

Supporting information for:  
**Sequential Birch reaction and asymmetric Ir-catalyzed hydrogenation as a route to chiral building blocks**

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**Table of contents**

General methods	S1
Preparation of Birch substrates	S2
Birch reductions	S6
Hydrogenations	S11
Other reactions	S17
References	S18

**General methods**

All reactions were conducted under dry nitrogen atmosphere using magnetic stirring. CH<sub>2</sub>Cl<sub>2</sub> (DCM) was freshly distilled from CaH<sub>2</sub> under nitrogen. THF was distilled from sodium with benzophenone under nitrogen prior to use. All reagents were used as supplied commercially without further purification. Lithium (99.9%) was purchased from Sigma-Aldrich as a wire with 0.01% sodium.

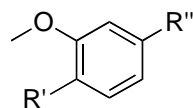
Chromatographic separations were performed on Kiesel gel 60 H silica gel (particle size: 0.063-0.100 mm). Thin layer chromatography (TLC) was performed on aluminum plates coated with Kieselgel 60 (0.20 mm, UV254) and visualized under ultraviolet light ( $\nu = 254$  nm), I<sub>2</sub> vapors, or by staining with basic aqueous KMnO<sub>4</sub> solution or ethanolic phosphomolybdic acid and heating.

<sup>1</sup>H NMR spectra were recorded at 500, 400 or 300 MHz in CDCl<sub>3</sub> at 25°C and referenced internally to the residual CHCl<sub>3</sub> peak (7.26 ppm). Prior to use, CDCl<sub>3</sub> was neutralized by passage through short plug of basic alumina. Chemical shifts are reported in ppm ( $\delta$  scale). Mass spectra were measured at 70 eV (EI). IR spectra was measured using an FT-IR apparatus. Enantiomeric excesses were determined using

chiral GC (see data for individual compounds for details) with a MS detector.

Racemic compounds were used for comparison.

### Preparation of Birch substrates



R'/R'' = Me/Me (**1m**), Me/iPr, (**1o**) iPr/Me (**1n**), H/iPr (**1c**)

A phenole (1 eq) was dissolved in dry THF (approx. 100 ml for each 70 mmol of phenole). NaOH prills were added (1.2 eq) and solution was heated in oil bath at 50°C until NaOH prills dissolve (approx. 1 hour). MeI (1.5 eq) was added in one portion and solution was left at 50°C o. n.. Water was added (approx. 50 ml for each 70 mmol of starting material), THF was evaporated and product was extracted two times with ether. Combined organic phase was washed with brine, dried over MgSO<sub>4</sub> and evaporated. Distillation or column chromatography (on short silica column using pentane:ether 100:0 to 95:5) afforded products as oils.

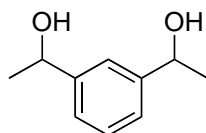
**1m**: Purified by chromatography. Colorless oil 9.88 g (89 %); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 2.36 (s, 3 H, Me), 2.49 (s, 3 H, Me), 3.94 (s, 3 H, MeO), 6.80 (m, 1 H, H-Ar), 6.83 (m, 1 H, J = 7.6 Hz, H-Ar), 7.16 (m, 1 H, J = 7.6 Hz, H-Ar)

**1o**: Purified by chromatography. Colorless oil 21.86 g (quant.); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 1.46 (d, 6 H, J = 6.9 Hz, 2xMe), 2.40 (s, 3 H, Me), 3.07 (sep, 1 H, J = 6.7 Hz, CH), 4.01 (s, 3 H, MeO), 6.90 (m, 1 H, J = 1.9 Hz, H-Ar), 6.93 (m, 1 H, J = 7.6 and 1.9 Hz, H-Ar), 7.24 (m, 1 H, H-Ar); MS (EI) (m/z) (rel. intensity): 165 (MH<sup>+</sup>, 15%), 164 (M<sup>+</sup>, 100%), 149 (100%) and 115 (20%)

**1n**: Purified by chromatography. Colorless oil 20.77 g (95 %); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ 1.22 (d, 6 H, J = 7.2 Hz, CH<sub>3</sub>×2), 2.36 (s, 3 H, CH<sub>3</sub>-Ar), 3.30 (m, 1 H, CH), 3.84 (s, 3 H, CH<sub>3</sub>O) 6.70 (m, 1 H, H-Ar), 6.77 (m, 1 H, J = 7.8 Hz, H-Ar), 7.12 (m, 1 H, J = 7.8 Hz, H-Ar); MS (EI) (m/z) (rel. intensity): 165 (MH<sup>+</sup>, 15%), 164 (M<sup>+</sup>, 73%), 149 (100%), 134 (18%), 119 (28%), 91 (33%)

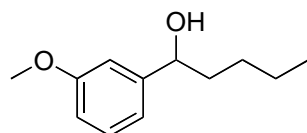
**1c**: purified by chromatography. Colorless oil 10.18 g (92 %); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 1.37 (d, 6 H, J = 6.9 Hz, 2xCH<sub>3</sub>), 3.00 (sep, 1 H, J = 6.9 Hz CH), 3.89 (s, 3 H, CH<sub>3</sub>O), 6.84 (m, 1 H, J = 8.2, 2.6 and 1.0 Hz, H-Ar), 6.91 (m, 1 H, H-Ar), 6.94 (m, 1 H, H-Ar), 7.32 (m, 1 H, H-Ar)

Compounds **1a**,<sup>1</sup> **1d**,<sup>2</sup> **1f**,<sup>3</sup> **1l**<sup>4</sup> and **1p**<sup>5</sup> were prepared using literature procedures. Attempts were made converting diphenoles using general NaOH/MeI/THF procedure as for monophenoles, although this produced significant amount of aromatic methylation byproducts.



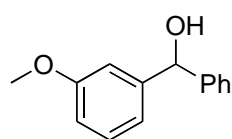
Compound **1g**: 1,3-diisopropenylbenzene (10.00 g, 1 eq) THF (400 ml), water (200 ml) and OsCl<sub>3</sub>·nH<sub>2</sub>O (53 mg) were combined and NaIO<sub>4</sub>(60 g) was added in one portion. After stirring o.n. solution was filtered, the inorganic precipitate was washed with THF and combined liquid was evaporated to remove all THF. Aqueous solution was extracted with ether (3 times), organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, evaporated to give crude 1,3-diacetyl benzene. Crude product was dissolved in 95% ethanol (150 ml) and NaBH<sub>4</sub> (2.57 g, 4 H<sup>-</sup>-eq) was added in portions over 10 minutes. After stirring o.n. reaction was quenched with 10% HCl (100 ml). Ethanol was evaporated and solution was basified with aqueous 20% NaOH (100 ml), product was extracted with DCM (3 times). Combined organic phase was washed with brine, dried over MgSO<sub>4</sub> and evaporated to give dark oil that partially crystallizes on standing.

Chromatography on silica with DCM:MeOH 100:0 to 90:10 affords 8.65 g of the semi-crystalline diol (82 % yield over two steps). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 1.41 (d, 6 H, J = 6.5 Hz, 2xCH<sub>3</sub>), 3.02 (s, 2 H, 2xOH), 4.77 (q, 2 H, J = 6.5 Hz, 2xCH), 7.16-7.20 (m, 2 H, H-Ar), 7.26 (m, 1 H, H-Ar), 7.32 (m, 1 H, H-Ar); MS (EI) (m/z) (rel. intensity): 166 (M<sup>+</sup>, 9%), 152 (31%), 149 (80%), 133 (33%), 105 (100%), 91 (28%), 79 (52%) and 77 (96%)

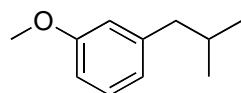


Compound **1e**: 3-methoxybenzaldehyde (15.00 g, 110 mmol, 1 eq) was dissolved in THF (150 ml) and cooled to -78°C. 2.5 M hexane solution of BuLi (58 ml, 145 mmol, 1.3 eq) was added drop wise over 1 hour. Reaction was stirred for an additional hour at -78°C, taken out from ice bath and stirred for 4 hours. After quenching with

saturated solution of  $\text{NH}_4\text{Cl}(\text{aq})$  (100 ml) the THF was evaporated and product was extracted 3 times with ether. Organic phase was washed with brine, dried over  $\text{MgSO}_4$  and evaporated. Chromatography on silica (DCM:ethanol 100:0 to 95:5) afforded 20.15 g (94 %) of product as an oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  0.89 (t, 3 H,  $J = 7.2$  Hz,  $\text{CH}_3$ ), 1.21-1.45 (m, 4 H,  $2\times\text{CH}_2$ ), 1.70 (m, 1 H,  $\text{CH}_2\text{CH}$ ), 1.79 (m, 1 H,  $\text{CH}_2\text{CH}$ ), 1.84 (br s, 1 H, OH), 3.81 (s, 3 H,  $\text{CH}_3\text{O}$ ), 4.64 (dd, 1 H,  $J = 7.6$  and  $5.8$  Hz, CH), 6.81 (m, 1 H,  $J = 8.2, 2.5$  and  $1.1$  Hz, H-Ar), 6.90-6.93 (m, 2 H, H-Ar), 7.26 (m, 1 H, H-Ar); MS (EI) ( $m/z$ ) (rel. intensity): 194 ( $\text{M}^+$ , 100%), 177 (90%), 137 (32%), 109 (74%), 94 (41%) and 77 (26%)

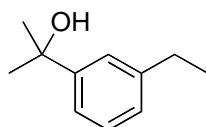


Compound **1k**: Phenylmagnesium bromide, prepared from Mg (2.50 g, 103 mmol, 1.4 eq) and benzyl bromide (10.0 ml, 95.5 mmol, 1.3 eq) in 150 ml THF, was added to 3-methoxybenzaldehyde (10.00 g, 73.4 mmol, 1 eq) in THF (50 ml) at  $-78^\circ\text{C}$  over 1.5 hours. Reaction was left in dry ice bath o. n. to heat up to RT. After quenching with saturated  $\text{NH}_4\text{Cl}(\text{aq})$  solution, THF was evaporated and product was extracted 3 times with ether. Organic phase was washed with brine, dried over  $\text{K}_2\text{CO}_3$  and evaporated. Flash chromatography (pentane:ether) afforded 15.23 g (97 %) of product as an oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  2.27 (br s, 1 H, OH), 3.80 (s, 3 H,  $\text{OCH}_3$ ), 5.81 (s, 1 H, CH), 6.82 (m, 1 H, H-Ar), 6.94-6.98 (m, 2 H, H-Ar), 7.24-7.30 (m, 2 H, H-Ar), 7.32-7.37 (m, 2 H, H-Ar), 7.38-7.41 (m, 2 H, H-Ar); MS (EI) ( $m/z$ ) (rel. intensity): 214 ( $\text{M}^+$ , 83), 197 (69%), 181 (20%), 165 (21), 153 (28%), 152 (33%), 135 (48%), 109 (100%), 108 (67%), 105 (51%), 94 (30%) and 77 (66%)



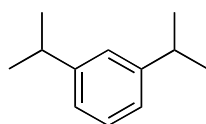
Compound **1j**:  $\text{PdCl}_2\text{dppf}^*\text{DCM}$  (55 mg, 67  $\mu\text{mol}$ , 0.25 mol%) was charged into a flask and air was displaced with argon. Ether solution (150 ml) of 3-bromoanisole (5.00 g, 27 mmol, 1 eq) was added and flask was cooled in ice bath. 2.0 M solution of isobutyl magnesium chloride (16.0 ml, 32 mmol, 1.2 eq) was added over 30 min. Reaction was removed from ice bath and refluxed o. n.. After careful quenching with

water (50 ml), organic phase was separated and aqueous phase was extracted 2 times with ether. Combined organic phase was washed with brine and left o. n. over  $\text{MgSO}_4$  and silica (approx. 0.5 g), filtered and evaporated. Chromatography on silica (6 cm column, pentane as eluent) afforded 3.98 g (91 %) of product as an oil.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  0.91 (d, 6 H,  $J = 6.7$  Hz,  $2 \times \text{CH}_3$ ), 1.88 (m, 1 H, CH), 2.46 (d, 2 H,  $J = 7.2$  Hz,  $\text{CH}_2$ ), 3.80 (s, 3 H,  $\text{OCH}_3$ ), 6.71 (m, 1 H, H-Ar), 6.72-6.76 (m, 2 H, H-Ar), 7.19 (m, 1 H, H-Ar); MS (EI) (m/z) (rel. intensity): 164 ( $\text{M}^+$ , 100%), 149 (13%), 122 (93%), 121 (53%), 107 (11%), 91(32%) and 77 (13%)



Compound **1h**: 2-(3-bromophenyl)propan-2-ol (prepared from m-bromoacetophenone and  $\text{MeMgI}$  in ether<sup>7</sup>) (5.53 g, 33.7 mmol, 1 eq) was added as a solution in dry ether (150 ml) to  $\text{PdCl}_2\text{dppf} \cdot \text{DCM}$  (52 mg, 64  $\mu\text{mol}$ , 0.25 mol%) under argon. Flask was cooled in ice-bath and a 2.54 M solution of  $\text{EtMgBr}$  was added (23.3 ml, 59.2 mmol, 2.3 eq) over 15 minutes. After removal of ice-bath and reflux for 24 h reaction was quenched carefully with 10%  $\text{HCl}$  (50 ml) and extracted with ether (3 times).

Combined organic phase was washed with brine and left to stand over night with  $\text{MgSO}_4$  and silica. After filtering and evaporation of solvent, residue was purified by chromatography on short silica column (7 cm, pentane:ether 95:5 to 50:50) to give 3.99 g of **1h** as colorless oil (94% yield).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  1.26 (t, 3 H,  $J = 7.6$  Hz,  $\text{CH}_3$ ), 1.59 (s, 6 H,  $2 \times \text{CH}_3$ ), 1.77 (br s, 1 H, OH), 2.67 (q, 2 H,  $J = 7.6$  Hz,  $\text{CH}_2$ ), 7.10 (m, 1 H, H-Ar), 7.25-7.32 (m, 2 H, H-Ar), 7.35 (m, 1 H, H-Ar); MS (EI) (m/z) (rel. intensity): 165 ( $\text{MH}^+$ , 12%), 149 (30%), 146 (96%), 133 (100%), 131 (97%), 118 (36%), 117 (46%), 115 (33%), 109 (20%), 105 (46%), 91 (48%), 79 (27%) and 77 (45%)



Compound **1i**: To 1,3-diisopropenylbenzene (10.0 g, 63.2 mmol) were added  $\text{DCM}$  (40 ml) and 10%  $\text{Pd/C}$  (50 mg). Reaction was stirred under atmosphere of 5 bar hydrogen for 19 hours. After removal of solvent, residue was dissolved in pentane, filtered through celite and pentane was removed. Residue was distilled at 10 torr to

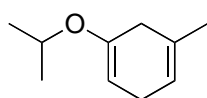
afford 9.00 g (88 %) of colorless liquid, bp 70 °C. <sup>1</sup>H NMR is in accordance to literature;<sup>6</sup> MS (EI) (m/z) (rel. intensity): 162 (M<sup>+</sup>, 35%), 147 (100%), 119 (56%), 105 (30%) and 91 (32%)

### Birch reductions

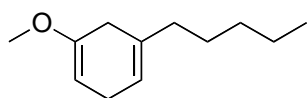
Compounds **2a**<sup>8</sup>, **2b**<sup>9</sup> and **2c**<sup>10</sup> were prepared according to literature procedures.

General procedure: Birch reductions were conducted in a 3 necked round bottomed flask with a dry ice condenser, an NH<sub>3</sub>(g) inlet and a stopper for Na addition. Ammonia was condensed from a commercial NH<sub>3</sub> tube into a mixture of aromatic substrate, alcohol and a co solvent while cooling flask in dry ice bath. Alcohols used were <sup>t</sup>BuOH, for unhindered substrates, in this case only a slight excess of the metal was required from theoretical amount. A co solvent was needed (ether or THF) to keep reaction stirrable in the beginning of ammonia condensation. In the case of more hindered substrates (specially tri- substituted arenes) ethanol was used in large excess (20-40 eq) as a proton source with a large excess Na or Li (8-30 eq), normally a co solvent was not needed in this case. Addition of the metal was done at reflux temperature of NH<sub>3</sub> with such speed as to prevent vigorous reaction/foaming. On discoloration of reaction, dry ice was removed from condenser and ammonia was evaporated. If unreacted Na was present, it was quenched with 95% ethanol. Reaction was carefully diluted with water, extracted with ether (3 times), washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. Solvent was removed and product was purified either by distillation under reduced pressure or by chromatography on deactivated (Et<sub>3</sub>N) silica with pentane as eluent.

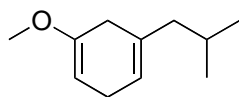
Products were stable for several months under argon at -20°C. At RT the methoxy enolate dienes disproportionated to a noticeable extent to aromatic starting material and reduced products after weeks. The produced ketones deactivated the Ir catalyst.



According to general procedure, following amounts were used: 1-isopropoxy-3-methylbenzene (5.00 g, 33.3 mmol, 1 eq), ethanol (8.4 ml, 144 mmol, 4.3 eq) and THF (20 ml). Ammonia condensed to a total volume of 125 ml. Na (2.75 g, 120 mmol, 3.6 eq) was added over 40 min. After general workup and distillation of crude material, 2.46 g (48 %) of **2d** was obtained as colorless oil, 75-78°C at 12 torr. <sup>1</sup>H NMR (d-benzene, 400 MHz): δ 1.14 (d, 6 H, J = 6.0 Hz, 2xCH<sub>3</sub>), 1.54-1.56 (m, 3 H, CH<sub>3</sub>), 2.64-2.70 (m, 2 H, CH<sub>2</sub>), 2.75-2.83 (m, 2 H, CH<sub>2</sub>), 4.13 (sept d, 1 H, J = 6.0 and 0.7 Hz, CH), 4.54 (m, 1 H, C=CH), 5.37 (m, 1 H, C=CH); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 22.1, 23.0, 27.1, 34.0, 67.4, 92.1, 118.8, 130.9, 150.3; MS (EI) (m/z) (rel. intensity): 152 (M<sup>+</sup>, 20%), 110 (40%), 95 (100%) and 77 (22%)

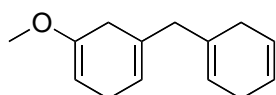


According to general procedure, following amounts were used: **1e** (5.00 g, 25.7 mmol, 1 eq) and ethanol (45 ml, 771 mmol, 30 eq). Ammonia condensed to a total volume of 250 ml. Na (3.60 g, 157 mmol, 6 eq) was added over 20 min. After general workup and chromatography on deactivated (Et<sub>3</sub>N) silica with pentane as eluent, 3.68 g (79 %) of **2e** was obtained as colorless oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 0.89 (t, 3 H, J = 7.2 Hz, CH<sub>3</sub>), 1.20-1.36 (m, 4 H, 2xCH<sub>2</sub>), 1.37-1.47 (m, 2 H, CH<sub>2</sub>), 1.96-2.02 (m, 2 H, CH<sub>2</sub>), 2.57-2.66 (m, 2 H, C=CCH<sub>2</sub>C=C), 2.75-2.83 (m, 2 H, C=CCH<sub>2</sub>C=C), 3.56 (s, 3 H, OCH<sub>3</sub>), 4.63 (m, 1 H, CH=CO), 5.41 (m, 1 H, CH=C); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 14.2, 22.7, 26.9, 27.1, 31.6, 31.7, 37.0, 54.0, 90.5, 118.3, 134.7, 153.2; MS (EI) (m/z) (rel. intensity): 180 (M<sup>+</sup>, 70 %), 137 (100%), 124 (35%), 109 (83%) and 91 (22%)

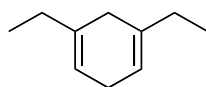


According to general procedure, following amounts were used: **1j** (2.00 g, 12.2 mmol, 1 eq), ethanol (3.6 ml, 61.6 mmol, 5 eq) and ether (5 ml). Ammonia condensed to a total volume of 80 ml. Na (0.84 g, 36.5 mmol, 5 eq) was added over 10 min. After general workup and chromatography on deactivated (Et<sub>3</sub>N) silica with pentane as eluent, 0.77 g (52 % with regard to recovered starting material) of **2j** was obtained as colorless oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ 0.86 (d, 6 H, J = 6.5 Hz, 2xCH<sub>3</sub>), 1.77

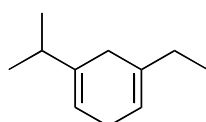
(m, 1 H, CH), 1.86 (m, 1 H, CH<sub>2</sub>) 1.89 (m, 1 H, CH<sub>2</sub>), 2.56-2.64 (m, 2 H, C=CCH<sub>2</sub>C=C), 2.75-2.85 (m, 2 H, C=CCH<sub>2</sub>C=C), 3.56 (s, 3 H, OCH<sub>3</sub>), 4.63 (m, 1 H, CH=CO), 5.39 (m, 1 H, CH=C); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz): δ 22.6, 25.8, 26.9, 31.6, 46.9, 54.0, 90.5, 119.8, 133.5, 153.2; MS (EI) (m/z) (rel. intensity): 166 (M<sup>+</sup>, 53%), 151 (25%), 124 (17%), 109 (100%), 91 (23%) and 77 (21%)



According to general procedure, following amounts were used: **1k** (5.00 g, 23.3 mmol, 1 eq) and ethanol (41 ml, 702 mmol, 30 eq). Ammonia condensed to a total volume of 250 ml. Na (4.29 g, 187 mmol, 8 eq) was added over 20 min. After general workup and chromatography on deactivated (Et<sub>3</sub>N) silica with pentane as eluent, 3.89 g (82 %) of **2k** was obtained as colorless oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 2.49-2.61 (m, 4 H, 2xCH<sub>2</sub>), 2.62-2.73 (m, 4 H, 2xCH<sub>2</sub>), 2.78-2.85 (m, 2 H, CH<sub>2</sub>), 3.55 (s, 3 H, OCH<sub>3</sub>), 4.62 (m, 1 H, CH=CO), 5.44-5.50 (m, 2 H, CH<sub>2</sub>), 5.66-5.70 (m, 2 H, CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 27.0 (2C), 28.6, 31.2, 45.8, 54.0, 90.4, 120.5, 120.7, 124.2, 124.6, 132.2, 132.6, 153.3; MS (EI) (m/z) (rel. intensity): 202 (M<sup>+</sup>, 5 %), 130 (10%), 109 (100%), 94 (25%) and 77 (21%)

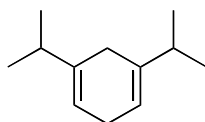


According to general procedure, following amounts were used: **1g** (3.00 g, 18.0 mmol, 1 eq) and ethanol (32 ml, 548 mmol, 30 eq). Ammonia condensed to a total volume of 250 ml. Na (4.15 g, 181 mmol, 10 eq) was added over 20 min. After general workup and chromatography on silica with pentane as eluent 1.01 g (41 %) of **2g** was obtained as colorless oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 1.04 (t, 6 H, J = 7.6 Hz, 2xCH<sub>3</sub>), 2.00 (app. q, 4 H, J = 7.6 Hz, 2xCH<sub>2</sub>), 2.50-2.55 (m, 2 H, CH<sub>2</sub>), 2.67-2.73 (m, 2 H, CH<sub>2</sub>), 5.42 (m, 2 H, 2xCH); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 12.2, 27.8, 30.1, 32.5, 117.0, 144.4; MS (EI) (m/z) (rel. intensity): 136 (M<sup>+</sup>, 35%), 107 (65%), 91 (25%), 79 (100%) and 77 (37%)

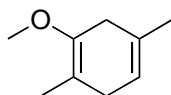




According to general procedure, following amounts were used: 2-(3-ethylphenyl)propan-2-ol (2.00 g, 12.2 mmol, 1 eq) and ethanol (21 ml, 360 mmol, 30 eq). Ammonia condensed to a total volume of 150 ml. Na (2.24 g, 97.4 mmol, 8 eq) was added over 20 min. After general workup and chromatography on silica with pentane as eluent 1.12 g (61 %) of **2h** was obtained as colorless oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  1.04 (d, 6 H,  $J = 6.9$  Hz,  $2\times\text{CH}_3$ ), 1.04 (t, 3 H,  $J = 7.5$  Hz,  $\text{CH}_3$ ), 2.01 (app. q, 2 H,  $J = 7.5$  Hz,  $\text{CH}_2$ ), 2.21 (sept, 1 H,  $J = 6.9$  Hz, CH), 2.51-2.58 (m, 2 H,  $\text{CH}_2$ ), 2.66-2.74 (m, 2 H,  $\text{CH}_2$ ), 5.42 (m, 1 H,  $\text{CH}=\text{C}$ ), 5.45 (m, 1 H,  $\text{CH}=\text{C}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  12.2, 21.4, 27.8, 30.1, 30.1, 34.8, 116.1, 117.0, 137.0, 140.9; MS (EI) (m/z) (rel. intensity): 150 ( $\text{M}^+$ , 25%), 121 (15%), 107 (60%), 106 (65%), 91 (40%), 79 (100%) and 77 (43%)

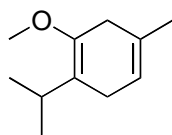


According to general procedure, following amounts were used: 1,3-diisopropylbenzene (4.66 g, 28.7 mmol, 1 eq) and ethanol (50 ml, 856 mmol, 30 eq). Ammonia condensed to a total volume of 250 ml. Na (6.60 g, 287 mmol, 10 eq) was added over 25 min. After general workup and chromatography on silica with pentane as eluent 2.11 g (45 %) of **2i** was obtained as colorless oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  1.04 (d, 12 H,  $J = 6.8$  Hz,  $4\times\text{CH}_3$ ), 2.21 (sept, 2 H,  $J = 6.8$  Hz,  $2\times\text{CH}$ ), 2.53-2.58 (m, 2 H,  $\text{CH}_2$ ), 2.67-2.73 (m, 2 H,  $\text{CH}_2$ ), 5.43 (m, 2 H,  $2\times\text{CH}=\text{C}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz):  $\delta$  21.4, 27.8, 28.0, 34.9, 116.0, 148.9; MS (EI) (m/z) (rel. intensity): 164 ( $\text{M}^+$ , 15%), 163 (18%), 147 (15%), 121 (64%), 120 (100%), 105 (70%), 91 (43%), 79 (93%) and 77 (52%)

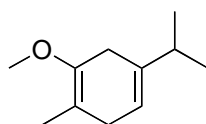


According to general procedure, following amounts were used: Aromatic compound **1m** (5.00 g, 36.7 mmol, 1 eq) and ethanol (39 ml, 668 mmol, 18 eq). Ammonia condensed to a total volume of 250 ml. Na (7.60 g, 331 mmol, 9 eq) was added over 30 min. After general workup and distillation at 9 torr, 3.93 g (77 %) of **2m** was obtained as colorless oil, 52-56°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  1.63 (app. s, 3 H,  $\text{CH}_3$ ), 1.70 (app. s, 3 H,  $\text{CH}_3$ ), 2.64-2.68 (m, 4 H,  $2\times\text{CH}_2$ ), 3.54 (s, 3 H,  $\text{OCH}_3$ ), 5.35

(m, 1 H, CH); MS (EI) (m/z) (rel. intensity): 138 ( $M^+$ , 58%), 123 (100%), 108 (23%), 91 (28%) and 77 (16%)

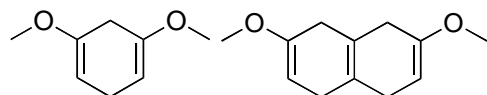


A mixture of anhydrous ammonia (60 ml), anhydrous tetrahydrofuran (40 ml) and *t*-butanol (5 ml) was treated with lithium wire (0.55 g, 79.1 mmol). The mixture was stirred vigorously for 40 min using a dry ice condenser to maintain the ammonia in the reaction mixture, at which time a solution of starting material (2.00 g, 12.2 mmol) in tetrahydrofuran (5 ml) was added over 5 min. The solution was stirred for 15 min and additional *t*-butanol (10 ml) was added. The condenser was removed and the ammonia allowed to evaporate o.n.. Solid ammonium chloride (6 g) and ethanol were added to quench any excess lithium. Ether (20 mL) and water (20 mL) were added and the layers separated. The aqueous layer was extracted with ether (200 mL). The combined ether layers were washed with solution of saturated ammonium chloride (50 ml) followed by water (80 ml). The combined aqueous layers were back-extracted with 100 mL of ether. All of the ether layers were combined, dried over anhydrous magnesium sulfate, filtered and the volatiles evaporated *in vacuo* to give a light yellow oil. The residue was purified by distillation to give 1.4 g (69%) of diene as colorless liquid (bp. 66-70 °C @ 8-9 mm Hg).  $^1\text{H}$  NMR (d-benzene, 400 MHz):  $\delta$  1.03 (d, 6 H,  $J = 6.8$  Hz, 2xCH<sub>3</sub>), 1.58 (app. s, 3 H, CH<sub>3</sub>), 2.46-2.49 (m, 2 H, CH<sub>2</sub>), 2.60-2.64 (m, 2 H, CH<sub>2</sub>), 3.25 (s, 3 H, OCH<sub>3</sub>), 3.40 (sept, 1 H,  $J = 6.8$  Hz, CH), 5.37 (m, 1 H, CH=C); MS (EI) (m/z) (rel. intensity): 167 ( $M^+$ , 10%), 166 (25%), 124 (13%), 123 (100%), 108 (15%), 91 (21%)



According to general procedure, following amounts were used: Aromatic compound **1o** (4.31 g, 26.4 mmol, 1 eq) and ethanol (48 ml, 822 mmol, 31 eq). Ammonia condensed to a total volume of 250 ml. Na (7.24 g, 315 mmol, 12 eq) was added over 40 min. After general workup and distillation at 9 torr, 3.01 g (69 %) of **2o** was obtained as colorless oil, 74-76°C.  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  1.04 (d, 6 H,  $J =$

9.2 Hz, 2xCH<sub>3</sub>), 1.64 (s, 3 H, CH<sub>3</sub>), 2.82 (m, 1 H, CH), 2.70 (m, 2xCH<sub>2</sub>), 3.55 (s, OCH<sub>3</sub>), 5.38 (m, 1 H, CH=C); MS (EI) (m/z) (rel. intensity): 167 (MH<sup>+</sup>, 25%), 166 (M<sup>+</sup>, 73%), 151 (35%), 123 (100%), 108 (%), 91 (%)



Compounds **2l**<sup>11</sup> and **2p**<sup>12</sup> were prepared using literature procedures.

## Hydrogenations

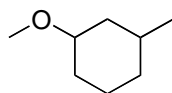
Substrate (1.25 mmol) was loaded into a vial with magnetic stirrer and a lid with septa, a stock solution of catalyst of ligands **A** or **B** (see main article) (5 ml, 6.25 μmol, 0.5 mol%) in dry DCM was added under argon, septa was pierced with a needle and vial was placed into high pressure hydrogenation equipment. After applying and releasing argon at 6 bar 8 times, a pressure of hydrogen was applied and left for specific time.

Hydrogen was released, solvent was evaporated and residue was analyzed by NMR and GC MS with chiral column. <sup>1</sup>H NMR was taken in CDCl<sub>3</sub> (priorly passed through basic alumina). For GC MS analysis a small part of reaction mixture was applied on a short plug of silica (deactivated by Et<sub>3</sub>N) and eluted with ether:pentane (1:1).

Racemates of **2a-j** were made by hydrogenating substrate (20-50 mg) in d-benzene (1 ml) in presence of 10% Pd/C (5 mg) and K<sub>2</sub>CO<sub>3</sub> (5 mg) at 10 bar hydrogen pressure for 20 hours.

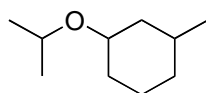
Racemate of **2k** was made by hydrogenating substrate (50 mg) in DCM (2 ml) in presence of 10% Pd/C (3 mg) and Et<sub>3</sub>N (4 drops) at 10 bar hydrogen pressure for 18 hours.

Racemates of **2l-n** were not prepared although both enantiomers were prepared using complexes of ligands **A** and **B** according to procedure for asymmetric hydrogenation. Racemate of **2o** was made using racemic complex of ligand **A** according to procedure for asymmetric hydrogenation.



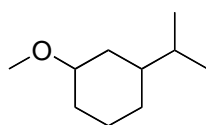
Catalyst used: [**B**-IrCOD]BA<sub>r</sub>F.

Trans: <sup>1</sup>H NMR (d-benzene, 500 MHz): δ 0.85 (d, J = 6.5 Hz, CH<sub>3</sub>), 3.11 (s, OCH<sub>3</sub>), 3.29 (m, CHO); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz): δ 20.5, 22.4, 26.8, 29.5, 34.6, 38.6, 55.8, 75.8; Cis: <sup>1</sup>H NMR (d-benzene, 500 MHz): δ 0.84 (d, J = 6.5 Hz, CH<sub>3</sub>), 2.93 (tt, J = 10.5 and 4.3 Hz, CHO), 3.19 (s, OCH<sub>3</sub>); Trans:cis = 76:24 (by NMR); MS (EI) (m/z) (rel. intensity): 127 ([M-H]<sup>+</sup>, 3%), 96 (61%), 85 (100%), 81 (58%), 71 (34%) and 55 (27%); GC MS (column: Chiraldex β-DM, temperature: 60 °C isothermal, pressure: 14.5 psi): trans: 8.3 (major) & 9.2 (minor) min, 97% ee; cis: 9.9 (major) & 10.4 (minor) min, 48% ee; Trans:cis = 91:9 (by GC MS)



Catalyst used: [**B**-IrCOD]BA<sub>r</sub>F.

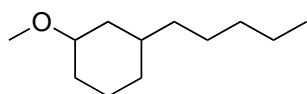
Trans: <sup>1</sup>H NMR (d-benzene, 400 MHz): δ 3.45 (sept, J = 6.1 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 3.53 (m, CHO(CH<sub>2</sub>)<sub>2</sub>); Cis: <sup>1</sup>H NMR (d-benzene, 400 MHz): δ 3.16 (tt, J = 10.6 and 4.2 Hz, CHO(CH<sub>2</sub>)<sub>2</sub>), 3.57 (sept, J = 6.1 Hz, CH(CH<sub>3</sub>)<sub>2</sub>); Trans:cis = 75:25 (by NMR); MS (EI) (m/z) (rel. intensity): 155 ([M-H]<sup>+</sup>, 2%), 113 (18%), 112 (23%), 97 (93%), 96 (100%), 81 (73%), 71 (96%) and 55 (50%); GC MS (column: Chiraldex β-DM, temperature: 60 °C isothermal, pressure: 14.5 psi): trans: 10.8 (minor) & 11.3 (major) min, 94% ee; cis: 14.7 (major) & 15.2 (minor) min, 77% ee; Trans:cis = 71:29 (by GC MS)



Catalyst used: [**B**-IrCOD]BA<sub>r</sub>F.

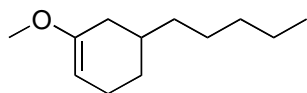
Trans: <sup>1</sup>H NMR (d-benzene, 400 MHz): δ 3.12 (s, OCH<sub>3</sub>), 3.35 (m, CHO); Cis: <sup>1</sup>H NMR (d-benzene, 400 MHz): δ 2.95 (m, CHO), 3.21 (s, OCH<sub>3</sub>); Trans:cis = 86:14 (by NMR); MS (EI) (m/z) (rel. intensity): 155 ([M-H]<sup>+</sup>, 2%), 124 (68%), 113 (62%), 109 (58%), 95 (13%), 81 (72%), 71 (100%), 67 (33%) and 55 (22%); GC MS (column: Chiraldex β-DM, temperature: 60 °C isothermal, pressure: 14.5 psi): trans: 13.6

(major) & 14.1 (minor) min, 94%; cis: 14.9 (major) & 15.4 (minor) min, 21% ee;  
Trans:cis = 90:10 (by GC MS)



Catalyst used: [A-IrCOD]BAR<sub>F</sub>.

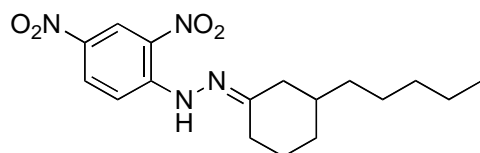
Trans: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 0.83 (t, J = 7.0 Hz), 3.24 (s, OCH<sub>3</sub>), 3.42 (m, CHO); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 14.1, 20.4, 22.8, 26.6, 29.8, 31.7, 32.3, 32.5, 36.7, 36.9, 55.6, 75.7; Cis: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 0.88 (t, J = Hz), 3.09 (tt, J = 11.0 and 4.2 Hz, CHO), 3.35 (s, OCH<sub>3</sub>); Trans:cis = 83:17 (by NMR); MS (EI) (m/z) (rel. intensity): 183 ([M-H]<sup>+</sup>, 3%), 152 (36%), 141 (35%), 123 (17%), 113 (49%), 109 (38%), 96 (45%), 95 (39%), 81 (82%), 71 (100%), 67 (47%) and 55 (23%); GC MS (column: Hydrodex β-6 TBDM, temperature: 100 °C isothermal, flow: 1.0 ml/min): trans: 23.7 (major) & 26.6 (minor) min, 98% ee; cis: 30.1 (minor) & 31.0 (major) min, 62% ee; Trans:cis = 91:9 (by GC MS); At 1 mol% catalyst loading 97% ee was obtained for the trans isomer.



Catalyst used: [A-IrCOD]BAR<sub>F</sub>, together with poly(4-vinylpyridine) (15 mg).

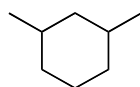
NMR of crude material taken, only olefinic and methoxy frequencies reported; <sup>1</sup>H NMR (d-benzene, 500 MHz): δ 4.52 (m, 1H, CH) 3.30 (s, 3H OCH<sub>3</sub>); MS (EI) (m/z) (rel. intensity): 182 (M<sup>+</sup>, 5%), 139 (5%), 111 (100%), 97 (4%), 81 (9%) and 79 (15%); GC MS (column: Hydrodex β-6 TBDM, temperature: 100 °C isothermal, flow: 1.0 ml/min): 42.4 (minor) & 43.3 (major) min, 89% ee.

At 1 mol% catalyst loading 95% ee was obtained.



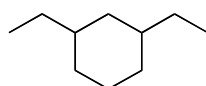
E/Z mixture ca 1:1; <sup>1</sup>H NMR (d-benzene, 500 MHz): δ 0.89 (t, E or Z, J=7.3 Hz, CH<sub>3</sub>), 0.90 (t, E or Z, J=7.0 Hz, CH<sub>3</sub>), 1.20-1.41 (m, 9H), 1.47-1.69 (m, 2H, CH<sub>2</sub>),

1.82-2.33 (m, 4H), 2.60 (m, 1H CH), 2.79 (m, 1H, CH), 7.96 (m, 1H, Ar-H), 8.28 (m, 1 H, Ar-H), 9.12 (m, 1H, Ar-H), 11.19 (brs., E or Z, NH), 11.23 (brs., E or Z, NH);



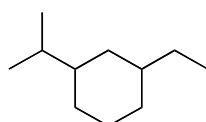
Catalyst used: [**A**-IrCOD]BAr<sub>F</sub>.

Trans: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 0.91 (d, J = 6.7 Hz, CH<sub>3</sub>); Cis: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 0.88 (d, J = 6.5 Hz, CH<sub>3</sub>); Trans:cis = 91:9 (by NMR); MS (EI) (m/z) (rel. intensity): 111 ([M-H]<sup>+</sup>, 10%), 97 (100%), 81 (8%), 69 (27%) and 55 (82%); GC MS (column: Chiraldex β-DM, temperature: 60 °C isothermal, pressure: 14.5 psi): trans: 4.5 (minor) & 4.6 (major) min, 97% ee; cis: 3.5 min; Trans:cis = 89:11 (by GC MS)



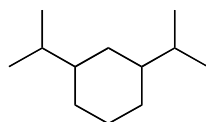
Catalyst used: [**A**-IrCOD]BAr<sub>F</sub>.

MS (EI) (m/z) (rel. intensity): 139 ([M-H]<sup>+</sup>, 3%), 111 (64%), 81 (9%), 69 (100%) and 55 (17%); GC MS (column: Hydrodex β-6 TBDM, temperature: 50 °C isothermal, flow: 1.0 ml/min): trans: 30.2 (minor) & 35.7 (major) min, 75% ee; cis: 25.9 min; Trans:cis = 54:46



Catalyst used: [**B**-IrCOD]BAr<sub>F</sub>.

MS (EI) (m/z) (rel. intensity): 153 ([M-H]<sup>+</sup>, 2%), 111 (62%), 110 (68%), 95 (7%), 81 (32%), 69 (100%) and 55 (17%); GC MS (column: Hydrodex β-6 TBDM, temperature: 50 °C isothermal, flow: 1.0 ml/min): trans: 56.7 (major) & 61.0 (minor) min, 96% ee; cis: 50.8 (major) & 52.9 (minor) min, 61% ee; Trans:cis = 56:44

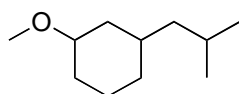


Catalyst used: [**B**-IrCOD]BAR<sub>F</sub>.

Trans: <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 20.5, 20.8, 21.6, 29.6, 29.7, 32.1, 39.6;

Cis: <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 19.8, 20.1, 26.9, 29.9, 33.4, 33.6, 44.4;

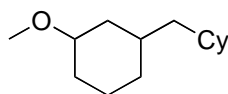
Trans:cis = 75:25 (by NMR); MS (EI) (m/z) (rel. intensity): 167 ([M-H]<sup>+</sup>, 1%), 125 (26%), 124 (66%), 109 (14%), 95 (7%), 83 (54%), 69 (100%), 67 (31%), 57 (27%) and 55 (37%); GC MS (column: Hydrodex β-6 TBDM, temperature: 50 °C isothermal, flow: 1.0 ml/min): trans: 99.3 (minor) & 107.6 (major) min, >99%; cis: 95.9 min; Trans:cis = 75:25



Catalyst used: [**B**-IrCOD]BAR<sub>F</sub>.

Trans: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 3.28 (s, OCH<sub>3</sub>), 3.45 (m, CHO); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz): δ 20.5, 22.9, 24.9, 29.2, 30.0, 32.7, 36.8, 46.5, 55.8, 75.8;

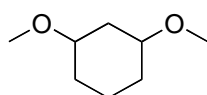
Cis: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 3.08 (tt, J = 11.0 and 4.1 Hz, CHO), 3.33 (s, OCH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz): δ 23.0, 23.2, 24.2, 32.2, 32.8, 34.1, 39.3, 46.8, 55.6, 79.7; Trans:cis = 82:18 (by NMR); MS (EI) (m/z) (rel. intensity): 169 ([M-H]<sup>+</sup>, 5%), 138 (100%), 127 (35%), 123 (71%), 113 (47%) and 109 (42%); GC MS (column: Hydrodex β-6 TBDM, temperature: 90 °C isothermal, flow: 1.0 ml/min): trans: 13.5 (minor) & 16.6 (major) min, 98% ee; cis: 17.7 (minor) & 19.0 (major) min, 66% ee; Trans:cis = 96:4



Catalyst used: [**A**-IrCOD]BAR<sub>F</sub>.

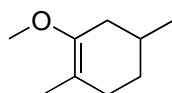
Trans: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 3.28 (s, OCH<sub>3</sub>), 3.45 (m, CHO); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 20.4, 26.6, 26.6, 26.9, 28.5, 29.9, 32.8, 33.7, 34.0, 34.5, 37.0, 45.0, 55.7, 75.8; Cis: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 3.07 (tt, J = 10.9 and 4.1 Hz,

CHO), 3.33 (s, OCH<sub>3</sub>); Trans:cis = 78:22 (by NMR); MS (EI) (m/z) (rel. intensity): 209 ([M-H]<sup>+</sup>, 2%), 178 (70%), 167 (3%), 149 (25%), 135 (100%), 121 (18%), 113 (25%) and 107 (17%); GC MS (column: Hydrodex β-6 TBDM, temperature: 110 °C isothermal, flow: 1.0 ml/min): trans: 66.3 (minor) & 73.7 (major) min, 99% ee; cis: 85.9 (minor) & 89.7 (major) min, 66% ee; Trans:cis = 97:3



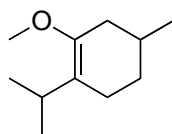
Catalyst used: [**B**-IrCOD]BAR<sub>F</sub>.

Trans: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 1.38-1.55 (m, 4 H), 1.56-1.66 (m, 2 H), 1.68-1.73 (m, 2 H), 3.27 (s, 6 H, 2xOCH<sub>3</sub>), 3.42-3.50 (m, 2 H, 2xCHO); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 19.0, 30.2, 35.9, 55.7, 75.8; Cis isomer is not seen by <sup>13</sup>C NMR; MS (EI) (m/z) (rel. intensity): 143 ([M-H]<sup>+</sup>, 1%), 113 (7%), 112 (100%), 111 (71%) and 101 (18%); GC MS (column: Hydrodex β-PM, temperature: 60 °C isothermal, flow: 1.0 ml/min): trans: 39.3 (minor) & 40.2 (major) min, >99% ee; cis: 26.8 min; Trans:cis = >99:1



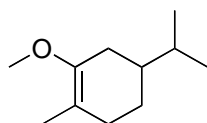
Catalyst used: [**A**-IrCOD]BAR<sub>F</sub>, together with poly(4-vinylpyridine) (15 mg).

MS (EI) (m/z) (rel. intensity): 140 (MH<sup>+</sup>, 51%), 125 (100%), 111 (27%), 93 (28%), 83 (30%), 77 (15%), 67 (25%) and 55 (24%); GC MS/FID (column: Chiraldex β-DM, temperature: 60 °C isothermal, pressure: 14.5 psi): 23.4 (minor) & 24.2 (major) min, 97% ee



Catalyst used: [**A**-IrCOD]BAR<sub>F</sub>, together with poly(4-vinylpyridine) (15 mg).

MS (EI) (m/z) (rel. intensity): 168 (MH<sup>+</sup>, 15%), 153 (100%), 125 (16%), 93 (15%) and 81 (15%); GC MS/FID (column: Chiraldex β-DM, temperature: 30 min at 60 °C followed by increase 3 °C/min, pressure: 14.5 psi): 41.5 (minor) & 42.2 (major) min, 89% ee

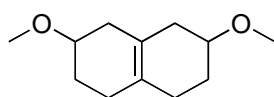


Catalyst used: [**A**-IrCOD]BAR<sub>F</sub>, together with poly(4-vinylpyridine) (15 mg).

MS (EI) (m/z) (rel. intensity): 168 (MH<sup>+</sup>, 52%), 153 (27%), 139 (15%), 125 (35%), 111 (28%), 93 (30%), 86 (100%) and 71 (33%); GC MS/FID (column: Chiraldex β-



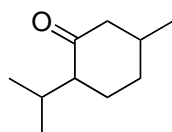
DM, temperature: 30 min at 60 °C followed by increase 3 °C/min, pressure: 14.5 psi):  
44.2 (minor) & 44.7 (major) min, 97% ee



Catalyst used: [**A**-IrCOD]BAR<sub>F</sub>.

Trans: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 1.45-1.61 (m, 2 H), 1.77-2.03 (m, 8 H), 2.15-2.26 (m, 2 H), 3.35 (s, 6 H, 2xOCH<sub>3</sub>), 3.39-3.47 (m, 2 H, 2xCHO); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz): δ 27.7, 28.3, 36.3, 55.9, 76.2, 122.9, 127.7; Cis isomer is not seen by <sup>13</sup>C NMR; MS (EI) (m/z) (rel. intensity): 196 (MH<sup>+</sup>, 2%), 164 (20%), 132 (100%), 117 (37%) and 104 (55%); GC MS/FID (column: Hydrodex β-6 TBDM, temperature: 120 °C isothermal, flow: 1.0 ml/min): trans: 49.0 (minor) & 51.4 (major) min, >99.9% ee; cis: 47.4 min; Trans:cis = >99:1

### Other reactions



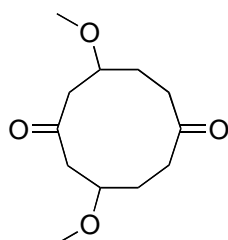
Hydrolysis of enolate: After completion of asymmetric hydrogenation of **2o** (416 mg, 2.5 mmol) solvent was removed and crude enolate **4o** was dissolved in methanol:water (5:1 ml). (COOH)<sub>2</sub>\*H<sub>2</sub>O (16 mg, 5 mol%) was added and reaction was stirred at RT for 2 hours until completion of reaction by TCL. Methanol was evaporated, reaction was diluted by water and extracted with ether (2 times). Organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Chromatography on silica (pentane:ether 100:0 to 90:10) afforded 232 mg clear oil (60% over two steps, asymmetric hydrogenation and hydrolysis) with 48:52 cis:trans ratio, determined by <sup>1</sup>H NMR.

NMR of a trans/cis mixture; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 0.86-0.90 (m, 6 H, 2xCH<sub>3</sub>), 0.99 (d, J=6.4 Hz, CH<sub>3</sub> major trans-isomer), 1.07 (d, J=7.1 Hz, CH<sub>3</sub> minor cis-isomer), 1.28 (qd, J=12.9 and 3.5 Hz, 1H), 1.42 (m, 1H), 1.49-1.72 (m, 2H), 1.83 (m, 1H), 2.00-2.11 (m, 2H), 2.26-2.45 (m, 2H); MS (EI) (m/z) (rel. intensity): 154 (M<sup>+</sup>, 49%), 125 (6%), 111 (100%), 95 (25%), 83 (24%), 69 (20%) and 55 (85%); GC

MS (column: Chiraldex  $\beta$ -DM, temperature: 30 min at 60 °C followed by increase 3 °C/min, pressure: 14.5 psi): cis: 44.1 min, trans: 45.9 min, absolute configuration is not defined.

Equilibration: Above ketone (117 mg, 0.759 mmol, 1 eq) was dissolved in dry ethanol (2 ml) and NaOMe (21 mg, 0.389 mmol, 0.5 eq) was added. After stirring for 2 h reaction was diluted with ether and washed with saturated  $\text{NH}_4\text{Cl}(\text{aq})$ . Aqueous phase was extracted with ether and combined organic phase was dried over  $\text{MgSO}_4$ .

Removal of solvent afforded 93 mg (79 %) pure product with 11:89 cis:trans ratio determined by  $^1\text{H}$  NMR.



To alkene **trans-6** (162 mg, 0.825 mmol, 1 eq) was added THF:water (5 ml, 2:1),  $\text{NaIO}_4$  (747 mg, 3.49 mmol, 4.2 eq) and  $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$  (1 mg). Reaction was stirred vigorously for 23 h, filtered, inorganic salts were washed with THF. After removal of THF, brine was added and solution was extracted with DCM (3 times). Combined organic phases were dried over  $\text{Na}_2\text{SO}_4$ , evaporated and residue was purified on silica (pentane:ether 20:80 to 0:100) to afford 102 mg of **7** as colorless crystals.

Mp = 116.6-119.7 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  1.78-1.86 (m, 2 H), 2.23-2.32 (m, 4 H), 2.48-2.61 (m, 4 H), 2.63-2.69 (m, 2 H), 3.34 (s, 6 H,  $2 \times \text{CH}_3$ ), 3.82 (m, 2 H,  $2 \times \text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  28.2 ( $2 \times \text{CH}_2\text{CH}_2\text{CO}$ ), 37.3 ( $2 \times \text{CH}_2\text{CO}$ ), 47.3 ( $2 \times \text{CH}_2\text{CO}$ ), 56.6 (CHO), 75.8 ( $2 \times \text{CH}_3$ ), 208.6 (CO), 212.7 (CO); MS (EI) (m/z) (rel. intensity): 229 ( $\text{MH}^+$ , 100%), 211 (42%), 197 (56%), 179 (67%), 164 (68%), 136 (49%), 123 (47%), 99 (62%), 95 (95%), 85 (59%), 81 (97%) and 67 (64%); IR (solid)  $\nu_{\text{max}}$  2931, 2823, 1696 (C=O), 1418, 1377, 1085, 975, 939 and 634  $\text{cm}^{-1}$

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