A very efficient Phosphoramidite Ligand for Asymmetric Iridium-Catalyzed Allylic Alkylation

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Supporting Information

General Procedures. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded in CDCl_3 , and chemical shift (δ) are given in ppm relative to residual CHCl_3 . Evolution of reaction was followed by GC-MS Hewlett Packard (EI mode) HP6890-5973. Optical rotations were measured at 22°C in a 10 cm cell in the stated solvent; $[\alpha]_{\text{D}}$ values are given in $10^{-1} \text{ deg.cm}^2 \text{ g}^{-1}$ (concentration c given as g/100 mL). Enantiomeric excesses were determined by chiral-GC (capillary column, 10 psi H_2) or chiral-SFC with the stated column. Temperature programs are described as follows: initial temperature (°C) – initial time (min) – temperature gradient (°C/min) – final temperature (°C); retention times (R_{T}) are given in min. Flash chromatography was performed using silica gel 32–63 μm , 60 Å. CH_2Cl_2 , was distilled from CaH_2 under nitrogen. THF was dried by passage over alumina (activated at 350 °C under nitrogen atmosphere for 12 h).

Substrates were synthesized by known experimental procedures.¹

Lithium chloride was dried over 24 hours at 80°C prior to use.

$[\text{Ir}(\text{COD})\text{Cl}]_2$ was purchased from Strem and used as received.

Ligands **L1b-L3b** were prepared according to the reported procedure.²

The sodium malonate solution was prepared as followed: NaH (dispersion on mineral oil, 50 %, 0.049 g, 1 mmol) was rinsed 3 times with portions of *n*-pentane (5 mL), one portion of dry THF (5 mL) and then suspended in 1.5 mL of dry THF. Dimethylmalonate (0.115 mL, 1 mmol) was added dropwise under stirring at room temperature. The resulting solution was immediately used.

General procedure for the Ir-catalyzed allylic alkylation.

In a flame-dried Schlenk tube, **L1** (0.022 mmol) and $\text{Ir}(\text{COD})\text{Cl}$ dimer (0.0067 g, 0.01 mmol) were dissolved in 0.5 mL of THF. The resulting orange solution was stirred for 20 minutes at room temperature and treated with the substrate (0.5 mmol) as well as a freshly prepared sodium malonate solution (1 mmol in 1.5 mL THF). The reaction mixture was stirred at the indicated temperature until complete disappearance of the starting material. The mixture was hydrolyzed with water, extracted with diethyl ether and dried over magnesium sulfate. The product was concentrated *in vacuo*, then 5 mL of pentane were added to let the catalyst sink. The resulting suspension is filtered, concentrated *in vacuo* and chromatographed on silica gel (*n*-pentane/diethyl ether 7:3) to afford the adduct as a colorless oil.

¹ Lehmann, J.; Lloyd-Jones, G. C. *Tetrahedron* **1995**, 51, 8863–8874.

² Alexakis, A.; Tissot-Croset, K.; Polet, D. *Angew. Chem. Int. Ed.* **2004**, 43, 2426–2428.

(R)-2-(1-Phenyl-allyl)-malonic acid dimethyl ester 2a ^1H NMR (400.13 MHz, CDCl_3) 7.40–7.23 (m, 5H), 6.03 (ddd, 1H, $J = 18.2, 10.1, 8.1$ Hz), 5.15 (d, 1H, $J = 18.0$ Hz), 5.12 (d, 1H, $J = 10.6$ Hz), 4.15 (dd, 1H, $J = 10.8, 8.1$ Hz), 3.90 (d, 1H, $J = 11.1$ Hz), 3.78 (s, 3H), 3.53 (s, 3H). ^{13}C NMR (100.59 MHz, CDCl_3) 168.2, 167.8, 139.9, 137.8, 128.7, 127.9, 127.2, 116.7, 57.4, 52.6, 52.4, 49.8. MS (EI) 189 (98), 157 (19), 129 (43), 117 (100), 91 (17), 77 (10). $[\alpha]_D^{22} = +34.1$ (c 1.08, CHCl_3) for 98 % ee. determined by comparison with published data.³ Ee was measured by chiral SFC analysis with a Regis (R,R) WHELK-O column (2% MeOH during 2 min, then 1 % min^{-1} , flow rate 2 mL/min, pressure 130 bars, 0°C) R_T : 3.05 (R), 3.29 (S).

(+)-2-(1-Naphthalen-2-yl-allyl)-malonic acid dimethyl ester 2b ^1H NMR (400.13 MHz, CDCl_3) 7.81–7.79 (m, 3H), 7.69 (s, 1H), 7.47–7.44 (m, 2H), 7.37 (dd, 1H, $J = 8.6, 1.5$ Hz), 6.08 (ddd, 1H, $J = 17.2, 10.4, 8.1$ Hz), 5.18 (d, 1H, $J = 17.2$ Hz), 5.04 (d, 1H, $J = 10.1$ Hz), 4.30 (dd, 1H, $J = 9.6, 8.4$ Hz), 4.01 (d, 1H, $J = 11.1$ Hz), 3.77 (s, 3H), 3.46 (s, 3H). ^{13}C NMR (100.59 MHz, CDCl_3) 168.3, 167.9, 137.7, 137.5, 133.5, 132.6, 128.4, 127.9, 127.7, 126.7, 126.2, 126.1, 125.9, 116.9, 57.3, 52.7, 52.5, 49.8. MS (EI) 298 (24), 239 (58), 207 (13), 179 (29), 167 (100), 152 (28). $[\alpha]_D^{22} = +39.3$ (c 0.925, CHCl_3) for 96 % ee. Ee was measured by chiral SFC analysis with a Chiralcel OB-H column (2% MeOH during 2 min, then 1 % min^{-1} , flow rate 2 mL/min, pressure 200 bars, 30°C) R_T : 7.43 (+), 8.05 (-).

³ Lloyd-Jones, G. C.; Pfaltz, A. *Angew. Chem. Int. Ed.* **1995**, *34*, 462-464.

⁴ Pretot, R.; Pfaltz, A. *Angew. Chem. Int. Ed.* **1998**, *37*, 323-325.

(+)-2-(1-Benzo[1,3]dioxol-5-yl-allyl)-malonic acid dimethyl ester 2c

^1H NMR (400.13 MHz, CDCl_3) 7.74–7.66 (m, 3H), 5.98–5.89 (m, 3H), 5.10 (d, 1H, $J = 15.4$ Hz), 5.07 (d, 1H, $J = 8.8$ Hz), 4.03 (dd, 1H, $J = 10.9, 8.1$ Hz), 3.79 (d, 1H, $J = 10.9$ Hz), 3.73 (s, 3H), 3.54 (s, 3H). ^{13}C NMR (100.59 MHz, CDCl_3) 168.3, 167.9, 139.9, 137.7, 137.5, 133.5, 132.6, 128.4, 127.9, 127.7, 126.7, 126.2, 126.1, 125.9, 116.9, 57.3, 52.7, 52.6, 52.5, 49.8. MS (EI) 298 (24), 239 (58), 207 (13), 179 (29), 167 (100), 152 (28).

HRMS (EI) calcd for $[\text{M}+\text{Na}]^+$ 315.0845, found 315.0834. $[\alpha]_D^{22} = +22.0$ (c 1.13, CHCl_3) for 97 % ee. Ee was measured by chiral SFC analysis with a Regis (R,R) WHELK-O column (1% MeOH during 6 min, then 1 %min $^{-1}$, flow rate 2 mL/min, pressure 130 bars, 30°C) R_T : 6.02 (+), 6.77 (-).

(+)-2-[1-(4-Trifluoromethyl-phenyl)-allyl]-malonic acid dimethyl ester 2d

^1H NMR (400.13 MHz, CDCl_3) 7.57 (d, 2H, $J = 8.1$ Hz), 7.36 (d, 2H, $J = 8.3$ Hz), 5.97 (ddd, 1H, $J = 16.9, 10.1, 8.1$ Hz), 5.16 (d, 1H, $J = 7.6$ Hz), 5.12 (s, 1H), 4.19 (dd, 1H, $J = 10.9, 8.6$ Hz), 3.90 (d, 1H, $J = 11.1$ Hz), 3.76 (s, 3H), 3.53 (s, 3H). ^{13}C NMR (100.59 MHz, CDCl_3) 167.8, 167.5, 144.1, 136.9, 129.6, 129.2, 128.3, 125.6–125.5 (q, 1C, $J = 3.3$ Hz), 125.4, 117.5, 56.9, 52.7, 52.5, 49.3. MS (EI) 260 (10), 257 (100), 224 (20), 197 (26), 185 (98), 177 (11), 165 (31), 151 (10), 128 (11), 115 (48), 59 (37). $[\alpha]_D^{22} = +40.1$ (c 0.81, CHCl_3) for 94 % ee. Ee was measured by chiral GC analysis with a Chiraldex LIPODEX E column (60-0-1-170-5) R_T : 59.09 (-), 59.68 (+).

(+)-2-[1-(4-Chloro-phenyl)-allyl]-malonic acid dimethyl ester 2e

^1H NMR (400.13 MHz, CDCl_3) 7.30 (d, 2H, $J = 8.3$ Hz), 7.20 (d, 2H, $J = 8.3$ Hz), 5.99 (ddd, 1H, $J = 16.9, 10.4, 8.1$ Hz), 5.16 (d, 1H, $J = 7.1$ Hz), 5.12 (d, 1H, $J = 0.8$ Hz), 4.13 (dd, 1H, $J = 10.9, 8.1$ Hz), 3.85 (d, 1H, $J = 10.8$ Hz), 3.78 (s, 3H), 3.56 (s, 3H). ^{13}C NMR (100.59 MHz, CDCl_3) 168.0, 167.7, 138.5, 137.3, 133.0, 129.4, 128.8, 117.1, 57.2, 52.7, 52.6, 49.0. MS (EI) 223 (100), 191 (17), 163 (23), 151 (85), 128 (19), 115 (53), 59 (15). $[\alpha]_D^{22} = +40.9$ (c 1.00, CHCl_3) for 97 % ee. Absolute configuration was determined by comparison with published data.³ Ee was measured by chiral SFC analysis with a Regis (R,R) WHELK-O column (2% MeOH during 2 min, then 1 %min⁻¹, flow rate 2 mL/min, pressure 130 bars, 30°C) R_T: 3.30 (+), 3.82 (-).

(+)-2-[1-(4-Methoxy-phenyl)-allyl]-malonic acid dimethyl ester 2f⁵

^1H NMR (400.13 MHz, CDCl_3) 7.14 (d, 2H, $J = 8.6$ Hz), 6.85 (d, 2H, $J = 8.6$ Hz), 5.97 (ddd, 1H, $J = 17.1, 10.1, 7.8$ Hz), 5.09 (d, 1H, $J = 15.4$ Hz), 5.06 (d, 1H, $J = 8.6$ Hz), 4.06 (dd, 1H, $J = 10.9, 8.3$ Hz), 3.82 (d, 1H, $J = 10.9$ Hz), 3.77 (s, 3H), 3.73 (s, 3H), 3.50 (s, 3H). ^{13}C NMR (100.59 MHz, CDCl_3) 168.3, 167.9, 158.6, 138.1, 131.9, 129.0, 116.3, 114.0, 57.5, 55.2, 52.5, 48.9. MS (EI) 278 (14), 219 (35), 147 (100), 115 (13), 91 (16). $[\alpha]_D^{22} = +23.3$ (c 1.10, CHCl_3) for 97 % ee. Ee was measured by chiral SFC analysis with a Regis (R,R) WHELK-O column (2% MeOH during 2 min, then 1 %min⁻¹, flow rate 2 mL/min, pressure 130 bars, 30°C) R_T: 4.99 (+), 5.61 (-).

⁵ You, S.-L.; Zhu, X.-Z.; Luo, Y.-M.; Hou, X.-L.; Dai, L.-X. *J. Am. Chem. Soc.* **2001**, *123*, 7471-7472.

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	4.993	MF	0.125	2407.85400	282.35570	50.8117
2	5.606	MF	0.125	2330.92505	310.07028	49.1883

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	4.909	MF	0.133	4781.50635	597.78931	98.6436
2	5.516	MF	0.111	65.74863	9.90229	1.3564

(+)-2-[1-(2-Methoxy-phenyl)-allyl]-malonic acid dimethyl ester 2g ^1H NMR (400.13 MHz, CDCl_3) 7.20 (td, 1H, $J = 7.6, 1.8$ Hz), 7.16 (dd, 1H, $J = 7.6, 1.5$ Hz), 6.90-6.84 (m, 2H), 6.14 (ddd, 1H, $J = 17.0, 10.1, 8.6$ Hz), 5.12 (dt, 1H, $J = 17.2, 1.3$ Hz), 5.04 (dd, 1H, $J = 10.1, 0.8$ Hz), 4.33 (dd, 1H, $J = 10.6, 8.6$ Hz), 4.18 (d, 1H, $J = 10.6$ Hz), 3.85 (s, 3H), 3.72 (s, 3H), 3.49 (s, 3H). ^{13}C NMR (100.59 MHz, CDCl_3) 168.7, 168.3, 157.1, 136.9, 129.5, 128.3, 128.1, 120.7, 116.8, 111.1, 55.5, 55.4, 52.4, 52.3, 46.2. MS (EI) 278 (10), 219 (53), 187 (16), 159 (12), 147 (100), 131 (11), 115 (17), 91 (26). Anal Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_5$: C, 64.74; H, 6.52; O, 28.74. Found: C, 64.46; H, 6.51; O, 29.03. $[\alpha]_D^{22} = +31.1$ (c 1.09, CHCl_3) for 79 % ee. Ee was measured by chiral SFC analysis with a Regis (R,R) WHELK-O column (1% MeOH, flow rate 2 mL/min, pressure 130 bars, 0°C) R_T : 5.67 (+), 6.30 (-).

(+)-2-[1-(3-Methoxy-phenyl)-allyl]-malonic acid dimethyl ester 2h ^1H NMR (400.13 MHz, CDCl_3) 7.25 (td, 1H, $J = 7.8, 1.0$ Hz), 6.85 (d, 1H, $J = 7.8$ Hz), 6.81-6.78 (m, 2H), 6.00 (ddd, 1H, $J = 17.2, 10.1, 8.3$ Hz), 5.17 (dt, 1H, $J = 16.9, 1.3$ Hz), 5.12 (d, 1H, $J = 10.4$ Hz), 4.12 (dd, 1H, $J = 10.8, 8.3$ Hz), 3.90 (d, 1H, $J = 10.8$ Hz), 3.82 (s, 3H), 3.77 (s, 3H), 3.56 (s, 3H). ^{13}C NMR (100.59 MHz, CDCl_3) 168.2, 159.7, 141.6, 137.7, 129.7, 120.1, 116.7, 113.8, 112.4, 57.3, 55.2, 52.6, 52.5, 49.8. MS (EI) 278 (28), 219 (100), 203 (10), 187 (38), 173 (10), 159 (40), 147 (86), 132 (12), 115 (34), 91 (35), 77 (13), 59 (12). Anal Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_5$: C, 64.74; H, 6.52; O, 28.74. Found: C, 64.49; H, 6.48; O, 29.03. $[\alpha]_D^{22} = +28.9$ (c 1.08, CHCl_3) for 96 % ee. Ee was measured by chiral SFC analysis with a Regis (R,R) WHELK-O column (1% MeOH, flow rate 2 mL/min, pressure 130 bars, 0°C) R_T : 5.95 (+), 6.54 (-).

(-)-2-(1-Cyclohexyl-allyl)-malonic acid dimethyl ester 2i⁶ ¹H NMR (400.13 MHz, CDCl₃) 5.73 (dt, 1H, *J* = 16.9, 10.1Hz), 5.08 (dd, 1H, *J* = 10.1, 2.0 Hz), 5.03 (dd, 1H, *J* = 17.2, 1.5 Hz), 3.73 (s, 3H), 3.68 (s, 3H), 3.63 (d, 1H, *J* = 9.1 Hz), 2.60-2.69 (m, 1H), 1.72-0.88 (m, 10H). ¹³C NMR (100.59 MHz, CDCl₃) 169.1, 168.8, 135.8, 118.2, 54.2, 52.4, 52.2, 50.1, 39.1, 28.6, 26.3. MS (EI) 195 (11), 172 (20), 140 (11), 133 (14), 122 (100), 113 (72), 107 (29), 101 (20), 93 (26), 81 (90), 77 (13), 67 (52), 59 (31), 55 (75). It was impossible to get rid of 6% of starting material. $[\alpha]_D^{22} = -0.9$ (*c* 0.98, CHCl₃) for 98 % ee and 6 % starting material. Ee was measured by chiral GC analysis with a Chiraldex G-TA column (80-0-1-170-5) *R_T*: 44.67 (-), 45.00 (+).

(+)-2-(1-Propyl-allyl)-malonic acid dimethyl ester 2j⁷ ¹H NMR (400.13 MHz, CDCl₃) 5.66 (dt, 1H, *J* = 16.9, 10.1Hz), 5.11 (m, 2H), 3.76 (s, 3H), 3.71 (s, 3H), 3.40 (d, 1H, *J* = 9.1 Hz), 2.79 (qd, 1H, *J* = 9.3, 3.0Hz), 1.45-1.21 (m, 4H), 0.91 (t, 3H, *J* = 6.8Hz). ¹³C NMR (100.59 MHz, CDCl₃) 168.8, 168.6, 138.1, 117.4, 57.0, 52.4, 52.2, 44.1, 34.5, 20.2, 13.8. MS (EI) 171 (41), 155 (100), 151 (32), 139 (66), 132 (69), 126 (30), 123 (29), 113 (49), 100 (48), 97 (10), 95 (36),

⁶ Evans, P. A.; Nelson, J. D. *Tetrahedron Letters* **1998**, 39, 1725-1728.

⁷ Takeuchi, R.; Kashio, M. *J. Am. Chem. Soc.* **1998**, 120, 8647-8655.

81 (50), 67 (41), 59 (51) , 55 (83). $[\alpha]_D^{22} = +2.3$ (*c* 1.12, CHCl₃) for 97 % ee. Ee was measured by chiral GC analysis with a Chiraldex G-TA column (70-0-0.5-110-15-170) R_T : 29.51 (+), 30.41 (-).

Signal		DP165.D\FID1A						
peak #	R.T.	Start	End	PK	peak	peak	peak	% of
	min	min	min	TY	height	area	% max.	total
1	29.511	29.330	29.759					
				M	94858	8995445	99.36%	49.840%
2	30.411	30.224	30.698					
				M	92668	9053363	100.00%	50.160%

Signal : DP251N02.D\FID1A								
peak #	R.T. min	START min	END min	PK TY	peak height	peak area	peak % max.	% of total
1	29.356	29.179	29.843	M	396556	50981048	100.00%	98.655%
2	30.474	30.288	30.656	M	6856	694839	1.36%	1.345%

DP167N02 CDCL3 400MHZ 1H

2a

DP167N02 CDCL3 400MHZ 13C

2a

2b

2b

2c

DP242N02 13C 100MHZ CDCL3

2c

2e

DP253N02 CDCL3 13C 100MHz

2e

2f

2g

DP255N02 CDCL3 13C 100MHZ

2g

2h

DP256N02 CDCL3 13C 100MHZ

2h

168.2237
159.7259
141.5763
137.6695
129.6744
120.1216
116.7340
113.7668
112.4398
77.4099
77.0885
76.7670
57.2822
55.2051
52.6335
52.5016
49.7734

*** Current Data Parameters ***

NAME : xr52fr4

EXPNO : 11

PROCNO : 1

*** Acquisition Parameters ***

BF1 : 100.6127690 MHz

*** Processing Parameters ***

SF : 100.6127750 MHz

*** 1D NMR Plot Parameters ***

XOffset : 1.00 cm

2i

169.1326
168.7534

135.8254

118.1786

77.3215
77.0000
76.6786

54.1853
52.3885
52.1824
50.0641

39.0606

31.5107
28.5599
26.3840
26.3180

2j

2j