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Diastereo- and Enantioselective Intramolecular C(sp^3)–H Arylation for the Synthesis of Fused Cyclopentanes

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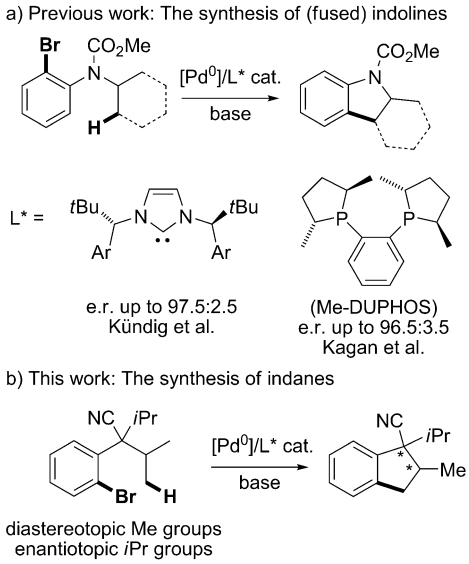
Transition-metal catalysis has recently emerged as a powerful tool to functionalize otherwise unreactive C(sp^2)–H and C(sp^3)–H bonds.[1–2] In this context, recent research from our group[3] and others[4] has focused on the intramolecular arylation of unactivated C(sp^3)–H bonds to aryl halides under palladium(0) catalysis, giving rise to original polycylic molecules.[5] To date, very few examples of catalytic enantioselective reactions involving the organometallic activation of unreactive C(sp^3)–H bonds have been described.[6–9]

While our own work in this area was in progress, the synthesis of (fused) indolines by palladium(0)-catalyzed enantioselective intramolecular C(sp^3)–H arylation was disclosed by the groups of Kündig[8a] and Kagan,[8b] who reported enantiomeric ratios (e.r. values) up to 97.5:2.5 by using chiral *N*-heterocyclic carbenes (NHCs) and diphosphines as the ligands, respectively (Scheme 1a). Herein, we report our preliminary results on the synthesis of indanes by use of a similar type of reaction (Scheme 1b). This substrate type raises an additional stereochemical challenge, that is, the presence of a quaternary benzylic carbon atom on the reaction substrate (instead of a nitrogen atom) that bears both diastereotopic and enantiotopic C–H bonds. In other words, both high diastereo- and enantioselectivity must be achieved to develop an efficient synthesis of the target carbocycles.

The reaction of aryl bromide **1a** in the presence of chiral ligands was studied extensively and Table 1 shows representative examples (see the Supporting Information for additional examples). As shown previously,[3b,e] compound **1a** may give rise to four different products by intramolecular C(sp^3)–H arylation, that is, both diastereoisomers of the desired indane (**2a** and **3a**), olefin **4a** (also arising from C(sp^3)–H activation), and protodebromination product **5a**. It has already been shown that the structure of the (achiral) ligand has a profound impact on the product selectivity, but



Scheme 1. Palladium(0)-catalyzed enantioselective intramolecular C(sp^3)–H arylation.

so far the major *cis* diastereoisomer **2a** could not be formed without significant proportions of **3a** or **4a**. For the asymmetric version of this reaction, we tested as a priority chiral ligands that gave good enantioselectivities in related processes (Table 1). We initially employed screening conditions that were previously optimized with achiral ligands, that is, 5 mol% $Pd(OAc)_2$ as the precatalyst, 20 mol% of the phosphine ligand, and K_2CO_3 as the base, in DMF at 140°C for 14 h. We first checked for a possible background reaction with $Pd(OAc)_2$ alone, which gave an 8% yield of **2a**+**3a** under the same conditions (Table 1, entry 1). As a consequence, there should be little impact of this racemic background reaction on the enantioselectivity observed with chiral ligands at this temperature. (*R*)-BINAP (**L1**) was evaluated first, and gave indane **2a** in moderate yield and good diastereoselectivity, but almost no enantioselectivity (Table 1, entry 2). (*R*,*R*)-Me-DUPHOS (**L2**), which gave good enantioselectivities in the related synthesis of indolines,[8b] furnished racemic **2a** in low yield (Table 1, entry 3). Josiphos (**L3**, Cy = cyclohexyl),[10] with different phosphorus substituents, gave similarly disappointing results (Table 1, entry 4), but its di(PCy_2) analogue **L4** proved much more efficient, providing an e.r. of 76:24 (Table 1, entry 5).[11] Decreasing the temperature to 110°C with this ligand did not

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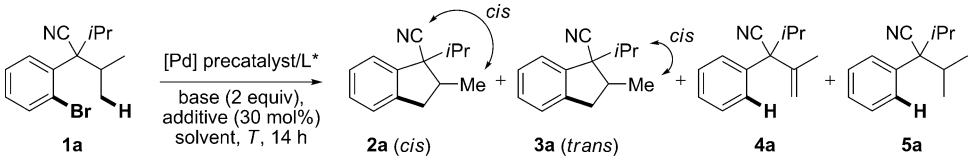
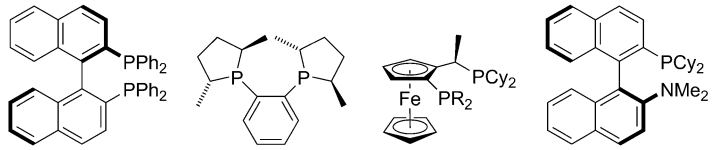
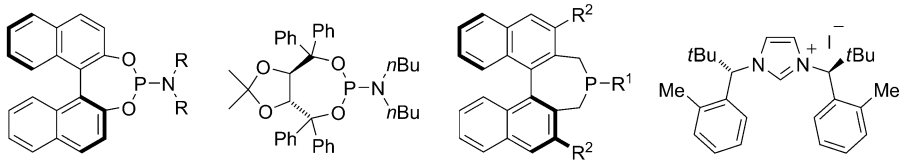
Table 1. Analysis of reaction parameters.







	Pd precatalyst ([mol%])	L* ([mol%])	Base	Additive (30 mol%)	Solvent	T [°C]	**2a**/**3a**/**4a**/**5a**[a]	d.r.[a]	Yield of **2a**+**3a** [%][b]	e.r. of **2a**[c]
1	$Pd(OAc)_2$ (5)	–	K_2CO_3	–	DMF	140	27.5:1:17:8	28:1	8 (18)	–
2	$Pd(OAc)_2$ (5)	**L1** (20)	K_2CO_3	–	DMF	140	12:1:3:1	12:1	57	52.5:47.5
3	$Pd(OAc)_2$ (5)	**L2** (20)	K_2CO_3	–	DMF	140	22.5:1:6.5:4	23:1	31	50:50
4	$Pd(OAc)_2$ (5)	**L3** (20)	K_2CO_3	–	DMF	140	17:1:7:2	17:1	36	52:48
5	$Pd(OAc)_2$ (5)	**L4** (20)	K_2CO_3	–	DMF	140	9.5:1.5:2:1	7:1	63	76:24
6	$Pd(OAc)_2$ (5)	**L4** (20)	K_2CO_3	–	DMF	110	14:2:1:1	8:1	63	75.5:24.5
7	$Pd(OAc)_2$ (5)	–	K_2CO_3	–	DMF	110	122:3:24:1	43:1	29 (47)	–
8	$Pd(OAc)_2$ (5)	**L5** (20)	K_2CO_3	–	DMF	140	42:2:12:1	21:1	74	50:50
9	$Pd(OAc)_2$ (5)	**L6** (20)	K_2CO_3	–	DMF	140	5.5:0:1:1	>98:2	53	50:50
10	$Pd(OAc)_2$ (5)	**L7** (20)	K_2CO_3	–	DMF	140	1.5:0:2.5:1	>98:2	12 (86)	n.d.
11	$Pd(OAc)_2$ (5)	**L8** (20)	K_2CO_3	–	DMF	140	36:3.5:12:1	10:1	74	53:47
12	$Pd(OAc)_2$ (5)	**L9** (20)	K_2CO_3	–	DMF	140	5:0:2:1	37:1	24 (64)	n.d.
13	$Pd(OAc)_2$ (5)	**L10** (20)	K_2CO_3	–	DMF	140	41:6:1:1	7:1	87	74:26
14	$Pd(OAc)_2$ (5)	**L11** (20)	K_2CO_3	–	DMF	140	30:4:4:1	8:1	88	71.5:28.5
15	$Pd(OAc)_2$ (5)	**L10** (20)	K_2CO_3	–	DMF	110	51:6:1:1	8:1	82	75.5:24.5
16	$Pd(OAc)_2$ (5)	**L11** (20)	K_2CO_3	–	DMF	110	84:11:3:1	8:1	89	78.5:21.5
17	$[Pd_2dba_3]$ (2.5)	**L11** (20)	K_2CO_3	–	DMF	140	30:1.5:31:1	20:1	43	n.d.
18	$[\{PdCl(cinnamyl)\}_2]$ (2.5)	**L11** (20)	K_2CO_3	–	DMF	140	19:1:46:1	19:1	24	n.d.
19	$Pd(OAc)_2$ (5)	**L11** (20)	Cs_2CO_3	–	DMF	140	12.5:1:3:0	12:1	74	61:39
20	$Pd(OAc)_2$ (5)	**L11** (20)	K_2CO_3	PivOH	DMF	140	159:28:3:1	6:1	81	78.5:21.5
21	$Pd(OAc)_2$ (5)	**L13** (10)	K_2CO_3	PivOH	DMF	140	90:3:15:1	29:1	56	66:34
22	$[\{PdCl(cinnamyl)\}_2]$ (5)	**L13** (10)	Cs_2CO_3[d]	tBuCO$_2$Cs[d]	mesitylene	160	19:2:16:1	11:1	39 (88)	69:31
23	$Pd(OAc)_2$ (5)	**L11** (20)	K_2CO_3	–	DMSO	140	46.5:2.5:1:1	20:1	84	79:21
24	$Pd(OAc)_2$ (5)	–	K_2CO_3	–	DMSO	140	1.5:0:1:0	n.d.	2 (33)	–
25	$Pd(OAc)_2$ (5)	**L12** (20)	K_2CO_3	–	DMSO	140	113:16:3:1	7:1	75	81:19
26	$Pd(OAc)_2$ (2.5)	**L11** (10)	K_2CO_3	–	DMSO	140	75.5:3:2:1	24:1	88	80:20

[a] Ratio of products estimated by GCMS analysis. The diastereomeric ratio (d.r.) of **2a**/**3a** was almost identical (±5%) from GC and ^{1}H NMR analysis. [b] GC yield calculated by using tetradecane as the internal standard. The conversion was 100% in all cases unless otherwise provided (in parentheses). [c] Determined by ^{19}F NMR analysis of the Mosher amides prepared after reduction of **2a** to the primary amine (see the Supporting Information). n.d. = not determined. [d] With Cs_2CO_3 (1.5 equiv) and tBuCO$_2$Cs (1 equiv).

seem to significantly affect the yield, d.r., or e.r. (Table 1, entry 6).

However, we discovered that there was significantly more of the background reaction at 110°C than at 140°C (Table 1, entry 7), and thus this might affect the selectivities observed with **L4** at this temperature. In light of this observation, the ligand screening was continued at 140°C to minimize the possible contribution of the "ligand-free" reaction. We next evaluated (*S*)-KenPhos (**L5**),[12] which has previously given e.r. values of up to 75:25 in intermolecular C(sp^3)–H arylation reactions (Table 1, entry 8).[9] Disappointingly, **L5** gave a good yield and d.r., but no enantioselectivity. We next

evaluated phosphoramidites **L6–8**,[13] which have furnished high enantioselectivities in related Pd^0-catalyzed intramolecular C(sp^2)–H arylation reactions (Table 1, entries 9–11).[14] However, these ligands did not give appreciable enantioselectivities in this reaction.

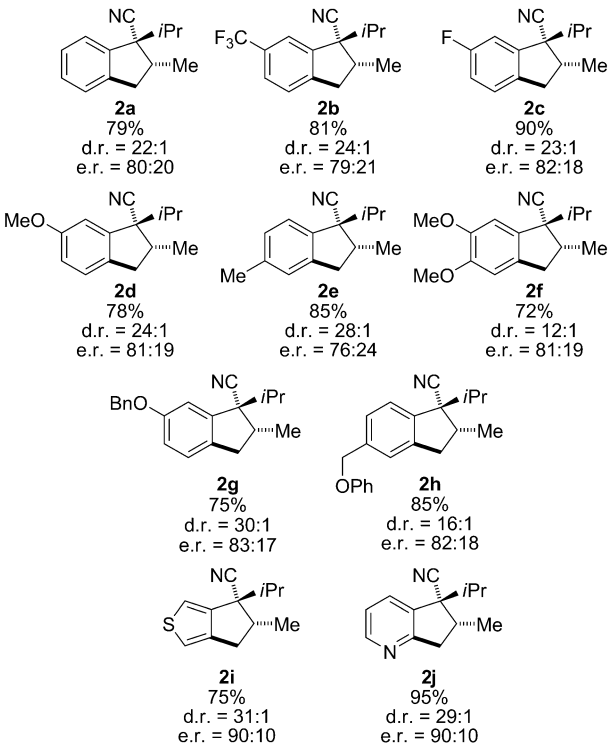
We then turned our attention to the binepine family of ligands **L9–12**.[15–16] Indeed, these ligands should possess the most similar electronic properties to trialkylphosphine ligands, which gave optimal results in the racemic reaction.[3e] Gratifyingly, although binepine **L9** was barely active (Table 1, entry 12), ligands **L10** and **11**, bearing cyclohexyl and *tert*-butyl P substituents, gave e.r. values above 70:30 (Table 1, entries 13 and 14), with a higher yield than Josiphos (**L4**; compare with Table 1, entry 5). The e.r. value could be further improved by decreasing the temperature to 110 °C (Table 1, entries 15 and 16), but we encountered problems with reproducibility that we attributed to the "ligand-free" background reaction (Table 1, entry 7).

As a consequence, more reliable conditions were sought with ligand **L11**, by first varying the nature of the Pd precatalyst (Table 1, entries 17 and 18), then the base (Table 1, entry 19), and finally by adding pivalic acid (PivOH; 30 mol %; Table 1, entry 20).[3c] Indeed, these last conditions were found to provide indane **2a** reproducibly in 81 % yield, with a d.r. of 6:1 and an e.r. of 78.5:21.5 at 140 °C. At this point, we were able to test NHC ligand **L13**, which gave an e.r. of 97.5:2.5 in the indoline system[8a] under the same conditions (Table 1, entry 21). For this system, this ligand gave a moderate yield and an e.r. of 66:34. Applying the same reaction conditions that were used for indolines[8a] failed to furnish better results (Table 1, entry 22).

A final significant improvement of the reaction catalyzed by Pd/**L11** was found by using DMSO as the solvent, which provided high diastereoselectivity (d.r. = 20:1), as well as a good yield (84 %) and enantioselectivity (e.r. = 79:21) without the need for added pivalic acid (Table 1, entry 23). In addition, no background reaction was found under these conditions (Table 1, entry 24). At this point the more bulky ligand **L12**, which was described by Fu and co-worker during the course of our study,[17] was synthesized and tested under these optimized conditions (Table 1, entry 25), but it did not provide any significant improvement on **L11**. Finally, the amount of catalyst could be decreased to a more reasonable loading (2.5 mol % $Pd(OAc)_2$/10 mol % **L11**), providing the optimized standard conditions for further studies (Table 1, entry 26).[18]

This comparison of different chiral ligands, some of which are known to provide good enantioselectivities in related processes, shows that different asymmetric C–H activation reactions require different chiral ligands, even for closely related systems (Scheme 1). In this case, binepines appear to be the most efficient and stereoselective ligands of the various types tested.

Next, we studied the reaction scope with substituted aryl bromides (Scheme 2).[19] Indanes **2a–h**, bearing various types of substituent on the benzene ring, were obtained from the corresponding aryl bromides in consistently good yields and diastereoselectivities, and with e.r. values between 76:24 (**2e**) and 83:17 (**2g**). The absolute configuration of indane **2d** was determined to be (*R*,*R*) by derivatization to form bromide **2k** and X-ray diffraction analysis of a single crystal (Figure 1).[20] The same absolute configuration was ascribed to other indanes (**2a–j**) by analogy. In addition to aryl bromides, the reaction was found to be applicable to pyridine and thiophene bromides, giving rise to bicyclic products **2i** and **j** in good yields and stereoselectivities. In particular, a better e.r. (9:1) was obtained for both **2i** and **j** than for **2a–h**, indicating that reduced steric hindrance at the *ortho* position of the incipient C_{Ar}–Pd bond has a positive influence on the enantioselectivity.



Scheme 2. Scope of the stereoselective synthesis of indanes. Reaction conditions: $Pd(OAc)_2$ (2.5 mol %), **L11** (10 mol %), K_2CO_3 (2 equiv), DMSO, 140 °C. For each compound: yield of the isolated mixture of diastereoisomers, d.r. determined by ^1H NMR analysis, e.r. determined by ^{19}F NMR analysis of the Mosher amides prepared after reduction of the nitrile to the primary amine (**2a–i**) or by HPLC on a chiral phase (**2j**). Absolute configurations of **2a–j** were ascribed by analogy to **2k**.

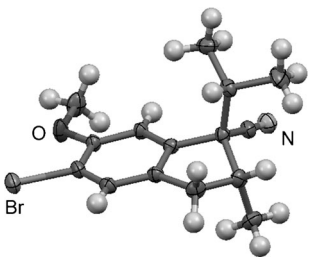


Figure 1. X-ray crystal structure of indane **2k**, obtained by electrophilic bromination of **2d** (ellipsoids are shown at 30 % probability).

As a first attempt at characterizing reaction intermediates to gain an insight into the origin of the enantioselectivity observed with binepine **L11**, we were able to isolate complex **6** from the oxidative addition of bromobenzene to a mixture of [Pd(cod)(CH_2SiMe_3)$_2$] (COD = 1,5-cyclooctadiene) and **L11** in hexane (Figure 2).[20] Complex **6**, which, to the best of our knowledge, is the first crystallographically characterized oxidative-addition complex with Pd and a binepine ligand, reveals a monomeric structure with two **L11** ligands bound to Pd. With the bulkier bromoarene **1a**, the intermediate Pd complex undergoing C–H activation should contain only one phosphine ligand,[3e] and thus it is difficult to extrapolate structural data from compound **6** to the corresponding oxidative-addition complex of **1a** (we have so far been unable to isolate the latter). In complex **6**, the Pd-bound benzene ring adopts a perpendicular orientation to the coordination plane, with its *ortho* hydrogen atoms in proximity to a naphthalene ring (H···C = 3.89 Å) and the *t*Bu group (H···C = 2.92 Å) of each binepine ligand (Figure 2). Such contacts, if preserved in the case of **1a**, would be key elements in the stereocontrol that could explain the stereochemical outcome of the reaction and could help in the design of more enantioselective ligand analogues. Future studies from our laboratory will be conducted along these lines.

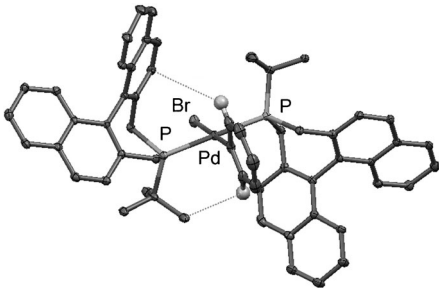


Figure 2. X-ray crystal structure of [Pd(Ph)Br(**L11**)$_2$] (**6**) obtained from the oxidative addition of PhBr to [Pd(cod)(CH_2SiMe_3)$_2$]/**L11**, with selected H···C contacts (ellipsoids are shown at 30% probability, most H atoms were omitted for clarity).

In conclusion, we have reported the first diastereo- and enantioselective synthesis of indanes and heterocyclic analogues by intramolecular C(sp^3)–H arylation by using a chiral Pd/binepine catalyst. The improvement in the enantioselectivity and the origins of the observed stereoinduction are currently being investigated.

Experimental Section

General procedure for the synthesis of indanes (Scheme 2): In a glovebox, $Pd(OAc)_2$ (1 mg, 0.0045 mmol), ligand **L11** (6.6 mg, 0.018 mmol), and K_2CO_3 (49 mg, 0.36 mmol) were added to a Schlenk tube containing a magnetic stirring bar. The flask was closed with a rubber septum and removed from the glovebox. A solution of aryl bromide (0.18 mmol) in dry DMSO (1 mL, c = 0.18 M) was added, the mixture was stirred for 5 min at room temperature and then for 14 h at 140 °C. After cooling to room temperature, the mixture was diluted with ethyl acetate and filtered through Celite. The solvents were evaporated under reduced pressure and the residue was purified by preparative TLC to provide the desired indane.

Acknowledgements

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Keywords: asymmetric catalysis · C–C coupling · C–H activation · palladium

[1] *Topics in Current Chemistry, Vol. 292* (Eds.: J.-Q. Yu, Z. Shi), Springer, Heidelberg, **2010**.

[2] For selected general reviews, see: a) F. Kakiuchi, N. Chatani, *Adv. Synth. Catal.* **2003**, *345*, 1077–1101; b) A. R. Dick, M. S. Sanford, *Tetrahedron* **2006**, *62*, 2439–2463; c) K. Godula, D. Sames, *Science* **2006**, *312*, 67–72; d) H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417–424; e) T. Newhouse, P. S. Baran, *Angew. Chem.* **2011**, *123*, 3422–3435; *Angew. Chem. Int. Ed.* **2011**, *50*, 3362–3374.

[3] a) O. Baudoin, A. Herrbach, F. Guéritte, *Angew. Chem.* **2003**, *115*, 5914–5918; *Angew. Chem. Int. Ed.* **2003**, *42*, 5736–5740; b) J. Hitce, P. Retailleau, O. Baudoin, *Chem. Eur. J.* **2007**, *13*, 792–799; c) M. Chaumontet, R. Piccardi, N. Audic, J. Hitce, J.-L. Peglion, E. Clot, O. Baudoin, *J. Am. Chem. Soc.* **2008**, *130*, 15157–15166; d) M. Chaumontet, R. Piccardi, O. Baudoin, *Angew. Chem.* **2009**, *121*, 185–188; *Angew. Chem. Int. Ed.* **2009**, *48*, 179–182; e) S. Rousseaux, M. Davi, J. Sofack-Kreutzer, C. Pierre, C. E. Kefalidis, E. Clot, K. Fagnou, O. Baudoin, *J. Am. Chem. Soc.* **2010**, *132*, 10706–10716.

[4] For selected examples, see: a) G. Dyker, *Angew. Chem.* **1992**, *104*, 1079–1081; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1023–1025; b) H. Ren, P. Knochel, *Angew. Chem.* **2006**, *118*, 3541–3544; *Angew. Chem. Int. Ed.* **2006**, *45*, 3462–3465; c) M. Lafrance, S. I. Gorelsky, K. Fagnou, *J. Am. Chem. Soc.* **2007**, *129*, 14570–14571; d) T. Watanabe, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2008**, *10*, 1759–1762; e) S. Rousseaux, S. I. Gorelsky, B. K. W. Chung, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 10692–10705.

[5] For recent reviews, see: a) R. Jazzar, J. Hitce, A. Renaudat, J. Sofack-Kreutzer, O. Baudoin, *Chem. Eur. J.* **2010**, *16*, 2654–2672; b) O. Baudoin, *Chem. Soc. Rev.* **2011**, *40*, 4902–4911.

[6] This definition excludes asymmetric C–H insertion. For a general review on stereoselective C–H functionalization, see: R. Giri, B.-F. Shi, K. M. Engle, N. Maugel, J.-Q. Yu, *Chem. Soc. Rev.* **2009**, *38*, 3242–3272.

[7] For asymmetric Pd^{II}-catalyzed C(sp^3)–H alkylation and arylation, see: a) B.-F. Shi, N. Maugel, Y.-H. Zhang, J.-Q. Yu, *Angew. Chem.* **2008**, *120*, 4960–4964; *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886; b) M. Wasa, K. M. Engle, D. W. Lin, E. J. Yoo, J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 19598–19601; for Ir^{I}-catalyzed C(sp^3)–H olefination, see: c) S. Pan, K. Endo, T. Shibata, *Org. Lett.* **2011**, *13*, 4692–4695.

[8] a) M. Nakanishi, D. Katayev, C. Besnard, E. P. Kündig, *Angew. Chem.* **2011**, *123*, 7576–7579; *Angew. Chem. Int. Ed.* **2011**, *50*, 7438–

7441; b) S. Anas, A. Cordi, H. B. Kagan, *Chem. Commun.* **2011**, *47*, 11483–11485.
[9] For a conceptually different enantioselective intermolecular C(sp^3)–H arylation, see: A. Renaudat, L. Jean-Gérard, R. Jazzar, C. E. Kefalidis, E. Clot, O. Baudoin, *Angew. Chem.* **2010**, *122*, 7419–7423; *Angew. Chem. Int. Ed.* **2010**, *49*, 7261–7265.
[10] H.-U. Blaser, W. Brieden, B. Pugin, F. Spindler, M. Studer, A. Togni, *Top. Catal.* **2002**, *19*, 3–16.
[11] We surmise that Me-DUPHOS and Josiphos diphosphines undergo in situ mono-oxidation concomitant to the reduction of $Pd(OAc)_2$ to give active phosphine–phosphinoxide ligands: I. Bonnaventure, A. Charette, *J. Org. Chem.* **2008**, *73*, 6330–6340.
[12] A. Chieffi, K. Kamikawa, J. Åhman, J. M. Fox, S. L. Buchwald, *Org. Lett.* **2001**, *3*, 1897–1900.
[13] J. F. Teichert, B. L. Feringa, *Angew. Chem.* **2010**, *122*, 2538–2582; *Angew. Chem. Int. Ed.* **2010**, *49*, 2486–2528.
[14] M. R. Albicker, N. Cramer, *Angew. Chem.* **2009**, *121*, 9303–9306; *Angew. Chem. Int. Ed.* **2009**, *48*, 9139–9142.
[15] S. Gladiali, E. Alberico, K. Junge, M. Beller, *Chem. Soc. Rev.* **2011**, *40*, 3744–3763.
[16] **L9–11** were synthesized from BINOL according to the literature procedure: K. Junge, G. Oehme, A. Monsees, T. Riermeier, U. Dingerdissen, M. Beller, *Tetrahedron Lett.* **2002**, *43*, 4977–4980.
[17] Y. Fujiwara, G. C. Fu, *J. Am. Chem. Soc.* **2011**, *133*, 12293–12297.
[18] The Pd/ligand ratio of 1:4 was found to be optimal.
[19] Bromo(hetero)arene reactants were synthesized in 2–6 steps from commercially available precursors. The diisopropyl substitution at the benzylic carbon was conserved for all examples because linear and cyclic alkyl groups preferentially give rise to olefins such as **4a** (for more details, see reference [3b]). In addition, only a nitrile group allowed the introduction of two isopropyl groups by dialkylation of the corresponding enolate. Compounds **2d–j** have not been reported before.
[20] CCDC-854015 (**2k**) and CCDC-848401 (**6**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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