Ru-Catalysed C–H Arylation of Indoles and Pyrroles with Boronic Acids: Scope and Mechanistic Studies

Carina Sollert,[a] Karthik Devaraj,[a] Andreas Orthaber,[b] Paul J. Gates,[c] and Lukasz T. Pilarski*[a]

Abstract: The Ru-catalysed C2–H arylation of indoles and pyrroles by using boronic acids under oxidative conditions is reported. This reaction can be applied to tryptophan derivatives and tolerates a wide range of functional groups on both coupling partners, including bromides and iodides, which can be further derivatised selectively. New indole-based ruthenacyclic complexes are described and investigated as possible intermediates in the reaction. Mechanistic studies suggest the on-cycle intermediates do not possess a para-cymene ligand and that the on-cycle metalation occurs through an electrophilic attack by the Ru centre.

Introduction

Transition metal-catalysed C–H activation has received enormous attention in recent years as a viable synthetic strategy; it offers previously impossible transformations, new selectivities and shortened routes in the preparation of organic molecules.[1, 2] The importance of indole and pyrrole units in bioactive molecules has fuelled continued efforts to develop new approaches to their selective C–H functionalisation.[3] For instance, the 2-arylindole unit appears in several natural products,[4] potential microtubulin polymerisation inhibitors, and molecules of interest for their antifungal and antimicrobial properties.[5] To date, indole and pyrrole C–H arylation has been developed most extensively by using aryl halide[6] and hypervalent iodine[7] electrophiles. Meanwhile, the complementary method in which anionic coupling partners[8] and an external oxidant are employed has received less attention. The dehydrogenative coupling of two (hetero)arene C–H units[9] represents, in principle, the most atom economical and desirable of these approaches. However, at present, the conjunction of two selective, compatible C–H activation processes often presents regioselectivity/scope limitations, the need for a large excess of one coupling partner, harsh conditions, and/or expensive additives. In this context, organoboronates[10] are an attractive alternative for oxidative direct arylation reactions,[11–14] by offering low cost, diversity, and ease of activation, amongst other advantages.

In Ru-catalysed C–H functionalisation reactions, which have attracted considerable recent interest (Figure 1),[15, 16] the use of boronates has remained rare. Ru0-catalysed C–H arylation reactions...
tions developed by the groups of Kakuchi,[17] and later Sames[18] and Schnürch,[19] require protected boronates. Unprotected boronic acids have been used in Ru-catalysed C–H arylation reactions with only a handful of substrates[20] and virtually no accompanying mechanistic investigation, despite a recent surge in the development of various related oxidative transformations.[21] In addition, the use of aryl halides by Ackermann and Lygin[22] under carboxylate-assisted conditions[23] stands as the only example to date of Ru-catalysed indole or pyrrole C–H arylation.[24]

Herein, we report the use of unprotected, diversely functionalised arylboronic acids in the Ru-catalysed C2–H arylation of indoles and pyrroles. We also describe the synthesis of new ruthenacyclic complexes and examine their role in the reaction, which is of direct relevance to commonly proposed mechanisms.

Results and Discussion

Reaction optimisation

We undertook our investigation with indole derivative 1a as the test-bed substrate. Sames and co-workers[18] and Ackermann and Lygin[20,24] pioneered the use of pyrimidine as a versatile, removable directing group[25] for catalytic C–H functionalisation. A number of groups have since described the use of this species in both the synthesis[24,26] and derivatisation of indoles and pyrroles by using various metals.[27–32]

In our initial experiments, we isolated 2a in 37% yield from the coupling of 1a and 4-tolylboronic acid with 2.5 mol% [RuCl(p-cymene)] and 1.5 equivalents of Ag2O in THF (Table 1, entry 1). Replacement of the oxidant with Cu(OAc)2-H2O (1 equiv) improved the yield to 64% and including water raised the yield further to 86% (Table 1, entry 3). A combination of substoichiometric amounts of Cu(OAc)2-H2O (0.5 equiv) and O2 proved less effective (Table 1, entry 4). As an additive, AgSbF6 proved superior to AgBF4, AgPF6, and KPF6. The addition of organic or inorganic bases, including carboxylates and carbonates (see Table 1, entry 5 and Table S5 in the Supporting Information),[33] was detrimental to the catalysis, whereas HOAc (up to 4 equiv) had no effect on the yield.[34] Replacement of the catalyst precursor with [Ru(OAc)2(p-cymene)] (5 mol%) or the more expensive [RhCp*Cl2]2 (2.5 mol%); Cp* = 1,2,3,4,5-pentamethylcyclopentadienyl) gave lower yields (Table 1, entries 9 and 10, respectively). As solvent, iPrOH proved slightly superior to the THF/H2O system (Table 1, entries 7 and 8), presumably due to the formation of alkoxoboronates in situ, giving improved nucleophile solubility and slower protodeborylation.[29] Accordingly, iPrOH was selected as the default solvent for the rest of our exploration of the reaction scope. All the arylation reactions occurred exclusively at C2. The desired reaction was not observed if the Ru catalyst, oxidant, or silver additive were excluded. Under the same conditions, arylation did not occur with indoles bearing oxygen-based directing groups, nor with a variety of other substrates commonly used in Ru-catalysed C–H arylation reactions (see the Supporting Information for further details). Thus, the pyrimidyl group seemed uniquely privileged under the conditions we explored.

Substrate scope

The reaction showed high tolerance towards a wide range of arylboronic acids, including those bearing nitro (2h), ketone (2i), alkenyl (2k), silyl (2l), sulfonyl (2m), ferrocenyl (2w), and halogen groups (Scheme 1). Tolerance of aryl iodides (2f) is both rare and complementary to their frequent use as oxidants/electrophiles in C–H arylation reactions. To the best of our knowledge, this C–H arylation of indoles is the first in which the C–I functionality is preserved. Reactions with 4-trifluoromethyl- and 4-ace-tlyphenylboronic acids gave higher yields when iPrOH was replaced with the THF/H2O solvent system. Protected boronic acids,[10,35] such as their pino-catal boronate (-Bpin), N-methylmimidacetyl boryl (-Bmida),[36] or potassium trifluoroborate (-BF,K)[37] derivatives, were not effective under our conditions. This outcome is in line with the requirement for their prior hydrolysis and the rate acceleration observed under acidic conditions in related C–H arylation reactions.[34] Variousily substituted indoles also selectively underwent the C–H arylation reaction (Scheme 2). Good yields were obtained with bromide and iodide groups on either or both coupling sites.

---

Table 1. Selected results from optimisation studies.[a]

| Entry | Catalyst [mol%] | Oxidant [equiv] | Additives | Solvent | Yield [%] |
|-------|-----------------|-----------------|-----------|---------|-----------|
| 1     | [RuCl2(p-cymene)] (2.5) | Ag2O (1.5) | AgSbF6 (0.12) | THF | 37[a] |
| 2     | [RuCl2(p-cymene)] (2.5) | Cu(OAc)2-H2O (1) | AgSbF6 (0.12) | THF | 64 |
| 3     | [RuCl2(p-cymene)] (2.5) | Cu(OAc)2-H2O (1) | AgSbF6 (0.12) | THF | 86 |
| 4     | [RuCl2(p-cymene)] (2.5) | Cu(OAc)2-H2O (0.5) | AgSbF6 (0.12) | THF | 56 |
| 5     | [RuCl2(p-cymene)] (2.5) | Cu(OAc)2-H2O (1) | AgSbF6 (0.12) | KOAc (1.0) | 0 |
| 6     | [RuCl2(p-cymene)] (2.5) | Cu(OAc)2-H2O (1) | AgSbF6 (0.12) | THF | 0 |
| 7     | [RuCl2(p-cymene)] (2.5) | Cu(OOCOCF3)2 (1) | AgSbF6 (0.12) | iPrOH | 89 |
| 8     | [RuCl2(p-cymene)] (2.5) | Cu(OAc)2-H2O (1) | AgSbF6 (0.12) | iPrOH | 98 |
| 9     | [Ru(OAc)2(p-cymene)] (5) | Cu(OAc)2-H2O (1) | AgSbF6 (0.12) | THF | 53 |
| 10    | [Cp*RhCl2(p-cymene)] (2.5) | Cu(OAc)2-H2O (1) | AgSbF6 (0.12) | H2O (3.7) | 52 |

[a] 1a (0.15 mmol), boronic acid (0.45 mmol), solvent (0.5 mL). [b] Yield was determined by H NMR spectroscopic analysis with respect to 1,3,5-trimethoxybenzene (0.05 mmol), which was added after the end of the reaction. [c] Yield of the isolated product.
The 3-methylindole derivative 3g was obtained in 75% yield, despite the proximate steric bulk, whereas indoles with 6-methoxycarbonyl (3c), 5-nitro (3f), and 3-cyano (3h) groups gave worse performance, hinting at the importance of the nucleophilicity of the indole unit. The protocol could further be extended to the phthaloyl-protected tryptophan derivative 1m (Scheme 3). In addition to standard analysis by NMR spectroscopy and mass spectrometry, products 2t, 3j, and 3m were characterised by X-ray crystallography studies.

Pyrroles also proved amenable to the arylation reaction with various boronic acids (Scheme 4). Substrate 4a (R1 = H) gave a separable mixture of mono- (5a) and diphenylated (5a') products in a combined yield of 42%. The 2-ethylpyrrole derivatives 4b-d afforded good-to-excellent yields, with arylation occurring exclusively at C2 for both electron-poor and electron-rich boronic acids to give products 5b-d. 2-Methoxycarbonyl-substituted pyrrole 5e was not formed, which is consistent with the nucleophilicity requirements of the indole substrates.

The iodide group of 3i underwent selective and efficient Heck alkenylation, highlighting the potential for derivatisation partners (Scheme 2; 3e and 3i-k). The 3-methylindole derivative 3g was obtained in 75% yield, despite the proximate steric bulk, whereas indoles with 6-methoxycarbonyl (3c), 5-nitro (3f), and 3-cyano (3h) groups gave worse performance, hinting at the importance of the nucleophilicity of the indole unit. The protocol could further be extended to the phthaloyl-protected tryptophan derivative 1m (Scheme 3). In addition to standard analysis by NMR spectroscopy and mass spectrometry, products 2t, 3j, and 3m were characterised by X-ray crystallography studies.

Pyrroles also proved amenable to the arylation reaction with various boronic acids (Scheme 4). Substrate 4a (R1 = H) gave a separable mixture of mono- (5a) and diphenylated (5a') products in a combined yield of 42%. The 2-ethylpyrrole derivatives 4b-d afforded good-to-excellent yields, with arylation occurring exclusively at C2 for both electron-poor and electron-rich boronic acids to give products 5b-d. 2-Methoxycarbonyl-substituted pyrrole 5e was not formed, which is consistent with the nucleophilicity requirements of the indole substrates.

The iodide group of 3i underwent selective and efficient Heck alkenylation, highlighting the potential for derivatisation partners (Scheme 2; 3e and 3i-k). The 3-methylindole derivative 3g was obtained in 75% yield, despite the proximate steric bulk, whereas indoles with 6-methoxycarbonyl (3c), 5-nitro (3f), and 3-cyano (3h) groups gave worse performance, hinting at the importance of the nucleophilicity of the indole unit. The protocol could further be extended to the phthaloyl-protected tryptophan derivative 1m (Scheme 3). In addition to standard analysis by NMR spectroscopy and mass spectrometry, products 2t, 3j, and 3m were characterised by X-ray crystallography studies.
of the newly installed aryl group whilst retaining an electrophilic coupling substrate on the indole (Scheme 5).

Mechanistic Considerations
Investigation of putative ruthenacyclic intermediates

We prepared the previously unreported complexes [7]Cl, [7]OAc, and [7-OH]SbF₆ (Scheme 6) to probe the potential role of ruthenacyclic intermediates. In addition to standard H and ¹³C NMR spectroscopy and mass spectrometry, complex [7]Cl was characterised by means of X-Ray crystallography (see the Supporting Information for further details).

Replacing [[RuCl₂(p-cymene)] with [7]Cl, [7]OAc, or [7-OH]SbF₆ gave 86, 60, and 40% spectroscopic yields of 2b, respectively, under the standard reaction conditions shown in Scheme 1. Thus, species 7 are either catalytically active or are converted into catalytically active species in situ (see below).

Species [7]tol was not observed on exposure of [7]Cl, [7]OAc, or [7-OH]SbF₆ to 4-tolyboronic acid with or without Cu(OAc)₂·H₂O present (Table 2). Product 2a formed in the absence of Cu(OAc)₂·H₂O from both [7]Cl and [7-OH]SbF₆ (15% and trace yields, respectively), indicating that transmetalation and reductive elimination are possible for Ru⁷ species. These results complement the finding by Lan and co-workers that a Rh⁷Cp⁺ analogue of [7]Cl underwent transmetalation and reductive elimination with benzo[b]thiophene in the absence of an oxidant. Traces of 2a were also observed for both [7]OAc and [7-OH]SbF₆ in the presence of Cu(OAc)₂·H₂O. An intractable mixture of indole-containing species constituted the mass balance of these reactions.

Hydrogen–deuterium exchange studies

Compound 1a gave no H/D exchange at either C2 or C3 in the presence of D₂O, catalytic [[RuCl₂(p-cymene)]], and AgSbF₆ (Table 3, entry 1) at 23 °C, although the ¹H NMR spectrum of the reaction mixture revealed the complete conversion of the catalyst precursor to ruthenacycle [7-OD]SbF₆. Substrate 1a underwent significant C3–H/D and modest C2–H/D exchange when the same experiment was performed at 60 °C, again with the quantitative formation of [7-OD]SbF₆ (Table 3, entry 2). On heating to 80 °C, only traces of [7-OD]SbF₆ were observed, with the concomitant formation of uncoordinated para-cymene and 64% deuterium incorporation at C3 (Table 3, entry 3). On heating to 100 °C, no [7-OD]SbF₆ remained and

Table 2. Transmetalation experiments.

| Entry | Complex | Cu(OAc)₂·H₂O | [7]tol | 2a |
|-------|---------|--------------|-------|----|
| 1     | [7]Cl   | yes          | –     | –  |
| 2     | [7]Cl   | no           | –     | –  |
| 3     | [7]OAc  | yes          | –     | traces |
| 4     | [7]OAc  | no           | –     | –  |
| 5     | [7-OH]SbF₆ | yes | –     | traces |
| 6     | [7-OH]SbF₆ | no | –     | traces |

[a] A symmetrical complex of the type [[Ru(p-cymene)]X₂] was observed by ¹H NMR spectroscopic analysis at the end of the reaction. [b] Traces of 2a were also observed for both [7]OAc and [7-OH]SbF₆ in the presence of Cu(OAc)₂·H₂O. An intractable mixture of indole-containing species constituted the mass balance of these reactions.

Table 3. Hydrogen–deuterium exchange studies.

| Entry | [7-OD]SbF₆ | temp, 18 h |
|-------|-------------|------------|
| 1     | [7]Cl       | –          |
| 2     | [7]Cl       | –          |
| 3     | [7]OAc     | –          |
| 4     | [7]OAc     | –          |
| 5     | [7-OH]SbF₆ | –          |
| 6     | [7-OH]SbF₆ | –          |

[a] Average of two runs. [b] Free para-cymene observed by ¹H NMR spectroscopic analysis. [c] [[RuCl₂(p-cymene)]₆] was excluded. [d] [[RuCl₂(p-cymene)]₆] and AgSbF₆ were excluded.

Scheme 5. Selective derivatisation of the aryl halide functionality. TBAB = tetrabutylammonium bromide.

Scheme 6. Preparation of ruthenacycles [7]Cl, [7]OAc, and [7-OH]SbF₆. Conditions: i) [[RuCl₂(p-cymene)]₆] (0.5 equiv), MeOH, RT, 24 h, 78% ; ii) AgOAc (2.5 equiv), MTBE, RT, 24 h, 80% ; iii) AgSbF₆ (1.1 equiv), H₂O (6.9 equiv), D₂O (3.7 equiv), temp, 18 h; iv) – – 100%.
uncoordinated *para*-cymene was observed, but C–H exchange increased only incrementally (Table 3, entry 4). Finally, heating to 120 °C gave no observable Ru–cymene complexes, with 1a showing 60% C2–H/D exchange (Table 3, entry 5). Thus, the greatest degree of reversible C2–H activation occurred after complete loss of *para*-cymene from the Ru centre. When ([RuCl(p-cymene)])2 was excluded from the reaction mixture, 15% C2–H/D and 68% C3–H/D exchange was observed at 120 °C. Kanai and co-workers found that simple Lewis acids, such as Sc(OTf)3, promote similar levels of C3-selective exchange for 1a,29 which we attribute to the presence of Ag+ ions in our reaction (Table 3, entries 6 and 7). Analogous experiments with N-acetylindole or 1-(pyrimidin-2-yl)benzimidazole did not give C2–H/D exchange, which is consistent with the requirement for nucleophilicity of the heteroarene and the inability of the acetyl group to effect C2 arylation under our catalytic conditions (see Figure S1 in the Supporting Information).

**Importance of the *para*-cymene ligand**

Cymene-ligated Ru complexes have frequently been invoked as catalytic intermediates in C–H functionalisation reactions. For the phenylation of 1a under our conditions, complete loss of the cymene ligand from the Ru coordination sphere could be confirmed by 1H NMR spectroscopic analysis on cooling the reaction mixture to room temperature just after 10 minutes (Scheme 7). Conversion into 2b was 50% at this point. The reaction mixture was reheated to 120 °C for a further 7 hours, after which the conversion into 2b increased to 67%, with cymene remaining uncoordinated.

![Scheme 7](image)

**Discussion of the mechanism**

We suggest that although initial ruthenation of the indole–pyrimidine unit occurs easily under our conditions, [7-OH]3SbF6 acts as a precursor rather than as a true catalytic intermediate. The inferior performance of several other transition-metal salts in our optimisation studies (see Table S2 in the Supporting Information) may indicate that the formation of such ruthenacycles at the beginning of the reaction—but prior to the catalysis—is advantageous. Facile exchange of the *para*-cymene ligand in ruthenacycles in the presence of excess nitrogen donors is well documented. For example, Jutand and co-workers reported that complexes of the type [Ru(k2-N,N-2-phenylpyridine)(MeCN)]OPiv (OPiv = dimethylpropanoate) formed easily in the presence of excess MeCN, but were catalytically inactive in the arylation of phenylpyridines with aryl halides.30 We propose that under our catalytic conditions the pyrimidine groups of substrates 1 or 4 displace the *para*-cymene ligand of cyclometalated species 7 and on-cycle intermediates may have more than one pyrimidyl heteroarene ligand in the ruthenium coordination sphere. Thus, 1 or 4 could act as spectator ligands in the cycle prior to their own C2 ruthenation. This outcome would be consistent with the poor performance of complexes [7Cl], [7]OAc, and [7-OH]3SbF6 in attempts to induce transmetalation and reductive elimination in the absence of unmetallated substrates 1 (Table 2). It is also in agreement with the need for a sufficiently strongly o-donating directing group, hence why oxygen-based directing groups42 proved ineffective.

With respect to the on-cycle C–H activation, the following observations suggest electrophilic attack by the ruthenium centre on the heteroarene: 1) the significant increase in efficiency when silver additives are used, 2) higher yields with electron-rich substrates, 3) failure of 1-(pyrimidin-2-yl)benzimidazole to undergo C–H/D exchange or C2 arylation, 4) that using Ag2O as an oxidant gives 2a in a moderate yield (Table 1, entry 1) in the absence of carboxylates, 5) that C–H ruthenation of 1a occurred in the absence of carboxylates during H/D exchange experiments (Table 3), suggesting the plausibility of an analogous on-cycle ruthenation reaction. In addition, KOAc had a detrimental effect on the catalysis (Table 1, entry 5) and no significant effect on the rate of C2–H/D exchange, whereas Cu(OAc)2 inhibited the rate of C2–H/D exchange (see Table S7 in the Supporting Information).

Therefore, our proposed mechanism is complementary to the carbonate-assisted Ru-catalysed C–H functionalisation reactions22 studied in depth by the groups of Ackermann43 and Dixneuf,44 in which aryl halide coupling partners were used. This mechanism also agrees with recent mechanistic proposals for related reactions in which electrophilic cationic Ru intermediates have been suggested.44

**Conclusion**

We have developed an oxidative, Ru-catalysed C2–H selective arylation reaction of indoles and pyrroles with boronic acids as the aryl source. The reaction shows high functional-group tolerance for both coupling partners, including halides, thus preserving the scope of the reaction for selective subsequent manipulation of the products. *Para*-Cymene-ligated ruthenacycles give, at best, poor yields in attempts at transmetalation, but lose the *para*-cymene ligand under our catalytic conditions; therefore, these complexes are unlikely on-cycle intermediates. Efforts to broaden this methodology to other transformations and substrates are ongoing in our laboratory.

**Experimental Section**

**General arylation procedure**

([RuCl(p-cymene)])2 (7.6 mg, 0.013 mmol, 2.5 mol%), substrate 1 or 4 (0.5 mmol), boronic acid (1.5 mmol), Cu(OAc)2·H2O (100 mg, 0.50 mmol), and AgSbF6 (21 mg, 0.06 mmol, 12 mol%) were added

[Experimental details and references to specific experimental procedures and conditions are provided in the Supporting Information.]
Keywords: catalysis - C-H activation - heterocycles - reaction mechanisms - ruthenium

[1] Handbook of C–H Transformations: Applications in Organic Synthesis (Ed.: G. Dyker), Wiley-VCH, Weinheim, 2005.

For selected reviews, see: a) J. Wencel-Delord, F. Glorius, Angew. Chem. Int. Ed. 2013, 52, 369–375; b) L.G. Mercier, M. Leclerc, Acc. Chem. Res. 2013, 46, 1597–1605; c) J.Y. Yamaguchi, A.D. Yamaguchi, K. Itami, Angew. Chem. 2012, 124, 9092–9142; Angew. Chem. Int. Ed. 2012, 51, 8960–8990; d) T. Brückl, R.D. Baxter, Y. Ishihara, P.S. Baran, Acc. Chem. Res. 2012, 45, 826–839; e) D.Y. Chen, S.W. Youn, Chem. Eur. J. 2012, 18, 9452–9474.

For selected reviews, see: a) S.A. Girard, T. Knauber, C.-J. Li, Angew. Chem. 2014, 126, 76–103; b) For Pd-catalysed examples, see: a) S.K. Kirchberg, S. Tani, K. Ueda, J. Org. Chem. 2009, 74, 4972–4973; b) R.J. Fritz, S.K. Kirchberg, S. Tani, K. Ueda, J. Org. Chem. 2009, 74, 4974–4979; c) For Pd-catalysed examples using indole substrates, see: a) S.K. Kirchberg, S. Tani, K. Ueda, J. Org. Chem. 2009, 74, 4972–4973; b) S.Y. Ichikawa, Y. Inoue, Y. Noda, T. Yamashita, K. Fujita, T. Watanabe, T. Sugasawa, Angew. Chem. Int. Ed. 2009, 48, 1081–1084; c) E.M. Beck, M.J. Gaunt, Top. Curr. Chem. 2010, 292, 85–121; d) G.Broggini, E.M. Beckalli, A. Fasana, S. Zaggia, Beilstein J. Org. Chem. 2012, 8, 1730–1746; e) N. Lebrasseur, I. Larroza in Advances in Heterocyclic Chemistry. Vol. 105 (Ed: K. Alcan), Academic Press, 2012, Chapter 4, pp. 309–351.

Acknowledgements

We are grateful to the Swedish Research Council (Vetenskapsrådet) for generous funding and Dr. Emilien Dehoy (Uppsala University) for help with the preparation of the starting materials. We also thank Professor Lars Engman, Dr. Eszter Borbas, and Dr. Johanna Larsson for proofreading of the manuscript.
For a Ru-catalysed example with unusual meta selectivity, see: a) N. Hofmann, L. Ackermann, J. Am. Chem. Soc. 2013, 135, 5877–5884; b) O. Saidi, J. Marofie, A. E. W. Ledger, P. M. Liu, M. F. Mahon, G. Kociok-Kohn, M. K. Whitley, C. G. Frost, J. Am. Chem. Soc. 2011, 133, 19298–19301; c) W. R. Reynolds, P. M. Liu, G. Kociok-Kohn, C. G. Frost, Synlett 2013, 24, 2687–2690.

(17) a) F. Kakikuchi, S. Kan, K. Igi, N. Chatani, S. Murali, J. Am. Chem. Soc. 2003, 125, 1698–1699; b) F. Kakikuchi, Y. Matsuura, S. Kan, N. Chatani, J. Am. Chem. Soc. 2005, 127, 5936–5945.

(18) S. J. Pastine, D. V. Grilbókov, D. Sames, J. Am. Chem. Soc. 2006, 128, 14220–14221.

(19) a) M. Schwarz, N. Dastbaravardeh, K. Kirchner, M. Schnürch, M. Mihovic, Monatsh. Chem. 2013, 144, 539–552; b) N. Dastbaravardeh, M. Schnürch, M. D. Mihovicová, Org. Lett. 2012, 14, 1930–1933; c) N. Dastbaravardeh, K. Kirchner, M. Schnürch, M. D. Mihovicová, J. Org. Chem. 2013, 78, 6518–6527.

(20) a) H. Li, W. Wei, Y. Xu, C. Zhang, X. Wan, Chem. Commun. 2011, 47, 1497–1499; b) R. K. Chinnagolla, M. Jeganmohan, Org. Lett. 2012, 14, 5246–5249; c) R. K. Chinnagolla, M. Jeganmohan, Chem. Commun. 2014, 50, 2442–2444; d) H. Li, Y. U. E, X. Shi, W. Wei, X. Wu, X. Wan, Chem. Commun. 2011, 47, 7880–7882.

(21) For a recent review of the role of carboxylates in C–H functionalisation, see: L. Ackermann, Chem. Rev. 2011, 111, 1315–1345.

(22) A single, low-yielding Ru-catalysed example has recently been reported by: Y. Zhao, V. Snekuks, Adv. Synth. Catal. 2014, 356, 1527–1532.

(23) L. Ackermann, A. V. Lygin, Org. Lett. 2012, 14, 764–767.

(24) For reviews on removable directing groups, see: a) G. Rousseau, B. Breit, Angew. Chem. 2011, 123, 2488–2543; Angew. Chem. Int. Ed. 2011, 50, 2450–2494; b) C. Wang, Y. Huang, Synlett 2013, 144, 145–149.

(25) a) J. Chen, Q. Peng, Y. Sun, X. Li, J. Org. Chem. 2011, 76, 3523–3526; b) W. Song, L. Ackermann, Chem. Commun. 2013, 49, 6638–6640.

(26) Cu-catalysed examples: a) X. Kou, M. Zhao, X. Qiao, Y. Zhu, X. Tong, Z. Shen, Chem. Eur. J. 2013, 19, 16888–16888; b) M. Nishino, K. Hirano, T. Satoh, M. Miura, Angew. Chem. 2012, 124, 7999–7933; Angew. Chem. Int. Ed. 2013, 52, 6993–6997; c) R. Odani, M. Nishino, K. Hirano, T. Satoh, M. Miura, Heterocycles 2014, 88, 595–602; d) C. Pan, H. Jin, P. Xu, X. Liu, Y. Cheng, C. Zhu, J. Org. Chem. 2013, 78, 9494–9498; e) H. Xu, X. Qiao, S. Yang, Z. Shen, J. Org. Chem. 2014, 79, 4414–4422.

(27) Pd-catalysed examples: a) C. Pan, H. Jin, X. Liu, Y. Cheng, C. Zhu, Chem. Commun. 2013, 49, 2933–2935; b) Z. Wang, F. Song, Y. Zhao, Y. Huang, L. Song, D. Zhao, J. Lan, J. Chem. Eur. J. 2012, 18, 16616–16620; c) S. Xu, X. Huang, X. Hong, B. Xu, Org. Lett. 2012, 14, 4614–4617; d) X.-B. Yan, Y.-W. Shen, D.-Q. Chen, P. Gao, Y.-X. Li, X.-R. Song, X.-Y. Liu, Y.-M. Liang, Tetrahedron 2014, 70, 7490–7495; e) W. Zhou, P. Li, Y. Zhang, L. Wang, Adv. Synth. Catal. 2013, 355, 2343–2352.