Birch Reaction Followed by Asymmetric Iridium-Catalysed Hydrogenation

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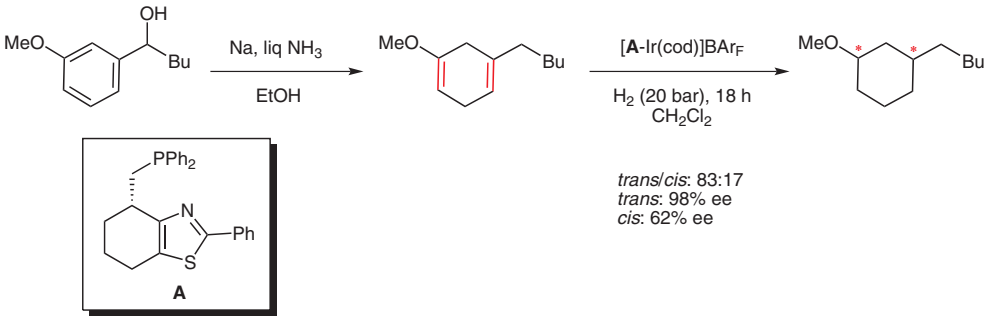
Abstract: Birch reaction products are asymmetrically hydrogenated with high enantio- and diastereoselectivity via iridium catalysts. This new method of producing chiral compounds was explored for a variety of 1,3-di- and 1,2,4-tri-substituted cyclohexadienes.

Key words: asymmetric catalysis, iridium, hydrogenation, reduction, radical reaction



Scheme 1 Birch reaction of substrate **1a** followed by asymmetric hydrogenation

Introduction

The Birch reaction is a well-known method of conversion of aromatic compounds into nonconjugated dienes.[1] It is a highly regioselective reaction, when the substitution pattern is chosen accordingly. The reaction is commonly used to synthesise natural product intermediates,[2] and the large selection of existing substituted benzene compounds offers a great variety of easily obtained target molecules. Iridium catalysis is a highly efficient method of asymmetric hydrogenation,[3] gaining in popularity over the recent years. However, asymmetric hydrogenation of Birch products has only been reported once so far,[4] despite the Birch reaction's regular use prior to introduction of chiral centres.[5]

The iridium catalysts used in this study, were originally developed on aryl alkene esters,[6] and have also been tested on vinyl fluorides and other olefins within this research group,[7] but lend themselves very well to being ported over to tri-substituted compounds such as the Birch products studied here (Scheme 1).

Scope and Limitations

A variety of 1,3, 1,4,[4] and 1,2,4 di- and trisubstituted benzenes were used; some commercially available and others had to be synthesised. They were reduced to substituted cyclohexadienes using Li or Na in liquid ammonia using large excess of EtOH for all compounds reported (though a near stoichiometric amount of *t*-BuOH for less encumbered compounds such as R^1 = OMe, R^2 = Me, R^3 = H, and R^1 = R^2 = Me, R^3 = H)[4] (Scheme 2). More hindered substrates needed larger excess of Na (8–30 equiv) and EtOH (20–40 equiv) to go to completion. For compounds where small amounts of alcohol were used, THF was used as a co-solvent to facilitate stirring. The metal was added to the mixture at ammonia's reflux temperature under powerful stirring to limit foaming or the reaction getting too vigorous. Afterwards, the ammonia was evaporated and any remaining metal was quenched with ethanol (Table 1).

Once purified by distillation or column chromatography, four representative substrates were screened against ten different compounds from our library of N,P-chelated iridium catalysts. The best catalysts were found to be [**A**-Ir(cod)]BAr_F and [**B**-Ir(cod)]BAr_F [BAr_F = tetrakis(3,5-bis(trifluoromethyl)-phenyl)borate]. No hydrolysis of the methoxy ethers were noticed during the hydrogenation process, though methoxy enolate dienes tend to disproportionate back to aromaticity over time at room temperature (though they are stable for months when stored under argon at –20 °C, in polypropylene containers).

Hydrogenation was conducted on a 1.25 mmol scale, by loading the substrate in anhydrous dichloromethane along with the appropriate catalyst ([**A**-Ir(cod)]BAr_F or [**B**-Ir(cod)]BAr_F, 0.5 mol%), flushing eight times with argon

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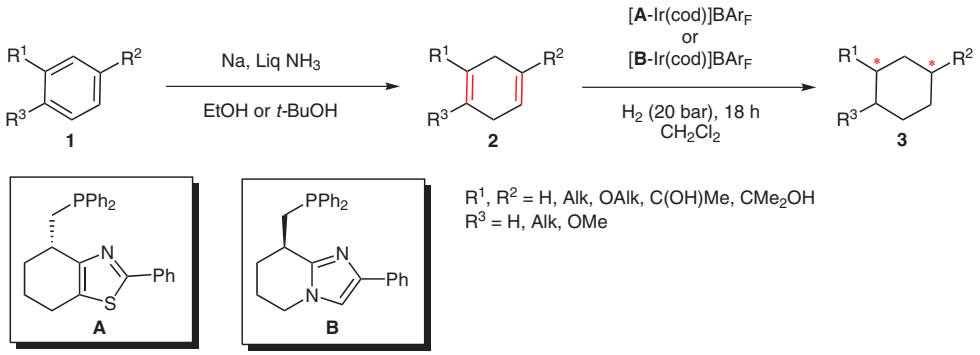


Scheme 2 General reaction scheme

Table 1 Reduction and Hydrogenation Steps on Substituted Aromatic Compounds (Scheme 2)

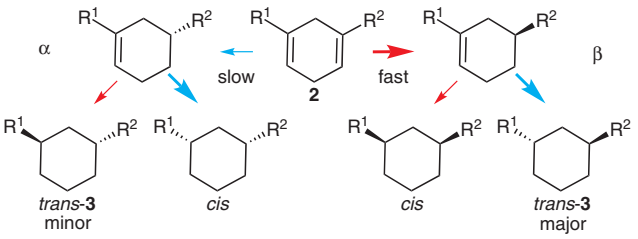
Entry	1	R^1	R^2	R^3	2[b]	Yield (%)[a]		ee (%)				Ligand[d]
						2	3	*trans*	*cis*[c]	*trans*	*cis*	
1	**1a**	OMe	CH(OH)Bu	H	**2a**, $R^2 = C_5H_{11}$	70	81	83	17	98	62	**A**
2	**1b**	OMe	*i*-Bu	H	**2b**	52	68	82	18	98	66	**A**
3	**1c**	OMe	CH(OH)Ph	H	**2c**[e]	82	84	78	22	>99	60	**A**
4	**1d**	OMe	OMe	H	**2d**	65	56	>99	<1	>99	–	**B**
5	**1e**	OMe	*i*-Pr	Me	**2e**	69	60[f]	–	–	97[g]	–	**A**
6	**1f**	*i*-Pr	*i*-Pr	H	**2f**	45	76	75	25	>99	–	**B**

[a] Isolated yields.
[b] Same substituents as compounds **1a–f**, unless specified.
[c] Determined by NMR spectroscopy.
[d] Ligand used: [**A**-Ir(cod)]BAr_F or [**B**-Ir(cod)]BAr_F.
[e] The alcohol is reduced to CH_2 and the Ph group is reduced to cyclohexa-1,4-diene.
[f] Isolated yield of the corresponding ketone.
[g] Poly(4-vinylpyridine) is used as an additive, the methoxy substituted double bond remains intact.

gas (6 bar), before applying H_2 (10 bar) for 18–20 hours, depending on substituents. It should be noted that the catalyst can be deactivated towards the methoxy-substituted π-bond using poly(4-vinylpyridine) as an additive.[4]

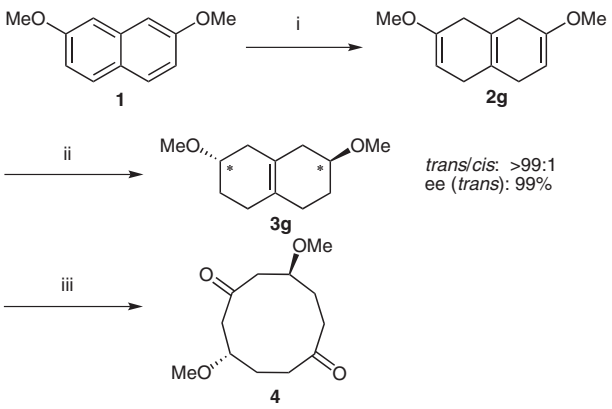
As depicted in Scheme 3, should the intermediate α be produced they will be converted subsequently to *cis*-isomer due to catalytic coordination preference, thus artificially enhancing the ee.

The hydrogenation gave, in most cases, a high preference towards *trans*- over *cis*-isomers (>75:25). In turn, the *trans*-isomers were hydrogenated with very high ee



Scheme 3 Source of the ee enhancement. Large arrows indicate preferred catalyst coordination. Red indicates coordination from below and blue from above.

(97%), whereas the *cis*-isomers gave middling ee values (60–66%), as per Table 1. This is especially marked for substrate **1d**, which displayed excellent stereo- (>99%) and regioselectivity (99:1). This was also true of the substituted naphthalene, which could in turn be oxidised by $RuCl_3/NaIO_4$, (Scheme 4). We can presume that this trend



Scheme 4 Conversion of the substituted naphthalene compound. *Reagents and conditions*: (i) Li, NH_3, EtOH, 93%; (ii) [**A**-Ir(cod)]BAr_F, H_2 (20 bar), CH_2Cl_2, 18 h, 72%; (iii) $RuCl_3 \cdot n\text{-}H_2O$, $NaIO_4$, 54% (absolute configuration unknown).

is not limited to monoaromatic, but in fact polyaromatic compounds could be subjected to similar treatments with similar results.

All reactions were conducted under dry N_2 atmosphere using magnetic stirring. CH_2Cl_2 was freshly distilled from CaH_2 under N_2. THF was distilled from Na with benzophenone under N_2 prior to use. All reagents were used as supplied commercially without further purification. Li (99.9%) was purchased from Sigma-Aldrich as a wire with 0.01% Na.

Chromatographic separations were performed on Kieselgel 60H silica gel (particle size: 0.063–0.100mm). TLC was performed on aluminum plates coated with Kieselgel 60 (0.20mm, UV 254) and visualised under ultraviolet light (λ = 254 nm), I_2 vapours, by staining with basic aqueous $KMnO_4$ solution, or ethanolic phosphomolybdic acid and heating.

^{1}H NMR spectra were recorded at 500, 400, or 300 MHz in $CDCl_3$ at 25 °C and referenced internally with the residual $CHCl_3$ peak (7.26 ppm). Prior to use, $CDCl_3$ was neutralised by passage through a short plug of basic alumina. Chemical shifts are reported in ppm (δ scale). Mass spectra were measured at 70 eV (EI). IR spectra were recorded on an FT-IR apparatus. Enantiomeric excesses were determined using chiral GC with an MS detector. Racemic compounds were used for comparison.

Birch Reaction; General Procedure

The reactions were conducted in a 3-necked round-bottomed flask with a dry ice condenser, an NH_3 (g) inlet, and a stopper for Na addition. Ammonia was condensed from a commercial NH_3 tube into a mixture of aromatic substrate, alcohol, and a cosolvent while cooling flask in a dry ice bath. Addition of the metal was done at reflux temperature of NH_3 with such a speed so as to prevent vigorous reaction/foaming. On discolouration of reaction, dry ice was removed from condenser and ammonia was evaporated. If unreacted Na was present, it was quenched with 95% EtOH. Reaction was carefully diluted with H_2O (50 mL), extracted with Et_2O (3 × 50 mL), the combined Et_2O extracts were washed with brine (30 mL), and dried (Na_2SO_4). Solvent was removed and product was purified either by distillation under reduced pressure or by chromatography on deactivated (Et_3N) silica gel with pentane as eluent.

1-Methoxy-5-pentylcyclohexa-1,4-diene (2a)

According to the general procedure, the following amounts were used: **1a** (5.00 g, 25.7 mmol, 1 equiv) and EtOH (45 mL, 771 mmol, 30 equiv). Ammonia was condensed to a total volume of 250 mL. Na (3.60 g, 157 mmol, 6 equiv) was added over 20 min. After general workup and chromatography, 3.68 g (79%) of **2a** was obtained as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, J = 7.2 Hz, 3 H, CH_3), 1.20–1.36 (m, 4 H, 2 × CH_2), 1.37–147 (m, 2 H, CH_2), 1.96–2.02 (m, 2 H, CH_2), 2.57–2.66 (m, 2 H, C=CCH_2C=C), 2.75–2.83 (m, 2 H, C=CCH_2C=C), 3.56 (s, 3 H, OCH_3), 4.63 (m, 1 H, CH=CO), 5.41 (m, 1 H, CH=C).

^{13}C NMR (100 MHz, $CDCl_3$): 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* (%) = 180 (M^+, 70), 137 (100), 124 (35), 109 (83), 91 (22).

1-Isobutyl-5-methoxycyclohexa-1,4-diene (2b)

According to the general procedure, the following amounts were used: **1b** (2.00 g, 12.2 mmol, 1 equiv) and EtOH (3.6 mL, 61.6 mmol, 5 equiv). Ammonia was condensed to a total volume of 80 mL. Na (0.84 g, 36.5 mmol, 5 equiv) was added over 10 min. After general workup and chromatography, 0.77 g (52% with regard to recovered starting material) of **2b** was obtained as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, J = 6.5 Hz, 6 H, 2 × CH_3), 1.77 (m, 1 H, CH), 1.86 (m, 1 H, CH_2) 1.89 (m, 1 H, CH_2), 2.56–2.64 (m, 2 H, C=CCH_2C=C), 2.75–2.85 (m, 2 H, C=CCH_2C=C), 3.56 (s, 3 H, OCH_3), 4.63 (m, 1 H, CH=CO), 5.39 (m, 1 H, CH=C).

^{13}C NMR (125 MHz, $CDCl_3$): 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* (%) = 166 (M^+, 53), 151 (25), 124 (17), 109 (100), 91 (23), 77 (21).

1-(Cyclohexa-1,4-dienylmethyl)-5-methoxycyclohexa-1,4-diene (2c)

According to the general procedure, the following amounts were used: **1c** (5.00 g, 23.3 mmol, 1 equiv) and EtOH (41 mL, 702 mmol, 30 equiv). Ammonia was condensed to a total volume of 250 mL. Na (4.29 g, 187 mmol, 8 equiv) was added over 20 min. After general workup and chromatography, 3.89 g (82%) of **2c** was obtained as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.49–2.61 (m, 4 H, 2 × CH_2), 2.62–2.73 (m, 4 H, 2 × CH_2), 2.78–2.85 (m, 2 H, CH_2), 3.55 (s, 3 H, OCH_3), 4.62 (m, 1 H, CH=CO), 5.44–5.50 (m, 2 H, CH_2), 5.66–5.70 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.0 (2 C), 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* (%) = 202 (M^+, 5), 130 (10), 109 (100), 94 (25), 77 (21).

4-Isopropyl-2-methoxy-1-methylcyclohexa-1,4-diene (2e)

According to the general procedure, the following amounts were used: **1e** (4.31 g, 26.4 mmol, 1 equiv) and EtOH (48 mL, 822 mmol, 31 equiv). Ammonia was condensed to a total volume of 250 mL. Na (7.24 g, 315 mmol, 12 equiv) was added over 40 min. After general workup and distillation at 9 Torr, 3.01 g (69%) of **2e** was obtained as a colourless oil; 74–76 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (d, J = 9.2 Hz, 6 H, 2 × CH_3), 1.64 (s, 3 H, CH_3), 2.82 (m, 1 H, CH), 2.70 (m, 2 × CH_2), 3.55 (s, OCH_3), 5.38 (m, 1 H, CH=C).

MS (EI): *m*/*z* (%) = 167 (MH^+, 25), 166 (M^+, 73), 151 (35), 123 (100), 108 (34), 91 (39).

1,5-Diisopropylcyclohexa-1,4-diene (2f)

According to the general procedure, the following amounts were used: **1f** (4.66 g, 28.7 mmol, 1 equiv) and EtOH (50 mL, 856 mmol, 30 equiv). Ammonia was condensed to a total volume of 250 mL. Na (6.60 g, 287 mmol, 10 equiv) was added over 25 min. After general workup and chromatography, 2.11 g (45%) of **2f** was obtained as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.04 (d, J = 6.8 Hz, 12 H, 4 × CH_3), 2.21 (sept, J = 6.8 Hz, 2 H, 2 × CH), 2.53–2.58 (m, 2 H, CH_2), 2.67–2.73 (m, 2 H, CH_2), 5.43 (m, 2 H, 2 × CH=C).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 27.8, 28.0, 34.9, 116.0, 148.9.

MS (EI): *m*/*z* (%) = 164 (M^+, 15), 163 (18), 147 (15), 121 (64), 120 (100), 105 (70), 91 (43), 79 (93), 77 (52).

Compounds **2d**[8] and the naphthalene derivative **2g**[9] were prepared using literature procedures.

Hydrogenation; General Procedure

Substrate **2** (1.25 mmol) was loaded into a vial with a magnetic stirrer and a lid with septa. A stock solution of the catalyst (5 mL, 6.25 μmol, 0.5 mol%) in anhyd CH_2Cl_2 was added under argon through the septa and the vial was placed into high pressure hydrogenation

equipment. Argon was applied 8 times at 6 bar, then H_2 atmosphere was applied, and left for the specified time (18–20 h). H_2 was released, the solvent evaporated, and the residue was analysed by NMR and GC–MS with a chiral column. ^{1}H NMR spectrum was taken in $CDCl_3$ (passed through basic alumina before use). For GC MS analysis, a small part of reaction mixture was applied on a short plug of silica gel (deactivated by Et_3N) and eluted with Et_2O–pentane (1:1). Flash chromatography (pentane–Et_2O, 100:0 to 90:10) was used for purification of the compounds.

1-Methoxy-3-pentylcyclohexane (3a)
With catalyst [**A**-Ir(cod)]BAr_F, using the general procedure; yield: 187 mg (81%); oil; *trans*/*cis* = 83:17 (by NMR); *trans*/*cis* = 91:9 (by GC–MS).

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*-**3a**) = 0.83 (t, *J* = 7.0 Hz), 3.24 (s, OCH_3), 3.42 (m, CHO).

^{13}C NMR (100 MHz, $CDCl_3$): δ (*trans*-**3a**) = 14.1, 20.4, 22.8, 26.6, 29.8, 31.7, 32.3, 32.5, 36.7, 36.9, 55.6, 75.7.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*cis*-**3a**) = 0.88 (t, *J* = 7.1 Hz), 3.09 (tt, *J* = 11.0, 4.2 Hz, CHO), 3.35 (s, OCH_3).

MS (EI): *m*/*z* (%) = 183 ([M – H]$^+$, 3), 152 (36), 141 (35), 123 (17), 113 (49), 109 (38), 96 (45), 95 (39), 81 (82), 71 (100), 67 (47), 55 (23).

GC–MS (column: Hydrodex β-6 TBDM, temp: 100 °C isothermal, flow: 1.0 mL/min): *trans*-**3a**: 23.7 (major) and 26.6 min (minor), 98% ee; *cis*-**3a**: 30.1 (minor) and 31.0 min (major), 62% ee.

1-Isobutyl-3-methoxycyclohexane (3b)
With catalyst [**B**-Ir(cod)]BAr_F using the general procedure; yield: 144 mg (68%); oil; *trans*/*cis* = 82:18 (by NMR); *trans*/*cis* = 96:4 (by GC–MS).

^{1}H NMR (500 MHz, $CDCl_3$): δ (*trans*-**3b**) = 3.28 (s, OCH_3), 3.45 (m, CHO).

^{13}C NMR (125 MHz, $CDCl_3$): δ (*trans*-**3b**) = 20.5, 22.9, 24.9, 29.2, 30.0, 32.7, 36.8, 46.5, 55.8, 75.8.

^{1}H NMR (500 MHz, $CDCl_3$): δ (*cis*-**3b**) = 3.08 (tt, *J* = 11.0, 4.1 Hz, CHO), 3.33 (s, OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ (*cis*-**3b**)= 23.0, 23.2, 24.2, 32.2, 32.8, 34.1, 39.3, 46.8, 55.6, 79.7.

MS (EI): *m*/*z* (%) = 169 ([M – H]$^+$, 5), 138 (100), 127 (35), 123 (71), 113 (47), 109 (42).

GC–MS (column: Hydrodex β-6 TBDM, temp: 90 °C isothermal, flow: 1.0 mL/min): *trans*: 13.5 (minor) and 16.6 min (major), 98% ee; *cis*: 17.7 (minor) and 19.0 min (major), 66% ee.

1-(Cyclohexylmethyl)-3-methoxycyclohexane (3c)
With catalyst [**A**-Ir(cod)]BAr_F, using the general procedure; yield: 222 mg (84%); **3c**; oil; *trans*/*cis* = 78:22 (by NMR); *trans*/*cis* = 97:3 (by GC–MS).

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*-**3c**) = 3.28 (s, OCH_3), 3.45 (m, CHO).

^{13}C NMR (100 MHz, $CDCl_3$): δ (*trans*-**3c**) = 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.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*cis*-**3c**) = 3.07 (tt, *J* = 10.9, 4.1 Hz, CHO), 3.33 (s, OCH_3).

MS (EI): *m*/*z* (%) = 209 ([M – H]$^+$, 2), 178 (70), 167 (3), 149 (25), 135 (100), 121 (18), 113 (25), 107 (17).

GC–MS (column: Hydrodex β-6 TBDM, temp: 110 °C isothermal, flow: 1.0 mL/min): *trans*: 66.3 (minor) and 73.7 min (major), 99% ee; *cis*: 85.9 (minor) and 89.7 min (major), 66% ee.

1,3-Dimethoxycyclohexane (3d)
With catalyst [**B**-Ir(cod)]BAr_F, using the general procedure; yield: 101 mg (56%); oil (volatile); *trans*/*cis* >99:1 (by ^{1}H NMR and GC–MS).

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*-**3d**) = 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, 2 × OCH_3), 3.42–3.50 (m, 2 H, 2 × CHO).

^{13}C NMR (100 MHz, $CDCl_3$): δ (*trans*-**3d**) = 19.0, 30.2, 35.9, 55.7, 75.8.

The *cis*-isomer was not seen by ^{13}C NMR spectroscopy.

MS (EI): *m*/*z* (%) = 143 ([M – H]$^+$, 1), 113 (7), 112 (100), 111 (71), 101 (18).

GC–MS (column: Hydrodex β-PM, temp: 60 °C isothermal, flow: 1.0 mL/min): *trans*: 39.3 (minor) and 40.2 min (major), >99% ee; *cis*: 26.8 min.

4-Isopropyl-2-methoxy-1-methylcyclohex-1-ene (3e)
With catalyst [**A**-Ir(cod)]BAr_F, together with poly(4-vinylpyridine) (30 mg) using the general procedure; the crude product (460 mg) was used without purification.

MS (EI): *m*/*z* (%) = 168 (MH$^+$, 52), 153 (27), 139 (15), 125 (35), 111 (28), 93 (30), 86 (100), 71 (33).

GC–MS (column: Chiraldex β-DM, temp: 30 min at 60 °C followed by an increase of 3 °C/min, pressure: 14.5 psi): 44.2 (minor) and 44.7 min (major); 97% ee.

5-Isopropyl-2-methylcyclohexanone (3e′)
*Hydrolysis of Enolate **2e***: After completion of asymmetric hydrogenation of **2e** (416 mg, 2.5 mmol), the solvent was removed and the crude enolate **3e** was dissolved in MeOH–H_2O (5 mL:1 mL). $(COOH)_2{\cdot}H_2O$ (16 mg, 5 mol%) was added and the reaction mixture was stirred at r.t. for 2 h until completion of reaction by TLC. MeOH was evaporated, the mixture diluted with H_2O (10 mL), and extracted with Et_2O (2 × 30 mL). The organic phase was dried (Na_2SO_4) and evaporated. Chromatography on silica gel (pentane–Et_2O, 100:0 to 90:10) afforded 232 mg of a clear oil (60% over two steps, asymmetric hydrogenation and hydrolysis) with 48:52 *cis*/*trans* ratio as determined by ^{1}H NMR spectroscopy.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.86–0.90 (m, 6 H, 2 × CH_3), 0.99 (d, *J* = 6.4 Hz, CH_3 major *trans*-isomer), 1.07 (d, *J* = 7.1 Hz, CH_3 minor *cis*-isomer), 1.28 (qd, *J* = 12.9, 3.5 Hz, 1 H), 1.42 (m, 1 H), 1.49–1.72 (m, 2 H), 1.83 (m, 1 H), 2.00–2.11 (m, 2 H), 2.26–2.45 (m, 2 H).

MS (EI): *m*/*z* (%) = 154 (M$^+$, 49), 125 (6), 111 (100), 95 (25), 83 (24), 69 (20), 55 (85).

GC–MS (column: Chiraldex β-DM, temp: 30 min at 60 °C followed by an increase of 3 °C/min, pressure: 14.5 psi): *cis*: 44.1 min, *trans*: 45.9 min, absolute configuration is not defined.

Equilibration: The above ketone (117 mg, 0.759 mmol, 1 equiv) was dissolved in anhyd EtOH (2 mL) and NaOMe (21 mg, 0.389 mmol, 0.5 equiv) was added. After stirring for 2 h, the mixture was diluted with Et_2O (30 mL) and washed with sat. aq NH_4Cl (10 mL). The aqueous phase was extracted with Et_2O (2 × 30 mL) and the combined organic phases were dried ($MgSO_4$). Removal of solvent afforded 93 mg (79%) of pure product with 11:89 *cis*/*trans* ratio as determined by ^{1}H NMR spectroscopy.

1,3-Diisopropylcyclohexane (3f)
With catalyst [**B**-Ir(cod)]BAr_F, using the general procedure; yield: 157 mg (76%); oil; *trans*/*cis* = 75:25 (by NMR).

^{13}C NMR (100 MHz; $CDCl_3$): δ (*trans*-**3f**) = 20.5, 20.8, 21.6, 29.6, 29.7, 32.1, 39.6.

^{13}C NMR (100 MHz; $CDCl_3$): δ (*cis*-**3f**) =19.8, 20.1, 26.9, 29.9, 33.4, 33.6, 44.4.

MS (EI): *m*/*z* (%) = 167 ([M – H]$^+$, 1), 125 (26), 124 (66), 109 (14), 95 (7), 83 (54), 69 (100), 67 (31), 57 (27), 55 (37).

GC–MS (column: Hydrodex β-6 TBDM, temp: 50 °C isothermal, flow: 1.0 mL/min): *trans*: 99.3 (minor) and 107.6 min (major), >99%; *cis*: 95.9 min.

2,7-Dimethoxy-1,2,3,4,5,6,7,8-octahydronaphthalene (*trans*-3g)
Catalyst used: [**A**-Ir(cod)]BAr_F. Flash chromatography (pentane–Et_2O, 90:10 to 80:20) afforded 177 mg (72%) of *trans*-**3g** as an oil; *trans*/*cis* >99:1 (by ^{1}H NMR and GC–MS).

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*-**3g**) = 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, 2 × OCH_3), 3.39–3.47 (m, 2 H, 2 × CHO).

^{13}C NMR (75 MHz, $CDCl_3$): δ (*trans*-**3g**) = 27.7, 28.3, 36.3, 55.9, 76.2, 122.9, 127.7.

The *cis*-isomer was not seen by ^{13}C NMR spectroscopy.

MS (EI): *m*/*z* (%) = 196 (MH$^+$, 2), 164 (20), 132 (100), 117 (37), 104 (55).

GC–MS (column: Hydrodex β-6 TBDM, temperature: 120 °C isothermal, flow: 1.0 mL/min): *trans*: 49.0 (minor) and 51.4 min (major), >99.9% ee; *cis*: 47.4 min.

3,9-Dimethoxycyclodecane-1,6-dione (4)
Alkene *trans*-**3g** (162 mg, 0.825 mmol, 1 equiv) was added to THF–H_2O (5 mL, 2:1), followed by $NaIO_4$ (747 mg, 3.49 mmol, 4.2 equiv) and $RuCl_3 \cdot nH_2O$ (1 mg). The reaction was stirred vigorously for 23 h, filtered, and inorganic salts were washed with THF (10 mL). After removal of THF, brine (20 mL) was added, followed by extraction with CH_2Cl_2 (3 × 30 mL). The combined organic phases were dried (Na_2SO_4), evaporated, and the residue was purified on silica gel (pentane–Et_2O, 20:80 to 0:100) to afford 102 mg (54%) of colourless crystals; mp 116.6–119.7 °C.

IR (neat): 2931, 2823, 1696 (C=O), 1418, 1377, 1085, 975, 939, 634 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 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 × CH_3), 3.82 (m, 2 H, 2 × CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.2 (2 × *C*$H_2$$CH_2$CO), 37.3 (2 × *C*$H_2$CO), 47.3 (2 × *C*$H_2$CO), 56.6 (CHO), 75.8 (2 × CH_3), 208.6 (C=O), 212.7 (C=O).

MS (EI): *m*/*z* (%) = 229 (MH$^+$, 100), 211 (42), 197 (56), 179 (67), 164 (68), 136 (49), 123 (47), 99 (62), 95 (95), 85 (59), 81 (97), 67 (64).

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