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New monoterpene-derived phosphinopyridine ligands and their application in the enantioselective iridium-catalyzed hydrogenation

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Dedicated to Professor Joe D. Connolly on the occasion of his 75th birthday and in appreciation of his contribution to terpene chemistry

ABSTRACT

Pyridine derivatives with a phosphine or phosphinite pendant (**1**–**11**) have been synthesized from (+)-α-pinene, (−)-isopinocampheol, and/or (+)-camphor via Kröhnke annulation or another annulation method as the key step for the construction of the pyridine nucleus. The iridium complex of **6** proved to catalyze hydrogenation of the prochiral unfunctionalized alkene **44** with 94% ee, whereas the complex of **2** was most efficient in the hydrogenation of the cinnamyl-type ester **45** (83% ee).

1. Introduction

Chiral P,N-ligands play an important role in asymmetric transition metal-catalyzed reactions.[1] Thus, for example, phosphinooxazolines have been developed for the highly enantioselective Pd-catalyzed allylic substitution,[2] Heck addition, hydrogenation, and other reactions.[3] The binaphthyl-type P,N-ligands, such as MAP and its congeners,[4] aside from also being employed in the Pd-catalyzed allylic substitution,[4–6] have revolutionized the Pd-catalyzed Hartwig-Buchwald amination of aromatic halides,[5,7,8] and enabled asymmetric Suzuki-Miyaura coupling.[9] Furthermore, the latter class has been shown to exhibit a unique way of coordination of Pd[5,6] and has contributed to a better understanding of the memory effect in the Pd-catalyzed allylic substitution.[6]

In recent years we have developed pyridine-type ligands with a chiral scaffold based on amino acids[7b,10,11,12] and/or monoterpenes,[13–17] and have demonstrated their application in the enantioselective Mo-catalyzed allylic substitution,[10] Pd-catalyzed allylic substitution[16b,18] Heck addition,[15] Cu-catalyzed conjugate addition,[11] allylic oxidation,[13,14,19] cyclopropanation,[14,20] Sn-catalyzed reduction of ketones with polymethylhydrosilane,[21] Rh-catalyzed hydroformylation[22] and hydrosilylation,[23] and the Pd-catalyzed Baeyer-Villiger oxidation.[24]

The *N*-oxides, prepared from some of our terpene-derived pyridines, became organocatalysts of choice for the asymmetric alkylation of aldehydes with allyl and crotyl trichlorosilane.[25,26]

Rhodium- and ruthenium-catalyzed asymmetric hydrogenation of functionalized olefins is one of the most powerful catalytic methods for the asymmetric synthesis of chiral molecules.[27] High enantioselectivity and low catalyst loadings are usually observed when the olefin substrate bears a coordinating group next to the C=C bond. Therefore, unfunctionalized olefins had remained for many years difficult substrates for asymmetric hydrogenation. During the last decade, inspired by the Crabtree catalyst,[28] Pfaltz,[29] and others[30] have developed various cationic iridium complexes, containing chiral P,N-ligands and weakly coordinating counterions, such as BArF (tetrakis[bis-3,5-(trifluoromethyl)phenyl]borate), which have shown to be particularly effective for the enantioselective hydrogenation of non-functionalized olefins.

Herein, we report on the synthesis of the terpene-derived phosphino-pyridine-type ligands **1**–**11** and their application in the iridium-catalyzed asymmetric hydrogenation of alkenes[30] and imines.[31]

2. Results and discussion

The monoterpene-derived phosphinopyridines **1**, **2**, and **4** (Chart 1) have been developed by us as efficient chiral ligands for

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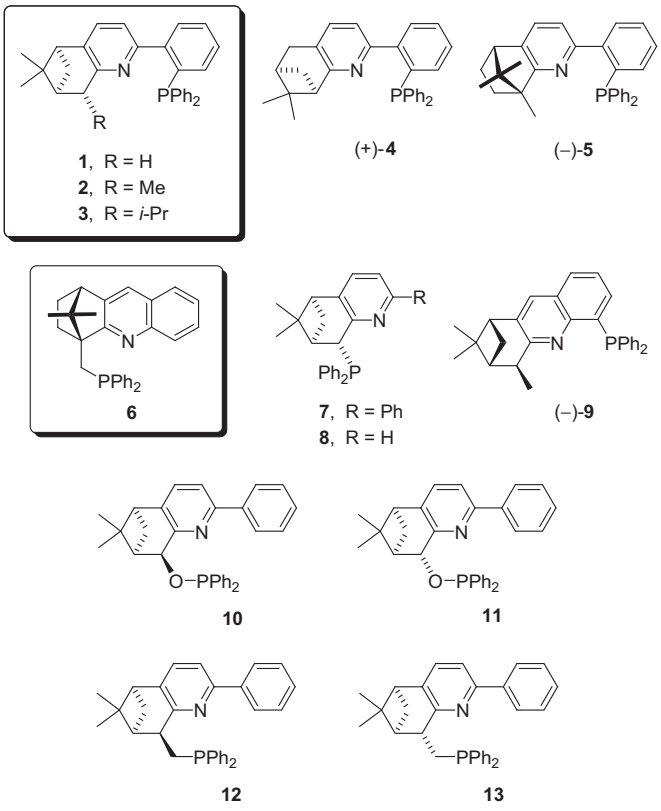
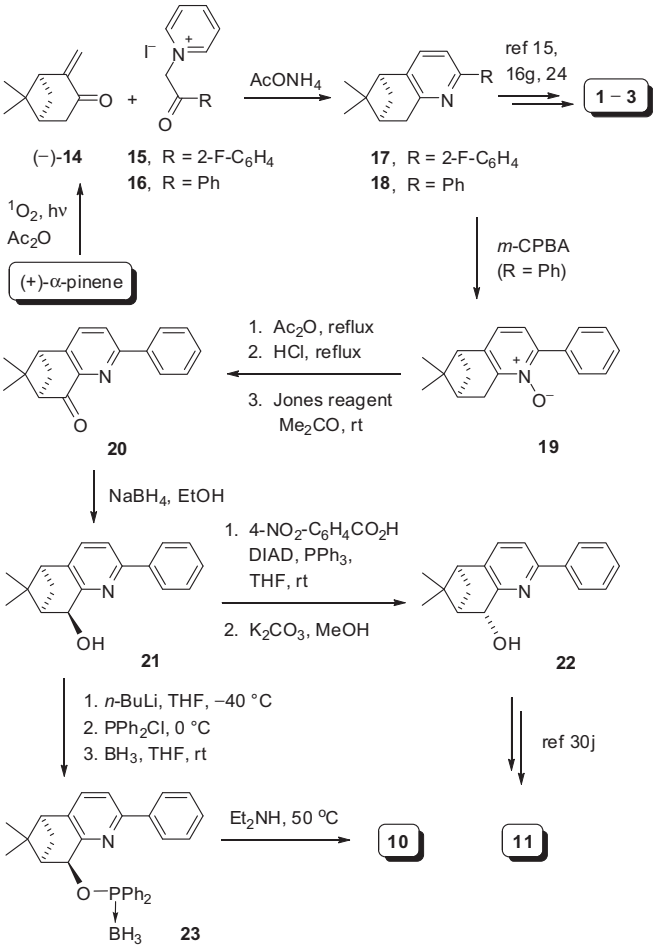


Chart 1.



Scheme 1.

the Pd-catalyzed Heck addition[15] and allylic substitution.[16b,18] More recently, we have introduced the isopropyl derivative **3** as one of the most efficient ligands in the Pd-catalyzed Baeyer-Villiger oxidation.[24] Aiming at an extension of the portfolio of this library of ligands, we embarked on the synthesis of the pyridine-type ligands **5**—**9** and the diastereoisomeric phosphinites **10** and **11**, with a view of their potential utilization to generate chelates of transition metals. While this work was in progress, Andersson added diastereoisomeric phosphines **12** and **13** and also synthesized phosphinites **10** and **11**.[30j]

2.1. Ligand synthesis

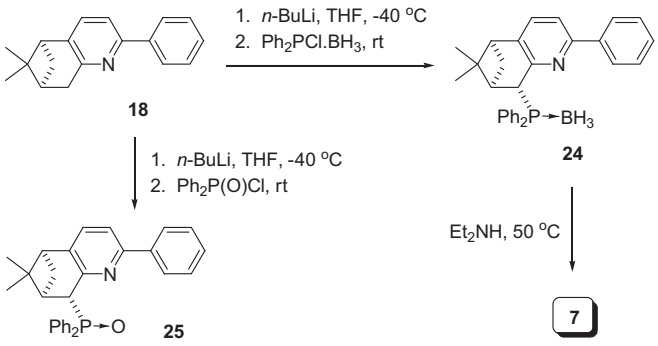
Kröhnke annulation[32] was employed as the key step in the construction of the terpene/pyridine scaffold (Scheme 1): thus, pinocarvone (−)-14, obtained from (+)-α-pinene,[33] was heated with the readily enolizable α-pyridinio ketones **15** and **16**, respectively (generated from the corresponding methyl aryl ketones on iodination in pyridine), in the presence of ammonium acetate, to produce the respective pyridine derivatives (+)-**17**[15,24] and (+)-**18**.[25b] Deprotonation of **17** in the 'benzylic' position with *n*-BuLi, followed by alkylation with MeI and *i*-PrI, respectively, and subsequent replacement of the fluoride with Ph_2PK, produced phosphines **1**—**3**, as described by us previously.[15,24] The enantiomeric (−)-**2** was prepared in the same way from (+)-pinocarvone, which in turn was obtained from (−)-α-pinene.[15,16g]

Ligand (+)-**4** was synthesized from (−)-β-pinene via (+)-nopinone, again by the Kröhnke annulation,[15,16g] and the same approach was employed for the synthesis of (−)-**5** from (+)-camphor.[16g] The quinoline-type ligand (+)-**6** was synthesized from (+)-camphor using a sequence involving functionalization of the methyl group and construction of the pyridine moiety of the quinoline nucleus.[18t]

The synthesis of phosphinites **10** and **11** (Scheme 1) required oxygenation of the 'benzylic' position in (+)-**18**, which was attained by the Boekelheide rearrangement[34] of the *N*-oxide (+)-**19**, whose preparation from (+)-**18** was straightforward (*m*-CPBA, CH_2Cl_2; 75%). The key rearrangement gave rise to a 1:3 mixture of epimeric alcohols **21** and **22** (70%), which were oxidized with Jones' reagent to afford ketone (+)-**20** (84%). As expected, reduction of the latter ketone with $NaBH_4$ gave alcohol (+)-**21** (91%), whose epimerization under Mitsunobu conditions, followed by hydrolysis, furnished alcohol **22** (50%). Deprotonation of alcohol **21**, followed by treatment with Ph_2PCl, generated the corresponding phosphinite, which was isolated and purified in its stable, protected form of the borane complex (+)-**23** (41%).[35] The free phosphinite **10** could then be released from the latter complex in situ by treatment with Et_2NH. Alcohol **22** was then converted into phosphinite **11** in the same way. While this work was in progress, Andersson reported on the synthesis of both **10** and **11** by using a similar strategy but with a different way of obtaining the pure diastereoisomeric alcohols **21** and **22**.[30j]

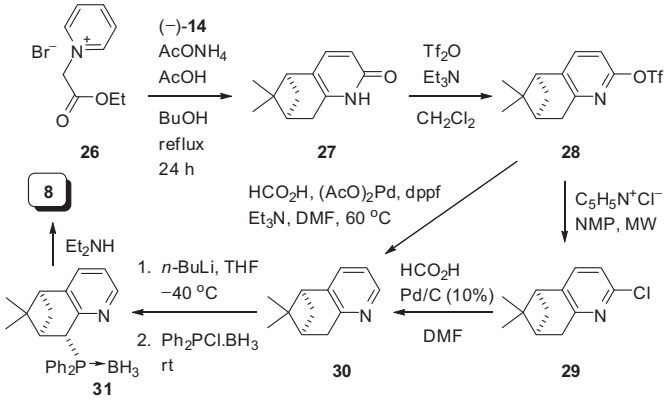
The synthesis of phosphine **7** (Scheme 2) required the usual 'benzylic' deprotonation of (+)-**18**,[14d–f,25b] followed by reaction with a complex of Ph_2PCl and BH_3, which provided (−)-**24** (35%) with excellent diastereoselectivity. The release of the desired phosphine **7** from its protected form (−)-**24** was effected by treatment with Et_2NH (99%) immediately before use.[36] The analogous phosphine oxide (−)-**25** was obtained from (+)-**18**[25b] via the sequence of deprotonation and reaction with $Ph_2P(O)Cl$ (34%); again, the reaction proved highly diastereoselective. However, reduction of (−)-**25**, expected to afford **7**, turned out to be sluggish and produced an intractable mixture.

The truncated phosphine **8**, lacking the phenyl substituent in the α-position of the pyridine nucleus, was synthesized as follows (Scheme 3): the Kröhnke salt **26**, readily available from ethyl



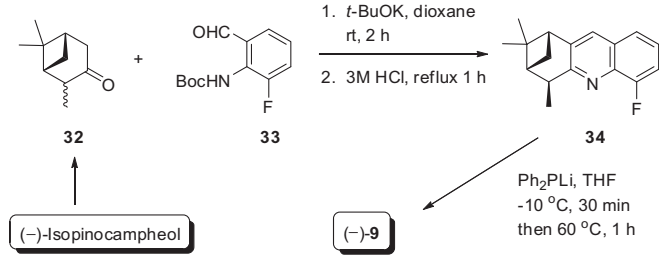
Scheme 2.

bromoacetate via an S_N2 substitution with pyridine,[32] was reacted with pinocarvone (−)-**14** in the presence of ammonium acetate to produce pyridone (+)-**27** (43%)[14b] that was converted into triflate (+)-**28** (99%).[14b] Reduction of the latter derivative with formic acid, catalyzed by palladium,[37] afforded the deoxygenated pyridine derivative (+)-**30** (65%), which was then converted into the phosphine/borane complex (+)-**31** (42%) as in the case of **24**. Again, free phosphine **8** was liberated from (+)-**31** on treatment with diethylamine. An alternative, two-step reduction of (+)-**28** included its conversion into the α-chloropyridine **29** (pyridinium chloride, microwave heating; 36%),[38] followed by a Pd(0)-catalyzed reduction with formic acid, which afforded (+)-**30** (95%); however, the overall yield was rather low compared to that of the direct reduction.



Scheme 3.

The synthesis of phosphine (−)-**9** (Scheme 4) commenced with the annulation reaction[39] of *tert*-butyl *N*-(2-formyl-6-fluorophenyl) carbamate **33** and the chiral ketone **32**, which in turn was obtained as a 4:1 mixture of epimers by oxidation of (−)-isopinocampheol. The 5-fluorotetrahydroacridine derivative, resulting from the annulation (70%), turned out to be a 4:1 mixture of epimers, from which the more abundant (1*R*,3*R*,4*S*)-diastereoisomer **34** (61% overall) was isolated by careful chromatography. The subsequent

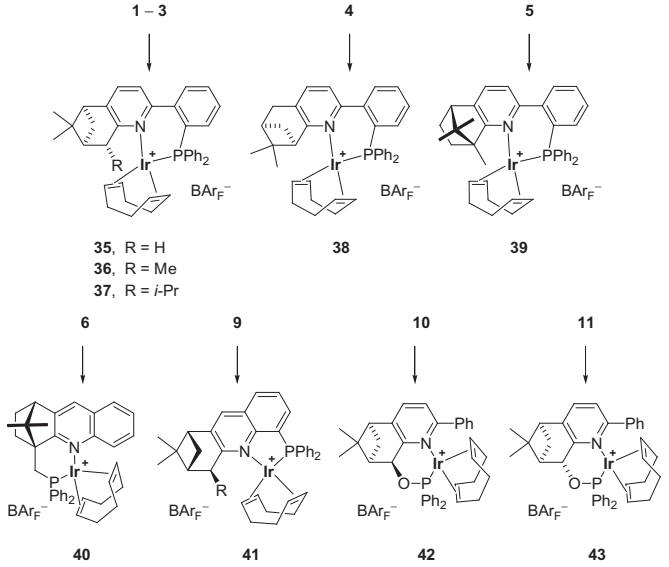


Scheme 4.

reaction of the pure fluoride **34** with Ph_2PLi[40] afforded the desired phosphine derivative but again as a 4:1 mixture of epimers, from which the predominant (1*R*,3*R*,4*S*)-stereoisomer **9** (63%) was obtained by chromatography, showing that purification of the fluoride **34** was actually redundant.

2.2. Preparation of iridium complexes with ligands 1–10

The P,N-ligands **1**–**10** were converted into the corresponding iridium complexes **35**–**42** on reaction with $[(COD)IrCl]_2$ in boiling CH_2Cl_2, followed by an anion exchange with $NaBAr_F$ (Scheme 5). All these complexes were air- and moisture-stable and were easily purified by flash chromatography in moderate yields [**35** (58%), **36** (52%), **37** (44%), **38** (63%), **39** (51%), **40** (75%), **41** (72%), and **42** (41%)]. Similarly, Andersson prepared the corresponding complexes from ligands **10**–**13**.[30j] Our complex **42**, which is identical to his,[30j] is shown here for comparison of its activity under slightly different conditions; for further comparison we also show one of the results he has attained with **43**[30j] (vide infra).



Scheme 5.

2.3. Hydrogenation of olefins 44–47 and imine 48 catalyzed by iridium complexes 35–43

Iridium complexes **35**–**43** were first evaluated as catalysts for the asymmetric hydrogenation of (*E*)-α-methylstilbene **44** (Chart 2 and Table 1, entries 1–15). The reactions were carried out at room temperature with 1–2 mol % catalyst loading and at various hydrogen

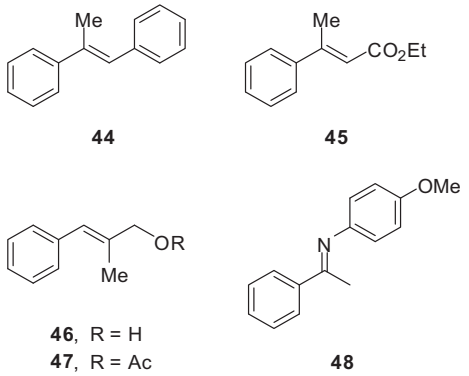


Chart 2.

Table 1
Hydrogenation of olefins **44**–**47** and imine **48** catalyzed by iridium complexes **35**–**43**[a]

Entry	Substrate	Catalyst (mol %)	Ligand	Pressure (atm)	Time (h)	Temp (°C)	Conversion[b] (%)	% ee[c,d] (configuration)
1	**44**	**35** (2)	**1**	10	48	rt	96	21 (*R*)[e]
2	**44**	**36** (2)	**2**	10	48	rt	7	n.d.
3	**44**	*ent*-**36** (1)	*ent*-**2**	50	24	25	13	17 (*R*)
4	**44**	**37** (2)	**3**	10	48	25	n.r.	n.d.
5	**44**	**38** (1)	**4**	50	72	25	34	29 (*R*)
6	**44**	**39** (1)	**5**	50	24	25	10	29 (*R*)
7	**44**	**39** (1)	**5**	50	24	50	56	33 (*R*)
8	**44**	**39** (1)	**5**	50	72	25	17	18 (*R*)
9	**44**	**39** (1)	**5**	50	456	25	29	4 (*R*)
10	**44**	**40** (1)	**6**	50	24	25	69	62 (*S*)
11	**44**	**40** (2)	**6**	10	24	25	**97**	**94** (*S*)
12	**44**	**41** (1)	**9**	50	72	25	n.r.	n.d.
13	**44**	**42** (0.5)	**10**	30	48	rt	30	12 (*S*)[f]
14	**44**	**42** (2)	**10**	10	48	rt	50	**80** (*S*)[e]
15	**44**	**43** (0.5)	**11**	30	48	rt	11	41 (*R*)[f]
16	**45**	**35** (2)	**1**	10	48	rt	>99	20 (*S*)[g]
17	**45**	**36** (2)	**2**	10	48	rt	**>99**	**83** (*S*)[g]
18	**45**	*ent*-**36** (1)	*ent*-**2**	50	72	25	48	55 (*R*)
19	**45**	**37** (2)	**3**	10	48	rt	>99	57 (*S*)[g]
20	**45**	**38** (1)	**4**	50	72	25	>99	17 (*S*)
21	**45**	**39** (1)	**5**	50	72	25	>99	38 (*R*)
22	**45**	**40** (1)	**6**	50	72	25	90	69 (*S*)
23	**45**	**40** (2)	**6**	10	48	25	97	77 (*S*)
24	**45**	**42** (2)	**10**	10	48	rt	15	n.d.
25	**45**	**42** (0.5)	**10**	30	48	rt	15	9 (*S*)[f]
26	**45**	**43** (0.5)	**11**	30	48	rt	10	16 (*S*)[f]
27	**46**	*ent*-**36** (1)	*ent*-**2**	50	72	25	n.r.	n.d.
28	**46**	**38** (1)	**4**	50	72	25	20	56[h]
29	**46**	**39** (1)	**5**	50	72	25	68	2[h]
30	**46**	**40** (1)	**6**	50	72	25	n.r.	n.d.
31	**46**	**40** (2)	**6**	10	72	25	n.r.	n.d.
32	**47**	**41** (2)	**9**	10	48	25	>99	12[h]
33	**48**	**35** (2)	**1**	10	48	rt	>99	0[h]
34	**48**	**36** (2)	**2**	10	48	rt	31	32 (*S*)[i]
35	**48**	**37** (2)	**3**	10	48	rt	6	n.d.
36	**48**	**42** (2)	**10**	10	48	rt	**>99**	**48** (*S*)[i]

[a] The reaction was carried out at a 0.2 mmol scale in CH_2Cl_2 (n.r.=no reaction; n.d.=not determined). The most significant results are highlighted by bold fonts in the last two columns.
[b] Determined by ^1H NMR of the crude mixture.
[c] Determined by chiral HPLC (see the Experimental section for details).
[d] The absolute configuration was established by comparison of the HPLC retention times with the literature values (see the Experimental section).
[e] The absolute configuration was assigned by comparison of the HPLC retention times with literature values (Ref. 41).
[f] Results reported by Andersson (Ref. 30j).
[g] The absolute configuration was assigned by comparison of the optical rotation and with the literature data (Ref. 42).
[h] The absolute configuration was not determined.
[i] The absolute configuration was assigned by comparison of the HPLC retention times with the literature values (Ref. 43).

pressures (10–50 bar). Steric parameters turned out to have a great influence on the reactivity of this class of substrate. Thus, catalysts **35**–**39** and **41** seem to be too encumbered to accommodate the rather bulky substrate, resulting in poor conversions. On the other hand, the more flexible catalysts **40** and **42** exhibited good conversions with moderate to good enantioselectivities (≤94%; entries 10, 11, and 14). Interestingly, lower hydrogen pressure seems to induce higher selectivity (entries 10 and 11).

Ethyl (*E*)-β-methylcinnamate **45** was found to be very sensitive to the type of ligand used (Table 1, entries 16–26). Iridium catalysts based on the chiral pyridine/phosphinite (**42** and **43**) showed very low reactivity (entries 24–26), whereas the catalysts based on the chiral phosphines (**35**–**40**; entries 16–23) promoted full conversion with moderate to good enantioselectivities, clearly controlled by the steric hindrance generated by the alkyl groups in the 'benzylic' position of the ligand (entries 16–21). The enantiomeric excess varied from 20% (ligand with no substituent **35**) to 83% (methyl-substituted ligand **36**).

Other olefinic substrates, such as **46** and **47**, showed rather poor reactivity and selectivity (Table 1, entries 27–32). Substantial differences were observed in the hydrogenation of imine **48**: thus, in the presence of complex **35**, the reaction, proceeded to completion but the product turned out to be racemic, suggesting dissociation of the ligand (entry 33). Complexes **36** and **37** proved to be mediocre catalysts (entries 34 and 35), whereas complex **42** catalyzed the reaction efficiently, affording the product of modest enantiopurity (48% ee, entry 36).

3. Conclusions

Pyridine-type ligands with a phosphine or phosphinite pendant (**1**–**11**) have been synthesized from (+)-α-pinene or (−)-β-pinene via Kröhnke annulation as the key step for the construction of the pyridine nucleus step (**1**–**4**, **7**, **8**, **10**, and **11**), from (−)-isopinocampheol, using another annulation method (**9**), and from (+)-camphor (**5** and **6**). Their iridium complexes **35**–**42** were examined as chiral catalysts in the hydrogenation of representative olefins. The complex **40** derived from ligand **6**, has been found to catalyze hydrogenation of the prochiral unfunctionalized alkene **44** with 94% ee, whereas the complex **36**, derived from ligand **2** was most efficient in the hydrogenation of the cinnamyl-type ester **45** (83% ee). Hydrogenation of imine **48** was less successful (48% ee with the complex of ligand **10**). In general, hydrogenation carried out at lower pressure (10 atm) and with higher catalyst loading (1–2 mol %) has been shown to result in a significant increase in enantioselectivity (compare entries 10 with 11 and 13 with 14 in Table 1).

4. Experimental

4.1. General methods

All reactions were carried out under an inert atmosphere in oven-dried glassware unless otherwise stated. Room temperature refers to ambient room temperature (20–22 °C); 0 °C refers to an ice slush bath. Heated experiments were conducted using thermostatically controlled oil baths. Reactions were monitored by Thin Layer Chromatography (TLC) using aluminum backed silica gel 60 (F_{254}) plates, visualized using UV_{254nm} and potassium permanganate, PMA, Drangendorf and ninhydrin dips as appropriate. Flash chromatography was carried out routinely using 60 Å silica gel (Fischer) as the stationary phase unless otherwise stated. Melting points were determined on a Kofler block and are uncorrected. Optical rotations were recorded in $CHCl_3$ at 20 °C unless otherwise indicated with an error of $<\pm 0.1$. The $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. The NMR spectra were recorded on a Bruker Spectrospin 400 (400 MHz) spectrometer. Chemical shifts are reported in δ units, parts per million (ppm) downfield from TMS. Coupling constants (J) are measured in Hertz (Hz) and are unadjusted; therefore, due to limits in resolution, in some cases there are small differences (<1 Hz) in the measured J value of the same coupling constant determined from different signals. Splitting patterns are designed as follows: s—singlet, d—doublet, t—triplet, dd—doublet of doublets, dt—doublet of triplets, td—triplet of doublets, ddd—doublet of doublet of doublets, tt—triplet of triplets, sp.—septet, m—multiplet, br—broad. Various 2D techniques and DEPT experiments were used to establish the structures and to assign the signals. The IR spectra were recorded on a JASCO FT-IR spectrophotometer for a thin film between NaCl plates, or as a KBr disc. The mass spectra (EI and/or CI) were measured on a Joel JMS700 spectrometer. Enantiomeric excess was determined by chiral HPLC analysis (using a Hewlett Packard Agilent 1100 Series quaternary pump, vacuum degasser, diode array detector, manual injector and Hewlett Packard ChemStation and a Diacel Chiracel IB or OJ-H 0.46 cm×25 cm column) as stated. The chiral GC and HPLC methods were calibrated with the corresponding racemic mixtures. Autoclave reactions were accomplished in a stainless steel autoclave manufactured by HEL Ltd.

4.2. Materials

All solvents were of reagent grade and were dried and distilled under argon or nitrogen immediately before use as follows: tetrahydrofuran, diethyl ether, and toluene from sodium/benzophenone, dichloromethane from calcium hydride. Petroleum ether refers to the fraction boiling in the range 40–60 °C. Methanol and ethanol were distilled over magnesium turnings and stored over molecular sieves. Triethylamine was distilled immediately before use from calcium hydride. (*R*)-(+)-α-Pinene was purchased from Aldrich with a 98% ee. The synthesis of ligands **1**, **2**, and **3** was reported previously.[24]

*4.2.1. (1R,3R,4S)-(−)-1,3-Methano-2,2,4-trimethyl-5-(diphenylphosphino)-1,2,3,4-tetrahydroacridine (−)-(**9**).* A solution of *n*-butyllithium in hexane (2.5 M, 0.541 mL, 1.35 mmol) was added dropwise to a cooled (−78 °C) solution of diphenylphosphine (252 mg, 1.35 mmol) in anhydrous THF (12 mL) under argon. The solution was stirred at that temperature for 10 min and then warmed to 0 °C. A solution of (+)-**34** (315 mg, 1.23 mmol) in anhydrous THF (3 mL) was added dropwise and the mixture was slowly warmed to room temperature and then heated at 60 °C for 1 h. The mixture was then cooled to room temperature and a purified and degassed Et_2O (30 mL) and water were added in sequence. The organic phase was separated, dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography on a column of silica gel (1.5×50 cm) under nitrogen using a mixture of petroleum ether and ethyl acetate (9:1) to give (−)-**9** as a white solid (328 mg, 63%): mp 96–97 °C; $[\alpha]_D^{26}$ −48.7 (*c* 0.015, $CHCl_3$); IR (KBr) cm^{-1}; ν 2957 (s, C—H), 2927(s, C—H), 1478 (s, arom C═C), 1434 (s, arom C═C), 1412 (s, arom C═C), 1257, 1179, 119, 1027, 784 (m, arom C—H), 659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.62 (s, 3H, 16-H), 0.92 (d, 3H, J=6.9 Hz, 17-H), 1.21 (d, 1H, J=10.2 Hz, 10-H), 1.39 (s, 3H, 15-H), 2.07 (dt, 1H, J=6.0, 2.4 Hz, 3-H), 2.50–2.11 (m, 1H, 3-H), 2.89 (t, 1H, J=5.4 Hz, 1-H), 2.23 (dt, 1H, J=6.0, 2.4 Hz, 3-H), 6.91–6.99 (m, 1H), 7.16–7.44 (m, 11H), 7.52 (s, 1H, 9-H), 7.68 (d, 1H, J=7.8 Hz, 8-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8 (CH_3-17), 21.1 (CH_3-16), 26.3 (CH_3-15), 28.7 (CH_2-10), 39.1 (CH-4), 41.4 (C-2), 46.4 (CH-3), 47.6 (CH-1), 125.6 (CH-7), 126.2 (C-14), 127.6 (CH-8), 127.8–128.4 (6× aromCH), 130.0 (CH-6), 131.9 (CH-9), 133.9 (d, J=20.7 Hz, C′PAr_2), 134.7 (d, J=20.7 Hz, C′PAr_2), 137.8–138.1 (C-5, 2× CPAr_2), 140.0 (C-11), 147.9 (d, J=15.6 Hz, C-13), 162.0 (C-14); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ −11.6 (s). Anal. Calcd for $C_{29}H_{28}NP$: C, 82.63; H, 6.70; N, 3.32. Found: C, 82.55; H, 6.73; N, 3.30.

*4.2.2. (8S,10S)-(+)-2-Phenyl-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene 1-oxide (+)-(**19**).* *m*-Chloroperoxybenzoic acid (70%, 0.70 g, 4 mmol, 2.0 equiv) was added portion-wise to a cooled (0 °C) solution of (+)-**18**[25b] (0.50 g, 2 mmol, 1.0 equiv) in CH_2Cl_2 (20 mL). The mixture was then allowed to warm up to room temperature and stirred overnight. The mixture was washed with an aqueous solution of $NaHCO_3$ (10%; 1×20 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was purified by chromatography on silica gel (25 g) using ethyl acetate to remove the unreacted starting material and some by-products, followed by methanol to afford pure (+)-**19** as a white solid (394 mg, 75%): mp 128–130 °C (hexane); $[\alpha]_D^{20}$ +100.2 (*c* 0.6, $CHCl_3$); IR (KBr) ν 3051 (m, C—H), 2938 (s, C—H), 1662 (m, arom C═C), 1477 (s, arom C═C), 1447 (m, arom C═C), 1265 (s, N—O), 770 (s, arom C—H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.73 (s, 3H, 12-H), 1.32 (d, J=9.8 Hz, 1H, 9-H), 1.42 (s, 3H, 13-H), 2.45 (m, 1H, 8-H), 2.69 (dt, J=9.8, 5.7 Hz, 1H, 9-H′), 2.81 (t, J=5.7 Hz, 1H, 10-H), 3.05–3.24 (m, 2H, 7-H), 6.92 (d, J=7.8 Hz, 1H, 3-H), 7.19 (d, J=7.8 Hz, 1H, 4-H), 7.42 (t, J=6.9 Hz, 1H, 4′-H), 7.45 (t, J=6.9 Hz, 2H, 3′-H, 5′-H), 7.79 (d, J=6.9 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (CH_3-12), 25.8 (CH_3-13), 31.2 (CH_2-7), 31.5 (CH_2-9), 39.31 (CH-8), 39.32 (C-11), 46.1 (CH-10), 122.9 (CH-3), 123.7 (CH-4), 128.0 (2× CH-3′,5′), 128.9 (CH-4′), 129.5 (2× CH-2′,6′), 133.3 (C-1′), 144.2 (C-5), 146.8 (C-2), 147.1 (C-6); MS (EI) *m*/*z* (%) 265 ($M^{\bullet+}$, 50), 248 ($M^{\bullet+}$−OH, 65), 206 ($M^{\bullet+}$−OH−C_3H_6, 100), 83 (62); HRMS (EI) 265.1466 ($C_{18}H_{19}NO$ requires 265.1467).

*4.2.3. (8R,10S)-(+)-2-Phenyl-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-trien-7-one (+)-(**20**).* A mixture of the *N*-oxide derivative (+)-**19** (105.2 mg, 0.40 mmol) and acetic anhydride (5 mL) was stirred at 110 °C for 2 h under argon. The reaction mixture was then cooled to room temperature and acetic anhydride was removed under vacuum. An aqueous solution of hydrochloric acid (3 M, 10 mL) was added to the residue and the resulting mixture was refluxed for 1.5 h, then cooled to room temperature and chilled with an ice bath. The solution was made alkaline (pH≈12–13) by a slow addition of an aqueous solution of sodium hydroxide (2 M). The aqueous layer was extracted with CH_2Cl_2 (3×15 mL) and the combined organic solutions were dried over $MgSO_4$ and concentrated under vacuum to obtain a diastereoisomeric mixture of benzylic alcohol derivatives (ratio 3:1) (74.2 mg, 70%). The latter mixture of alcohols (74.2 mg, 0.28 mmol, 1.0 equiv) was dissolved in acetone (2 mL) and Jones' reagent (70 μL, 0.28 mmol, 1.0 equiv) was added and the mixture was stirred at room temperature for 30 min. The reaction was then quenched by addition of propan-2-ol (10 drops) and the mixture was filtered over a silica pad. The filtrate

was then made alkaline by addition of an aqueous solution of sodium hydroxide (2M). CH_2Cl_2 (10 mL) was then added, the two layers were separated, the aqueous phase was extracted with CH_2Cl_2 (3×15 mL). The combined organic solutions were dried over $MgSO_4$ and concentrated under vacuum to give pure (+)-**20** as a white solid (62 mg, 84%): mp 155–157 °C; $[\alpha]_D^{20}$ +163.7 (*c* 0.6, $CHCl_3$); IR (KBr) *ν* 2975 (m, C–H), 1705 (s, C=O), 1585 (m, arom C=C), 1558 (s, arom C=C), 1455 (m, arom C=C), 779 (m, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.83 (s, 3H, 12-H), 1.62 (s, 3H, 13-H), 2.18 (dt, *J*=8.2, 5.0 Hz, 1H, 9-H), 3.09–3.13 (m, 3H, 8-H, 9-H′, 10-H), 7.41 (tt, *J*=7.2, 1.3 Hz, 1H, 4′-H), 7.47 (t, *J*=7.2 Hz, 2H, 3′-H, 5′-H), 7.64 (d, *J*=7.9 Hz, 1H, 3-H), 7.78 (d, *J*=7.9 Hz, 1H, 4-H), 8.08 (d, *J*=7.2 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 22.7 (CH_3-12), 26.7 (CH_3-13), 39.3 (CH_2-9), 47.1 (CH-10), 52.7 (C-11), 58.2 (CH-8), 123.2 (CH-4), 127.1 (2× CH-2′,6′), 128.7 (2× CH-3′,5′), 129.1 (CH-4′), 134.9 (CH-3), 138.5 (C-2′), 144.8 (C-5), 147.9 (C-2), 156.6 (C-6), 199.9 (C=O); MS (CI-isobutane) *m*/*z* (%) 264 ($(M+H)^+$, 100); HRMS (CI-isobutane) 264.1389 ($C_{18}H_{18}NO$ $(M+H)^+$ requires 264.1388).

*4.2.4. (7S,8R,10S)-(+)-2-Phenyl-11,11-dimethyl-1-azatricyclo [7.1.1.0^{5,6}]undeca-2,4,6-trien-7-ol (+)-(**21**).* Sodium borohydride (4 mg, 0.103 mmol, 1.0 equiv) was added portion-wise to a solution of ketone (+)-**20** (27 mg, 0.103 mmol, 1.0 equiv) in ethanol (1 mL) and the reaction mixture was stirred at room temperature for 20 min. Water (2 mL) was then added to quench the remaining sodium borohydride and the aqueous layer was extracted with CH_2Cl_2 (3×5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum to afford pure (+)-**21** as a white solid (25 mg, 91%): mp 85–87 °C; $[\alpha]_D^{20}$ +86.9 (*c* 1.5, $CHCl_3$); IR (KBr) *ν* 3430 (s, OH), 2933 (s, C–H), 1586 (m, arom C=C), 1568 (m, arom C=C), 1441 (m, arom C=C), 772 (m, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.61 (s, 3H, 12-H), 1.39 (s, 3H, 13-H), 1.50 (d, *J*=9.9 Hz, 1H, 9-H), 2.44 (td, *J*=5.8, 3.3 Hz, 1H, 8-H), 2.50–2.60 (m, 1H, 9-H′), 2.74 (t, *J*=5.8 Hz, 1H, 10-H), 3.42 (br s, 1H, OH), 4.88 (d, *J*=3.3 Hz, 1H, 7-H), 7.29 (d, *J*=7.8 Hz, 1H, 4-H), 7.33 (t, *J*=7.0 Hz, 1H, 4′-H), 7.39 (t, *J*=7.0 Hz, 2H, 3′-H, 5′-H), 7.47 (d, *J*=7.8 Hz, 1H, 3-H), 7.95 (d, *J*=7.0 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 22.0 (CH_3-12), 25.7 (CH_3-13), 33.0 (CH_2-9), 39.5 (C-11), 45.1 (CH-8), 45.9 (CH-10), 73.2 (CH-7), 117.8 (CH-3), 125.64 (2× CH-2′,6′), 125.69 (CH-4′), 127.7 (2× CH-3′,5′), 132.9 (CH-4), 137.9 (C-1′), 138.4 (C-5), 153.9 (C-2), 156.9 (C-6); MS (EI) *m*/*z* (%) 265 ($M^{\bullet+}$, 50), 248 ($M^{\bullet+}$–OH, 26), 206 ($M^{\bullet+}$–OH–C_3H_6, 50), 196 (100), 28 (39); HRMS (EI) 265.1469 ($C_{18}H_{19}NO$ requires 265.1467).

*4.2.5. (7R,8R,10S)-2-phenyl-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}] undeca-2,4,6-trien-7-ol (**22**).* Diisopropyl azodicarboxylate (0.62 mL, 3.12 mmol, 4 equiv) was added dropwise to a cold (0 °C) solution of alcohol (+)-**21** (200 mg, 0.78 mmol, 1 equiv), *p*-nitrobenzoic acid (520 mg, 3.12 mmol, 4 equiv), and triphenylphosphine (820 mg, 3.12 mmol, 4 equiv) in dry THF (6 mL). After completion of the addition, the reaction mixture was allowed to warm to room temperature and was stirred overnight at that temperature. The mixture was then diluted with ether (10 mL) and the organic layer was washed with a saturated aqueous solution of sodium carbonate (2×15 mL), dried over $MgSO_4$, and concentrated under vacuum. The crude material was dissolved in methanol (3 mL) and potassium carbonate (570 mg, 4.1 mmol, 10 equiv) was added portion-wise and the reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated under reduced pressure, the residue was diluted with water (5 mL) and made alkaline by addition of an aqueous solution of 2 M sodium hydroxide. The aqueous layer was extracted with CH_2Cl_2 (3×20 mL) and the organic extract was dried over $MgSO_4$, and concentrated under vacuum to provide pure alcohol **22** as a colorless oil (100.3 mg, 50%): ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.70 (s, 3H, 12-H), 1.48 (s, 3H, 13-H), 1.59 (d, *J*=9.9 Hz, 1H, 9-H), 2.53 (td, *J*=5.8, 3.2 Hz, 1H, 8-H), 2.64 (dt, *J*=9.9, 5.8 Hz, 1H, 9-H′), 2.83 (t, *J*=5.8 Hz, 1H, 10-H), 3.51 (br s, 1H, OH), 4.97 (d, *J*=3.2 Hz, 1H, 7-H), 7.35 (d, *J*=7.8 Hz, 1H, 3-H), 7.38 (t, *J*=7.4 Hz, 1H, 4′-H), 7.45 (t, *J*=7.4 Hz, 2H, 3′-H, 5′-H), 7.52 (d, *J*=7.8 Hz, 1H, 4-H), 8.00 (d, *J*=7.4 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 21.0 (CH_3-12), 26.6 (CH_3-13), 29.6 (CH_2-9), 44.9 (C-11), 45.5 (CH-8), 46.6 (CH-10), 71.5 (CH-7), 118.9 (CH-4), 126.7 (2× CH-2′,6′), 128.5 (CH-4′), 128.6 (2× CH-3′,5′), 133.8 (CH-3), 139.2 (C-1′), 139.8 (C-5), 155.0 (C-2), 157.2 (C-6); HRMS (EI) 265.1469 ($C_{18}H_{19}NO$ requires 265.1467).

*4.2.6. Borane-protected (7S,8R,10S)-(+)-2-phenyl-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-trien-7-yl diphenylphosphinite (+)-(**23**).* A solution of *n*-butyllithium in hexane (2.5M; 0.38 mL, 0.94 mmol, 1.0 equiv) was added dropwise to a solution of (+)-**21** (250 mg, 0.94 mmol, 1.0 equiv) in anhydrous THF (2 mL) under argon at −40 °C. The solution was stirred at that temperature for 30 min and then allowed to gradually warm to 0 °C. Diphenylphosphine chloride (0.20 mL, 1.04 mmol, 1.1 equiv) was then added dropwise and the reaction mixture was warmed up to room temperature and stirred for 3 h. A solution of borane in THF (1 M, 0.94 mL, 0.94 mmol, 1.0 equiv) was added dropwise to the latter solution and the reaction mixture was stirred overnight. The reaction was then quenched by addition of water (15 mL), the aqueous phase was extracted with CH_2Cl_2 (3×20 mL), and the combined organic extracts were washed with brine (20 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was purified by chromatography on a column of silica gel (13 g) using a mixture of petroleum ether and AcOEt (95:5) to give pure (+)-**23** (176 mg, 41%) as a white solid: mp 117–120 °C (hexane); $[\alpha]_D^{19}$ +170.5 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.82 (s, 3H, 12-H), 1.42 (s, 3H, 13-H), 1.48 (d, *J*=9.7 Hz, 1H, 9-H), 1.54 (br s, 3H, BH_3), 2.73–2.79 (m, 2H, 10-H, 9-H′), 2.84 (td, *J*=6.4, 3.3 Hz, 1H, 8-H), 5.78 (dd, J_{H,P^2}=10.0 Hz, *J*=3.3 Hz, 1H, 7-H), 7.33 (d, *J*=7.8 Hz, 1H, 4-H), 7.35–7.49 (m, 9H, 3′-H, 5′-H, 4′-H, 6× aromH), 7.55 (d, *J*=7.8 Hz, 1H, 3-H), 7.72–7.77 (m, 2H, aromH), 7.90 (dd, *J*=8.0, 1.6 Hz, 2H, 2′-H, 6′-H), 8.02–8.07 (m, 2H, aromH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 23.5 (CH_3-12), 26.6 (CH_3-13), 35.1 (CH_2-9), 40.6 (C-11), 46.6 (CH-10), 47.0 (CH-8), 80.1 (CH-7), 118.6 (CH-3), 126.6 (2× CH-2′,6′), 128.3 (d, *J*=10 Hz, 2× aromCH), 128.4 (d, *J*=10 Hz, 2× aromCH), 128.49 (CH-4′), 128.51 (2× CH-3′,5′), 131.2 (d, *J*=11 Hz, 2× aromCH), 131.37 (d, *J*=2 Hz, aromCH), 131.46 (d, *J*=2 Hz, aromCH), 132.1 (d, *J*=11 Hz, 2× aromCH), 133.0 (d, *J*=65 Hz, C), 133.7 (CH-4), 133.9 (d, *J*=65 Hz, C), 139.1 (C-1′), 140.2 (C-5), 154.0 (d, *J*=6 Hz, C-6), 155.0 (C-2); ^{31}P NMR (162.0 MHz, $CDCl_3$) *δ* 105.9 (m). Anal. Calcd for $C_{30}H_{31}BNOP$: C, 77.76; H, 6.74; N, 3.02. Found: C, 77.30; H, 6.69; N, 3.22.

*4.2.7. Borane-protected (7R,8R,10S)-(−)-2-phenyl-7-(diphenylphosphino)-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (−)-(**24**).* A solution of *n*-butyllithium in hexane (2.5 M; 0.4 mL, 1.0 mmol, 1.0 equiv) was added dropwise to a solution of (+)-**18** (0.25 g, 1.0 mmol, 1.0 equiv) in THF (2 mL) at −40 °C. The solution was stirred at that temperature for 1 h and then a solution of $Ph_2PCl\cdot BH_3$ (3.0 mmol, 3.0 equiv) was added dropwise at −40 °C [the $Ph_2PCl\cdot BH_3$ solution was prepared by stirring for 30 min a mixture of borane in THF (1 M, 3 mL, 3 mmol, 1.0 equiv) and chlorodiphenylphosphine (0.54 mL, 3 mmol, 1.0 equiv) in diethyl ether (2 mL) at room temperature]. The resulting solution was then gradually warmed up to room temperature and stirred overnight. A saturated aqueous solution of NH_4Cl (2 mL) was then added to quench the reaction, the mixture was extracted with CH_2Cl_2 (3×20 mL) and the combined organic extracts were washed with brine (20 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was purified by chromatography on silica gel (20 g) using a mixture of hexane and diethyl ether (20:1) to give pure (−)-**24** as a white solid (154 mg, 35%): mp 190–192 °C (MeOH); $[\alpha]_D^{25}$ −112.4 (*c* 1.0, $CHCl_3$); IR (KBr) *ν* 3050–2950 (s, C–H), 2397 (m, B–H), 1560 (m, arom C=C),

1425 (m, arom C=C), 771 (s, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.74 (s, 3H, 12-H), 1.21 (d, J=10.3 Hz, 1H, 9-H), 1.41 (s, 3H, 13-H), 1.54 (s, 3H, BH_3), 2.45 (dt, J=10.3, 5.8 Hz, 1H, 9-H′), 2.66 (t, J=5.8 Hz, 1H, 10-H), 2.77 (qd, J=6.2, 2.0 Hz, 1H, 8-H), 4.43 (dd, J_{H,P^2}=13.4 Hz, J=2.0 Hz, 1H, 7-H), 7.19–7.23 (m, 3H, 4-H, 3′-H, 5′-H), 7.25–7.29 (m, 3H, 4′-H, 2× aromH), 7.35–7.43 (m, 3H, 2′-H, 6′-H, aromH), 7.47–7.57 (m, 4H, 3-H, 3× aromH), 7.68–7.73 (m, 2H, aromH), 7.83–7.88 (m, 2H, aromH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9 (CH_3-12), 25.9 (CH_3-13), 28.3 (CH_2-9), 42.4 (CH-8), 42.5 (C-11), 42.7 (d, J=29 Hz, CH-7), 45.8 (CH-10), 117.1 (CH-3), 126.1 (2× CH-2′,6′), 128.2 (d, J=10 Hz, 2× aromCH), 128.33 (2× CH-3′,5′), 128.39 (CH-4′), 128.45 (d, J=55 Hz, C), 128.5 (d, J=10 Hz, 2× aromCH), 130.1 (d, J=2 Hz, aromCH), 131.0 (d, J=2 Hz, aromCH), 131.7 (d, J=55 Hz, C), 132.5 (d, J=9 Hz, 2× aromCH), 134.2 (CH-4), 134.4 (d, J=9 Hz, 2× aromCH), 138.5 (C-1′), 140.8 (d, J=4 Hz, C-5), 153.1 (d, J=7 Hz, C-6), 153.3 (C-2); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 25.8 (m); MS (EI) m/z (%) 447 ($M^{\bullet+}$, 14), 433 ($M^{\bullet+}-BH_3$, 58), 248 ($M^{\bullet+}-PPh_2\cdot BH_3$, 57), 206 ($M^{\bullet+}-PPh_2\cdot BH_3-C_3H_6$, 100), 91 (73); HRMS (EI) 447.2286 ($C_{30}H_{31}BNP$ requires 447.2293).

*4.2.8. (7R,8R,10S)-(−)-2-Phenyl-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-trien-7-yl(diphenyl)phosphine oxide (−)-(**25**).* A 2.5 M solution of *n*-butyllithium in hexane (0.8 mL, 2.0 mmol, 1.0 equiv) was added dropwise to a solution of (+)-**18** (0.50 g, 2.0 mmol, 1.0 equiv) in anhydrous THF (5 mL) under an argon atmosphere at −40 °C. The red color of the mixture turned darker and darker. The solution was stirred at that temperature for 1 h and then a solution of diphenylphosphinic chloride (0.40 mL, 2.0 mmol, 1.0 equiv) in THF (2 mL) was added dropwise at −40 °C. The solution was then gradually warmed up to room temperature and stirred overnight. The reaction was then quenched by addition of water (20 mL), the mixture was extracted with CH_2Cl_2 (3×20 mL), the organic solution was washed with brine (20 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was purified by chromatography on silica gel (30 g) using a mixture of petroleum ether and ethyl acetate (1:1) at the beginning, followed by a regular increase of the ethyl acetate ratio to pure ethyl acetate to give pure (−)-**25** as a white solid (307 mg, 34%): mp 104–106 °C (hexane); $[\alpha]_D^{25}$ −54.0 (*c* 1.0, $CHCl_3$); IR (KBr) ν 3016 (s, C–H), 1596 (m, arom C=C), 1525 (m, arom C=C), 1432 (m, arom C=C), 1216 (s, P=O), 771 (s, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.63 (s, 3H, 12-H), 1.32 (s, 3H, 13-H), 1.54 (d, J=10.2 Hz, 1H, 9-H), 2.45 (dt, J=10.2, 5.8 Hz, 1H, 9-H′), 2.60–2.65 (m, 2H, 8-H, 10-H), 4.32 (dd, J_{H,P^2}=13.9 Hz, J=1.0 Hz, 1H, 7-H), 7.10 (td, J=7.2, 1.5 Hz, 2H, 3′-H, 5′-H), 7.14–7.20 (m, 4H, 4-H, 4′-H, 2′-H, 4′-H), 7.30 (td, J=7.4, 3.0 Hz, 2H, aromH), 7.35–7.51 (m, 5H, 3-H, aromH), 7.69–7.75 (m, 2H, aromH), 7.82–7.89 (m, 2H, aromH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8 (CH_3-12), 25.7 (CH_3-13), 28.4 (CH_2-9), 41.1 (CH-8), 41.9 (C-11), 45.3 (d, J=21 Hz, CH-7), 45.9 (CH-10), 116.9 (CH-3), 126.0 (2× CH-2′,6′), 128.1 (d, J=12 Hz, 2× aromCH), 128.2 (2× CH-3′,5′), 128.22 (CH-4′), 128.5 (d, J=12 Hz, 2× aromCH), 130.9 (d, J=3 Hz, aromCH), 131.0 (d, J=3 Hz, aromCH), 131.15 (d, J=9 Hz, 2× aromCH), 131.85 (d, J=9 Hz, 2× aromCH), 133.0 (d, J=97 Hz, C), 134.2 (CH-4), 134.6 (d, J=97 Hz, C), 138.4 (C-1′), 141.0 (d, J=5 Hz, C-5), 152.0 (d, J=7 Hz, C-6), 153.3 (C-2); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 33.4 (P=O); MS (EI) m/z (%) 449 ($M^{\bullet+}$, 15), 248 ($M^{\bullet+}-P(O)Ph_2$, 100), 206 ($M^{\bullet+}-P(O)Ph_2-C_3H_6$, 18); HRMS (EI) 449.1906 ($C_{30}H_{28}NOP$ requires 449.1909).

*4.2.9. (8S,10S)-2-Chloro-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (**29**).* Pyridinium chloride (100 mg, 0.864 mmol, 2 equiv) was added to a solution of triflate (+)-**28**[14b] (139 mg, 0.431 mmol, 1 equiv) in *N*-methyl-2-pyrrolidone (2.6 mL) and the mixture was stirred under microwave irradiation (250 °C) for 15 min. The resulting mixture was diluted with ethyl acetate (4 mL), the organic layer was washed with water (2×10 mL), dried over $MgSO_4$, and concentrated under vacuum. The resulting brownish oil was purified by column chromatography on silica gel (4 g) using a mixture of hexane and ethyl acetate (1:1) to give pure **29** (32 mg, 36%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 0.63 (s, 3H, 12-H), 1.27 (d, J=9.8 Hz, 1H, 9-H), 1.40 (s, 3H, 13-H), 2.38 (m, 1H, 8-H), 2.69 (dt, J=9.8, 5.7 Hz, 1H, 9-H′), 2.75 (t, J=5.7 Hz, 1H, 10-H), 3.08 (d, J=2.1 Hz, 2H, 7-H), 7.01 (d, J=8.9 Hz, 1H, 3-H), 7.17 (d, J=8.9 Hz, 1H, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0 (CH_3-12), 25.9 (CH_3-13), 31.9 (CH_2-7), 36.2 (CH_2-9), 39.3 (C-11), 39.9 (CH-8), 45.8 (CH-10), 120.5 (CH-3), 135.7 (CH-4), 140.7 (C-5), 147.8 (C-6), 157.8 (C-2); LCMS (GSK-gold) 3.31 min—mass 208.1.

*4.2.10. (8S,10S)-(+)-11,11-Dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (+)-(**30**). Method A.* A mixture of 10% Pd/C (10 mg, 0.0077 mmol, 0.05 equiv) and 2-chloropyridine derivative **29** (32 mg, 0.155 mmol, 1.00 equiv) in formic acid 99% (0.25 mL) and DMF (1.25 mL) was heated at 60 °C for 5 h. The mixture was then cooled to room temperature, diluted with CH_2Cl_2 (4 mL), and filtered through a plug of Celite. The filtrate was made alkaline by addition of an aqueous solution of sodium hydroxide (2 M). The mixture was then extracted with CH_2Cl_2 (3×20 mL), dried over $MgSO_4$, and concentrated under vacuum to afford the pure pyridine (+)-**30** (25.4 mg, 95%).

Method B. Formic acid 99% (38 μL, 1.00 mmol, 2.00 equiv) was added dropwise to a solution of triflate (+)-**28**[14b] (160 mg, 0.50 mmol, 1.00 equiv), triethylamine (0.21 mL, 1.50 mmol, 3.00 equiv), palladium(II) acetate (2.3 mg, 0.01 mmol, 0.02 equiv), and 1,1′-bis(diphenylphosphino)ferrocene (12 mg, 0.02 mmol, 0.04 equiv) in DMF (1 mL). The reaction mixture was stirred at 60 °C for 2 h under argon, then cooled to room temperature and diluted with water (4 mL). The resulting mixture was extracted with ether (3×10 mL) and the combined organic layers were washed successively with a saturated aqueous solution of $NaHCO_3$ (30 mL) and brine (30 mL), dried over Na_2SO_4, and evaporated. The brown residue was then purified by column chromatography on silica gel (4 g) using a mixture of hexane and ethyl acetate (9:1), to afford pure (+)-**30** (55.6 mg, 65%) as a colorless oil: $[\alpha]_D^{20}$ +51.8 (*c* 1.0, $CHCl_3$); IR (KBr) ν 3020 (m, C–H), 1573 (m, arom C=C), 1524 (m, arom C=C), 1430 (m, arom C=C), 758 (s, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.61 (s, 3H, 12-H), 1.24 (d, J=9.5 Hz, 1H, 9-H), 1.37 (s, 3H, 13-H), 2.33 (tt, J=5.8, 2.8 Hz, 1H, 8-H), 2.64 (dt, J=9.5, 5.8 Hz, 1H, 9-H′), 2.71 (t, J=5.8 Hz, 1H, 10-H), 3.08 (d, J=2.8 Hz, 2H, 7-H), 6.93 (dd, J=7.4, 5.0 Hz, 1H, 3-H), 7.15 (dd, J=7.4, 1.3 Hz, 1H, 4-H), 8.31 (dd, J=5.0, 1.4 Hz, 1H, 2-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (CH_3-12), 26.0 (CH_3-13), 31.8 (CH_2-9), 36.4 (CH_2-7), 39.3 (C-11), 40.1 (CH-8), 46.4 (CH-10), 120.2 (CH-3), 132.8 (CH-4), 141.7 (C-5), 146.6 (CH-2), 156.8 (C-6); MS (CI-isobutane) m/z (%) 174 ($(M+H)^+$, 100), 95 (11), 69 (61); HRMS (CI-isobutane) 174.1284 ($C_{12}H_{16}N$ $(M+H)^+$ requires 174.1283).

*4.2.11. Borane-protected (7R,8S,10S)-(+)-7-(diphenylphosphino)-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (+)-(**31**).* A solution of *n*-butyllithium in hexane (1.6 M; 0.42 mL, 0.67 mmol, 1.0 equiv) was added dropwise to a solution of (+)-**30** (120 mg, 0.67 mmol, 1.0 equiv) in THF (2 mL) at −40 °C. The solution was stirred at that temperature for 1 h and then a solution of $Ph_2PCl\cdot BH_3$ (1.0 mmol, 1.5 equiv) was added dropwise at −40 °C [the $Ph_2PCl\cdot BH_3$ solution was prepared by stirring for 30 min a mixture of borane in THF (1 M, 1 mL, 1.0 mmol, 1.0 equiv) and chlorodiphenylphosphine (0.18 mL, 1.0 mmol, 1.0 equiv) in diethyl ether (2 mL) at room temperature]. The resulting solution was then gradually warmed up to room temperature and stirred overnight. A saturated aqueous solution of NH_4Cl (2 mL) was then added to quench the reaction, the mixture was extracted with CH_2Cl_2 (3×20 mL), and the combined organic extracts were washed with brine (20 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was purified by chromatography on silica gel (20 g) using a mixture of hexane and ether (20:1) to give

pure (+)-**31** as a white solid (103 mg, 42%): $[\alpha]_D^{26}$ +45.7 (*c* 1.0, $CHCl_3$); IR (KBr) ν 3018 (m, C–H), 2389 (m, B–H), 1576 (m, arom C=C), 1525 (m, arom C=C), 1432 (m, arom C=C), 1213 (s, P–BH_3), 758 (s, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.69 (s, 3H, 12-H), 1.40 (s, 3H, 13-H), 1.50 (d, *J*=10.3 Hz, 1H, 9-H), 2.53 (dt, *J*=10.3, 5.8 Hz, 1H, 9-H′), 2.67 (t, *J*=5.8 Hz, 1H, 10-H), 2.70 (qd, *J*=6.2, 2.1 Hz, 1H, 8-H), 4.33 (dd, J_{H,P^2}=13.8 Hz, *J*=2.0 Hz, 1H, 7-H), 7.91–6.96 (m, 1H, 3-H), 7.15 (dd, *J*=7.5, 1.5 Hz, 1H, 4-H), 7.29 (td, *J*=7.6, 2.0 Hz, 2H, aromH), 7.38 (td, *J*=7.6, 1.4 Hz, 1H, aromH), 7.45–7.52 (m, 3H, 3× aromH), 7.74 (ddd, *J*=10.7, 8.0, 1.2 Hz, 2H, 2× aromH), 7.92 (ddd, *J*=10.3, 7.7, 1.8 Hz, 2H, 2× aromH), 8.23 (dd, *J*=4.9, 1.7 Hz, 1H, 2-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7 (CH_3-12), 25.8 (CH_3-13), 28.4 (CH_2-9), 42.0 (d, *J*=10 Hz, C-11), 42.4 (d, *J*=29 Hz, CH-7), 42.7 (CH-8), 45.8 (d, *J*=2 Hz, CH-10), 121.1 (CH-3), 127.8 (d, *J*=10 Hz, 2× aromCH), 128.3 (d, *J*=10 Hz, 2× aromCH), 129.3 (d, *J*=53 Hz, C), 130.5 (d, *J*=2 Hz, aromCH), 130.6 (d, *J*=2 Hz, aromCH), 130.9 (d, *J*=55 Hz, C), 133.2 (CH-4), 133.21 (d, *J*=9 Hz, 2× aromCH), 134.2 (d, *J*=9 Hz, 2× aromCH), 141.8 (d, *J*=4 Hz, C-5), 146.4 (d, *J*=2 Hz, CH-2), 153.6 (d, *J*=6 Hz, C-6); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 26.7 (m); MS (EI) *m*/*z* (%) 371 ($M^{\bullet+}$, 22), 357 ($M^{\bullet+}-BH_3$, 100), 172 ($M^{\bullet+}-PPh_2\cdot BH_3$, 86), 130 ($M^{\bullet+}-PPh_2\cdot BH_3-C_3H_6$, 100); HRMS (EI) 371.1653 ($C_{24}H_{27}BNP$ requires 371.1646). Anal. Calcd for $C_{24}H_{27}BNP$: C, 77.64; H, 7.33; N, 3.77. Found: C, 77.74; H, 7.44; N, 3.71.

*4.2.12. (1R,3R,4S)-(+)-5-Fluoro-1,3-methano-2,2,4-trimethyl-1,2,3,4-tetrahydroacridine (+)-(**34**).* (1*R*,5*S*)-2,6,6-Trimethylbicyclo[3.1.1]heptan-3-one **32**[39,44] (365 mg, 2.40 mmol) was added to a suspension of *t*-BuOK (539 mg, 4.80 mmol) in dry 1,4-dioxane (15 mL) and the solution was stirred at room temperature for 10 min. *tert*-Butyl *N*-(2-formylphenyl)carbamate **33**[45] (478 mg, 2.00 mmol) was then added and the reaction mixture was stirred at room temperature for 7 h. A 3.0 M solution of HCl (6 mL) was added and the resulting mixture was heated under reflux from 4 h. Most part of the solvent was then evaporated under reduced pressure and the residue was taken up with a 5% NaOH solution and extracted with Et_2O. The organic phase was dried over anhydrous Na_2SO_4, the solvent was evaporated, and the residue was purified by flash chromatography on a column of silica gel (2×16 cm) using a mixture of petroleum ether and ethyl acetate (4:1) to give **34** as a 4:1 mixture of epimers at C4 (539.3 mg). This epimeric mixture was submitted to further flash chromatography on a column of silica gel (2×32 cm) using a mixture of CH_2Cl_2 and Et_2O (9:1) to give the most abundant isomer (1*R*,3*R*,4*S*)-**34** as a white solid (329 mg, 61%): mp 96–97 °C; $[\alpha]_D^{25}$ +45.8 (*c* 4.59, $CHCl_3$); IR (KBr) ν 2927 (s, C–H), 1561 (s, arom C=C), 1465 (s, arom C=C), 1379 (s, arom C=C), 1271, 1174, 862, 801 (m, arom C–H), 735 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.66 (s, 3H, 16-H), 1.38 (d, 1H, *J*=10.2, 10-H), 1.46 (s, 3H, 15-H), 1.51 (d, 3H, *J*=6.9 Hz, 17-H), 2.23 (dt, 1H, *J*=6.0, 2.4 Hz, 3-H), 2.62–2.71 (m, 1H, 10-H′), 2.96 (t, 1H, *J*=5.4 Hz, 1-H), 3.45 (dq, 1H, *J*=6.9, 1.5 Hz, 4-H), 7.24–7.4 (m, 2H, 6,7-H), 7.48 (d, 1H, *J*=8.1 Hz, 8-H), 7.59 (d, 1H, *J*=1.8 Hz, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.8 (CH_3-17), 21.0 (CH_3-16), 26.2 (CH_3-15), 28.8 (CH_2-10), 39.5 (CH-4), 41.3 (C-2), 46.6 (CH-3), 47.7 (CH-1), 112.2 (d, *J*=19.1 Hz, CH-6), 122.5 (d, *J*=4.5 Hz, CH-8), 125.4 (d, *J*=19.1 Hz, CH-7), 128.7 (d, *J*=19.1 Hz, CH-11), 130.0 (d, *J*=130.0 Hz, C-5), 137.1 (d, *J*=11.4 Hz, C-4), 141.0 (s, CH-9), 157.8 (d, *J*=253.1 Hz, C-12), 163.7 (s, C-13). Anal. Calcd for $C_{17}H_{18}FN$: C, 79.97; H, 7.11; N, 5.49. Found: C, 79.78; H, 7.23; N, 5.45.

4.3. General procedure for the borane adduct deprotection

Borane-protected phosphine or phosphinite was dissolved in diethylamine (1–2 mL) and stirred for 6 h. The conversion was monitored by TLC. After completion of the reaction all volatiles were removed under high-vacuum at 60 °C to afford the free phosphine/phosphinite. The free phosphine/phosphinite was then immediately used for complexation with iridium.

4.4. General procedure for the preparation of iridium(I) catalysts 35–43

$[Ir(COD)Cl]_2$ (33.58 mg, 0.05 mmol, 0.5 equiv) and the respective P,N-ligand (0.10 mmol, 1.0 equiv) were dissolved in CH_2Cl_2 (2 mL). The resulting red solution was heated at 50 °C until disappearance of the starting P,N-ligand (TLC monitoring). The solution was then cooled to room temperature and $Na[BAr_F]$[46] (133 mg, 0.15 mmol, 1.5 equiv) was added, followed by water (2 mL), and the resulting mixture was stirred vigorously for 30 min. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×3 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was then purified by flash chromatography on silica gel (15 g) using a mixture of hexane and CH_2Cl_2 (1:1) to give **35**–**43** as orange solids.

*4.4.1. (8S,10S)-(+)-2-[2′-(Diphenylphosphino)phenyl]-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene-η^4-(1,5-cyclooctadiene) iridium(I) tetrakis-[3,5-bis(trifluoromethyl)phenyl] borate (+)-(**35**).* Obtained from **1** (92.6 mg, 58%): mp 65–67 °C (hexane/Et_2O 1:1); $[\alpha]_D^{26}$ +7.8 (*c* 1.0, $CHCl_3$); IR (KBr) ν 3022 (s, C–H), 1424 (m, arom C=C), 1353 (m, arom C=C), 1277 (m, arom C=C), 772 (s, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.29 (d, *J*=10.0 Hz, 1H, 9-H), 0.52 (s, 3H, 12-H), 0.95–1.00 (m, 1H, C*H*$_2$(COD)), 1.17–1.22 (m, 1H, C*H*$_2$(COD)), 1.24 (s, 3H, 13-H), 1.27–1.34 (m, 1H, C*H*$_2$(COD)), 1.58–1.70 (m, 2H, C*H*$_2$(COD)), 1.93–2.03 (m, 1H, C*H*$_2$(COD)), 2.25–2.34 (m, 1H, C*H*$_2$(COD)), 2.36–2.61 (m, 4H, C*H*$_2$(COD), 8-H, 9-H′, 10-H), 3.25 (dd, *J*=18.0, 2.7 Hz, 1H, 7-H), 3.32 (dd, *J*=18.0, 2.7 Hz, 1H, 7-H′), 3.44–3.62 (m, 1H, C*H*(COD)), 3.85–3.95 (m, 1H, C*H*(COD)), 4.32–4.51 (m, 1H, C*H*(COD)), 5.11–5.17 (m, 1H, C*H*(COD)), 7.02–7.14 (m, 7H, aromH), 7.17–7.30 (m, 3H, aromH), 7.34–7.53 (m, 9H, aromH), 7.57–7.65 (m, 9H, aromH); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 19.2 (s); MS (FAB) *m*/*z* (%) 734 ($M^{\bullet+}$, 100), 626 ($M^{\bullet+}-$COD, 16), 450 (42); HRMS (FAB) 734.2529 ($C_{38}H_{40}NPIr$ requires 734.2530). Anal. Calcd for $C_{70}H_{52}BF_{24}NPIr$: C, 52.64; H, 3.28; N, 0.88. Found: C, 52.38; H, 3.23; N, 1.01.

*4.4.2. (7R,8S,10S)-(+)-2-[2′-(Diphenylphosphino)phenyl]-7,11,11-trimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene-η^4-(1,5-cyclooctadiene) iridium(I) tetrakis-[3,5-bis(trifluoromethyl)phenyl] borate (+)-(**36**).* Obtained from **2** (83.8 mg, 52%): mp 61–63 °C (hexane/CH_2Cl_2 1:1); $[\alpha]_D^{25}$ +2.8 (*c* 0.25, $CHCl_3$); IR (KBr) ν 3020 (s, C–H), 1428 (m, arom C=C), 1354 (m, arom C=C), 1279 (m, arom C=C), 770 (s, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.51 (s, 3H, 12-H), 0.55 (d, *J*=10.2 Hz, 1H, 9-H), 0.80–0.85 (m, 1H, C*H*$_2$(COD)), 1.00–1.10 (m, 2H, C*H*$_2$(COD)), 1.34 (s, 3H, 13-H), 1.36–1.44 (m, 1H, C*H*$_2$(COD)), 1.60–1.70 (m, 1H, C*H*$_2$(COD)), 1.85 (d, *J*=7.1 Hz, 3H, C*H*$_3$C(7)), 2.02–2.04 (m, 1H, C*H*$_2$(COD)), 2.08–2.12 (m, 1H, C*H*$_2$(COD)), 2.40 (m, 1H, 9-H′), 2.52–2.62 (m, 2H, C*H*$_2$(COD), 8-H), 2.67 (t, *J*=5.9 Hz, 1H, 10-H), 3.33–3.41 (m, 2H, C*H*(COD), 7-H), 4.10–4.15 (m, 1H, C*H*(COD)), 4.24–4.29 (m, 1H, C*H*(COD)), 5.27–5.33 (m, 1H, C*H*(COD)), 6.98–7.09 (m, 3H, aromH), 7.15–7.25 (m, 2H, aromH), 7.31–7.53 (m, 10H, aromH), 7.54–7.63 (m, 3H, aromH), 7.66–7.74 (m, 10H, aromH); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 11.1 (s); MS (FAB) *m*/*z* (%) 748 ($M^{\bullet+}$, 100), 636 (48), 558 (22); HRMS (FAB) 748.2685 ($C_{39}H_{42}NPIr$ requires 748.2687). Anal. Calcd for $C_{71}H_{54}BF_{24}NPIr$: C, 52.93; H, 3.38; N, 0.87. Found: C, 52.88; H, 3.26; N, 0.98.

*4.4.3. (7R,8S,10S)-(+)-2-[2′-(Diphenylphosphino)phenyl]-7-isopropyl-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene-η^4-(1,5-cyclooctadiene) iridium(I) tetrakis-[3,5-bis(trifluoromethyl) phenyl] borate (+)-(**37**).* Obtained from **3** (71 mg, 44%): mp 64–66 °C (hexane/Et_2O 2:1); $[\alpha]_D^{22}$ +28.8 (*c* 0.5, $CHCl_3$); IR (KBr) ν 3020 (s, C–H), 1426 (m, arom C=C), 1353 (m, arom C=C), 1272 (m,

arom C=C), 770 (s, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.35 (d, J=6.6 Hz, 3H, CH_3CH), 0.38 (s, 3H, 12-H), 0.66–0.76 (m, 1H, CH_2(COD)), 0.83 (d, J=10.2 Hz, 1H, 9-H), 0.96–1.09 (m, 2H, CH_2(COD)), 1.18–1.22 (m, 1H, CH_2(COD)), 1.26 (s, 3H, 13-H), 1.35 (d, J=6.6 Hz, 3H, $CH_3'CH$), 1.45–1.51 (m, 1H, CH_2(COD)), 1.90–2.00 (m, 1H, CH_2(COD)), 2.22 (td, J=6.1, 1.8 Hz, 1H, 8-H), 2.30–2.38 (m, 2H, CH_2(COD), 9-H′), 2.57 (t, J=6.1 Hz, 1H, 10-H), 2.58–2.66 (m, 1H, CH_2(COD)), 3.06 (br s, 1H, 7-H), 3.16 (td, J=6.6, 3.5 Hz, 1H, CH_3CHCH_3), 3.55–3.43 (m, 1H, CH(COD)), 3.90–3.96 (m, 1H, CH(COD)), 3.97–4.04 (m, 1H, CH(COD)), 5.05–5.11 (m, 1H, CH(COD)), 6.84–6.90 (m, 2H, aromH), 6.91–6.97 (m, 2H, aromH), 7.04 (tq, J=7.1, 1.5 Hz, 1H, aromH), 7.20–7.28 (m, 3H, aromH), 7.30–7.50 (m, 10H, aromH), 7.52–7.66 (m, 10H, aromH); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 8.9 (s); MS (FAB) m/z (%) 776 ($M^{\bullet+}$, 100), 668 ($M^{\bullet+}$–COD, 5), 262 (58); HRMS (FAB) 776.3004 ($C_{41}H_{46}NPIr$ requires 776.3000). Anal. Calcd for $C_{73}H_{58}BF_{24}NPIr$: C, 53.49; H, 3.57; N, 0.85. Found: C, 53.12; H, 3.38; N, 0.97.

*4.4.4. (6R,8R)-(+)-5,7-Methano-6,6,8-trimethyl-2-(2-diphenylphosphinophenyl)-5,6,7,8-tetrahydroquinoline-η^4-(1,5-cyclooctadiene) iridium(I) tetrakis-[3,5-bis(trifluoromethyl)phenyl] borate (+)-(**38**).* Obtained from **4** (100.6 mg, 63%): mp 74 °C (hexane/CH_2Cl_2 1:1); $[\alpha]_D^{25}$ +14.7 (c 1.0 $CHCl_3$); IR (KBr) ν 2927 (s, C–H), 1436 (m, arom C=C), 1354 (arom C=C), 1277 (m, arom C=C), 748 (m, arom C–H); ^1H NMR (400 MHz, $CDCl_3$) δ 0.60 (d, J=10 Hz, 1H, 10-H), 0.63 (d, J=10 Hz, 1H, 10-H), 0.73 (s, 3H, 9-H), 0.95–1.02 (m, 1H, CH_2(COD)), 1.20–1.22 (m, 1H, CH_2(COD)), 1.25 (s, 3H, 9′-H), 1.31–1.34 (m, 1H, CH_2(COD)), 1.59–1.71 (m, 1H, CH_2(COD)), 1.98–2.13 (m, 2H, CH_2(COD)), 2.35–2.47 (m, 1H, CH_2(COD)), 2.53–2.57 (m, 3H, CH_2(COD), 8-H, 10-H), 2.62 (dd, J=18.0, 2.5 Hz, 1H, 5-H), 2.81 (dd, J=18.0, 2.5 Hz, 1H, 5-H′), 3.58–3.70 (m, 1H, CH(COD)), 3.72–3.85 (m, 1H, CH(COD)), 4.45–4.48 (m, 1H, CH(COD)), 4.84–4.91 (m, 1H, CH(COD)), 7.14–7.17 (m, 7H, aromH), 7.22–7.27 (m, 3H, aromH), 7.32–7.54 (m, 9H aromH), 7.61–7.73 (m, 9H, aromH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7 (CH_3-9), 25.5 (CH_3-9′), 28.5 (CH_2-10), 30.8 (CH_2(COD)), 33.1 (CH_2-5), 39.4 (d, J=10 Hz, C-7), 43.3 (CH-6), 45.6 (CH-8), 117.4 (C-3), 124.7 (q, J=540 Hz, CF_3), 127.3 (CH-4′), 127.6 (CH-6′), 128.7 (CH(COD)), 128.9 (C-12), 129.1 (CH-5′), 129.3 (CH-arom), 129.5 (CH-arom), 131.3 (*C*-arom), 131.8(*C*-arom), 137.9 (CH-4), 144.9 (C-1′), 161.4 (C-2), 166.9 (C-11); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 20.0. Anal. Calcd for $C_{70}H_{52}BF_{24}IrNP$: C, 52.64; H, 3.28; N, 0.88. Found: C, 52.31; H, 3.24; N, 0.86.

*4.4.5. (5S,8R)-(+)-5,7-Methano-8,9,9-trimethyl-2-(2-diphenylphosphinophenyl)-5,6,7,8-tetrahydroquinoline-η^4-(1,5-cyclooctadiene) iridium(I) tetrakis-[3,5-bis(trifluoromethyl)phenyl] borate (+)-(**39**).* Obtained from **5** (82.2 mg, 51%): mp 72 °C (hexane/CH_2Cl_2 1:1); $[\alpha]_D^{25}$ +4.2 (c 0.75 $CHCl_3$); IR (KBr) ν 2920 (s, C–H), 1420 (m, arom C=C), 1354 (arom C=C), 1277 (m, arom C=C), 744 (m, arom C–H); ^1H NMR (400 MHz, $CDCl_3$) δ 0.53 (s, 3H, 10-H), 0.59 (s, 3H, 10-H), 1.00–1.08 (m, 1H, CH_2(COD)), 1.15 (s, 3H, 11-H), 1.33–1.45 (m, 1H, CH_2(COD)), 1.59–1.65 (m, 2H, CH_2(COD), 7-H), 1.68–174 (m, 1H, 6-H), 1.89–1.93 (m, 2H, CH(COD), 7-H′), 1.95–1.98 (m, 1H, 6-H′), 2.00–2.04 (m, 1H, CH_2(COD)), 2.08–2.11 (m, 1H, CH_2(COD)), 2.50–2.59 (m, 1H, CH_2(COD)), 2.77 (t, J=6.1 Hz, 1H, 5-H), 3.30–3.39 (m, 2H, CH_2(COD)), 4.09–4.15 (m, 1H, CH(COD)), 4.24–4.30 (m, 1H, CH(COD)), 5.61–5.69 (m, 1H, CH(COD)), 7.15–7.25 (m, 6H, aromH), 7.52–7.67 (m, 4H, aromH), 7.68–7.75 (m, 9H, aromH), 7.77–7.86 (m, 9H, aromH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2 (CH_3-11), 18.5 (CH_3-10), 19.2 (CH_2-10), 25.1 (CH_2-7), 25.5 (CH_2-6), 28.1 (CH_2(COD)), 50.7 (CH_2-5), 57.1 (C-9), 59.1 (C-8), 117.4 (C-3), 123.2 (CH-4′), 124.7 (q, J=540 Hz, CF_3), 125.2 (CH-6′), 125.9 (CH-5′), 128.4 (CH(COD)), 129.1 (C-13), 129.5 (CH-arom), 129.3 (CH-arom), 131.3 (*C*-arom), 131.8 (*C*-arom), 134.1 (C-3′), 136.2 (C-2′), 137.4 (*C*-arom), 137.6 (CH-4), 144.0 (C-1′), 161.9 (C-2), 172.8 (C-12); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 12.1. Anal. Calcd for $C_{71}H_{54}BF_{24}IrNP$: C, 52.93; H, 3.38; N, 0.87. Found: C, 52.62; H, 3.33; N, 0.88.

*4.4.6. (1S,4S)-(−)-1,4-Methano-11,11-dimethyl-4-(diphenylphosphanylmethyl)-1,2,3,4-tetrahydroacridine-η^4-(1,5-cyclooctadiene) iridium(I) tetrakis-[3,5-bis(trifluoromethyl)phenyl]borate (−)-(**40**).* Obtained from **6** (113.4 mg, 75%): mp 87 °C (hexane/CH_2Cl_2 1:1); $[\alpha]_D^{25}$ −37.1 (c 0.35 $CHCl_3$); IR (KBr) ν 2965 (s, C–H), 2926 (s, C–H), 2891 (s, C–H), 1457 (m, arom C=C), 1354 (arom C=C), 1277 (m, arom C=C), 744 (m, arom C–H); ^1H NMR (400 MHz, $CDCl_3$) δ 0.15 (s, 6H, 12-H, 12H′), 0.80–0.85 (m, 1H, CH_2(COD)), 0.93–1.00 (m, 2H, CH_2(COD)), 1.15 (s, 2H, 13-H), 1.30–1.40 (m, 1H, CH_2(COD)), 1.55–1.64 (m, 2H, CH_2(COD), 3-H), 1.67–1.71 (m, 2H, 2-H), 1.88–1.91 (m, 1H, 3-H′), 1.93–1.98 (m, 1H, CH_2(COD)), 2.01–2.03 (m, 1H, CH_2(COD)), 2.73 (t, J=5.9 Hz, 1H, 1-H), 3.29–3.37 (m, 2H, CH_2(COD)), 4.10–4.15 (m, 1H, CH(COD)), 4.20–4.27 (m, 1H, CH(COD)), 4.51–4.60 (m, 1H, CH(COD)), 7.18–7.32 (m, 10H, aromH), 7.35–7.57 (m, 4H, aromH), 7.70–7.83 (m, 10H, aromH), 7.91–8.04 (m, 3H, 8-H, 9-H, 5-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.25 (CH_3-12), 19.27 (CH_3-12′), 27.0 (CH_2-2), 28.0 (CH_2(COD)), 30.1 (CH_2-3), 35.0 (CH_2-13), 50.1 (C-1), 51.2 (C-11), 58.6 (C-4), 124.5 (q, J=540 Hz, CF_3), 126.0 (CH-7), 127.2 (C-10, C-8′), 127.9 (C-5, C-8), 128.5 (C-6), 128.7 (CH(COD)), 128.9 (CH-arom), 129.3 (CH-arom), 131.3 (*C*-arom), 131.8 (*C*-arom), 132.7 (CH-arom), 135.4 (CH-9), 139.2 (*C*-arom), 146.2 (C-5′), 192 (C-10′); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 28.1. Anal. Calcd for $C_{69}H_{52}BF_{24}IrNP$: C, 52.28; H, 3.31; N, 0.88. Found: C, 52.56; H, 3.34; N, 0.85.

*4.4.7. (1R,3R,4S)-(−)-5-Fluoro-1,3-methano-2,2,4-trimethyl-5-(diphenylphosphino)-1,2,3,4-tetrahydroacridine-η^4-(1,5-cyclooctadiene) iridium(I) tetrakis-[3,5-bis(trifluoromethyl)phenyl]borate (−)-(**41**).* Obtained from **9** (108.9 mg, 72%): mp 86–88 °C (hexane/CH_2Cl_2 1:1); $[\alpha]_{D^{25}}$ −35.5 (c 0.35 $CHCl_3$); IR (KBr) ν 2974 (s, C–H), 2932 (s, C–H), 2889 (s, C–H), 1456 (m, arom C=C), 1348 (arom C=C), 741 (m, arom C-H); ^1H NMR (400 MHz, $CDCl_3$) δ 0.71 (s, 3H, 15-H), 0.80–0.83 (m, 1H, CH_2(COD)), 0.93–1.00 (m, 2H, CH_2(COD)), 1.24–1.29 (m, 1H, CH_2(COD)), 1.33 (d, 1H, J=9.8 Hz, 10-H), 1.43 (s, 3H, 16-H), 1.49 (d, J=6.7 Hz, 3H, 17-H), 1.54–1.63 (m, 1H, CH_2(COD)), 1.93–1.97 (m, 1H, CH_2(COD)), 2.01–2.03 (m, 1H,CH_2(COD)), 2.28 (dt, J=6.0, 2.3 Hz, 1H, 3-H), 2.57–2.65 (m, 1H, 10-H′), 2.93 (t, J=5.6 Hz, 1H, 1-H), 3.29–3.32 (m, 2H, CH_2(COD)), 3.42 (dq, J=6.9, 1.5 Hz, 1H, 4-H), 4.05–4.12 (m, 1H, CH(COD)), 4.20–4.25 (m, 1H, CH(COD)), 4.54–4.61 (m, 1H, CH(COD)), 7.20–7.38 (m, 2H, 6-H, 7-H), 7.40–7.47 (m, 10H, aromH), 7.51 (d, J=8.1 Hz, 1H, 8-H), 7.55–7.65 (m, 4H, aromH), 7.67 (s, 1H, 9-H), 7.72–7.85 (m, 8H, aromH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9 (CH_3-17), 22.4 (CH_3-10), 22.5 (CH_3-16), 24.4 (CH_2-10), 28.1 (CH_2(COD)), 34.8 (CH-4), 42.7 (C-2), 51.3 (CH-1), 55.6 (CH-3), 124.5 (q, J=540 Hz, CF_3), 125.6 (CH-7), 126.4 (C-14), 128.3 (CH(COD)), 128.9 (CH-arom), 129.3 (CH-arom), 131.3 (*C*-arom), 131.8 (*C*-arom), 132.1 (C-11), 133.1 (CH-6), 133.4 (CH-arom), 133.9 (CH-9), 136.5 (C-5), 137.1 (*C*-arom), 151.7 (C-13), 162.0 (C-12); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 24.0. Anal. Calcd for $C_{69}H_{52}BF_{24}IrNP$: C, 52.28; H, 3.31; N, 0.88. Found: C, 51.583; H, 3.36; N, 0.91.

*4.4.8. (7S,8R,10S)-(+)-2-Phenyl-11,11-dimethyl-1-azatricyclo[7.1.1.$0^{5,6}$]undeca-2,4,6-trien-7-yl diphenylphosphinite-η^4-(1,5-cyclooctadiene) iridium(I) tetrakis-[3,5-bis(trifluoromethyl)phenyl] borate (+)-(**42**).* Obtained from **10** (66.2 mg, 41%): mp 69–71 °C (Et_2O/CH_2Cl_2 1:1); $[\alpha]_D^{25}$ +32.3 (c 0.25, $CHCl_3$); IR (KBr) ν 3020 (s, C–H), 1638 (br m, arom C=C), 1279 (m), 1215 (s, P–O), 770 (s, arom C–H) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.68 (s, 3H, 12-H), 1.46 (m, 4H, 9-H, 13-H), 1.50–1.52 (m, 2H, CH_2(COD)), 1.66–1.76 (m, 1H, CH_2(COD)), 1.80–1.90 (m, 2H, CH_2(COD)), 1.91–2.12 (m, 3H, CH_2(COD)), 2.72–2.80 (m, 1H, CH(COD)), 2.82–2.94 (m, 3H, 8-H, 9-H′, 10-H), 3.00–3.60 (m, 1H, CH(COD)), 4.27–4.35 (m, 2H, CH(COD)), 6.30 (dd, J=8.6, 3.7 Hz, 1H, 7-H), 7.16–7.20 (m, 2H, aromH), 7.31–7.39 (m, 5H, aromH), 7.40–7.42 (m, 7H, aromH), 7.43–7.50 (m,

5H, aromH), 7.56–7.70 (m, 10H, aromH); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 99.2 (s); MS (FAB) m/z (%) 750 ($M^{\bullet+}$, 100), 642 ($M^{\bullet+}$–COD, 28), 462 (48); HRMS (FAB) 750.2498 ($C_{38}H_{40}NOPIr$ requires 750.2479). Anal. Calcd for $C_{70}H_{52}BF_{24}NOPIr$: C, 52.12; H, 3.25; N, 0.87. Found: C, 52.21; H, 3.32; N, 0.81.

4.5. General procedure for the hydrogenation of alkenes 44–47 and imine 48

A solution of the alkene **44**–**47** (0.2 mmol, 1 equiv), or imine **48** (45 g, 0.2 mmol, 1 equiv) and the respective iridium catalyst (4.0 μmol, 2 mol %) in CH_2Cl_2 (2 mL) was sealed in an autoclave and the hydrogenation was performed at room temperature under hydrogen gas; for the pressure, temperature, and duration, see Table 1. The hydrogen was then released, the autoclave was purged with nitrogen, and the reaction mixture was directly passed through a short silica gel plug and flashed with a mixture of petroleum ether and ethyl acetate (4:1). The filtrate was evaporated and the residue was analyzed by ^{1}H NMR to obtain the conversion of the reaction; chiral HPLC was used to determine the enantiomeric excess.

4.5.1. 1,2-Diphenylpropane. Obtained from **44** on hydrogenation (Table 1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (d, J=6.8 Hz, 3H, CH_3CH), 2.71 (dd, J=12.9, 8.0 Hz, 1H, 2-H), 2.86–3.00 (m, 2H, 1-H, 2-H′), 7.02 (d, J=7.0 Hz, 2H, aromH), 7.10–7.25 (m, 8H, aromH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (CH_3), 41.8 (CH-1), 45.0 (CH_2-2), 125.8 (CH-4′), 126.0 (CH-4″), 127.0 (2× aromCH), 128.0 (2× aromCH), 128.3 (2× aromCH), 129.1 (2× aromCH), 140.8 (C-1′), 146.9 (C-1″) in agreement with the literature data;[41] chiral HPLC (Chiracel OJ-H, 0.5 mL min^{-1}, hexane/2-propanol, 99:1), t_R=13.2 min, t_S=19.3 min.

4.5.2. Ethyl 3-phenylbutanoate. Obtained from **45** on hydrogenation (Table 1): $[\alpha]_D^{26}$ +6.4 (*c* 1.4, $CHCl_3$, 83% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, J=7.1 Hz, 3H, CH_3CH$_2$), 1.23 (d, J=7.2 Hz, 3H, 4-H), 2.46 (dd, J=15.0, 7.2 Hz, 1H, 2-H), 2.54 (dd, J=15.0, 7.2 Hz, 1H, 2-H′), 3.20 (q, J=7.2 Hz, 1H, 3-H), 4.00 (q, J=7.2 Hz, 2H, CH$_3$CH_2), 7.13 (t, J=7.1 Hz, 1H, 4′-H), 7.15 (d, J=6.9 Hz, 2H, 2′-H, 6′-H), 7.22 (t, J=7.1 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1 (CH_3CH$_2$), 21.8 (CH_3-4), 36.5 (CH-3), 43.0 (CH_2CH$_3$), 60.2 (CH_2-2), 126.3 (CH-4′), 126.7 (2× CH-2′,6′), 128.4 (2× CH-3′,5′), 145.7 (C-1′), 172.4 (C=O-1) in agreement with the literature data;[47] chiral HPLC (Chiralpak IB, 0.75 mL min^{-1}, hexane/2-propanol, 99:1), t_R=6.8 min, t_S=9.8 min.

4.5.3. 2-Methyl-3-phenylpropan-1-ol. Obtained from **46** on hydrogenation (Table 1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, J=6.8 Hz, 3H, 4-H), 1.31 (br s, 1H, O*H*), 1.92–1.82 (m, 1H, 2-H), 2.35 (dd, J=8.0, 13.4 Hz, 1H, 3-H), 2.68 (dd, J=6.3, 13.4 Hz, 1H, 3-H′), 3.40 (dd, J=5.9, 10.6 Hz, 1H, 1-H), 3.46 (dd, J=5.9, 10.6 Hz, 1H, 1-H′), 7.12 (t, J=7.1 Hz, 1H, 4′-H), 7.14 (d, J=6.9 Hz, 2H, 2′-H, 6′-H), 7.23 (t, J=7.1 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9 (CH_3-4), 38.2 (CH-2), 40.1 (CH_2-3), 68.1 (CH_2-1), 126.3 (CH-4′), 128.7 (2× CH-2′,6′), 129.5 (2× CH-3′,5′), 141.0 (C-1′) in agreement with the literature data;[48] chiral HPLC (Chiracel OD, 1.0 mL min^{-1}, hexane/2-propanol, 95:5) t_1=8.5 min, t_2=10.0 min.

4.5.4. 2-Methyl-3-phenylpropyl ethanoate. Obtained from **47** on hydrogenation (Table 1): ^{1}H NMR (400 MHz, $CDCl_3$) δ ($CDCl_3$ 500 MHz): δ=0.94 (d, J=6.7 Hz, 3H, 4-H), 2.07 (s, 3H, $COCH_3$), 2.13 (m, 1H, 2-H), 2.47 (dd, J=7.8, 13.4 Hz, 1H, 3-H), 2.75 (dd, J=6.4, 13.4 Hz, 1H, 3-H′), 3.93 (dd, J=6.4, 10.8 Hz, 1H, 1-H), 3.98 (dd, J=6.2, 10.8 Hz, 1H, 1-H′), 7.09 (t, J=7.0 Hz, 1H, 4′-H), 7.11 (d, J=6.9 Hz, 2H, 2′-H, 6′-H), 7.20 (t, J=7.0, 2H, 3′-H, 5′-H); ^{13}C NMR ($CDCl_3$) δ 14.4 (CH_3-4), 16.8 (CH_3–CO), 34.6 (CH-2), 40.1 (CH_2-3), 68.7 (CH_2-1), 126.1 (CH-4′), 128.4 (2× CH-2′,6′),129.2 (2× CH-3′,5′),141.6 (C-1′), 171.1 (C=O), in agreement with the literature data;[49] chiral HPLC (Chiracel OD, 1.0 mL min^{-1}, hexane/2-propanol, 95:5) t_1=9.5 min, t_2=11.9 min.

4.5.5. 4-Methoxy-N-(1′-phenylethyl)aniline. Obtained from **48** on hydrogenation (Table 1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (d, J=6.7 Hz, 3H, CH_3), 3.61 (s, 3H, OCH_3), 4.34 (q, J=6.7 Hz, 1H, 1-H), 6.40 (d, J=8.9 Hz, 2H, 2′-H, 6′-H), 6.61 (d, J=8.9 Hz, 2H, 3′-H, 5′-H), 7.13 (tt, J=7.3, 1.5 Hz, 1H, 4″-H), 7.23 (td, J=7.3, 2.0 Hz, 2H, 3″-H, 5″-H), 7.29 (dd, J=7.3, 1.5 Hz, 2H, 2″-H, 6″-H) in agreement with the literature data;[43] chiral HPLC (Chiralpak IB, 0.75 mL min^{-1}, hexane/2-propanol, 99:1) t_R=13.2 min, t_S=19.3 min.

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