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Phosphoramidite Ligands in Iridium-Catalyzed Allylic Substitution

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Abstract: A new phosphoramidite ligand was used in the iridium-catalyzed allylic substitution reaction. This permitted high regio- and enantioselectivities on a wide variety of substrates and nucleophiles. Because of the stereospecificity of the reaction obtained by using branched substrates, a kinetic resolution reaction was attempted. The origin of the impressive efficiency of this ligand in terms of kinetics was explored in detail, as was the role of the substituent in the *ortho*-position of the amine moiety.

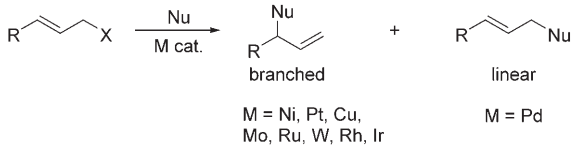
Keywords: allylic substitution · asymmetric catalysis · chiral ligands · iridium · phosphoramidite

Introduction

Among the methodologies that synthetic chemists employ to create chiral centers, allylic substitution is of considerable importance. The products of this reaction are particularly interesting because they contain a double bond, which is one of the most versatile functional groups in organic synthesis.

Although the most-studied catalytic system is that with palladium as the metal source, its applicability is limited mostly to symmetrical substrates in which the enantioselectivity is a result of regioselectivity.[1]

Regarding the nonsymmetrical prochiral substrates (Scheme 1), the situation is more complex and challenging, as one has to control both regio- and enantioselectivity. For this purpose, metals, such as nickel,[2] platinum,[3] copper,[4] molybdenum,[5] ruthenium,[6] tungsten,[7] rhodium,[8] and iridium,[9,10] have emerged as efficient systems. Although the regiochemistry of palladium normally favours the linear product, there is an increasing number of examples favouring the branched regioisomer.[11]



Scheme 1.

Following the pioneering work of Takeuchi et al.[9,10a–c] and Helmchen et al.,[10d–g] Hartwig and co-workers achieved high enantioselectivities by using **L1** as ligand in iridium-catalyzed allylic amination[10m] and etherification[10n] (Scheme 2). They later identified the active species **C1** in their reaction;[12] it came from an insertion into the C–H bond in the methyl group on the amine part of the ligand (Scheme 3). Helmchen et al. had previously observed such an insertion into an aromatic C–H bond of triphenylphosphite as ligand.[10f]

Here, we describe improved conditions and ligands for allylic alkylation, which result not only in higher regio- and enantioselectivities, but also in improved kinetics.

Results and Discussion

Allylic alkylation reaction: The results obtained by Helmchen et al. using **L1** were good, but limited in scope.[10g] Moreover, this catalyst system needed to be improved regarding its long reaction time (from 18 hours to 4 days), its only moderate to good regioselectivities (branched/linear (b/

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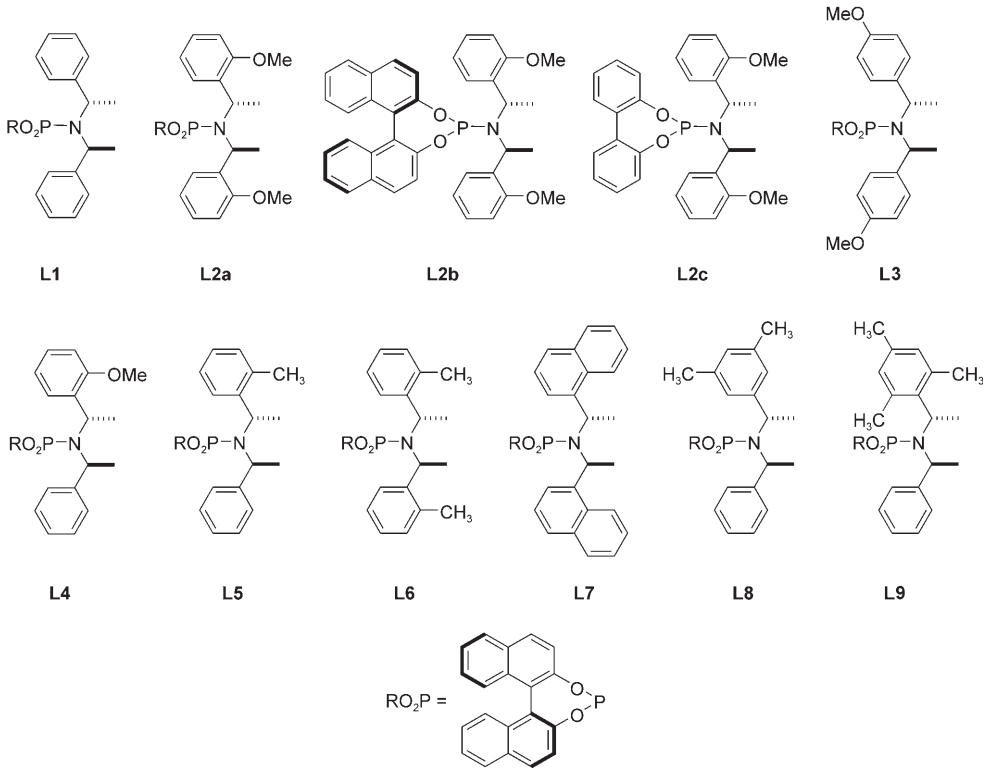
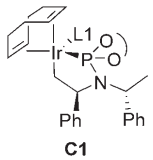


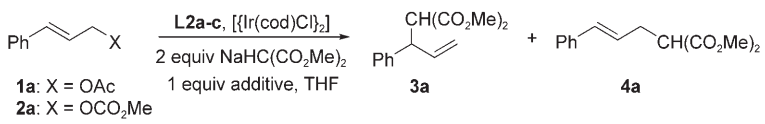
Scheme 2. Ligands used in this study.



Scheme 3.

l) ratios 30:70 to 91:9), and its imperfect enantioselectivities (86% for the classical substrate cinnamyl acetate).

Hartwig et al.[10o,p] and Helmchen et al.[13] recently achieved improvement by using additives, such as 1,4-diazabicyclo[2.2.2]octane (DABCO) or 1,5,7-triazabicyclo-[4.4.0]dec-5-ene (TBD), respectively, to control the formation of the catalytic species **C1**. In contrast, we examined the potential of structural modifications of **L1** to improve the scope and kinetics of the reaction, as there was a need for a general and simple catalytic methodology in asymmetric allylic alkylation. To accelerate the reaction, we developed a new family of phosphoramidite ligands **L2a–c**, bearing two *ortho*-methoxy substituents on the amine moiety, which provided excellent regio- and enantioselectivities in Cu-catalyzed allylic substitution[14] (Scheme 4).



Scheme 4.

Under the original conditions developed by Helmchen and co-workers (4% Ir catalyst and 4% ligand) for the cinnamyl derivative **1a**,[10g] ligand **L1** did not seem to be optimal (regioselectivity of 70:30 and enantioselectivity of 70%, Table 1, entry 1), although the introduction of LiCl as an additive improved the result remarkably (**3a**/**4a** ratio of 91:9 and 86% optical purity, Table 1, entry 2).

Knowing that the carbonate derivative **2a** was much more active than **1a** in the amination version of the same reaction,[10m] we[15] initially tested **2a** under the classical conditions without any additive. The reaction was sluggish, even at 60°C, and led to only low regio- and enantioselectivities (Table 1, entry 3). The addition of lithium chloride led to an impressive acceleration of the reaction, together with an improvement of the regio- (99:1) and enantioselectivities (98%) (Table 1, entry 4). The role of LiCl is discussed below. This result again demonstrates the superiority of the new ligand **L2a** relative to **L1**, both in terms of regio- and enantioselectivities. We even tested a much lower catalyst loading (0.5 mol% of Ir catalyst), which did not seem to be deleterious, as after 4 h at 40°C, 83% conversion was obtained together with an *ee* of 96% and a regioselectivity of 99:1 (Table 1, entry 5). Such a small amount of catalyst (0.5%) is impressive for C–C bond formation methodologies. This represents a turnover number (TON) of 200 and a turnover frequency (TOF) of 50 at 40°C.

Table 1. Enantioselective Ir-catalyzed allylic alkylation of carbonates.[a]

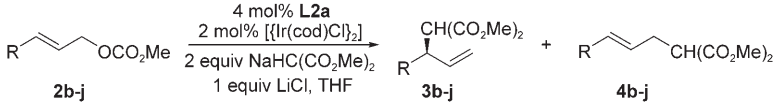
Entry	Substrate	Ligand	Additive	T [°C]	Time [h]	Yield[b] [%]	**3**/**4**[c]	*ee*[d] [%]
1[e]	**1a**	**L1**	–	25	18	41	70:30	70 (*R*)
2[e]	**1a**	**L1**	LiCl	25	18	98	91:9	86 (*R*)
3	**2a**	**L2a**	–	60	22	31	65:35	44 (*R*)
4[f]	**2a**	**L2a**	LiCl	25	2	82	99:1	98 (*R*)
5[g]	**2a**	**L2a**	LiCl	40	4	(83)	99:1	96 (*R*)
6	**2a**	**L2b**	LiCl	25	14	28	97:3	89 (*S*)
7	**2a**	**L2c**	LiCl	25	14	81	99:1	93 (*R*)

[a] Molar ratio: substrate/LiCl/$NaHC(CO_2Me)_2$/[{Ir(cod)Cl}$_2$]/**L** = 1:1:2:0.02:0.044; scale: 0.5 mmol substrate. [b] Isolated yield; in parenthesis: conversion determined by GC–MS. [c] Determined by 400 MHz ^{1}H NMR spectroscopy or GC–MS. [d] Determined by chiral SFC (HPLC for entries 1 and 2); in parentheses: absolute configuration attributed by comparison with published data (ref. [7]). [e] Taken from ref. [10g]. [f] Performed on a 1-mmol scale. [g] Performed on a 4-mmol scale with a molar ratio: substrate/LiCl/$NaHC(CO_2Me)_2$/[{Ir(cod)Cl}$_2$]/**L** = 1:1:2:0.0025:0.0055.

Comparison of the diastereomeric ligands **L2a** (*aS*,*SS*) and **L2b** (*aR*,*SS*) clearly shows a matched/mismatched situation, with **L2b** being mismatched (entry 6, 89% *ee*). It should be stressed that the inversion of the binaphthol part of the ligand translates into an inversion of stereochemistry on the resulting allylic adduct, indicating that the binaphthyl chiral element is dominant. Interestingly, the simpler ligand **L2c** affords a relatively high *ee* (Table 1, entry 7, 93%). The absolute stereochemistry of the adduct corresponds to that obtained with the matched ligand **L2a**. Thus, the biphenyl part of the axially labile ligand **L2c** seems to adopt the same configuration as the (*S*)-binaphthyl of **L2a**. This adaptive behavior is similar to that observed in Cu-catalyzed reactions, in which the induced atropoisomerism of the biphenyl has the same configuration as the matched diastereomeric pair in the binaphthyl-type ligand.[16]

We next focused our efforts on expanding the scope of the reaction. We tested different allylic substrates (Scheme 5), starting with the 2-naphthyl derivative **2b** that regioselectively (99:1) gave the branched isomer in 96% *ee* (Table 2, entry 1). We then modulated the electron demand of the aromatic ring. With the −OMe group in the *para*- or *meta*-positions, substrates **2c** and **2d** behaved similarly and gave excellent regioselectivities and enantiomeric excesses (Table 2, entries 2 and 3). However, for steric or coordination reasons, if the same substituent as that in **2e** was in the *ortho*-position, it was deleterious for the stereoselectivity (Table 2, entry 4). An excess of only 79% was obtained for this substrate. This was observed previously by Hartwig et al. in the amination reaction.[10m] With *para*- and *meta*-donor substituents, the dioxolane derivative **2f** led to excellent results (Table 2, entry 5).

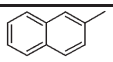
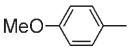
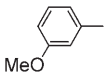
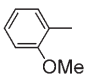
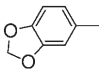
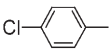
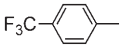
Of particular interest is the substrate bearing a *para*-chloro substituent **2g**. Its transformation into **3g** is known to give



2b-j 3b-j 4b-j

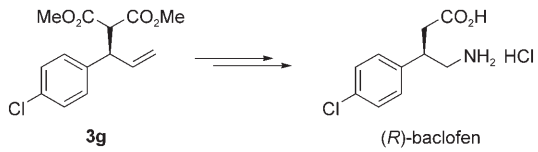
Scheme 5.

Table 2. Enantioselective Ir-catalyzed allylic alkylation of carbonates with **L2a**.[a]

Entry	Substrate	R	T [°C]	Time [h]	Yield[b] [%]	**3**/**4**[c]	*ee*[d] [%]
1	**2b**		25	20	73	99:1	96 (*R*)
2	**2c**		35	24	99	>99:1	97 (*R*)
3	**2d**		30	6	58	99:1	96 (*R*)
4	**2e**		30	6	98	>99:1	79 (*R*)
5	**2f**		30	44	70	99:1	97 (*R*)
6	**2g**		35	24	90	>99:1	97 (*R*)[e]
7	**2h**		30	65	40	94:6	94 (*R*)
8	**2i**	*n*-Pr–	30	30	92	80:20	96 (*R*)
9	**2j**		30	65	65	97:3	98 (*R*)

[a] Molar ratio: substrate/LiCl/$NaHC(CO_2Me)_2$/[{Ir(cod)Cl}$_2$]/**L2a** = 1:1:2:0.02:0.044; scale: 0.5 mmol substrate. [b] Isolated yield. [c] Determined by 400 MHz ^{1}H NMR spectroscopy or GC–MS. [d] Determined by chiral SFC; in parentheses: absolute configuration. [e] The absolute configuration was determined by comparison with published data (ref. [7]); all other configurations were attributed by analogy with **3a**.

straightforward access to the therapeutically useful $GABA_B$ receptor agonist (*R*)-baclofen hydrochloride (Scheme 6).[17] We obtained **3g** with an optical purity of 97% without any trace of the regioisomer **4g** (Table 2, entry 6).



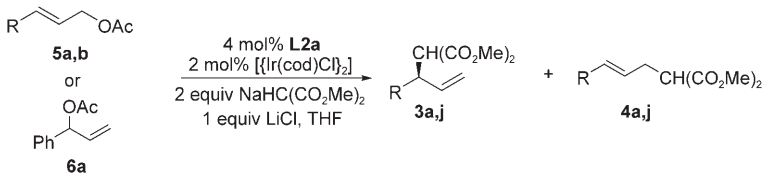
3g (*R*)-baclofen

Scheme 6.

An electron-withdrawing group on the aromatic core of the substrate was also tested (Table 2, entry 7). Although very good enantioselectivity was measured for **3h**, a significant amount of **4h** was detected (6%).

Alkyl groups as substituents were investigated. Primary (**2i**, Table 2, entry 8) and secondary (**2j**, Table 2, entry 9) alkyl derivatives gave high enantioselectivites (96 and 98%, respectively), but lower regioselectivities (80:20 and 97:3, respectively) than aromatic derivatives.

Allylic carbonates are usually the substrates of choice, and allylic acetates are used less often, owing to their lower reactivity and selectivity.[10m] However, despite requiring a longer reaction time, the latter (Scheme 7) gave similar results (Table 3, entry 1) under the conditions employed in this study. Thus, substrate **5b** needed to be heated slightly for the reaction to be completed. This affected the regioselectivity (Table 3, entries 2–5) rather than the enantioselectivity. Finally, we also tested a branched substrate **6a**. However, the enantioselectivity dropped dramatically, showing that the isomerization of the Ir π-complex is a very slow process, a result also reported by Helmchen et al.[10e] and Moberg et al.[17b]



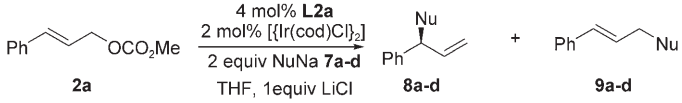
Scheme 7.

Table 3. Ir-catalyzed allylic alkylation of acetates with ligand **L2a**.[a]

Entry	Substrate	R	*T* [°C]	Time [h]	Yield[b] [%]	**3**/**4**[c]	*ee*[d] [%]
1[e]	**5a**		25	22	79	99:1	97 (*R*)
2	**5b**	*n*-Pr–	25	60	21	91:9	94 (*R*)
3	**5b**	*n*-Pr–	30	66	87	87:13	97 (*R*)
4	**5b**	*n*-Pr–	42	15	71	86:14	97 (*R*)
5	**5b**	*n*-Pr–	55	18	82	82:18	97 (*R*)
6	**6a**		25	3	81	>99:1	10 (*R*)

[a] Molar ratio: substrate/LiCl/$NaHC(CO_2Me)_2$/$[\{Ir(cod)Cl\}_2]$/**L2a** = 1:1:2:0.02:0.04; scale: 0.5 mmol substrate. [b] Isolated yield. [c] Determined by 400 MHz ^{1}H NMR spectroscopy or GC–MS. [d] Determined by chiral GC or SFC; in parentheses: absolute configuration. [e] Performed on a 1-mmol scale.

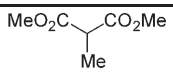
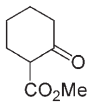
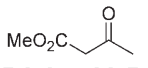
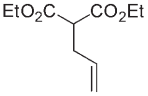
In addition to studying various electrophiles, we were interested in testing different stabilized alkyl nucleophiles under these conditions (Scheme 8). Among them, trisubstituted methyl malonate **7a** required slight heating to lead to full conversion (Table 4, entry 1). The resulting regio- and enantioselectivities were as high as those obtained with the simple malonate. Two nucleophiles containing a prostereogenic center, **7b** and **7c**, were also tested. Although high regio- and enantioselectivities were achieved, no stereocontrol on the nucleophile occurred, leading to the corresponding diastereoisomers in a 1:1 mixture (Table 4, entries 2 and 3). Of particular interest was nucleophile **7d**, bearing an allyl substituent (Table 4, entry 4). In addition to the good regioselectivity obtained, we transformed product **7d** into the cyclohexene derivative **10** by a ring-closing metathesis by using the first generation Grubb's catalyst[18] (Scheme 9). The optical purity of **10** was extremely high (98.7% *ee*).



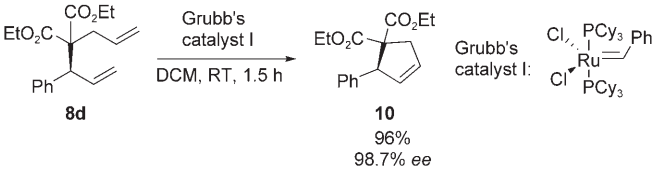
Scheme 8.

Attempts at kinetic resolution: In view of the intriguing result obtained by using **6a** as substrate (Table 3, entry 6), we

Table 4. Allylic alkylation with different stabilized nucleophiles.

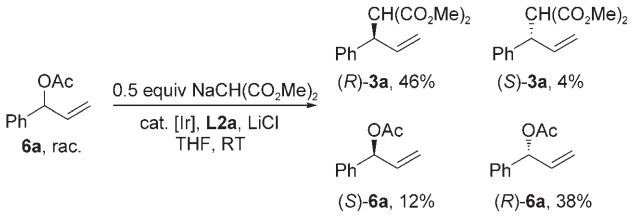
Entry	Nu	Structure	*T* [°C]	Time [h]	**8**/**9**[a]	Yield[b] [%] (d.r.)	*ee*[c] [%]
1	**7a**		40	15	>99:1	95 (–)	97
2	**7b**		25	3	94:6	79 (51:49)	95[d]
3	**7c**		25	5	>99:1	68 (53:47)	95[e]
4	**7d**		40	3	94:6[f]	85 (–)	n.d.

[a] Measured by GC–MS, unless otherwise stated. [b] Isolated yield; in parenthesis: diastereomeric ratio. [c] Measured by chiral SFC. [d] Measured on the minor diastereoisomer. [e] Measured on the major diastereoisomer. [f] Measured by ^{1}H NMR spectroscopy.



Scheme 9.

wondered if it would be possible to use this memory effect in a kinetic resolution reaction. Treatment of racemic starting material **6a** with half an equivalent of sodium dimethyl malonate gave **3a** with 84% *ee* (*R*) and the recovered starting material with 52% of the predominant *R* enantiomer (Scheme 10). The ratio **6a**/**2a** was 49:51.



Scheme 10.

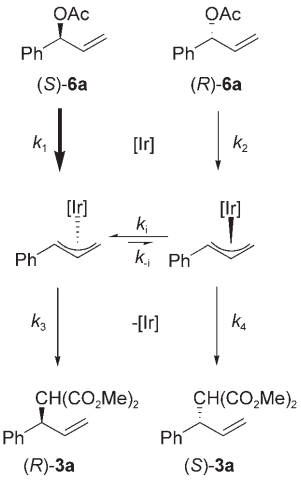
As already proved by Helmchen et al.,[10f] the reaction can be seen as a double inversion process, and, hence, as a formal retention event. Consequently, we can state that the branched allylic acetate (*S*)-**5a** is more reactive than its enantiomer. This corresponds to the same face-preference as ligand **L2a** in the allylic substitution on the nonchiral substrates cinnamyl acetate **5a** or carbonate **2a** (see above).

The enantioface preference (*s*) is expressed as a function of conversion (*C*) and the enantiomeric excess of the remaining starting material (*ee*) [Eq. (1)]:[19]

$$s = k_S/k_R = \ln[(1-C)(1-ee)]/\ln[(1-C)(1+ee)] = 4.9 \qquad (1)$$

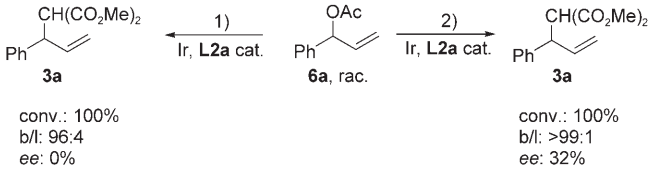
This means that the bottom face is preferred to the upper face by a factor of 4.9 for the oxidative addition. We assume that the oxidative addition is an irreversible process. In view of the *ee* of the product, we can then state that a racemization process occurs during the reaction, because the *ee* of the product does not reflect the optical purity of the remaining starting material. Two racemization pathways are possible:[20] enantioinversion by another complex, or the σ–π–σ process (Scheme 11). If the oxidative addition is irreversible and the nucleophilic attack is stereospecific, then a racemization process takes place. In the absence of racemization, the *ee* of the product should reflect that of the remaining starting material (52%), which is clearly not the case (84%).

The enantioface inversion equilibrium is a first-order process (k_i), whereas nucleophilic attack is a second-order process (k_3[Nu] and k_4[Nu]), dependent on the concentration of the nucleophile. The sum of the amounts of (*R*)-**3a** and the rest of (*S*)-**6a** is 58%. As the remainder is 42%, it can be stated that 8% racemization occurred, meaning that $k_i \neq 0$. Therefore, by decreasing the concentration of the nucleophile, we should theoretically be able to get an efficient dynamic kinetic resolution. This would be reached under real Curtin–Hammet conditions (see below).



Scheme 11.

From the results of this simple experiment, we have established that there are two stereoselection processes in our reaction: kinetic (important) and thermodynamic (less important). The kinetic process is the enantioface preference of our catalyst ($k_1 = 4.9k_2$). The thermodynamic one is the equilibrium of the intermediate, which favours the same face in terms of stability ($k_i > k_{-i}$). An efficient dynamic kinetic resolution (DKR) would be theoretically possible by lowering the concentration of the nucleophile, for example, by using a weaker base, such as the BSA/KOAc system (Scheme 12).

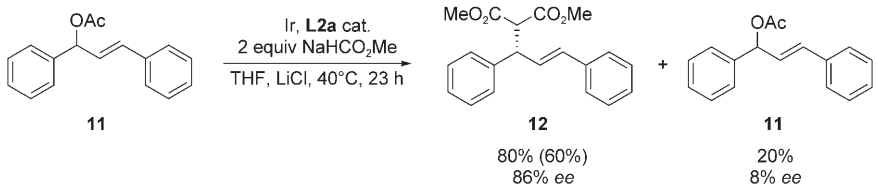


Scheme 12. Conditions: 1) RT, 16 h, 3 equiv $CH_2(CO_2Me)_2$, 3 equiv BSA, cat. KOAc; 2) substrate/catalyst ratio = 10:1, temperature 65 °C, reaction time 16 h, slow addition of 1.1 equiv $NaCH(CO_2Me)_2$ over 5 h.

Under these classical conditions for palladium catalysis, no enantiomeric excess was obtained (conditions 1). We tried (conditions 2) to increase the temperature to 65 °C and the amount of catalyst to 10 mol%, and treated the substrate with 1.1 equivalent of $NaCH(CO_2Me)_2$ introduced very slowly (addition time of 5 h) to give the system a chance to reach the Curtin–Hammett conditions. As a result, we obtained 32% *ee*, which is not spectacular, but confirmed our

hypothesis. This result was promising and may be improved in the future.

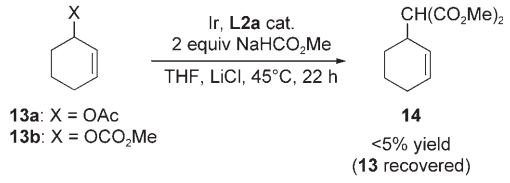
Symmetrical substrates: We tested the symmetrical substrate **11** under the conditions described previously (Scheme 13).



Scheme 13.

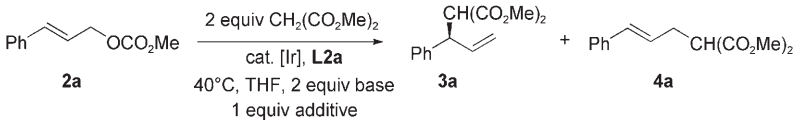
Interestingly, although this substrate was more inert than the other allylic acetates used, it led to 80% conversion and 86% *ee* after 23 h at 40°C. The recovered starting material gave an enantiomeric excess of only 8%. This experiment confirms the above result obtained with **6a**. The low *ee* of the remaining starting material shows that the face selectivity is not very high; instead, the high enantiodiscrimination occurs on the *meso*-π-allyl complex.

Allylic acetate **13a** (Scheme 14) is also a classical substrate in allylic substitution and has been extensively studied in the Pd-catalyzed system.[21] However, it led to no conversion under our conditions. Even the more reactive carbonate congener **13b** was inert under the same treatment. Because they feature a defined *Z* geometry of the double bond, these substrates do not behave like their isomers, as previously observed by Takeuchi.[9]



Scheme 14.

Role of LiCl and catalyst recycling: Although the advantage of adding LiCl in the allylic alkylation reaction is clear, we have not so far discussed a rationale for its role. An initial naive hypothesis is that LiCl does not change the nature of the true catalyst. Indeed, this additive is not required for other nucleophiles, such as amines (see below). Both systems (RNH_2 and $NaCH(CO_2Me)_2$/LiCl) give similar regio- and enantioselectivities. Therefore, we turned our attention to the nature of the alkyl nucleophiles. Two hypotheses could be formulated: 1) an Na–Li transmetallation results in a lithium malonate salt or 2) LiCl breaks the aggregates of the sodium salt of the malonate anion. To evaluate these suppositions, we employed several bases, such as lithium hydride, lithium carbonate, and lithium methylate to deprotonate the nucleophile (Scheme 15). The results are shown in Table 5. The use of lithium hydride did not result in any conversion (Table 5, entry 1), probably for reasons of solubility. Lithium carbonate seemed equally inefficient in deprotonating the nucleophile (Table 5, entry 2), and lithium methylate, which was more basic and soluble under our conditions, did not lead to conversion (Table 5, entry 3). We can, therefore, conclude that Na–Li metal exchange does not occur. The addition of LiCl to this latter base gave totally different results (Table 5, entry 4). After only 4 h at 45°C, the conversion was complete and the regio- and enantioselectivities were excellent (98:2 and 97%, respectively). Thus, LiCl seems to play a role already observed by Seebach[22] for Li or Na enolates: the "pure" aggregates of the latter exhibit a different reactivity than the "mixed" aggregates formed with LiX additives.



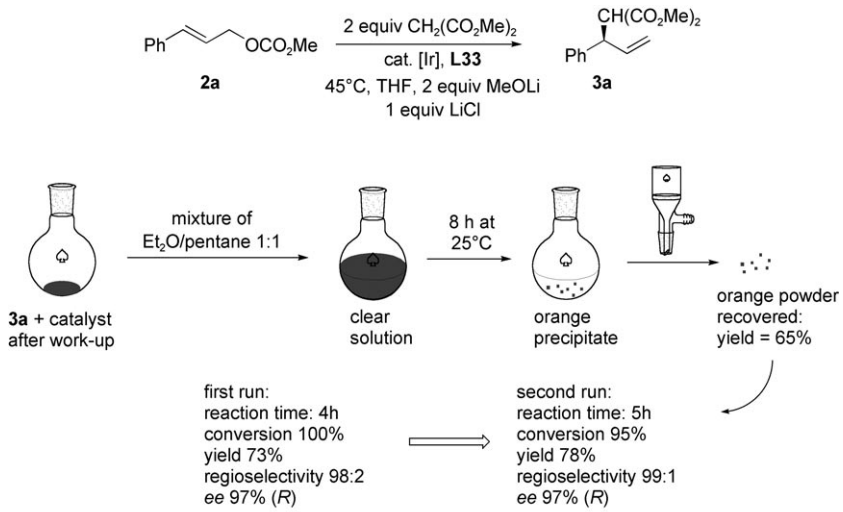
Scheme 15.

Table 5. Evaluation of several bases in the Ir-catalyzed allylic alkylation.[a]

Entry	Base	Additive	*T* [°C]	Time [h]	Conv.[b] [%]	**3**/**4**[c]	*ee*[d] [%]
1	LiH	–	40	22	0	n.d.	n.d.
2	Li_2CO_3	–	40	22	0	n.d.	n.d.
3	MeOLi	–	40	22	0	n.d.	n.d.
4	MeOLi	LiCl	45	4	100 (73)	98:2	97 (*R*)
5[e]	MeOLi	LiCl	45	5	95 (78)	99:1	97 (*R*)

[a] Molar ratio: **2a**/base/additive/$CH_2(CO_2Me)_2$/[{Ir(cod)Cl}$_2$]/**L2a** = 1:2:1:2:0.02:0.04; scale: 0.5 mmol substrate. [b] Conversion determined by GC–MS; in parenthesis: isolated yield. [c] Determined by GC–MS. [d] Determined by chiral SFC; in parentheses: absolute configuration. [e] Catalyst recovered from reaction of entry 4 and reused.

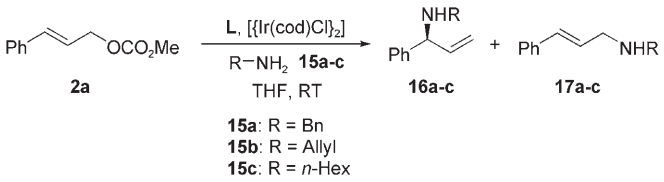
By employing these simpler conditions, we were also able to demonstrate that the iridium catalyst was recoverable without any drawbacks (Table 5, entry 5). The reaction run with the recycled catalyst required an additional hour to reach completion. No loss of regio- or enantioselectivity was



Scheme 16. Catalyst recycling technique.

observed. Scheme 16 shows the procedure used to recycle the catalyst (see Experimental Section). This method allowed us to recover 65% of the catalyst without the need to take any precautions regarding oxygen or water.

Allylic amination reaction: In addition to the previous nucleophiles, we tested primary amines under the conditions described previously by Hartwig et al.[10m] (Scheme 17). The results are presented in Table 6.



Scheme 17.

Table 6. Enantioselective Ir-catalyzed allylic amination.[a]

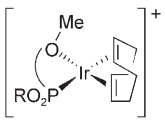
Entry	Amine	Ligand	Conv.[b] [%]	**16**/**17**[c,e]	*ee*[d–f] [%]
1	**15a**	**L2a**	98 (88)	98:2 [99:1]	97 (*S*) [95]
2	**15b**	**L2a**	>99 (91)	99:1 [n.d.]	97 (+) [97]
3	**15c**	**L2a**	>99 (89)	98:2 [98:2]	98 (*S*) [96]
4	**15a**	**L2b**	62	50:50	47 (*R*)
5	**15a**	**L2c**	92	99:1	92 (*S*)

[a] Molar ratio: **2a**/**15**/[{Ir(cod)Cl}$_2$]/**L** = 1:1.3:0.01:0.02; scale: 1 mmol substrate. [b] In parentheses: isolated yields after silica gel chromatography. [c] Determined by ^{1}H NMR analysis of the crude reaction mixtures. [d] Determined by chiral SFC analysis of the corresponding acetamide. [e] In square brackets, Hartwig's results with **L1** (ref. [10m]). [f] In parentheses, absolute configuration.

By using **L2a** as the chiral ligand (Table 6, entries 1–3), we were able to get high enantio- and regioselectivities in favour of the branched products **16**. Enantioselectivities remained constantly high (97–98%), irrespective of the amine **15** used, and these reflected the values obtained with alkyl nucleophiles. With ligand **L2a**, the results were as high or even slightly higher than those obtained by Hartwig et al. with **L1**.

Comparison with ligands **L2b** (Table 5, entry 4) and **L2c** (Table 5, entry 5) allows approximately the same observations to be made as for the alkylation reaction. Ligand **L2b** was the mismatched diastereomeric pair (47% *ee*) and led to the opposite enantiomer, whereas the flexible biphenyl derivative **L2c** gave relatively high *ee* (92%), in favour of the same enantiomer as for the matched ligand **L2a**.

Mechanistic considerations: Apparently, the iridium catalyst resulting from ligand **L2a** was not only more enantioselective, but also showed impressively higher kinetics than the one obtained by using **L1**.[14,15] To explain the higher efficiency of **L2a** over **L1**, we initially postulated a P–O hemilabile character, although this would lead to a seven-membered metallo-ring **C2** (Scheme 18) and the exclusion of the chloride anion from the first coordination sphere.



C2

Scheme 18.

Indeed, it was legitimate to consider **L2a** as a bidentate ligand, which would allow a stronger positive character to enhance the oxidative addition to the substrate.[23] Preliminary calculations (see Experimental Section) on the related ligand **L4** support such an assumption (Figure 1). Interestingly, the square-planar arrangement favoured by d^8 transition metals, such as Ir^I, is not distorted by a bidentate mode of coordination of the ligand **L4**. However, we have not been able to observe any coordination of the *ortho*-methoxy group by ^{1}H or ^{31}P NMR spectroscopy or to get any crystals suitable for X-ray crystallography.

Although these calculations were promising for our hypothesis, experimental proof was not obtained. To confirm or deny our initial hypothesis, we focused on generating specific structural changes in the amine part of this family of phosphoramidite ligands (Table 7).[24]

The secondary amines were prepared very easily by condensation of the corresponding enantiopure primary amine and ketone [25] (Scheme 19). Notably, amine **25** bearing a mesityl group could not be synthesized if starting from α-

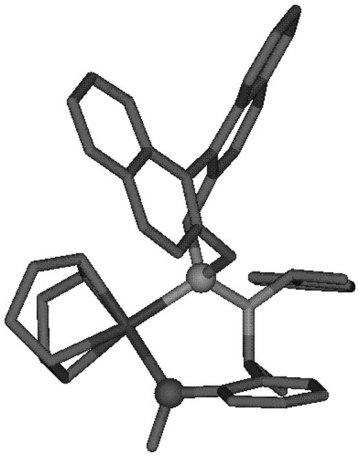


Figure 1. Density functional theory model of **L4**.

Table 7. Synthesis of different secondary amines and the corresponding (*S*)-BINOL-based ligands.

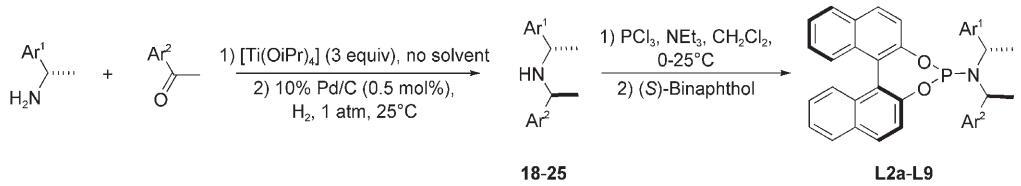
Entry	Ar^1	Ar^2	Amine[a] (d.r.)	Yield of amine[b] [%]	Ligand	Yield of **L** [%]
1	*o*-$MeOC_6H_4$	*o*-$MeOC_6H_4$	**18** (82:18)	59	**L2a**	94
2	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	**19** (89:11)	47	**L3**	32
3	Ph	*o*-$MeOC_6H_4$	**20** (82:18)	55[c]	**L4**	34[d]
4	Ph	*o*-$CH_3C_6H_4$	**21** (92:8)	64	**L5**	82
5	*o*-$CH_3C_6H_4$	*o*-$CH_3C_6H_4$	**22** (94:6)	64	**L6**	63
6	1-naphthyl	1-naphthyl	**23** (94:6)	34	**L7**	74
7	Ph	xylyl	**24** (88:12)	25[d]	**L8**	67
8	mesityl	Ph	**25** (98:2)	25[d]	**L9**	52

[a] In parenthesis, diastereomeric ratio measured by GC–MS. [b] Isolated yield after recrystallization of the corresponding hydrochloric salt, unless otherwise stated. [c] Purification by silica gel chromatography. [d] Yield not optimized.

Me-benzylamine and the corresponding ketone. Under the conditions used for all other amines, no formation of imine occurred, probably for steric reasons. However, the inverted strategy was successful, as seen in entry 8.

We evaluated these new ligands in the iridium-catalyzed allylic alkylation reaction by using sodium dimethyl malonate as the nucleophile. The kinetic data is presented in Figure 2. As shown by Hartwig et al.,[10n] in the amination process **L1** gave only low conversion during the first two hours of the reaction. Because it bears a methoxy substituent in the *para*-position, ligand **L3** was used to indicate a possible electronic effect of the OMe group. This did not seem to be the case, as the kinetics of **L3** were much slower than those of **L2a**, and gave a slope similar to that of **L1**.

Next, we investigated the influence of a sole *ortho*-methoxy substituent, as the calculations for this ligand (**L4**) have already been performed. The reaction showed a rate significantly higher than that for **L1** and **L3**, but lower than that for **L2a**. To confirm a possible coordination role of the methoxy substituent, we replaced it by a simple methyl group in the *ortho*-position, as in **L5**. This ligand afforded a kinetic slope similar to that of **L4**, which suggests that our first postulated model



Scheme 19.

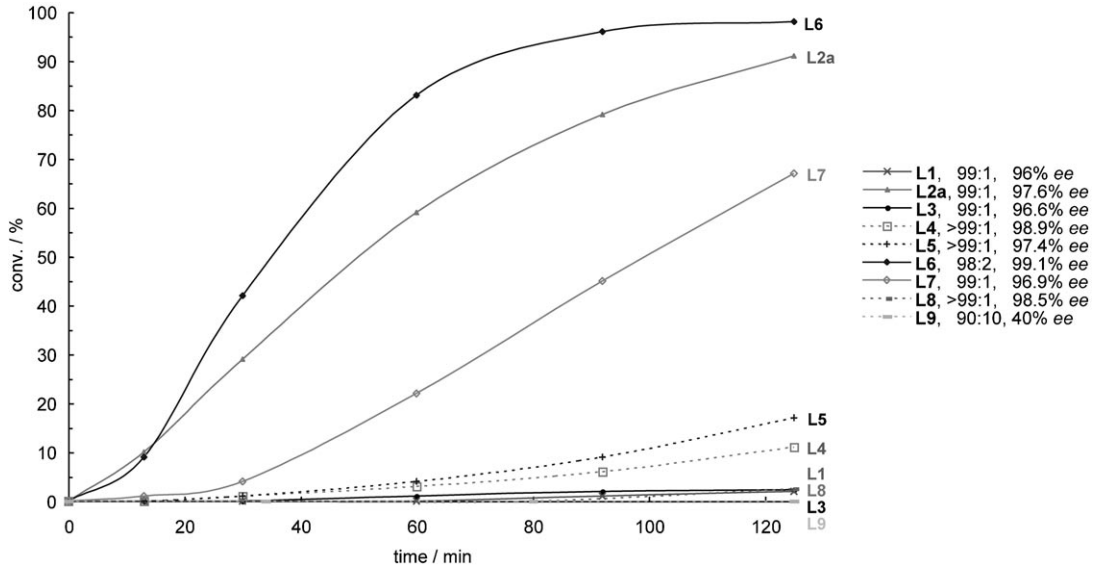


Figure 2. Kinetics of Ir-catalyzed allylic alkylation with sodium dimethyl malonate, using catalysts with the corresponding ligands **L**.

(Ir–OMe coordination) might be wrong. To confirm this, we synthesized the C_2-symmetrical ligand **L6**, bearing two *ortho*-methyl substituents. This ligand showed even more spectacular kinetics than **L2a**, enabling completion of the reaction in less than two hours at room temperature! For comparison, we studied the congener featuring the 1-naphthyl moiety **L7** used by Hartwig et al.[10o,p] This gave a slower reaction rate than that observed for **L2a** and **L6**.

Reaction using the ligand featuring a xylyl group, **L8**, showed a kinetic slope similar to that for **L1**. However, the mesityl group in **L9** seemed to be deleterious both in terms of kinetics and selectivity, giving the lowest *ee* (40%) and the poorest regioselectivity (90:10) of the series.

A similar study was conducted on the allylic amination (Figure 3).[24] Again, the slowest reaction was obtained with the ligand bearing a mesityl group, **L9**. Ligands that resulted in gradual slopes were those bearing either no substituent, **L1**, a xylyl group, **L8**, or a methoxy group in the *para*-position, **L3**, as in the alkylation reaction. The two pseudo-C_2-symmetrical ligands, **L4** and **L5**, gave more impressive kinetic slopes than that of **L1**; **L5** afforded a catalyst as efficient as that with **L2a**. Ligand **L6** showed impressive kinetic results, facilitating a faster reaction than that with **L2a**. Once again, **L7** was less efficient in terms of kinetics, although it surpassed **L2a**.

These two kinetic studies reveal that our initial postulation was wrong. Indeed, **L6**, bearing two methyl groups in the *ortho*-position of the amine part of the ligand, gave even more spectacular results than our, until now, best catalyst derived from **L2a**. That suggests that there is a more subtle explanation for the effect of the substituents in the *ortho*-position, as an electronic or even a coordination effect does not seem to explain the improvement of the kinetics.

We can, however, postulate from this study that the *ortho*-methoxy group plays a steric role, because ligand **L6**, bearing no oxygen, but rather a methyl group at the same position, gave even better results. Such steric effects are well known with phosphorus ligands (for example, Tol-BINAP versus BINAP; Tol = toluene, BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl),[26] in which the ligand cone angle θ plays a crucial role.[27]

Furthermore, the position at which steric hindrance occurs is of critical importance, as testified by the experiments with ligands **L8** and **L9**. Indeed, neither two Me groups in the *meta*-position (as in **L8**) nor two Me groups in the *ortho*-position of the same aromatic core could improve the kinetics of the reaction. An η^2 effect of the aryl group[28] neighboring the amine part cannot be excluded; further studies are currently in progress.

Concerning the enantio- or regioselectivities, all the ligands gave results within the same range (up to >99:1, 92–99% *ee*, respectively, Figure 4), except for **L9**, which we excluded from the figure (40% *ee* in alkylation and 0% *ee* in amination reaction). This suggests that only the kinetics of the reaction are dramatically affected by the steric bulk of the amine moiety of the ligand. Nevertheless, ligand **L6**

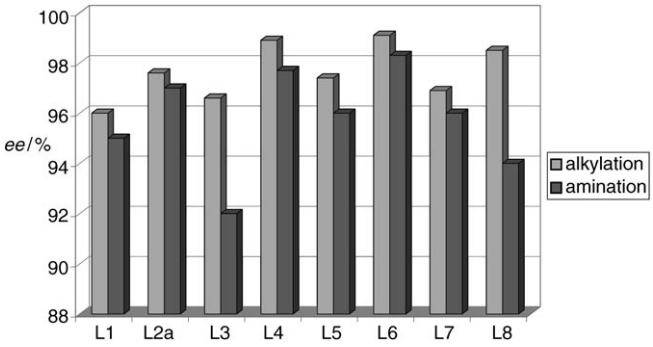


Figure 4. Recapitulative comparison of the *ee* values (%) resulting from the Ir-catalyzed allylic alkylation with sodium dimethyl malonate and the amination with benzylamine, with ligands **L1**–**L8**.

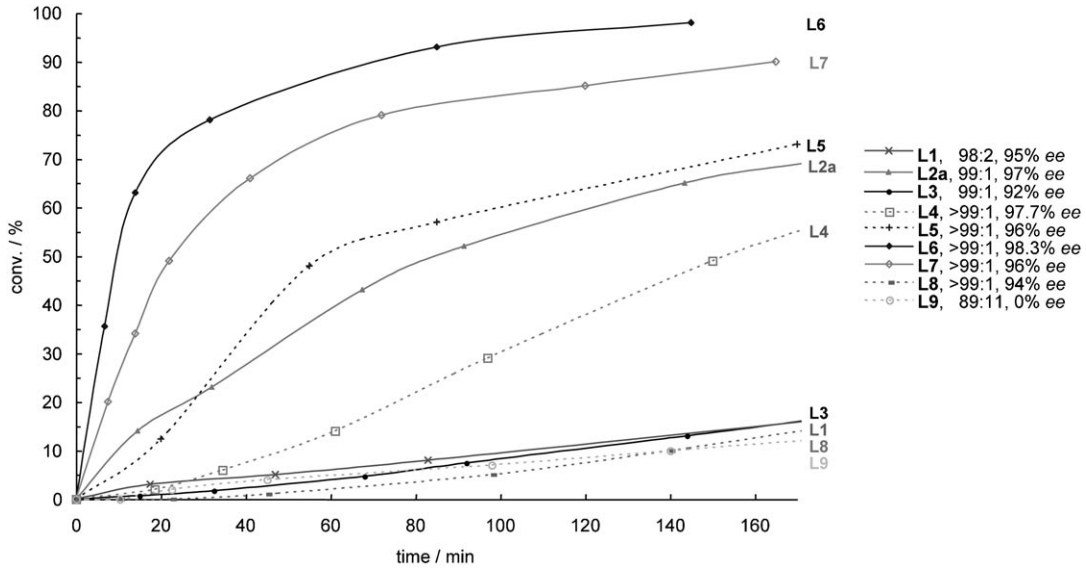


Figure 3. Kinetics of Ir-catalyzed allylic amination with benzylamine, using catalysts with the corresponding ligands **L**.

gave the best enantioselectivities for both reactions, 98.3 and 99.1 %, respectively.

Conclusion

Ligand **L2a** appears to be an extremely efficient ligand for iridium-catalyzed allylic alkylation. In conjunction with [{Ir(cod)Cl}$_2$] and LiCl as an additive it provided a successful system that permitted the use of a wide range of electrophiles (allylic carbonates or acetates) or nucleophiles (secondary or tertiary) with high enantio- and regioselectivities. This general methodology could be extended to the development by ring-closing metathesis of other interesting products, such as cyclic molecules. Similarly, C–N bonds could be created by using several amines as nucleophiles.

The results also provide mechanistic insight into the role of the *ortho*-methoxy substituent in terms of kinetics. Our first, and most obvious, hypothesis was a coordination role, which was later confirmed by theoretical calculations. Nevertheless, we designed several other ligands that revealed that neither a coordination nor an electronic role could provide an explanation. Instead, we found a steric effect, as the ligand bearing only methyl groups, **L6**, gave the most impressive kinetics. We are studying this hypothesis further.

Experimental Section

General remarks: ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded in CDCl3 by using a Bruker 400F NMR spectrometer, and chemical shifts (δ) are given in ppm relative to residual $CHCl_3$. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), ddd (doublet of doublet of doublets), qd (quartet of doublets), brs (broad singlet). Coupling constants are reported in Hertz (Hz). The evolution of reactions was monitored by GC–MS (EI mode) with an HP6890. Optical rotations were recorded by using a Perkin–Elmer 241 polarimeter at 20 °C in a 10-cm cell in the stated solvent; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1} (concentration c is given as g per 100 mL). Enantiomeric excesses were determined by performing chiral supercritical-fluid chromatography (SFC) with a Berger SFC and the stated column. Gradient programs are described as follows: initial methanol concentration (%), initial time (min), percent gradient of methanol (% min^{-1}), final methanol concentration (%); retention times (R_T) are given in min.

Enantiomeric excesses were in some cases determined by chiral GC measurement by using either an HP6890 (H_2 as vector gas) or HP6850 (H_2 as vector gas) with the stated column. Temperature programs are described as follows: initial temperature (°C), initial time (min), temperature gradient (°C min^{-1}), final temperature (°C); retention times (R_T) are given in min. Flash chromatography was performed by using silica gel 32–63 μm, 60 Å. THF and dichloromethane were dried by filtration over alumina (activated at 350 °C under nitrogen atmosphere for 12 h). Allylic carbonates and acetates were synthesized by using known experimental procedures.[29]

All chiral primary amines were obtained from BASF. Chiral secondary amines **18**–**23** were prepared according to the procedure described previously.[25]

All chiral ligands **L1**–**L7** were prepared according to the literature procedure.[14,15] Lithium chloride was dried for 24 h at 80 °C prior to use. [{Ir(cod)Cl}$_2$] was purchased from Strem and was used as received. Primary amines **15** were distilled over CaH_2 prior to use. Sodium malonate or sodium β-ketoester solutions were prepared as follows: NaH (dispersion in mineral oil, 50 %, 0.049 g, 1 mmol) was rinsed with *n*-pentane (3 × 5 mL), followed by dry THF (2 × 5 mL), and then suspended in dry THF (2 mL). Neat malonate or β-ketoester (1 mmol) was added dropwise under nitrogen and stirring at RT to give a colorless solution, which was immediately used.

Computational calculation remarks: Geometry optimization and electronic structure calculation for the ligand **L4** were performed by using density functional theory as implemented in the Gaussian 03 program.[30] The PW91 functional was used for treating both the exchange and correlation effects. The relativistic ECP and its associate basis set, SBKJC VDZ ECP, were employed to describe the iridium metal center, and all others atoms were described by the 6–31G* Pople type basis. A frequency calculation was performed on the optimized structure to ensure it was a minimum on the potential-energy surface.

General procedure for the preparation of new secondary amines: A mixture of ketone (9 mmol), amine (9 mmol), and titanium(IV) isopropoxide (8 mL, 27 mol) was stirred at RT for 20 min. The mixture was then hydrogenated at 1 atm with 10 % palladium on charcoal (180 mg, 2 mol %) under vigorous stirring at RT. The reaction course was monitored by GC–MS. Upon complete conversion, the reaction mixture was treated with an aqueous solution of 1 M sodium hydroxide. After stirring for 10 min, the solution was extracted five times with ethyl acetate. The combined organic layers were filtered over celite, dried over sodium sulfate, and evaporated under reduced pressure. After dissolving the resulting oil in diethyl ether (10 mL), an aqueous solution of 37 % HCl was added dropwise until a slightly acidic medium was reached, to afford the crude hydrochloric acid salt of the amine. The latter was recrystallized by slow evaporation of an ethyl acetate/methanol saturated solution followed by desalinification by treatment with an aqueous solution of 1 M NaOH, extraction with dichloromethane, and drying over sodium sulfate for analysis.

(*S,S*)-1-Phenylethyl-1-xylylethylamine (24): Synthesized according to the general procedure described. Yield: 25 %; $[\alpha]_D^{20} = -150.7$ ($c = 1.25$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.35$–7.24 (m, 5H), 6.90 (s, 1H), 6.84 (s, 2H), 3.55 (q, $J = 6.8$ Hz, 1H), 3.46 (q, $J = 6.8$ Hz, 1H), 2.33 (s, 6H), 1.80–1.50 (brs, 1H), 1.30 (d, $J = 7.8$ Hz, 3H), 1.28 ppm (d, $J = 7.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 137.9$, 128.5, 128.4, 126.8, 124.5, 55.2, 55.1, 25.0, 24.9, 21.4 ppm; MS (EI): m/z (%): 239 (15), 238 (79), 148 (10), 133 (98), 120 (37), 117 (10), 105 (100); HRMS (ES): m/z calcd for $C_{17}H_{20}N$ $[M-H-CH_3]^+$: 238.1596; found: 238.1596.

(*S,S*)-1-Phenylethyl-1-mesitylethylamine (25): Synthesized according to the general procedure described. Yield: 25 %; $[\alpha]_D^{20} = -129.1$ ($c = 1.24$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.27$–7.20 (m, 5H), 6.83 (brs, 2H), 4.07 (q, $J = 7.0$ Hz, 1H), 3.51 (q, $J = 6.8$ Hz, 1H), 2.61 (brs, 3H), 2.31 (s, 3H), 1.76 (brs, 4H), 1.38 (d, $J = 7.0$ Hz, 3H), 1.35 ppm (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 135.5$, 128.4, 126.8, 55.6, 51.0, 25.3, 20.8, 20.7 ppm; MS (EI): m/z (%): 267 (7) $[M]^+$, 252 (36), 146 (100), 131 (17), 105 (76); HRMS (ES): m/z calcd for $C_{19}H_{25}N$ $[M-H]^+$: 267.1987; found: 267.1986.

General procedure for the preparation of new phosphoramidite ligands: The hydrochloric acid salt of the amine (3.33 mmol) was added neat in one portion to a stirred mixture of Et_3N (16.67 mmol, 2.3 mL) and PCl_3 (3.33 mmol, 0.29 mL) at 0 °C in dichloromethane (6 mL) under nitrogen atmosphere. The reaction mixture was stirred for 3–5 h at RT until complete disappearance of the PCl_3 (monitored by ^{31}P NMR spectroscopy). Neat (*S*)-binaphthol (3.33 mmol, 0.95 g) was added in one portion to the reaction mixture at 0 °C and the suspension was stirred at RT overnight. The reaction was quenched with water, dried over sodium sulfate, and purified by flash chromatography on silica gel (cyclohexane/ethyl acetate or pentane/dichloromethane) affording the ligand as white foam.

***O,O′*-(*S*)-1,1′-Dinaphthyl-2,2′-diyl-*N,N′*-(*S,S*)-1-phenylethyl-1-xylylethylphosphoramidite (L8)**: Synthesized according to the general procedure described. Yield: 67 %; $[\alpha]_D^{20} = +5.4$ ($c = 1.03$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.06$ (d, $J = 8.6$ Hz, 1H), 7.97 (d, $J = 8.1$ Hz, 1H), 7.86 (d, $J = 7.8$ Hz, 1H), 7.78 (d, $J = 8.8$ Hz, 1H), 7.63 (d, $J = 8.6$ Hz, 1H), 7.48–7.23 (m, 12H), 6.86 (s, 1H), 6.80 (s, 2H), 4.42 (m, 2H), 2.27 (s, 6H), 1.74 (d, $J = 7.1$ Hz, 3H), 1.71 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$): δ = 149.9, 143.4, 142.7, 137.1, 133.0, 132.8, 131.4, 130.5, 130.4, 129.6, 128.3, 128.1, 127.7, 127.3, 127.2, 126.7, 126.1, 125.9, 124.8, 124.3, 122.6, 122.5, 121.2, 54.7, 54.6, 54.4, 26.6, 23.3, 22.9, 22.7, 21.4 ppm; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 151.3 ppm.

***O,O′*-(*S*)-1,1′-Dinaphthyl-2,2′-diyl-*N,N′*-(*S,S*)-1-phenylethyl-1-mesitylethylphosphoramidite (L9)**: Synthesized according to the general procedure described. Yield: 52%; $[\alpha]_D^{20}$ = +300.8 (c = 1.11 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 8.8 Hz, 1H), 7.92 (t, J = 8.6 Hz, 2H), 7.87 (d, J = 7.3 Hz, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.43–6.94 (m, 11H), 6.55 (brs, 2H), 4.88 (m, 1H), 4.69 (m, 1H), 2.35 (brs, 6H), 2.14 (s, 3H), 1.74 (m, 3H), 1.61 ppm (d, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.7, 149.7, 136.5, 136.4, 135.9, 132.9, 131.5, 130.5, 130.4, 129.5, 128.4, 128.1, 127.8, 127.2, 127.1, 126.2, 126.1, 126.0, 124.8, 124.4, 122.6, 122.4, 121.3, 22.2, 21.9, 20.8, 20.6 ppm; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 144.2 ppm.

General procedure for the Ir-catalyzed allylic alkylation: In a flame-dried Schlenk tube, lithium chloride (0.021 g, 0.5 mmol), chiral ligand (0.022 mmol), and [{Ir(cod)Cl}$_2$] (0.0067 g, 0.01 mmol) were dissolved in THF (0.5 mL) at RT. The resulting orange solution was stirred for 20 min and treated with substrate (0.5 mmol) as well as a freshly prepared sodium malonate or ketoester solution (1 mmol in 2.0 mL THF) at RT. The reaction mixture was stirred at the indicated temperature until complete disappearance of the starting material. The mixture was hydrolyzed with water, extracted with diethyl ether, and dried over magnesium sulfate. GC–MS analysis of the crude mixture indicated the ratio of regioisomers. The product was concentrated in vacuo and subjected to chromatography on silica gel (*n*-pentane/diethyl ether 7:3) to afford the alkylated adduct as a colorless oil.

Dimethyl (*R*)-2-(1-phenylallyl) malonate (3a):[7] Product prepared from substrate **2a** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 82%. The absolute configuration was determined by comparison with published data.[7] *Ee* was measured by chiral SFC analysis with a Regis (*R,R*) WHELK-O column (2% MeOH for 2 min, then 1% min^{-1}, flow rate 2 mL min^{-1}, pressure 130 bars, 0°C); R_T: 3.05 (*R*), 3.29 (*S*); $[\alpha]_D^{20}$ = +34.1 (c = 1.08 in $CHCl_3$) for 98% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.40–7.23 (m, 5H), 6.03 (ddd, J = 18.2, 10.1, 8.1 Hz, 1H), 5.15 (d, J = 18.0 Hz, 1H), 5.12 (d, J = 10.6 Hz, 1H), 4.15 (dd, J = 10.8, 8.1 Hz, 1H), 3.90 (d, J = 11.1 Hz, 1H), 3.78 (s, 3H), 3.53 ppm (s, 3H); ^{13}C NMR (100.59 MHz, CDCl3): δ = 168.2, 167.8, 139.9, 137.8, 128.7, 127.9, 127.2, 116.7, 57.4, 52.6, 52.4, 49.8 ppm; MS (EI): *m/z* (%): 189 (98), 157 (19), 129 (43), 117 (100), 91 (17), 77 (10).

Dimethyl (*R*)-2-(1-naphthalen-2-yl-allyl) malonate (3b):[11a] Product prepared from substrate **2b** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 73%. *Ee* was measured by chiral SFC analysis with a chiralcel OB-H column (2% MeOH for 2 min, then 1% min^{-1}, flow rate 2 mL min^{-1}, pressure 200 bars, 30°C); R_T: 7.43 (+), 8.05 (−); $[\alpha]_D^{20}$ = +39.3 (c = 0.925 in $CHCl_3$) for 96% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.81–7.79 (m, 3H), 7.69 (s, 1H), 7.47–7.44 (m, 2H), 7.37 (dd, J = 8.6, 1.5 Hz, 1H), 6.08 (ddd, J = 17.2, 10.4, 8.1 Hz, 1H), 5.18 (d, J = 17.2 Hz, 1H), 5.04 (d, J = 10.1 Hz, 1H), 4.30 (dd, J = 9.6, 8.4 Hz, 1H), 4.01 (d, J = 11.1 Hz, 1H), 3.77 (s, 3H), 3.46 ppm (s, 3H); ^{13}C NMR (100.59 MHz, CDCl3): δ = 168.3, 167.9, 137.7, 137.5, 133.5, 132.6, 128.4, 127.9, 127.7, 126.7, 126.2, 126.1, 125.9, 116.9, 57.3, 52.7, 52.5, 49.8 ppm; MS (EI): *m/z* (%): 298 (24), 239 (58), 207 (13), 179 (29), 167 (100), 152 (28).

Dimethyl (*R*)-2-[1-(4-methoxyphenyl)allyl] malonate (3c):[11c] Product prepared from substrate **2c** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 99%. *Ee* was measured by chiral SFC analysis with a Regis (*R,R*) WHELK-O column (2% MeOH for 2 min, then 1% min^{-1}, flow rate 2 mL min^{-1}, pressure 130 bars, 30°C); R_T: 4.99 (+), 5.61 (−); $[\alpha]_D^{20}$ = +23.3 (c = 1.10 in $CHCl_3$) for 97% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.14 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 5.97 (ddd, J = 17.1, 10.1, 7.8 Hz, 1H), 5.09 (d, J = 15.4 H z, 1H), 5.06 (d, J = 8.6 Hz, 1H), 4.06 (dd, J = 10.9, 8.3 Hz, 1H), 3.82 (d, J = 10.9 Hz, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.50 ppm (s, 3H); ^{13}C NMR (100.59 MHz, CDCl3): δ = 168.3, 167.9, 158.6, 138.1, 131.9, 129.0, 116.3, 114.0, 57.5, 55.2, 52.5, 48.9 ppm; MS (EI): *m/z* (%): 278 (14), 219 (35), 147 (100), 115 (13), 91 (16).

Dimethyl (*R*)-2-[1-(3-methoxyphenyl)allyl] malonate (3d): Product prepared from substrate **2d** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 58%. *Ee* was measured by chiral SFC analysis with a Regis (*R,R*) WHELK-O column (1% MeOH, flow rate 2 mL min^{-1}, pressure 130 bars, 0°C); R_T: 5.95 (+), 6.54 (−); $[\alpha]_D^{20}$ = +28.9 (c = 1.08 in $CHCl_3$) for 96% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.25 (td, J = 7.8, 1.0 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.81–6.78 (m, 2H), 6.00 (ddd, J = 17.2, 10.1, 8.3 Hz, 1H), 5.17 (dt, J = 16.9, 1.3 Hz, 1H), 5.12 (d, J = 10.4 Hz, 1H), 4.12 (dd, J = 10.8, 8.3 Hz, 1H), 3.90 (d, J = 10.8 Hz, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 3.56 ppm (s, 3H); ^{13}C NMR (100.59 MHz, CDCl3): δ = 168.2, 159.7, 141.6, 137.7, 129.7, 120.1, 116.7, 113.8, 112.4, 57.3, 55.2, 52.6, 52.5, 49.8 ppm; MS (EI): *m/z* (%): 278 (28), 219 (100), 203 (10), 187 (38), 173 (10), 159 (40), 147 (86), 132 (12), 115 (34), 91 (35), 77 (13), 59 (12); elemental analysis: calcd (%) for $C_{15}H_{18}O_5$: C 64.74, H 6.52; found: C 64.49, H 6.48.

Dimethyl (*R*)-2-[1-(2-methoxyphenyl)allyl] malonate (3e): Product prepared from substrate **2e** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 98%. *Ee* was measured by chiral SFC analysis with a Regis (*R,R*) WHELK-O column (1% MeOH, flow rate 2 mL min^{-1}, pressure 130 bars, 0°C); R_T: 5.67 (+), 6.30 (−); $[\alpha]_D^{20}$ = +31.1 (c = 1.09 in $CHCl_3$) for 79% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.20 (td, J = 7.6, 1.8 Hz, 1H), 7.16 (dd, J = 7.6, 1.5 Hz, 1H), 6.90–6.84 (m, 2H), 6.14 (ddd, J = 17.0, 10.1, 8.6 Hz, 1H), 5.12 (dt, J = 17.2, 1.3 H, 1H z), 5.04 (dd, J = 10.1, 0.8 Hz, 1H), 4.33 (dd, J = 10.6, 8.6 Hz, 1H), 4.18 (d, J = 10.6 Hz, 1H), 3.85 (s, 3H), 3.72 (s, 3H), 3.49 ppm (s, 3H); ^{13}C NMR (100.59 MHz, CDCl3) 168.7, 168.3, 157.1, 136.9, 129.5, 128.3, 128.1, 120.7, 116.8, 111.1, 55.5, 55.4, 52.4, 52.3, 46.2 ppm; MS (EI): *m/z* (%): 278 (10), 219 (53), 187 (16), 159 (12), 147 (100), 131 (11), 115 (17), 91 (26); elemental analysis calcd (%) for $C_{15}H_{18}O_5$: C 64.74, H 6.52; found: C 64.46, H 6.51.

Dimethyl (*R*)-2-(1-benzo[1,3]dioxol-5-yl-allyl) malonate (3f): Product prepared from substrate **2f** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 70%. *Ee* was measured by chiral SFC analysis with a Regis (*R,R*) WHELK-O column (1% MeOH during 6 min, then 1% min^{-1}, flow rate 2 mL min^{-1}, pressure 130 bars, 30°C); R_T: 6.02 (+), 6.77 (−); $[\alpha]_D^{20}$ = +22.0 (c = 1.13 in $CHCl_3$) for 97% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.74–7.66 (m, 3H), 5.98–5.89 (m, 3H), 5.10 (d, J = 15.4 Hz, 1H), 5.07 (d, J = 8.8 Hz, 1H), 4.03 (dd, J = 10.9, 8.1 Hz, 1H), 3.79 (d, J = 10.9 Hz, 1H), 3.73 (s, 3H), 3.54 ppm (s, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$): δ = 168.3, 167.9, 139.9, 137.7, 137.5, 133.5, 132.6, 128.4, 127.9, 127.7, 126.7, 126.2, 126.1, 125.9, 116.9, 57.3, 52.7, 52.6, 52.5, 49.8 ppm; MS (EI): *m/z* (%): 298 (24), 239 (58), 207 (13), 179 (29), 167 (100), 152 (28); HRMS (EI) calcd for $[M+Na]^+$ 315.0845, found 315.0834.

Dimethyl (*R*)-2-[1-(4-chlorophenyl)allyl] malonate (3g):[11c] Product prepared from substrate **2g** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 90%. Absolute configuration was determined by comparison with published data.[7] *Ee* was measured by chiral SFC analysis with a Regis (*R,R*) WHELK-O column (2% MeOH during 2 min, then 1% min^{-1}, flow rate 2 mL min^{-1}, pressure 130 bars, 30°C); R_T: 3.30 (+), 3.82 (−); $[\alpha]_D^{20}$ = +40.9 (c = 1.00 in $CHCl_3$) for 97% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.30 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H), 5.99 (ddd, J = 16.9, 10.4, 8.1 Hz, 1H), 5.16 (d, J = 7.1 Hz, 1H), 5.12 (d, J = 0.8 Hz, 1H), 4.13 (dd, J = 10.9, 8.1 Hz, 1H), 3.85 (d, J = 10.8 Hz, 1H), 3.78 (s, 3H), 3.56 ppm (s, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$): δ = 168.0, 167.7, 138.5, 137.3, 133.0, 129.4, 128.8, 117.1, 57.2, 52.7, 52.6, 49.0 ppm; MS (EI): *m/z* (%): 223 (100), 191 (17), 163 (23), 151 (85), 128 (19), 115 (53), 59 (15).

Dimethyl (*R*)-2-[1-(4-trifluoromethylphenyl)allyl] malonate (3h):[11c] Product prepared from substrate **2h** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 40%. *Ee* was measured by chiral GC analysis with a Chiraldex LIPODEX E column (60-0-1-170-5); R_T: 59.09 (−), 59.68 (+); $[\alpha]_D^{20}$ = +40.1 (c = 0.81 in $CHCl_3$) for 94% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.57 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 5.97 (ddd, J = 16.9, 10.1, 8.1 Hz, 1H), 5.16 (d, J = 7.6 Hz, 1H), 5.12 (s, 1H), 4.19 (dd, J = 10.9,

8.6 Hz, 1H), 3.90 (d, $J=11.1$ Hz, 1H), 3.76 (s, 3H), 3.53 ppm (s, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta=167.8$, 167.5, 144.1, 136.9, 129.6, 129.2, 128.3, 125.6–125.5 (q, $J=3.3$ Hz, 1C), 125.4, 117.5, 56.9, 52.7, 52.5, 49.3 ppm; MS (EI): *m*/*z* (%): 260 (10), 257 (100), 224 (20), 197 (26), 185 (98), 177 (11), 165 (31), 151 (10), 128 (11), 115 (48), 59 (37).

Dimethyl (*R*)-2-(1-propylallyl) malonate (3i):[32] Product prepared from substrate **2i** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 82%. *Ee* was measured by chiral GC analysis with a Chiraldex G-TA column (70-0-0.5-110-15-170); R_T: 29.51 (+), 30.41 (−); $[\alpha]_D^{20}=+2.3$ ($c=1.12$ in $CHCl_3$) for 97% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta=5.66$ (dt, $J=16.9$, 10.1 Hz, 1H), 5.11 (m, 2H), 3.76 (s, 3H), 3.71 (s, 3H), 3.40 (d, $J=9.1$ Hz, 1H), 2.79 (qd, $J=9.3$, 3.0 Hz, 1H), 1.45–1.21 (m, 4H), 0.91 ppm (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$) 168.8, 168.6, 138.1, 117.4, 57.0, 52.4, 52.2, 44.1, 34.5, 20.2, 13.8 ppm; MS (EI) *m*/*z* (%): 171 (41), 155 (100), 151 (32), 139 (66), 132 (69), 126 (30), 123 (29), 113 (49), 100 (48), 97 (10), 95 (36), 81 (50), 67 (41), 59 (51), 55 (83).

Dimethyl (*S*)-2-(1-cyclohexylallyl) malonate (3j):[31] Product prepared from substrate **2j** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield: 65%. It was impossible to remove the 6% of starting material that remained. *Ee* was measured by chiral GC analysis with a Chiraldex G-TA column (80-0-1-170-5); R_T: 44.67 (−), 45.00 (+); $[\alpha]_D^{20}=-0.9$ ($c=0.98$ in $CHCl_3$) for 98% *ee* and 6% starting material; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta=5.73$ (dt, $J=16.9$, 10.1 Hz, 1H), 5.08 (dd, $J=10.1$, 2.0 Hz, 1H), 5.03 (dd, $J=17.2$, 1.5 Hz, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.63 (d, $J=9.1$ Hz, 1H), 2.60–2.69 (m, 1H), 1.72–0.88 ppm (m, 10H); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta=169.1$, 168.8, 135.8, 118.2, 54.2, 52.4, 52.2, 50.1, 39.1, 28.6, 26.3 ppm; MS (EI): *m*/*z* (%): 195 (11), 172 (20), 140 (11), 133 (14), 122 (100), 113 (72), 107 (29), 101 (20), 93 (26), 81 (90), 77 (13), 67 (52), 59 (31), 55 (75).

Dimethyl (*S*)-2-methyl-2-(1-phenylallyl) malonate (8a): Product prepared from substrate **2a** and nucleophile **7a** according to the general allylic alkylation procedure described. Yield: 95%. *Ee* was measured by chiral SFC analysis with a Daicel OJ column (0% MeOH, flow rate 2 mL min^{-1}, pressure 200 bars, 45 °C); R_T: 2.76 (*S*), 3.06 (*R*); $[\alpha]_D^{20}=+39.3$ ($c=1.4$ in $CHCl_3$) for 97% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta=7.30$–7.2 (m, 5H), 6.32 (ddd, $J=16.9$, 10.2, 8.6 Hz, 1H), 5.12 (m, 2H), 4.15 (d, $J=8.6$ Hz, 1H), 3.71 (s, 3H), 3.62 (s, 3H), 1.43 ppm (s, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta=171.5$, 171.3, 139.1, 136.9, 129.6, 128.2, 127.2, 117.8, 58.9, 54.6, 52.5, 52.4, 18.5 ppm; MS (EI): *m*/*z* (%): 262 (2) $[M]^+$, 203 (30), 170 (10), 117 (100); HRMS (ESI) calcd for $C_{15}H_{19}O_4$ $[M+H]^+$ 263.1277; found: 263.1298.

Methyl (*S*)-2-oxo-1-(1-phenylallyl) cyclohexanecarboxylate (8b): Product prepared from substrate **2a** and nucleophile **7b** according to the general allylic alkylation procedure described. Yield: 79% as a mixture of the two unseparable diastereoisomers in a 51:49 ratio. "Maj" refers to the signals of the majority diastereoisomer, and "Min" to the signals of the minor one. *Ee* was measured by chiral SFC analysis with a Daicel OJ column (0% MeOH, flow rate 2 mL min^{-1}, pressure 175 bars, 30 °C); R_T: 2.93 (Min, *R*), 3.39 (Min, *S*); $[\alpha]_D^{20}=+32.7$ ($c=0.87$ in $CHCl_3$) for 95% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta=7.42$–7.21 (m, 5H; Maj+Min), 6.40–6.25 (m, 1H; Maj+Min), 5.16–5.08 (m, 2H; Maj+Min), 4.18 (d, $J=8.3$ Hz, 1H; Maj+Min), 4.02 (d, $J=9.4$ Hz, 1H; Min), 3.62 (s, 3H; Min), 3.56 (s, 3H; Maj), 2.61–2.36 (m, 3H; Maj+Min), 2.01–1.56 ppm (m, 5H; Maj+Min); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta=206.5$ (Min), 206.3 (Maj), 171.2 (Min), 171.1 (Maj), 139.8 (Min), 139.5 (Maj), 137.2 (Min), 130.1 (Min), 129.8 (Maj), 128.1 (Maj), 128.0 (Min), 127.0 (Min), 126.8 (Maj), 117.5 (Maj), 117.4 (Min), 65.8 (Maj), 65.7 (Min), 54.2 (Min), 53.4 (Maj), 52.2 (Min), 52.1 (Maj), 42.0 (Maj), 41.9 (Min), 34.6 (Min), 33.0 (Maj), 27.0 (Min), 26.7 (Maj), 22.6 (Maj), 22.6 ppm (Min); MS (EI): *m*/*z* (%): 272 (1) $[M]^+$, 254 (18), 195 (16), 117 (100); HRMS (ESI) calcd for $C_{17}H_{21}O_3$ $[M+H]^+$ 273.1485, found 273.1504.

Methyl (*R*)-2-acetyl-3-phenyl-pent-4-enoate (8c): Product prepared from substrate **2a** and nucleophile **7c** according to the general allylic alkylation procedure described. Yield: 68% as a mixture of the two inseparable diastereoisomers in a 53:47 ratio. "Maj" refers to the signals of the majority diastereoisomer, and "Min" to the signals of the minor one. *Ee* was measured by chiral SFC analysis with a Daicel OJ column (2% MeOH, then 2% min^{-1}, flow rate 2 mL min^{-1}, pressure 175 bars, 30 °C); R_T: 2.67 (Maj, *S*), 3.05 (Maj, *R*); $[\alpha]_D^{20}=+27.1$ ($c=1.29$ in $CHCl_3$) for 95% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta=7.34$–7.18 (m, 5H; Maj+Min), 6.03–5.90 (m, 1H; Maj+Min), 5.16–5.09 (m, 2H; Maj+Min), 4.16 (dd, $J=11.9$, 8.3 Hz, 1H; Min), 4.06 (dd, $J=15.2$, 11.4 Hz, 1H; Maj), 3.76 (s, 3H; Maj), 3.49 (s, 3H; Min), 2.32 (s, 3H; Min), 2.01 ppm (s, 3H; Maj); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta=201.7$ (Min), 201.5 (Maj), 168.4 (Maj), 168.1 (Min), 140.1 (Maj), 139.8 (Min), 138.2 (Maj), 137.8 (Min), 128.9 (Maj), 128.7 (Min), 128.0 (Maj), 127.9 (Min), 127.2 (Maj), 127.1 (Min), 116.8 (Maj), 116.3 (Min), 65.2 (Min), 64.8 (Maj), 52.6 (Maj), 52.4 (Min), 49.6 (Min), 49.4 (Maj), 30.2 (Min), 29.8 ppm (Maj); MS (EI): *m*/*z* (%): 214 (39), 189 (48), 173 (25), 157 (35), 129 (35), 117 (100); HRMS (ESI) calcd for $C_{14}H_{17}O_3$ $[M+H]^+$ 233.1172, found 233.1155.

Diethyl (*S*)-2-allyl-2-(1-phenylallyl) malonate (8d):[18] Product prepared from substrate **2a** and nucleophile **7d** according to the general allylic alkylation procedure described. Following chromatography, the product still contained some allyldiethyl malonate, which was removed by kugelrohr distillation (80 °C, 0.1 mmHg) and afforded 0.134 g of a colorless oil (85%). *Ee* was measured by chiral GC analysis of the cyclized metathesis product **11**; $[\alpha]_D^{20}=+55.3$ ($c=1.4$ in $CHCl_3$); ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta=7.27$–7.20 (m, 5H), 6.46 (ddd, $J=17.0$, 10.2, 8.3 Hz, 1H), 5.87–5.76 (m, 1H), 5.16–5.02 (m, 4H), 4.25 (q, $J=7.3$ Hz, 2H), 4.19–4.16 (m, 2H), 4.05 (d, $J=8.4$ Hz, 1H), 2.63 (ddt, $J=14.1$, 6.6, 1.2 Hz, 1H), 2.45 (dd, $J=14.2$, 8.1 Hz, 1H), 1.30 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta=$ 170.3, 170.1, 139.2, 138.0, 133.4, 129.4, 128.3, 127.2, 118.6, 117.1, 62.4, 61.2, 54.3, 39.4, 14.1, 14.0 ppm; MS (EI): *m*/*z* (%): 316 (2) $[M]^+$, 229 (14), 117 (100), 115 (29), 91 (21); HRMS (ESI) calcd for $C_{19}H_{25}O_4$ $[M+H]^+$ 317.1747, found 317.1761.

Diethyl (*S*)-2-phenyl-cyclopent-3-ene-1,1-dicarboxylate (10):[18] Product **8d** (0.25 mmol, 0.079 g) was dissolved in dichloromethane (5 mL) and treated with Grubb's first generation catalyst (0.0125 mmol, 0.010 g) for 1.5 h at RT. After solvent removal in vacuo, the crude product was subjected to chromatography (SiO_2, pentane/diethyl ether 7:3) to afford 0.069 g (96%) of **10** as a white product. M.p. 75–77 °C. *Ee* was measured by chiral GC analysis with a Chiraldex BTA column (80-0-1-170-10); R_T: 68.97 (*R*), 69.34 (*S*); $[\alpha]_D^{20}=-336.3$ ($c=0.82$ in $CHCl_3$) for 98.8% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta=7.24$–7.18 (m, 5H), 5.87–5.84 (m, 1H), 5.71–5.68 (m, 1H), 4.87 (d, $J=1.3$ Hz, 1H), 4.32–4.14 (m, 2H), 3.68 (dq, $J=10.8$, 7.1 Hz, 1H), 3.50 (dq, $J=17.4$, 2.3 Hz, 1H), 3.39 (dq, $J=10.6$, 7.4 Hz, 1H), 2.78 (dd, $J=17.7$, 2.5 Hz, 1H), 1.25 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta=172.2$, 169.6, 139.2, 132.3, 129.2, 128.6, 128.0, 127.2, 64.9, 61.6, 61.1, 56.9, 40.7, 14.1, 13.5 ppm; MS (EI): *m*/*z* (%): 288 (21) $[M]^+$, 242 (10), 214 (100), 197 (25), 169 (32), 155 (19), 141 (90), 128 (20), 115 (29); HRMS (ESI) calcd for $C_{17}H_{21}O_4$ $[M+H]^+$ 289.1434, found 289.1414.

Dimethyl (*S*)-2-(1,3-diphenylallyl) malonate (12):[33] Product prepared from substrate **11** and sodium dimethyl malonate according to the general allylic alkylation procedure described. Yield 60%. *Ee* was measured by chiral SFC analysis with a Regis (*R*,*R*) WHELK-O column (2% MeOH during 2 min, then 1% min^{-1}, flow rate 2 mL min^{-1}, pressure 130 bars, 30 °C); R_T: 2.83 (*S*), 3.13 (*R*); $[\alpha]_D^{20}=-11.2$ ($c=1.04$ in $CHCl_3$) for 86% *ee*, lit. data: −22.4 ($c=1.8$ in $CHCl_3$);[30] ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta=7.35$–7.20 (m, 10H), 6.50 (d, $J=15.8$ Hz, 1H), 6.35 (dd, $J=15.8$, 8.8 Hz, 1H), 4.28 (dd, $J=10.8$, 9.8 Hz, 1H), 3.97 (d, $J=11.0$ Hz, 1H), 3.72 (s, 3H), 3.53 ppm (s, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta=$ 168.2, 167.8, 140.1, 136.8, 131.8, 129.1, 128.7, 128.5, 127.8, 127.6, 127.2, 126.4, 57.6, 52.6, 52.4, 49.2 ppm; MS (EI): *m*/*z* (%): 324 (8) $[M]^+$, 292 (8), 232 (12), 205 (81), 193 (86), 178 (26), 165 (13), 128 (13), 115 (100).

Procedure for recycling of the iridium catalyst: After the normal course of the reaction, the crude mixture was treated with 10 mL of a 1:1 mixture of diethyl ether and pentane. The resulting solution was stored at RT for about 8 h. An orange precipitate formed and settled to the bottom of the solution. Filtration gave an orange powder that was rinsed with diethyl ether/pentane (1:1, 3×). The catalyst was dried in vacuo and could be used for another run.

General procedure for the iridium-catalyzed enantioselective allylic amination: $[\{Ir(cod)Cl\}_2]$ (0.01 mmol) and chiral ligand (0.02 mmol) were dissolved in THF (0.5 mL) in a 3-mL test tube under argon. A small mag-

netic stirring bar was added, the test tube was capped with a septum, and the mixture was stirred for 10 min at RT. Amine **15** (1.3 mmol) and cinnamyl methyl carbonate **2a** (0.18 mL, 0.98 mmol) were added to the reaction mixture by using a syringe. The reaction mixture was stirred at RT until the starting material had disappeared completely. The solvent was removed in vacuo. GC–MS analysis of the crude mixture indicated the ratio of regioisomers **16**/**17**. The mixture was then purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate 8:2) to give the secondary amine as a white oil. A small amount of the product was converted to the corresponding acetamide by treatment with acetic anhydride in diethyl ether for 5 min. The acetamide was washed with water and filtered on silica gel. Chiral SFC analysis indicated the enantiomeric excess.

(*S*)-*N*-(1-Phenyl-2-propenyl)benzylamine (16a):[10m] Product prepared from substrate **2a** and amine **15a** according to the general allylic amination procedure described. Yield: 88%. The absolute configuration was determined by comparison of the optical rotation with literature data.[10m] *Ee* was measured by chiral SFC analysis of the acetamide with a chiralcel OB-H column (2% MeOH, flow rate 2 mL min^{-1}); R_T: 5.99 (*S*), 7.00 (*R*); $[\alpha]_D^{20} = +6.2$ ($c = 1.12$ in $CHCl_3$) for 97% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta = 7.30$–7.22 (m, 10H), 5.99 (ddd, $J = 17.3$, 10.2, 7.1 Hz, 1H), 5.26 (d, $J = 17.1$ Hz, 1H), 5.17 (d, $J = 10.2$ Hz, 1H), 4.27 (d, $J = 7.2$ Hz, 1H), 3.81 (d of AB pattern, $J = 13.4$ Hz, 1H), 3.75 (d of AB pattern, $J = 13.4$ Hz, 1H), 1.72 ppm (br s, 1H); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta =$ 142.8, 141.0, 140.5, 128.6, 128.4, 128.2, 127.4, 127.3, 126.9, 115.2, 65.2, 51.3 ppm; MS (EI): *m*/*z* (%): 223 (10) $[M]^+$, 196 (38), 146 (22), 132 (56), 117 (35), 115 (17), 106 (13); HRMS (ESI$^+$) calcd for $C_{16}H_{18}N$ $[M+H]^+$ 224.1433, found 224.1438.

(*S*)-*N*-(1-Phenyl-2-propenyl)allylamine (16b):[10m] Product prepared from substrate **2a** and amine **15b** according to the general allylic amination procedure described. Yield: 91%. The *ee* was measured by chiral SFC analysis of the acetamide with a chiralcel OB-H column (1% MeOH, flow rate 2 mL min^{-1}); R_T: 3.92 (+), 4.53 (−); $[\alpha]_D^{20} = +15.1$ ($c = 1.23$ in $CHCl_3$) for 97% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta = 7.45$–7.26 (m, 5H), 5.91–6.02 (m, 2H), 5.29–5.13 (m, 4H), 4.27 (d, $J = 7.1$ Hz, 1H), 3.29–3.19 (m, 2H), 1.50–1.30 ppm (br s, 1H); ^{13}C NMR (100.59 MHz, $CDCl_3$): $\delta = 142.7$, 140.9, 136.8, 128.6, 127.3, 127.3, 116.0, 115.2, 65.2, 49.9 ppm; MS (EI): *m*/*z* (%): 173 (7) $[M]^+$, 146 (100), 132 (48), 117 (74), 104 (16); HRMS (ESI$^+$) calcd for $C_{12}H_{16}N$ $[M+H]^+$ 174.1277, found 174.1275.

(*S*)-*N*-(1-Phenyl-2-propenyl)-*n*-hexylamine (16c):[10m] Product prepared from substrate **2a** and amine **15c** according to the general allylic amination procedure described. Yield: 89%. *Ee* was measured by chiral SFC analysis of the acetamide with a chiralcel OD-H column (3% MeOH, flow rate 1.8 mL min^{-1}); R_T: 5.50 (+), 6.23 (−); $[\alpha]_D^{20} = +20.6$ ($c = 1.21$ in $CHCl_3$) for 98% *ee*; ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta = 7.40$–7.26 (m, 5H), 5.98 (ddd, $J = 17.2$, 8.6, 7.0 Hz, 1H), 5.25 (dt, $J = 17.2$, 1.3 Hz, 1H), 5.14 (dt, $J = 10.4$, 1.6, 1.3 Hz, 1H), 4.21 (d, $J = 7.0$ Hz, 1H), 2.65–2.50 (m, 2H), 1.55–1.28 (m, 9H), 0.92 ppm (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100.59 MHz, $CDCl_3$): 143.1, 141.3, 128.5, 127.3, 127.1, 114.8, 66.3, 47.8, 31.8, 30.2, 27.1, 22.7, 14.1 ppm; MS (EI): *m*/*z* (%): 217 (3) $[M]^+$, 190 (21), 146 (29), 132 (17), 117 (100), 115 (20); HRMS (ESI$^+$) calcd for $C_{15}H_{24}N$ $[M+H]^+$ 218.1903, found 218.1918.

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