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Palladium-Catalysed Dehydrogenative sp^3 C–H Bonds Functionalisation into Alkenes: A Direct Access to *N*-Alkenylbenzenesulfonamides

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Dedicated to Professor Max Malacria on the occasion of his 65th birthday.

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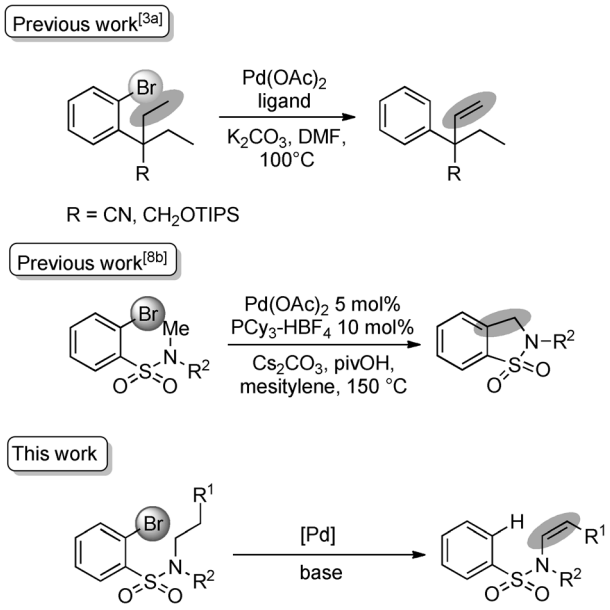
Abstract: The palladium-catalysed dehydrogenation of sp^3 carbon-hydrogen bonds of *N*-alkylbenzenesulfonamides allows a simple access to *N*-alkenylbenzenesulfonamides. The reaction proceeds with easily accessible catalysts, with pivalate as a base, and allows a variety of substituents both on nitrogen and on the arene moiety.

Keywords: aryl halides; atom economy; C–H bond functionalisation; dehydrogenation; palladium

In recent years, the metal-catalysed functionalisation of C–H bonds has emerged as a powerful method for the simple access to useful molecules for materials or biological applications. Most of the examples of C–H bond functionalisation concern the formation of C–C bonds *via* arylations, alkenylations or alkylations.[1,2] On the other hand, the dehydrogenation process of alkanes to produce reactive alkenes *via* sp^3 C–H bond activation has attracted less attention despite its potential.

In 2003, Baudoin and co-workers described the palladium-catalysed C–H functionalisation of alkyl groups linked at a benzylic carbon to give alkenes (Scheme 1, *top*).[3a–d] The formation of enamines from alkylamines,[4] by iridium or cobalt hydrogen transfer catalysts, has initially been described by Goldman[4a] and Brookhart[4b] and co-workers. The palladium-catalysed dehydrogenation of alkyl groups linked to a carbonyl in the presence of benzoquinone has been recently reported by Yu and co-workers, from a cyclopentylcarboxylic amide derivative, but containing an *N*,*N*-chelating group.[5] The dehydrogenation of cyclohexanones and also the coupling of propiophenones with benzoic acids combining dehydrogenation and decarboxylation has also been reported.[6,7] Ruthenium- and iridium-catalysed alkylations at the β-position of alkylamines have been performed and shown to proceed *via* dehydrogenation into enamines.[4e]

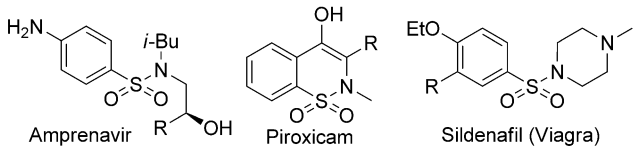
Fagnou has reported the intramolecular alkane arylation of *N*-methylsulfonamides using $Pd(OAc)_2/PCy_3$ catalyst with Cs_2CO_3 as base in the presence of pivalate as Pd-ligand (Scheme 1, *middle*).[8,9] By contrast, to the best of our knowledge, the synthesis of *N*-alk-



Scheme 1.

enylbenzenesulfonamides easily obtained *via* dehydrogenation of *N*-alkylbenzenesulfonamides has not been reported yet (Scheme 1, *bottom*).

However, benzenesulfonamides are a very important class of pharmaceutical compounds. For example, Amprenavir is a protease inhibitor used to treat HIV infection, Piroxicam is a non-steroidal anti-inflammatory drug and Sildenafil is used to treat erectile dysfunction (Scheme 2).



Scheme 2. Examples of bioactive benzenesulfonamides.

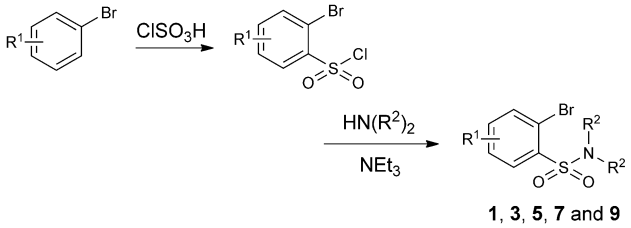
Among the benzenesulfonamides, reactive *N*-alkenylbenzenesulfonamides are an important family of substrates allowing the access to a very wide variety of functional benzenesulfonamides.[10] For example, in tetrahydropyridines, their carbon-carbon double bonds have been transformed into β-cyanohydrins,[10a] or allylated with allylsilane.[10b] They are also simply transformed into cyclobutanes,[10d] cyclopropanes,[10e] diols,[10f] epoxides[10g] and to pyrido-fused tetrahydroquinolines.[10h]

Only a few methods lead to the synthesis of *N*-alkenylbenzenesulfonamides, including the Ru-catalysed ring closing methathesis,[11a,b] the Ru or Rh isomerisation of *N*-allyl derivatives,[11c,i] the Au or Rh cycloisomerisation,[11d–f] or the elimination of HBr[11g] or H_2O.[11h] To the best of our knowledge, no direct dehydrogenative synthesis of *N*-alkenylbenzenesulfonamides, from easily accessible *N*-alkylbenzenesulfonamides, has been reported.

Herein, we describe a novel dehydrogenation process based on an intramolecular reaction with palladium(II) species and a direct access to a variety of *N*-alkenylbenzenesulfonamide derivatives using simple palladium(II)-catalysed sp^3 C–H functionalisation/dehydrogenation of *N*-alkyl-2-bromobenzenesulfonamides under economically viable conditions using a moderate catalyst loading associated to pivalate base.

The bromobenzenesulfonamides were first easily prepared by the chlorosulfonation of some bromobenzene derivatives in the presence of chlorosulfonic acid, which allows the one step access to a variety of 2-bromobenzenesulfonyl chlorides,[12] and then by the reaction of secondary amines with these benzenesulfonyl chlorides which provides a variety of the 2-bromobenzenesulfonamides in high yields (Scheme 3).

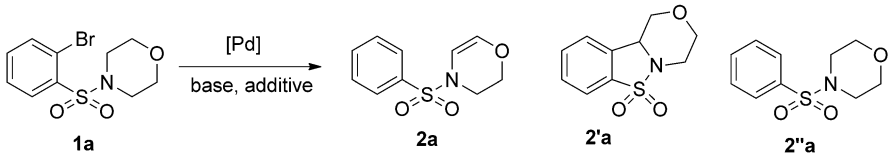
We then examined the influence of the conditions on the product formation (Table 1). The reaction of 4-



Scheme 3. Synthesis of 2-bromobenzenesulfonamides.

(2-bromobenzenesulfonyl)-morpholine **1a** using $Pd(OAc)_2$/Xantphos catalyst and K_2CO_3 as base led to a mixture of dehydrogenated morpholine derivative **2a** in 65% selectivity and debrominated side-product **2″a** in 23% selectivity with full conversion of **1a** (Table 1, entry 1). The intramolecular alkane arylation product **2′a** was detected in only 12% selectivity, although formation of such 5- to 7-membered rings *via* intramolecular palladium-catalysed direct sp^2[13] or sp^3[14] C–H arylations seems to occur easily. As the presence of benzoquinone as oxidant in some dehydrogenation reactions has been found to be profitable,[5] we employed 0.2 equiv. of this additive to obtain a more selective reaction, and **2a** was formed in 86% selectivity (Table 1, entry 2). The use of KOAc as base in the presence of benzoquinone led to a slightly lower selectivity in **2a** (70%) (Table 1, entry 3). Dppf as ligand or $PdCl(C_3H_5)$(dppb) catalyst did not increase the selectivity in the desired product **2a**; whereas, ligand-free $Pd(OAc)_2$ produces **2a** in 87–91% selectivity (Table 1, entries 4–7). The use of Ag_2CO_3 was completely ineffective; whereas a clean reaction was observed in the presence of KOpiv as base/ligand, (Table 1, entries 8 and 9). We then found that a complete conversion of **1a** with a high selectivity in **2a** could also be obtained in the absence of benzoquinone, but using 2.5 mol% of ligand-free $Pd(OAc)_2$ and KOpiv as base/ligand to give **2a** in 89% selectivity and in 75% isolated yield (Table 1, entry 10). Then, the influence of several bases in the absence of benzoquinone was examined using 2.5 mol% of ligand-free $Pd(OAc)_2$. Lower conversions of **1a** were obtained with KOAc or CsOAc than with KOpiv (Table 1, entries 11 and 12). In the presence of K_2CO_3, **2a** was formed in 69% selectivity, and the intramolecular cyclisation product **2′a** was also obtained in 15% selectivity and in 11% isolated yield (Table 1, entry 13). No formation of intramolecular cyclisation product **2′a** was detected using other carbonate bases, Na_2CO_3 or Li_2CO_3, but the selectivity in **2a** was not improved (Table 1, entries 14 and 15). The use of stronger base *t*-BuOK led to an exclusive formation of debrominated compound **2″a** (Table 1, entry 16). The reaction performed with ligand-free $Pd(OAc)_2$/KOpiv at 130 °C instead of 150 °C produces **2a** in 95% selectivity and 69% yield (Table 1, entry 17). On the

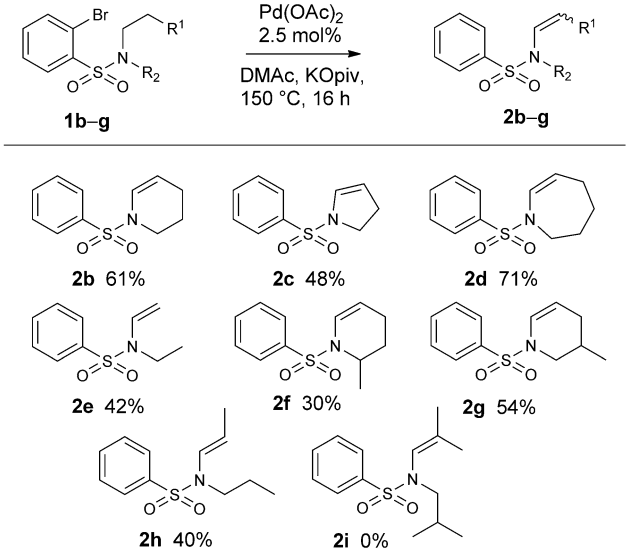
Table 1. Influence of the reaction conditions for the palladium-catalysed intramolecular functionalisation of **1a**.



Entry	Catalyst (mol%)	Base (equiv.)	Benzoquinone (equiv.)	Conv. of **1a** [%]	Ratio **2a**:**2′a**:**2″a**	Yield [%]
1	$Pd(OAc)_2$ (2.5)/Xantphos (10)	K_2CO_3 (2)	–	100	65:12:23	
2	$Pd(OAc)_2$ (2.5)/Xantphos (10)	K_2CO_3 (2)	(0.2)	95	86:0:14	
3	$Pd(OAc)_2$ (5)/Xantphos (10)	KOAc (2)	(0.2)	80	70:14:16	
4	$Pd(OAc)_2$ (5)/dppf (10)	KOAc (2)	(0.5)	100	58:0:42	
5	$Pd(C_3H_5)Cl$(dppb) (5)	KOAc (2)	(1)	100	85:0:15	60 (**2a**)
6	$Pd(OAc)_2$ (2.5)	K_2CO_3 (2)	(0.2)	100	87:0:13	55 (**2a**)
7	$Pd(OAc)_2$ (2.5)	K_2CO_3 (2)	(0.5)	100	91:0:9	57 (**2a**)
8	$Pd(OAc)_2$ (2.5)	Ag_2CO_3 (2)	(0.5)	0	–	
9	$Pd(OAc)_2$ (5)	KOpiv (3)	(0.2)	81	82:0:18	
10	$Pd(OAc)_2$ (2.5)	KOpiv (3)	–	100	89:0:11	75 (**2a**)
11	$Pd(OAc)_2$ (2.5)	KOAc (3)	–	86	81:0:19	
12	$Pd(OAc)_2$ (2.5)	CsAcO (3)	–	59	85:0:15	
13	$Pd(OAc)_2$ (2.5)	K_2CO_3 (3)	–	100	69:15:16	11 (**2′a**)
14	$Pd(OAc)_2$ (2.5)	Na_2CO_3 (3)	–	100	85:0:15	64 (**2a**)
15	$Pd(OAc)_2$ (2.5)	Li_2CO_3 (3)	–	40	62:0:38	
16	$Pd(OAc)_2$ (2.5)	*t*-BuOK (3)	–	100	0:0:100	
17[b]	$Pd(OAc)_2$ (2.5)	KOpiv (3)	–	100	95:0:5	69 (**2a**)
18[c]	$Pd(OAc)_2$ (2.5)	KOpiv (3)	–	33	70:0:30	

[a] Base (2 equiv.), DMAc, 150 °C, 16 h.
[b] 8 h, 130 °C.
[c] 100 °C.

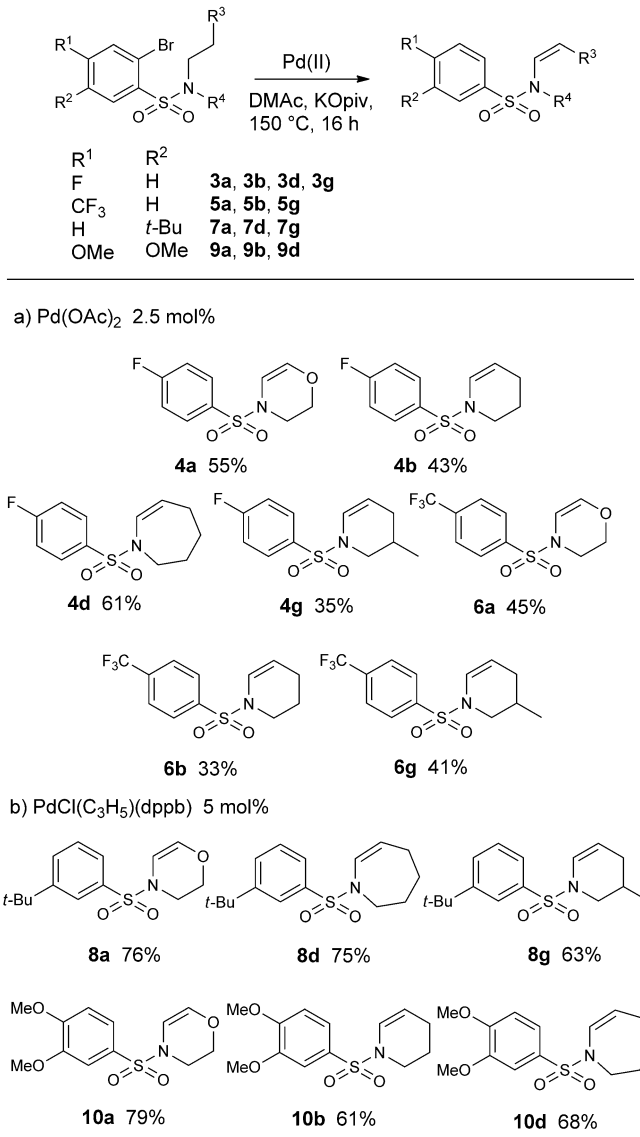
other hand, at 100 °C, a low conversion of **1a** and a poor selectivity in favour of the formation of **2a** was observed (Table 1, entry 18). It is noteworthy that these conditions of $Pd(OAc)_2$ in DMAc at 130–150 °C are relevant for the formation of nanoparticules.[15]



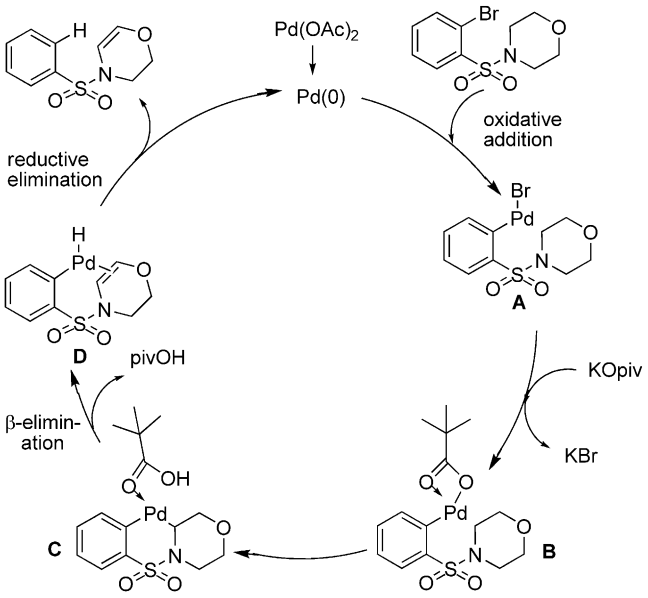
Scheme 4. Scope of the substituents on the NR_2 moiety.

Then, the scope of the substituents on the NR_2 moiety for this reaction was examined using 2.5 mol% $Pd(OAc)_2$ catalyst in the presence of KOpiv base/ligand (Scheme 4). The piperidine-substituted benzenesulfonamide **1b** led to **2b** in 61% yield. From the 5-membered ring pyrrolidine-sulfonamide **1c**, **2c** was produced in a yield of 48%; whereas, the 7-membered ring produces **2d** in 71% yield. A moderate yield of **2e** was obtained from 2-bromo-*N*,*N*-diethylbenzenesulfonamide **1e**. From the two methyl-substituted piperidine derivatives **1f** and **1g**, a completely regioselective dehydrogenation at the C-5/C-6 positions was observed to produce 2- or 3-methyl-1,2,3,4-tetrahydropyridines **2f** and **2g**. A selective dehydrogenation of 2-bromo-*N*,*N*-dipropylbenzenesulfonamide **1h** gave the desired (*E*)-*N*-propenyl-*N*-propylbenzenesulfonamide **2h** in moderate yield. It should be noted that no formation of the *Z*-isomer or of the allyl derivative was observed. On the other hand, no dehydrogenation of 2-bromo-*N*,*N*-diisobutylbenzenesulfonamide **1i** to produce **2i** was detected by GC/MS analysis. With this reactant, only the debrominated side-product was formed.

The influence of the substituents on the aryl moiety was also examined (Scheme 5). From 2-bromo-4-fluorobenzenesulfonamides **3a**–**3g**, the dehydrogenated products **4a**–**4g** were obtained in 35–61% yields. An



Scheme 5. Dehydrogenation of 2-bromobenzenesulfonamides.



Scheme 6. Proposed catalytic cycle.

electron-withdrawing substituent on the benzene ring was also tolerated for this coupling; and from 2-bromo-4-trifluoromethylbenzenesulfonamides **5a**, **5b** and **5g**, the new dehydrogenated compounds **6a**, **6b** and **6g** were isolated in 33–45% yields. On the other hand, with substrates containing electron-donating substituents, ligand-free $Pd(OAc)_2$ catalyst led to very low yields due to poor conversions, and 5 mol% $PdCl(C_3H_5)(dppb)$ catalyst had to be employed to obtain complete conversions of **7** or **9**, as the dppb ligand certainly favours the oxidative addition of the aryl bromides to palladium. A *tert*-butyl substituent at C-5 of benzene gave products **8a**, **8d** and **8g** in 63–76% yield from the morpholine, azepane or 3-methylpiperidine sulfonamides **7a**, **7d** and **7g**. Even the presence of two methoxy substituents at the C-4 and C-5 positions of benzene was tolerated to give **10a**, **10b** and **10d** in 61–79% yields.

Although the mechanism is not yet elucidated, a catalytic cycle as shown in Scheme 6 can be proposed. The first step of the catalytic cycle is certainly the oxidative addition of the aryl bromide to Pd(0) species to afford the Pd(II) intermediate **A** as for Heck-type and Baudoin reactions.[3] Then, the **A** species undergoes an exchange of the bromide by a pivalate to give **B**. A concerted metallation–deprotonation (CMD) process[9c,14a] is expected to produce **C**, giving **D** after β-elimination. Finally, a reductive elimination from **D** affords the *N*-alkenylbenzenesulfonamide and regenerates the Pd(0) catalytic species. The SO_2N functional group is likely favouring the β-elimination process rather than the reductive elimination as for an alkyl group linked to a benzylic position.[3]

In summary, we show here the first palladium-catalysed dehydrogenative sp^3 C–H functionalisation of *N*-alkylbenzenesulfonamides to produce *N*-alkenylbenzenesulfonamides. The reaction proceeds with easily accessible ligand-free $Pd(OAc)_2$ for aryl bromides bearing electron-withdrawing groups or $PdCl(C_3H_5)(dppb)$ catalyst for aryl bromides with electron-donating substituents, and KOpiv as non-expensive base/ligand. The reaction can be successful for a variety of substituents both on nitrogen and on the arene moiety. Due to the described usefulness of alkenylsulfonamides, such simple reaction conditions and functional group tolerance is offering a new attractive method for access to such structures. This work also shows that simple palladium(II) precursors have potential to dehydrogenate the frequent alkyl moieties of functional molecules and molecular materials.

Experimental Section

General

All reactions were performed in Schlenck tubes under argon. DMA analytical grade was not distilled before use. Commercial aryl bromide derivatives and amines were used without purification. ^{1}H (300 or 400 MHz), ^{13}C (75 or 100 MHz) spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm relative to $CDCl_3$ (^{1}H: 7.26 and ^{13}C: 77.0). Flash chromatography was performed on silica gel (230–400 mesh).

Synthesis of 1a–1g, 3a–3g, 5a–5g, 7a–7g and 9a, 9b

A mixture of the 2-bromobenzenesulfonyl chloride derivative (2 mmol) and triethylamine (6 mmol) in CH_2Cl_2 (10 mL) was treated with the appropriate secondary amine (2.2 mmol) in a dropwise fashion at 0 °C. Stirring was continued for 12 h and the reaction mixture was gradually warmed to room temperature. The solvent was removed under reduced pressure and CH_2Cl_2 (20 mL) and H_2O (20 mL) were added. The resultant aqueous layer was further extracted with CH_2Cl_2 (2×20 mL) and the combined CH_2Cl_2 extracts were dried over $MgSO_4$. Filtration followed by solvent removal under vacuum afforded the crude product, which was purified by flash column chromatography (pentane:diethyl ether; 4:1) affording the product.

General Procedure for the Synthesis of 2a–2g, 4a–4g, 6a–6g, 8a–8g, and 10a, 10b

A dry Schlenk tube was charged with 2-bromoarylsulfonamide derivative (0.5 mmol) and potassium pivalate (0.210 g, 1.5 mmol). The catalyst $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol) or [PdCl(allyl)(dppb)] (15.4 mg, 0.025 mmol) dissolved in DMA (0.5 mL) was quickly added to the Schlenk tube with a flow of argon, then DMA (1.5 mL) was added. The Schlenk tube was closed and the reaction mixture stirred at room temperature for 15 min. After heating at 150 °C for 16 h, and cooling, the solvent was removed under vacuum, and the residue purified by flash chromatography (diethyl ether:pentane).

Acknowledgements

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References

[1] a) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174–238; b) L.-C. Campeau, D. R. Stuart, K. Fagnou, *Aldrichimica Acta* **2007**, *40*, 35–41; c) I. V. Seregin, V. Gevoryan, *Chem. Soc. Rev.* **2007**, *36*, 1173–1193; d) T. Satoh, M. Miura, *Chem. Lett.* **2007**, *36*, 200–205; e) C. Lewis, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2008**, *41*, 1013–1025; f) O. Daugulis, H.-Q. Do, D. Skabashov, *Acc. Chem. Res.* **2009**, *42*, 1074–1086; g) F. Bellina, R. Rossi, *Tetrahedron* **2009**, *65*, 10269–10310; h) P. Thansandote, M. Lautens, *Chem. Eur. J.* **2009**, *15*, 5874–5883; i) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem.* **2009**, *121*, 5196–5217; *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115; j) L. Ackermann, R. Vicente, A. Kapdi, *Angew. Chem.* **2009**, *121*, 9976–10011; *Angew. Chem. Int. Ed.* **2009**, *48*, 9792–9826; k) J. Roger, A. L. Gottumukkala, H. Doucet, *ChemCatChem* **2010**, *2*, 20–40; l) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem.* **2012**, *124*, 10382–10401; *Angew. Chem. Int. Ed.* **2012**, *51*, 10236–10254.

[2] For reviews on sp^3 C–H bond functionalisation: a) R. Giri, B.-F. Shi, K. M. Engle, N. Maugel, J.-Q. Yu, *Chem. Soc. Rev.* **2009**, *38*, 3242–3272; b) F. Bellina, R. Rossi, *Chem. Rev.* **2010**, *110*, 1082–1146; c) O. Baudoin, *Chem. Soc. Rev.* **2011**, *40*, 4902–4911; d) H. Li, B.-J. Li, Z.-J. Shi, *Catal. Sci. Technol.* **2011**, *1*, 191–206.

[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, O. Baudoin, *Adv. Synth. Catal.* **2007**, *349*, 2054–2060; c) J. Hitce, P. Retailleau, O. Baudoin, *Chem. Eur. J.* **2007**, *13*, 792–799; d) N. Martin, C. Pierre, M. Davi, R. Jazzar, O. Baudoin, *Chem. Eur. J.* **2012**, *18*, 4480–4484; e) E. Motti, M. Catellani, *Adv. Synth. Catal.* **2008**, *350*, 565–569.

[4] For examples of formation of enamines from alkylamines using cobalt, iridium, platinum or iron catalyst, see: a) X. Zhang, A. Fried, S. Knapp, A. S. Goldman, *Chem. Commun.* **2003**, 2060–2061; b) A. D. Bolig, M. Brookhart, *J. Am. Chem. Soc.* **2007**, *129*, 14544–14545; c) X.-F. Xia, X.-Z. Shu, K.-G. Ji, Y.-F. Yang, A. Shaukat, X.-Y. Liu, Y.-M. Liang, *J. Org. Chem.* **2010**, *75*, 2893–2902; d) N. Takasu, K. Oisaki, M. Kanai, *Org. Lett.* **2013**, *15*, 1918–1921. For sp^3 functionalisation of alkylamines with Ru and Ir catalysts, see also: e) B. Sundararaju, Z. Tang, M. Achard, G. V. M. Sharma, L. Toupet, C. Bruneau, *Adv. Synth. Catal.* **2010**, *352*, 3141–3146; f) B. Sundararaju, M. Achard, G. V. M. Sharma, C. Bruneau, *J. Am. Chem. Soc.* **2011**, *133*, 10340–10343; g) X.-F. Xia, X.-Z. Shu, K.-G. Ji, A. Shaukat, X.-Y. Liu, Y.-M. Liang, *J. Org. Chem.* **2011**, *76*, 342–345; h) K. Yuan, F. Jiang, Z. Sahli, M. Achard, T. Roisnel, C. Bruneau, *Angew. Chem.* **2012**, *124*, 9006–9010; *Angew. Chem. Int. Ed.* **2012**, *51*, 8876–8880; i) T. Boudiar, Z. Sahli, B. Sundararaju, M. Achard, Z. Kabouche, H. Doucet, C. Bruneau, *J. Org. Chem.* **2012**, *77*, 3674–3678; j) A. Millet, P. Larini, E. Clot, O. Baudoin, *Chem. Sci.* **2013**, *4*, 2241–2247.

[5] R. Giri, N. Maugel, B. M. Foxman, J.-Q. Yu, *Organometallics* **2008**, *27*, 1667–1670.

[6] a) Y. Izawa, D. Pun, S. S. Stahl, *Science* **2011**, *333*, 209–213; b) Y. Moon, D. Kwon, S. Hong, *Angew. Chem.* **2012**, *124*, 11495–11498; *Angew. Chem. Int. Ed.* **2012**, *51*, 11333–11336.

[7] J. Zhou, G. Wu, M. Zhang, X. Jie, W. Su, *Chem. Eur. J.* **2012**, *18*, 8032–8036.

[8] a) D. K. Rayabarapu, A. Zhou, K. O. Jeon, T. Samarakoon, A. Rolfe, H. Siddiqui, P. R. Hanson, *Tetrahedron* **2009**, *65*, 3180–3188; b) S. Rousseaux, S. I. Gorelesky, B. K. W. Chung, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 10692–10705.

[9] a) D. L. Davies, S. M. A. Donald, S. A. Macgregor, *J. Am. Chem. Soc.* **2005**, *127*, 13754–13755; b) M. Lafrance, K. Fagnou, *J. Am. Chem. Soc.* **2006**, *128*, 16496–16497; 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) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem.* **2009**, *121*, 5196–5217; *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115.

[10] For the use of such unsaturated sulfonamides in synthesis: a) S. Yamasaki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2001**, *123*, 1256–1257; b) L. C. Pattenden, H. Adams, S. A. Smith, J. P. A. Harrity, *Tetrahedron* **2008**, *64*, 2951–2961; c) S. Toumieux, P. Compain, O. R. Martin, *J. Org. Chem.* **2008**, *73*, 2155–2162; d) J. B. Feltenberger, R. Hayashi, Y. Tang, E. S. C. Babiash, R. P. Hsung, *Org. Lett.* **2009**, *11*, 3666–3669; e) N. C. Mancey, N. Sandon, A.-L. Auvinet, R. J. Butlin, W. Czechtizky, J. P. A. Harrity, *Chem. Commun.* **2011**, *47*, 9804–9806; f) R. W. Bates, K. Sivarajan, B. F. Straub, *J. Org. Chem.* **2011**, *76*, 6844–6848; g) D. F. Taber, P. W. DeMatteo, *J. Org. Chem.* **2012**, *77*, 4235–4241; h) N. Gigant, I. Gillaizeau, *Org. Lett.* **2012**, *14*, 4622–4625.

[11] For examples of the synthesis of such enamines, see: a) R. Grigg, M. York, *Tetrahedron Lett.* **2000**, *41*, 7255–7258; b) S. S. Kinderman, J. H. van Maarseveen, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *Org. Lett.* **2001**, *3*, 2045–2048; c) M. G. Hamilton, C. E. Hughes, A. M. Irving, C. M. Vogels, S. A. Westcott, *J. Organomet. Chem.* **2003**, *680*, 143–147; d) P. Lu, S. Ma, *Org. Lett.* **2007**, *9*, 2095–2097; e) C.-M. Chao, D. Beltrami, P. Y. Toullec, V. Michelet, *Chem. Commun.* **2009**, 6988–6990; f) Y. T. Lee, Y. K. Kang, Y. K. Chung, *J. Org. Chem.* **2009**, *74*, 7922–7934; g) C. A. Sperger, J. E. Tungen, A. Fiksdahl, *Eur. J. Org. Chem.* **2011**, 3719–3722; h) P. Evans, T. McCabe, B. S. Morgan, S. Reau, *Org. Lett.* **2005**, *7*, 43–46; i) C. R. Larsen, D. B. Grotjahn, *J. Am. Chem. Soc.* **2012**, *134*, 10357–10360.

[12] For the synthesis of sulfonated bromobenzenes from bromobenzenes: a) A. L. Borror, E. Chinoporos, M. P. Filosa, S. R. Herchen, C. P. Petersen, C. A. Stern, K. D. Onan, *J. Org. Chem.* **1988**, *53*, 2047–2052; b) P. Evans, T. McCabe, B. S. Morgan, S. Reau, *Org. Lett.* **2005**, *7*, 43–46.

[13] a) D. E. Ames, A. Opalko, *Synthesis* **1983**, 234–235; b) D. E. Ames, A. Opalko, *Tetrahedron* **1984**, *40*, 1919–1925; c) M. Butwood, B. Davies, I. Diazt, R. Grigg, P. Molina, V. Sridharan, M. Hughes, *Tetrahedron Lett.* **1995**, *36*, 9053–9056; d) I. C. F. R. Ferreira, M.-J. R. P. Queiroz, G. Kirsch, *Tetrahedron* **2003**, *59*, 3737–3743; e) J.-P. Leclerc, M. André, K. Fagnou, *J. Org. Chem.* **2006**, *71*, 1711–1714; f) D. García-Cuadrado, P. de Mendoza, A. A. C. Braga, F. Maseras, A. M. Echavarren, *J. Am. Chem. Soc.* **2007**, *129*, 6880–6886; g) L. C. Campeau, P. Thansandote, K. Fagnou, *Org. Lett.* **2005**, *7*, 1857–1860.

[14] For examples of formation of 5-membered rings *via* direct sp^3 C–H arylations, see: a) M. Lafrance, S. I. Gorelsky, K. Fagnou, *J. Am. Chem. Soc.* **2007**, *129*, 14570–14571; b) H. Ren, Z. Li, P. Knochel, *Chem. Asian J.* **2007**, *2*, 416–433; c) 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; d) S. Anas, A. Cordi, H. B. Kagan, *Chem. Commun.* **2011**, *47*, 11483–11485.

[15] A. H. M. de Vries, J. M. C. A. Mulders, J. H. M. Mommers, H. J. W. Henderickx, J. G. de Vries, *Org. Lett.* **2003**, *5*, 3285–3288.

