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Supplementary Material

(7 pages)

General

Acetic acid hex-5-enyl ester^[1] and undec-10-enoic^[2] acid methyl ester were prepared according to literature reported procedures. All other reagents were obtained commercially unless otherwise noted. Reactions were performed using oven-dried glassware under an atmosphere of argon. Air- and moisture sensitive liquids and solutions were transferred via syringe. Organic solutions were concentrated under reduced pressure (ca. 20 mbar) by rotary evaporation. Toluene was distilled from sodium and stored under an atmosphere of argon. Chromatographic purification of products was accomplished using flash chromatography^[3] on Macherey-Nagel silica gel 60 (230-400 mesh).

Nuclear magnetic resonance spectra were acquired on a Varian Mercury spectrometer (300 MHz, 121.5 MHz and 75.5 MHz for ¹H, ³¹P and ¹³C respectively) and on a Bruker AMX 400 (400 MHz and 100.6 MHz for ¹H and ¹³C respectively) and are referenced internally according to residual protio solvent signals. Data for ¹H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet), coupling constant (Hz), integration. Data for ¹³C NMR are reported in terms of chemical shift (δ, ppm). GC-MS analysis was done on a Varian GC/MS Workstation CP3800/Saturn 2000 on a CP-SIL 5 CB low bleed column. High-resolution mass spectra were obtained on a Finnigan MAT 8200 instrument. Hydroformylation experiments were performed either with an Argonaut Endeavour[®] Catalyst Screening System or in stainless steel tube autoclaves. Synthesis gas (CO 3.7, H₂ 4.3, 1:1) was obtained from Messer.

Caution: All operations involving carbon monoxide must be carried out in a well-ventilated fume hood. Use of a gas-leak detector for carbon monoxide is highly recommended.

Experimental procedures and characterizations

2-*tert*-Butoxy-6-chloro-pyridine (1)

C₉H₁₂ClNO

Mol. Wt.: 185.65

To a solution of 10.00 g 2,6-dichloro-pyridine (67.6 mmol, 1.0 eq) in 150 ml toluene was added 9.10 g potassium-*tert*-butylate (81.1 mmol, 1.2 eq). After heating 6 h to 80 °C the suspension was filtered through a plug of silica to remove solid byproducts. The filtrate was concentrated in vacuo and the residual yellow oil was purified via bulb to bulb distillation (200 °C, 10⁻¹ mbar). Compound **1** was obtained as a colorless liquid (11.98 g, 95.5%).

¹H NMR (400 MHz, CDCl₃, ppm) 7.43 (t, *J* = 7.7 Hz, 1H), 6.81 (d, *J* = 7.3 Hz, 1H), 6.53 (d, *J* = 8.2 Hz, 1H), 1.58 (s, 9H)

¹³C (100.6 MHz, CDCl₃, ppm) 163.3, 147.7, 140.2, 115.7, 111.3, 80.9, 28.6

CHN calcd C: 58.23, H: 6.52, N: 7.54 found C: 58.27, H: 6.65, N: 7.48

2-*tert*-Butoxy-6-diphenylphosphanyl-pyridine (2)

C₂₁H₂₂NOP

Mol. Wt.: 335.38

To liquid ammonia (ca. 500 ml) at – 78 °C was added 5.40 g sodium (235.0 mmol, 2.03 eq) during 10 min. The dark blue solution was treated portionwise first with 30.40 g triphenylphosphine (115.9 mmol, 1 eq) and then, after stirring for 2 h at –78 °C, with 21.50 g (115.8 mmol, 1 eq) 2-*tert*-butoxy-6-chloro-pyridine (**1**). After the addition of 175 ml of tetrahydrofuran the ammonia was allowed to evaporate over night. The residue was quenched with 200 ml of water (dest.), extracted three times with 150 ml diethylether each and dried over Na₂SO₄. Evaporation of the solvent in vacuo and recrystallisation of the residual oil from methanol yielded 31.0 g (79.8%) 2-*tert*-butoxy-6-diphenylphosphanyl-pyridine (**2**) as a white solid.

mp = 77 °C

^1H (400 MHz, C_6D_6 , ppm) 7.51-7.44 (m, 4H), 7.11-7.04 (m, 6H), 6.91 (ddd, $J = 8.3, 7.3, 2.8$ Hz, 1H), 6.75 (dd, $J = 7.3, 2.8$ Hz, 1H), 6.45 (d, $J = 8.3$ Hz, 1H)

^{13}C (100.6 MHz, C_6D_6 , ppm) 164.1 (d, $J_{\text{C,P}} = 9.7$ Hz), 160.5, 138.0 (d, $J_{\text{C,P}} = 5.8$ Hz), 137.6 (d, $J_{\text{C,P}} = 11.7$ Hz), 134.7 (d, $J_{\text{C,P}} = 18.9$ Hz), 128.9, 128.7 (d, $J_{\text{C,P}} = 7.2$ Hz), 121.4 (d, $J_{\text{C,P}} = 24.7$), 112.2, 79.6, 28.5

^{31}P (121.5 MHz, C_6D_6 , ppm) -3.1

CHN calcd C: 75.21, H: 6.61, N: 4.18 found C: 74.98, H: 6.57, N: 4.09

6-Diphenylphosphanyl-1*H*-pyridin-2-one (6-DPPon) (**3**)

$\text{C}_{17}\text{H}_{14}\text{NOP}$
Mol. Wt.: 279.27

9.70 g (28.92 mmol) 2-*tert*-butoxy-6-diphenylphosphanyl-pyridine (**2**) was dissolved in 100 ml of conc. formic acid which has been saturated with argon. After stirring for 30 min the solution was diluted with 120 ml water (dest.). The precipitate was collected by filtration, washed with 30 ml aqueous formic acid (2:1, v/v) and dried. 6-Diphenylphosphanyl-1*H*-pyridin-2-on (**3**) was obtained as a white solid (5.6 g, 69.3%). The combined aqueous formic acid solutions were concentrated in vacuo and the residue was recrystallized from acetone. This yielded another 1.8 g (22.2%) of 6-diphenylphosphanyl-1*H*-pyridin-2-on (**3**).

mp 187 °C

^1H (400 MHz, CDCl_3 , ppm) 9.29 (br s, 1H), 7.45-7.25 (m, 11H), 6.51 (d, $J = 9.0$ Hz, 1H), 6.20 (t, $J = 6.3$ Hz, 1H)

^{13}C (100.6 MHz, CDCl_3 , ppm) 163.8, 146.6 (d, $J_{\text{C,P}} = 26.2$ Hz), 140.5 (d, $J_{\text{C,P}} = 7.3$ Hz), 133.9 (d, $J_{\text{C,P}} = 20.4$ Hz), 132.6 (d, $J_{\text{C,P}} = 10.2$ Hz), 130.2, 129.3 (d, $J_{\text{C,P}} = 7.3$ Hz), 120.7, 114.0 (d, $J_{\text{C,P}} = 21.8$)

^{31}P (121.5 MHz, CDCl_3 , ppm) -9.8

CHN calcd C: 73.11, H: 5.05, N: 5.02 found C: 72.97, H: 5.18, N: 4.73

Phenyl-carbamic acid hex-5-enyl ester (4)

$C_{13}H_{17}NO_2$

Mol. Wt.: 219.28

To a solution of 2.54 g hex-5-en-1-ol (25.3 mmol, 1 eq) in 25 ml benzene was added dropwise 3.3 g isocyanato-benzene (27.9 mmol, 1.1 eq). After stirring for 16 h at rt some precipitated 1,3-diphenyl-urea was removed by filtration. The filtrate was concentrated in vacuo and the residue was purified by flash chromatography on silica gel (5:1 cyclohexane:EtOAc). Compound **4** was obtained as a colorless oily liquid (5.40 g, 97.0%).

1H (300 MHz, C_6D_6 , ppm) 7.38 (d, $J = 7.9$ Hz, 2H), 7.09 (t, $J = 7.9$ Hz, 2H), 6.84 (t, $J = 7.9$ Hz, 2H), 6.61 (br s, 1H), 6.60-5.78 (m, 1H), 5.10-4.90 (m, 2H), 4.03 (t, $J = 6.6$, 2H), 1.88 (q, $J = 7.1$ Hz, 2H), 1.50-1.35 (m, 2H), 1.33-1.18 (m, 2H)

^{13}C (75.5 MHz, C_6D_6 , ppm) 153.8, 138.9, 138.5, 128.3, 123.3, 118.8, 114.9, 65.0, 33.5, 28.6, 25.4

HRMS (EI) calcd for $C_{13}H_{17}NO_2$ 219.1260 found 219.1259 (M^+)

2-Hydroxy-benzoic acid hex-5-enyl ester (5)^[4]

$C_{13}H_{16}O_3$

Mol. Wt.: 220.26

To a suspension of 6.99 g 2-hydroxy-benzoic acid (50.6 mmol, 2.0 eq) in 50 ml CH_2Cl_2 was added 3.09 g dimethyl-pyridin-4-yl-amine (25.3 mmol, 1.0 eq), followed by 2.53 g hex-5-en-1-ol (25.3 mmol, 1 eq) and 7.85 g dicyclohexyl-carbodiimide (63.2 mmol, 2.5 eq). The suspension was stirred for 3 d and then filtrated. The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel (2:1 hexanes: CH_2Cl_2). Compound **4** was obtained as a colorless oily liquid (5.51 g, 98.8%).

1H (300 MHz, C_6D_6 , ppm) 10.72 (s, 1H), 7.74 (dd, $J = 8.0, 1.7$ Hz, 1H), 7.35 (td, $J = 7.8, 1.7$ Hz, 1H), 6.88 (dd, $J = 8.4$ Hz, 1H), 6.81 (td, $J = 7.6, 1.0$ Hz, 1H), 5.80-5.65 (m, 1H), 5.00-4.85 (m, 2H), 4.26 (t, $J = 6.6$ Hz, 2H), 2.04 (q, $J = 7.1$ Hz, 2H), 1.78-1.64 (m, 2H), 1.53-1.39 (m, 2H)

^{13}C (100.6 MHz, CDCl_3 , ppm) 170.2, 161.8, 138.2, 135.6, 129.9, 119.1, 117.6, 115.0, 112.7, 65.3, 33.3, 28.0, 25.3

HRMS (EI) calcd for $\text{C}_{13}\text{H}_{16}\text{NO}_3$ 220.1099 found 220.1099 (M^+)

CHN calcd C: 70.89, H: 7.32 found C: 70.68, H: 7.40

General procedure for the hydroformylation of 1-octene

To a solution of 1.8 mg (6.98 μmol) $[\text{Rh}(\text{CO})_2\text{acac}]$ in 24 ml toluene in a schlenk tube was added 140 μmol of the particular ligand (*see* below and **table 1**). Subsequently an aliquot of 3 ml (0.87 μmol $[\text{Rh}]$ -catalyst, 1 eq) of the above prepared catalyst solution was injected in each of the 8 reaction vessels. Catalyst preformation was done at 5 bar (CO/H_2 , 1:1) and 90 $^\circ\text{C}$ for 30 min. The reaction vessels were adjusted to the appropriate reaction temperatures and pressurized to 8 bar (CO/H_2 , 1:1). Under these conditions each vessel was loaded with 0.68 g (6.1 mmol, 7000 eq) 1-octene and additional 0.5 ml toluene. The pressure was adjusted to 10 bar (CO/H_2 , 1:1) for each vessel. Pressure and temperature were kept constant over the complete reaction time. After 4 h the reaction vessels were cooled down to rt, depressurized and the solutions were analyzed via GC.

General procedure for the hydroformylation of functionalized terminal alkenes

Hydroformylations of functionalized olefines were performed each with in situ prepared $[\text{Rh}]$ -catalyst modified with the ligands TPP and 6-DPPon (**3**), respectively.

To a solution of 1.8 mg (6.98 μmol , 1 eq) $[\text{Rh}(\text{CO})_2\text{acac}]$ in 10 ml toluene in a schlenk tube was added 140 μmol (20 eq) of the particular ligand. The solution was stirred for 5 min and then charged with 6.98 mmol (1000 eq) of alkenic substrate. The solution was transferred to the autoclave via syringe, pressurized to 10 bar (CO/H_2 , 1:1) and heated to 70 $^\circ\text{C}$ in an oil bath. After 20 h the autoclave was cooled down to rt and depressurized. The *l/b*-ration was analyzed via ^1H -NMR spectra or GC analysis of the crude reaction mixture. The solution was filtrated over a plug of silica (5 x 2 cm) with 50 ml AcOEt and concentrated in vacuo. The conversion was always

quantitative, the isolated yields were typically in the range of 90 to 95% and the products obtained were essentially pure. For the aldehydes 7-bromo-heptanal^[5] (**table 2: entry 1**), acetic acid 7-oxo-heptyl ester^[6] (**table 2: entry 2**), 12-oxo-dodecanoic acid methyl ester^[7] (**table 2: entry 3**), 6-oxo-heptanal^[8] (**table 2: entry 4**), 4-hydroxy-butyraldehyde (tetrahydro-furan-2-ol)^[9] (**table 2: entry 7**) and 12-hydroxy-dodecanal^[10] (**table 2: entry 8**) the spectral and analytical data correspond to those reported previously. The hydroformylation products derived from phenyl-carbamic acid hex-5-enyl ester (**4**) and 2-hydroxy-benzoic acid hex-5-enyl ester (**5**) have not been reported in literature before. The corresponding aldehydes were purified by flash chromatography on silica gel (cyclohexane/AcOEt 1:1) to afford analytically pure samples.

Phenyl-carbamic acid 6-oxo-hexyl ester (**6**)

C₁₃H₁₇NO₃
Mol. Wt.: 235.28

Compound **6** was obtained as a white solid (1.50 g, 91.4%).

mp 51 °C

¹H (400 MHz, CDCl₃, ppm) 9.76 (t, *J* = 1.6 Hz, 1H), 7.40-7.34 (m, 2H), 7.32-7.26 (m, 2H), 7.08-7.02 (m, 1H), 6.61 (br s, 1H), 4.15 (t, *J* = 6.7 Hz, 2H), 2.43 (td, *J* = 7.3, 1.7 Hz, 2H), 1.73-1.60 (m, 4H), 1.47-1.32 (m, 4H)

¹³C (100.6 MHz, CDCl₃, ppm) 202.6, 152.9, 138.1, 129.1, 125.5, 118.7, 65.2, 43.9, 28.8, 25.8, 22.0

CHN calcd C: 67.45, H: 7.68, N: 5.62 found C: 67.42, H: 7.77, N: 5.55

2-Hydroxy-benzoic acid 7-oxo-heptyl ester (**7**)

C₁₄H₁₈O₄
Mol. Wt.: 250.29

Compound **7** was obtained as a white solid (1.53 g, 87.4%).

mp 34 °C

¹H (300 MHz, CDCl₃, ppm) 10.80 (s, 1H), 9.76 (t, *J* = 1.8 Hz, 1H), 7.82 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.44 (td, *J* = 7.9, 1.7 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.87 (td, *J* = 7.6, 1.0 Hz, 1H), 4.34 (t,

$J = 6.6$ Hz, 2H), 2.44 (td, $J = 7.0, 1.8$ Hz, 2H), 1.86-1.73 (m, 2H), 1.72-1.60 (m, 2H), 1.55-1.34 (m, 2H)

^{13}C (75.5 MHz, CDCl_3 , ppm) 202.4, 170.2, 161.7, 135.6, 129.8, 119.1, 117.6, 112.6, 65.2, 43.7, 28.7, 28.4, 25.8, 21.9

HRMS (EI) calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_4$ 250.1208 found 220.1205 (M^+)

CHN calcd C: 67.18, H: 7.25 found C: 67.17, H: 7.25

[*cis*- $\text{PtCl}_2(6\text{-DPPon})_2$] (**8**)

To a solution of 68.4 mg (182 μmol , 1 eq) [*cis*- $\text{PtCl}_2(\text{COD})_2$] in 2.5 ml CH_2Cl_2 was added 102 mg (366 μmol , 2 eq) 6-diphenylphosphanyl-*1H*-pyridin-2-one (**3**). The citreous suspension was diluted with additional 2.5 ml CH_2Cl_2 and the yellow solution was stirred for 5 min. The solvent was removed in vacuo and the residue was washed two times with pentane. The remaining white solid was dried in oil pump vacuo. Suitable crystals for x-ray analysis were grown from a solution of 20 mg [*cis*- $\text{PtCl}_2(6\text{-DPPon})_2$] in 1 ml CH_2Cl_2 at rt.

Literature

- [1] Brown, H. C.; Lynch, G. C. *J. Org. Chem.* **1981**, 46(3), 531-538.
- [2] Strother, T.; Cai, W.; Zhao, X.; Hamers, R. J.; Smith, L. M. *J. Amer. Chem. Soc.* **2000**, 122(6), 1205-1209.
- [3] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, 43, 2923-2925.
- [4] Höfle, G.; Steglich, W.; Vorbrüggen, H. *Angew. Chem.* **1978**, 90, 602-615.
- [5] Hester, J. B.; Gibson, J. K.; Buchanan, L. V.; Cimini, M. G.; Clark, M. A.; Emmert, D. E.; Glavanovich, M. A.; Imbordino, R. J.; LeMay, R. J.; McMillan, M. W.; Perricone, S. C.; et al. *J. Med. Chem.* **2001**, 44(7), 1099-1115.
- [6] Muchowski, J. M.; Venuti, M. C. *J. Org. Chem.* **1981**, 46(2), 459-461.
- [7] Myers, A. G.; Gin, D. Y.; Rogers, D. H. *J. Amer. Chem. Soc.* **1994**, 116(11), 4697-4718.
Baldwin, J. E.; Adlington, R. M.; Ramcharitar, S. H. *Tetrahedron* **1992**, 48(14), 2957-2976.
- [8] Shin, H. S.; Lee, C. W.; Lee, J. Y.; Huh, T. S. *Eur. J. Org. Chem.* **2000**, 2, 335 – 348.
- [9] Bergman, N.-A.; Halvarsson, T. *J. Org. Chem.* **1988**, 53(11), 2548-2552.
Chickos, J. S.; Uang, J. Y.-J.; Keiderling, T. A. *J. Org. Chem.* **1991**, 56(7), 2594-2596.
Nakano, T.; Terada, T.; Ishii, Y.; Ogawa, M. *Synthesis* **1986**, 9, 774-776.
- [10] Cuny, G. D.; Buchwald, S. L. *J. Amer. Chem. Soc.* **1993**, 115(5), 2066-2068.