

Palladium-Catalyzed Direct and Site-Selective Desulfitative Arylation of Indoles with Sodium Sulfinates

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Abstract: An efficient method was developed for the desulfitative arylation of indoles with sodium sulfinates using palladium as catalyst and copper chloride dihydrate as oxidant. The direct arylation occurred exclusively in the C-2 position of indoles and proceeded well for a range of different substrates.

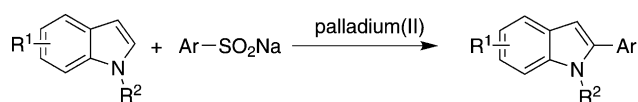
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The direct conversion of C–H bonds into C–C bonds can potentially lead to more efficient synthesis with a reduced number of synthetic operations and thus has attracted great interest recently. Since the seminal work reported by Murai et al.^[1] and Fujiwara and co-workers,^[2] remarkable progress has been made in the transition metal-catalyzed activation and subsequent reaction of C–H bonds.^[3] In the past few years the direct arylation of *sp*² C–H bonds has emerged as a very powerful synthetic method for rapid C–C bond forming reactions.^[4] Specifically, palladium has been reported predominantly as a versatile catalyst for constructing C–C bonds through C–H activation.^[5]

Indoles and their derivatives exist widely in nature. Since the first preparation of indole by Baeyer in 1886,^[6] the synthesis of these compounds and their functionalization has attracted much attention in both industrial and academic research because of their biological and pharmaceutical properties.^[7] In particular, the direct arylation of indoles at C-2 and/or C-3 *via* C–H activation has received considerable attention over the past decade.^[8] This method avoids the pre-

functionalization of indoles and thus affords a shortcut for the arylation of indoles. Apart from aryl halides,^[9–11] a variety of coupling species, including organoboranes,^[12] hypervalent iodine arylating agents,^[13] arylsiloxanes,^[14] and even arene C–H bonds,^[15] have been explored in the direct arylation reaction of indoles. Recently, the widely commercially available aromatic carboxylic acids have been successfully used as the aryl sources in the direct arylation of various arene C–H bonds *via* decarboxylative coupling reactions.^[16,17] This strategy has been also successfully applied for the direct arylation of indoles, and various benzoic acids are selectively coupled with indoles in the C-2 or C-3 position using palladium salts as the catalysts and silver salts as the oxidants.^[18] However, this approach is generally limited to the *ortho*-substituted aromatic benzoic acids.

Compared with the widely studied carboxylic acid partners, aromatic sulfinic acid sodium salts are rarely used as aryl sources *via* desulfination. Sulfinic acid sodium salts are relatively stable, easy to handle, and when necessary, are accessible preparatively from their corresponding sulfonyl chlorides. Sulfinic acid sodium salts have the potential to serve as the ideal aryl sources for C–C bond forming reactions *via* releasing SO₂ under relatively mild conditions.^[19] However, sulfinic acids (or sodium salts) are mainly used as sulfonylation reagents and rarely used as aryl sources *via* desulfitative reactions.^[20] We have recently reported a palladium-catalyzed desulfitative Heck-type reaction of aromatic sulfinic acid sodium salts with various olefins with oxygen as the terminal oxidant under mild conditions.^[21] The desulfination proceeded smoothly at 85 °C, which is much lower than the temperature required by most of the decarboxylative reactions. We also developed an efficient method for



Scheme 1. General reaction.

the synthesis of aryl ketones by palladium-catalyzed desulfative addition of aromatic sodium sulfinates to various nitriles under mild conditions.^[22] In continuation of our interest in using aromatic sulfinic acids (salts) as the aryl sources, herein we describe the first palladium-catalyzed desulfative C-2 arylation of indoles with sodium sulfinates *via* C–H activation (Scheme 1).

We began our study by examining the reaction of 1-methylindole (**1a**) with *p*-toluenesulfinic acid sodium salt (**2a**) in toluene/dioxane by using Pd(OAc)₂ as catalyst and oxygen as oxidant. No desired product was detected as determined by GC-MS and ¹H NMR methods (Table 1, entry 1). Other oxidants such as TBP (*tert*-butyl peroxide), FeCl₃, Cu(OAc)₂·H₂O and CuBr₂ were inefficient for this kind of transformation (entries 2–5). To our delight, the desired product (**3a**) was obtained in 84% yield when 2 equivalents of CuCl₂·2H₂O were used as the oxidant (entry 6). Other palladium salts were also investigated and moderate to good yield was obtained (entries 7–13). Among them, Pd(COD)Cl₂ showed the best reactivity, and the desired product **3a** was obtained in 88% yield (isolated yield 73%, entry 13). The solvent had a significant impact on the reaction yield. The reaction yield decreased when the ratio of toluene to dioxane was changed (entries 14 and 15). A much lower yield was obtained when the reaction was carried out in dioxane and DMF, and the desired product was obtained in 23% and 32% yield, respectively (entries 17 and 18). Decreasing the catalyst loading decreased the reaction yield (entry 19).

With the optimized reaction conditions in hand, we then explored the scope and generality of this transformation. Various indoles bearing electron-withdrawing and electron-donating substituents were investigated (Table 2). The reaction temperature was increased slightly to 120°C and Pd(OAc)₂ was used as the catalyst to afford higher reaction yields for indoles bearing substituents. Indoles with a methyl group in C-3, C-6 and C-7 all smoothly coupled with **2a** and gave the desired products in 80%, 66% and 81% yields, respectively (table 2, entries 2–4). Notably, the methoxy, bromo, fluoro, nitro and even ester moieties on indoles were all well tolerated under these reaction conditions and the desired products were obtained in good yields (entries 5–10). Under similar conditions, 1-ethylindole (**1k**) and 1-acetylindole (**1l**) also could couple with **2a** to give the desired products in 70% and 65% yields, respectively (entries 11 and 12). However, only a trace amount of product was ob-

Table 1. Optimization of the reaction conditions.^[a]

Entry	Catalyst	Oxidant	Solvent	Yield [%] ^[b]
1	Pd(OAc) ₂	O ₂	toluene/dioxane (1:1)	trace
2	Pd(OAc) ₂	TBP	toluene/dioxane (1:1)	trace
3	Pd(OAc) ₂	FeCl ₃	toluene/dioxane (1:1)	8
4	Pd(OAc) ₂	Cu(OAc) ₂	toluene/dioxane (1:1)	trace
5	Pd(OAc) ₂	CuBr ₂	toluene/dioxane (1:1)	trace
6	Pd(OAc) ₂	CuCl ₂	toluene/dioxane (1:1)	79
7	PdCl ₂	CuCl ₂	toluene/dioxane (1:1)	65
8	PdBr ₂	CuCl ₂	toluene/dioxane (1:1)	53
9	Pd(CH ₃ CN) ₂ Cl ₂	CuCl ₂	toluene/dioxane (1:1)	63
10	Pd(acac) ₂	CuCl ₂	toluene/dioxane (1:1)	62
11	Pd(OH) ₂	CuCl ₂	toluene/dioxane (1:1)	74
12	Pd(TFA) ₂	CuCl ₂	toluene/dioxane (1:1)	41
13	Pd(COD)Cl₂	CuCl₂	toluene/dioxane (1:1)	88
14	Pd(COD)Cl ₂	CuCl ₂	toluene/dioxane (1:2)	65
15	Pd(COD)Cl ₂	CuCl ₂	toluene/dioxane (2:1)	75
16	Pd(COD)Cl ₂	CuCl ₂	toluene	56
17	Pd(COD)Cl ₂	CuCl ₂	dioxane	23
18	Pd(COD)Cl ₂	CuCl ₂	DMF	32
19 ^[c]	Pd(COD)Cl ₂	CuCl ₂	toluene/dioxane (1:1)	70

^[a] Conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), catalyst (5 mol%), oxidant (2 equiv.), 110°C, 24 h under argon unless otherwise noted.

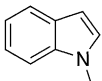
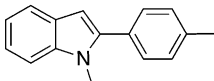
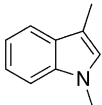
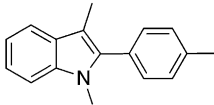
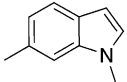
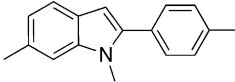
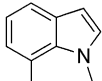
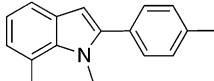
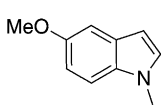
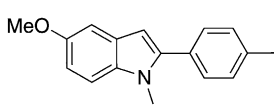
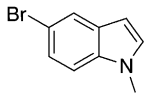
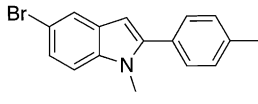
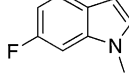
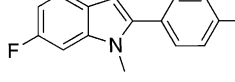
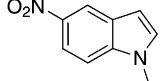
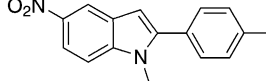
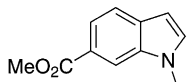
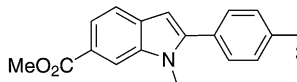
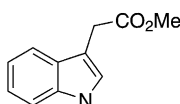
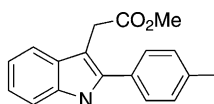
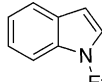
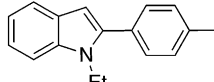
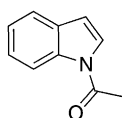
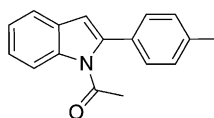
^[b] GC-MS yield based on **1a**.

^[c] 2.5 mol% catalyst were used.

served when the more bulky substrate 1-pivaloylindole was used.

The reaction results of various arylsulfinic acid sodium salts with 1-methylindole (**1a**) are presented in Table 3. A series of functional groups including *tert*-butyl, methoxy, fluoro, bromo and trifluoromethyl was tolerated under the optimal reaction conditions, and the desired products were obtained in moderate to good yields (entries 2–6). Only a trace of product was observed when (4-nitrophenyl)sulfinic acid sodium salt (**2h**) reacted with **1a** (entry 7). More bulky substrates such as 2-naphthylsulfinic acid sodium salt (**2i**) also efficiently reacted with **1a** and gave the product in 80% yield (entry 8). In most cases, the desulfative arylation occurred exclusively

Table 2. Desulfurative arylation of **2a** with various indoles.^[a]

Entry	Indole	Product	Yield [%] ^[b]
1			73
2 ^[c]			80
3 ^[c]			60
4 ^[c]			81
5			67
6 ^[c]			78
7 ^[c]			80
8 ^[c]			60
9 ^[c]			79
10 ^[c]			78
11			70
12			65

^[a] Conditions: **1** (0.2 mmol), **2a** (0.4 mmol), Pd(COD)Cl₂ for entry 1 and Pd(OAc)₂ for entries 2–12 (5 mol%), CuCl₂·2H₂O (2 equiv.), 110 °C, 24 h under argon unless otherwise noted.

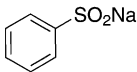
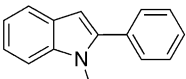
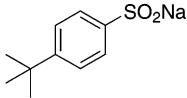
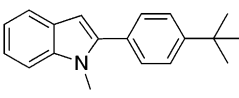
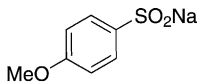
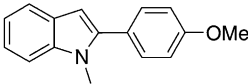
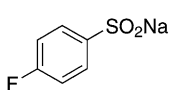
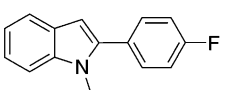
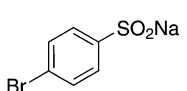
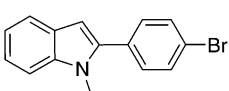
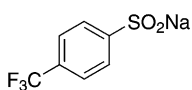
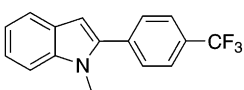
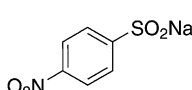
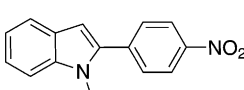
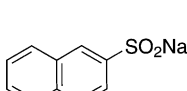
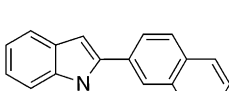
^[b] Isolated yield.

^[c] 120 °C.

in the C-2 position of indoles as determined by ¹H NMR methods.^[23] No desired product was observed when free NH-indole was used as substrate under the same conditions.

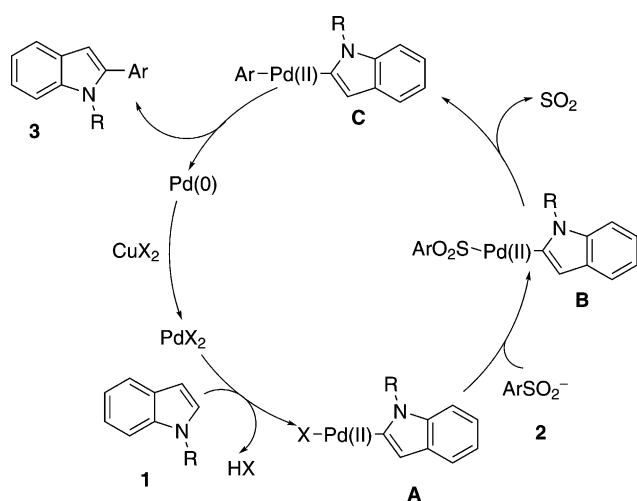
Although the exact mechanism of this coupling is still not clear, on the basis of the results reported by us and others,^[24] a plausible mechanism is proposed and shown in Scheme 2. First, the Pd(II) catalyst reacts with the indole **1** in the C-2 position to form an

Table 3. Desulfitative arylation of **1a** with various sodium sulfinates.^[a]

Entry	Sodium sulfinate	Product	Yield [%] ^[b]
1	 2b	 3m	67
2	 2c	 3n	84
3	 2d	 3o	59
4	 2e	 3p	71
5	 2f	 3q	81
6	 2g	 3r	70
7	 2h	 3s	trace
8	 2i	 3t	80

^[a] Conditions: **1a** (0.2 mmol), **2** (0.4 mmol), Pd(COD)Cl₂ (5 mol%), CuCl₂·2H₂O (2 equiv.), 110°C, 24 h in argon unless otherwise noted.

^[b] Isolated yield.

**Scheme 2.** Proposed mechanism.

Ar-Pd(II)-X intermediate **A** (X=OAc), which is subsequently displaced by sulfinic acid **2** to form intermediate **B**. This intermediate species undergoes desulfination to generate the aryl-palladium complex **C**. A reductive elimination of **C** affords the desired product **3** and the Pd(0) catalyst is reoxidized to Pd(II) by the CuCl₂, thus closing the catalytic cycle.

In summary, we have demonstrated a novel palladium-catalyzed desulfitative direct arylation of indoles in the presence of an oxidant. Various aromatic sulfinic acid sodium salts with or without substituents selectively coupled with indoles and exclusively afforded the C-2 arylated indole adducts. Unlike the decarboxylative coupling reaction, no electron-withdrawing or electron-donating group *ortho* to the sulfinic acid group was necessary to ensure the desulfitative coupling. Functional groups such as methoxy, bromo, fluoro, nitro and even ester moieties on the indoles were all well tolerated under these reaction condi-

tions. The scope, mechanism, and synthetic applications of this reaction are under further investigation.

Experimental Section

Typical Procedure

A 10-mL oven-dried reaction vessel was charged with Pd(COD)Cl₂ (2.8 mg, 0.01 mmol), CuCl₂·2H₂O (68.1 mg, 0.4 mmol), sodium *p*-toluenesulfonate (**2a**, 71.3 mg, 0.4 mmol), and purged with argon three times. 1-Methyl-1H-indole (**1a**, 26.2 mg, 0.2 mmol), toluene (0.3 mL) and 1,4-dioxane (0.3 mL) were added to the sealed reaction vessel by syringe. The resulting solution was stirred at 110°C for 24 h. After cooling to room temperature, the volatiles were removed under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate=30:1) to give **3a** as white solid; yield: 32.3 mg (73%).

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References

- [1] S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, *Nature* **1993**, 366, 529.
- [2] C. Jia, D. Piao, J. Oyamada, W. Lu, T. Kitamura, Y. Fujiwara, *Science* **2000**, 287, 1992.
- [3] For representative reviews on C–H functionalization, see: a) G. Dyker, *Handbook of C–H Transformations: Applications in Organic Synthesis*, Wiley-VCH, Weinheim, **2005**; b) J. Q. Yu, Z. J. Shi, *C–H Activation*, Springer, Berlin, Germany, **2010**; c) *Activation and Functionalization of C–H Bond*, (Eds.: K. I. Goldberg, A. S. Goldman), ACS Symposium Series No. 885, American Chemical Society, Washington DC, **2004**; d) A. E. Shilov, G. B. Shul'pin, *Chem. Rev.* **1997**, 97, 2879; e) T. Naota, H. Takaya, S. I. Murahashi, *Chem. Rev.* **1998**, 98, 2599; f) G. Dyker, *Angew. Chem.* **1999**, 111, 1808; *Angew. Chem. Int. Ed.* **1999**, 38, 1698; g) C. Jia, T. Kitamura, Y. Fujiwara, *Acc. Chem. Res.* **2001**, 34, 633; h) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev.* **2002**, 102, 1731; i) J. A. Labinger, J. E. Bercaw, *Nature* **2002**, 417, 507; j) R. H. Crabtree, *J. Organomet. Chem.* **2004**, 689, 4083; k) L. A. Goj, T. B. Gunnoe, *Curr. Org. Chem.* **2005**, 9, 671; l) A. R. Dick, M. S. Sanford, *Tetrahedron* **2006**, 62, 2439; m) K. Godula, D. Sames, *Science* **2006**, 312, 67; n) J. C. Lewis, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2008**, 41, 1013; o) B. Li, S. Yang, Z. Shi, *Synlett* **2008**, 949; p) M. Diaz-Requejo, P. Pérez, *Chem. Rev.* **2008**, 108, 3379; q) J. Hartwig, *Nature* **2008**, 455, 314; r) R. Giri, B. Shi, K. Engle, N. Maugel, J. Yu, *Chem. Soc. Rev.* **2009**, 38, 3242; s) C. J. Li, *Acc. Chem. Res.* **2009**, 42, 335; t) C. Copéret, *Chem. Rev.* **2010**, 110, 656; u) I. Mkhaliid, J. Barnard, T. Marder, J. Murphy, J. Hartwig, *Chem. Rev.* **2010**, 110, 890; v) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, 110, 624; w) M. Zhang, *Appl. Organomet. Chem.* **2010**, 24, 269.
- [4] For selected reviews on direct C–H arylations, see: a) L. Ackermann, *Modern Arylation Methods*, Wiley-VCH, Weinheim, **2009**; b) F. Kakiuchi, N. Chatani, *Adv. Synth. Catal.* **2003**, 345, 1077; c) K. Godula, D. Sames, *Science* **2006**, 312, 67; d) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, 107, 174; e) L. C. Campeau, D. R. Stuart, K. Fagnou, *Aldrichimica Acta* **2007**, 40, 35; f) G. McGlacken, L. Bateman, *Chem. Soc. Rev.* **2009**, 38, 2447; g) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem.* **2009**, 121, 9976; *Angew. Chem. Int. Ed.* **2009**, 48, 9792; h) M. Zhang, *Adv. Synth. Catal.* **2009**, 351, 2243; i) J. A. Ashenhurst, *Chem. Soc. Rev.* **2010**, 39, 540.
- [5] a) X. Chen, K. M. Engle, D. H. Wang, J. Q. Yu, *Angew. Chem.* **2009**, 121, 5196; *Angew. Chem. Int. Ed.* **2009**, 48, 5094; b) E. M. Beccalli, G. Brogini, M. Martinelli, S. Sottocornola, *Chem. Rev.* **2007**, 107, 5318; c) O. Daugulis, H. Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, 42, 1074; d) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, 110, 1147.
- [6] A. Baeyer, *Justus Liebigs Ann. Chem.* **1886**, 140, 295.
- [7] a) P. L. Julian, E. W. Meyer, H. C. Printy, in: *Heterocyclic Compounds*, (Ed.: R. C. Elderfield), Wiley: New York, **1952**, Vol. 3, pp 1–274; b) R. J. Sundberg, *The Chemistry of Indoles*, Academic Press, New York, **1970**; c) R. J. Sundberg, *Indoles*, Academic Press, London, UK, **1996**; d) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2005**, 105, 2873; e) G. R. Humphrey, J. T. Kuethe, *Chem. Rev.* **2006**, 106, 2875; f) A. Brancale, R. Silvestri, *Med. Res. Rev.* **2007**, 27, 209; g) K. Krüger, A. Tillack, M. Beller, *Adv. Synth. Catal.* **2008**, 350, 2153; h) P. Thansandote, M. Lautens, *Chem. Eur. J.* **2009**, 15, 5874; i) M. Bandini, A. Eichholzer, *Angew. Chem.* **2009**, 121, 9786; *Angew. Chem. Int. Ed.* **2009**, 48, 9608.
- [8] For selected reviews, see: a) L. Joucla, L. Djakovitch, *Adv. Synth. Catal.* **2009**, 351, 673; b) M. Bandini, A. Eichholzer, *Angew. Chem.* **2009**, 121, 9786; *Angew. Chem. Int. Ed.* **2009**, 48, 9608; c) J. Roger, A. Gottumukkala, H. Doucet, *ChemCatChem* **2010**, 2, 20; d) L. Djakovitch, N. Batail, M. Genelot, *Molecules* **2011**, 16, 5241; e) F. Bellina, C. Calandri, S. Caeteruccio, R. Rossi, *Tetrahedron* **2007**, 63, 1970; f) T. Satoh, M. Miura, *Chem. Lett.* **2007**, 36, 200; g) I. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, 36, 1173. For excellent examples on highly site-selective indole arylation, see: h) L. Joucla, L. Djakovitch, *Adv. Synth. Catal.* **2009**, 351, 673; i) L. Joucla, N. Batail, L. Djakovitch, *Adv. Synth. Catal.* **2010**, 352, 2929.
- [9] a) B. S. Lane, D. Sames, *Org. Lett.* **2004**, 6, 2897; b) C. Bressy, D. Alberico, M. Lautens, *J. Am. Chem. Soc.* **2005**, 127, 13148; c) X. Wang, B. S. Lane, D. Sames, *J. Am. Chem. Soc.* **2005**, 127, 4996; d) F. Bellina, S. Caeteruccio, R. Rossi, *Eur. J. Org. Chem.* **2006**, 6, 137; e) B. B. Toure, B. S. Lane, D. Sames, *Org. Lett.* **2006**, 8,

- 1979; f) X. Wang, D. V. Gribkov, D. Sames, *J. Org. Chem.* **2007**, *72*, 1476; g) Z. Zhang, Z. Hu, Z. Yu, P. Lei, H. Chi, Y. Wang, R. He, *Tetrahedron Lett.* **2007**, *48*, 2415; h) F. Bellina, C. Calandri, S. Cauteruccio, R. Rossi, *Tetrahedron* **2007**, *63*, 1970; i) N. Lebrasseur, I. Larrosa, *J. Am. Chem. Soc.* **2008**, *130*, 2926; j) N. S. Nandurkar, M. J. Bhanushali, M. D. Bhor, B. M. Bhanage, *Tetrahedron Lett.* **2008**, *49*, 1045; k) J. Roger, H. Doucet, *Adv. Synth. Catal.* **2009**, *351*, 1977; l) B. Liégault, I. Petrov, S. I. Gorelsky, K. Fagnou, *J. Org. Chem.* **2010**, *75*, 1047; m) F. Shibahara, E. Yamaguchi, T. Murai, *Chem. Commun.* **2010**, *46*, 2471; n) L. Wang, W. B. Yi, C. Cai, *Chem. Commun.* **2011**, *47*, 806; o) O. Vakuliuk, B. Koszarna, D. T. Gryko, *Adv. Synth. Catal.* **2011**, *353*, 925.
- [10] For direct C-2 arylation of indoles using palladium nanoparticles as catalysts, see: L. Wang, W. B. Yi, C. Cai, *Chem. Commun.* **2011**, *47*, 806.
- [11] For palladium-catalyzed C-3 arylation of free NH-indoles, see: G. Cusati, L. Djakovitch, *Tetrahedron Lett.* **2008**, *49*, 2499.
- [12] a) S. D. Yang, C. L. Sun, Z. Fang, B. J. Li, Y. Li, Z. J. Shi, *Angew. Chem.* **2008**, *120*, 1495; *Angew. Chem. Int. Ed.* **2008**, *47*, 1473; b) J. L. Zhao, Y. H. Zhang, K. Cheng, *J. Org. Chem.* **2008**, *73*, 7428; c) S. Kirchberg, R. Fröhlich, A. Studer, *Angew. Chem.* **2009**, *121*, 4299; *Angew. Chem. Int. Ed.* **2009**, *48*, 4235.
- [13] a) N. R. Deprez, D. Kalyani, A. Krause, M. S. Sanford, *J. Am. Chem. Soc.* **2006**, *128*, 4972; b) R. J. Phipps, N. P. Grimster, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 8172.
- [14] Z. J. Liang, B. B. Yao, Y. H. Zhang, *Org. Lett.* **2010**, *12*, 3185.
- [15] a) M. Lafrance, K. Fagnou, *J. Am. Chem. Soc.* **2006**, *128*, 16496; b) D. R. Stuart, K. Fagnou, *Science* **2007**, *316*, 1172; c) D. R. Stuart, E. Villemure, K. Fagnou, *J. Am. Chem. Soc.* **2007**, *129*, 12072; d) S. Potavathri, A. S. Dumas, T. A. Dwight, G. R. Naumiec, J. M. Hammann, B. DeBoef, *Tetrahedron Lett.* **2008**, *49*, 4050; e) Z. Liang, J. Zhao, Y. Zhang, *J. Org. Chem.* **2010**, *75*, 170; f) A. García-Rubia, B. Urones, R. Gómez Arraías, J. C. Carretero, *Chem. Eur. J.* **2010**, *16*, 9676; g) D. G. Pintori, M. F. Greaney, *J. Am. Chem. Soc.* **2011**, *133*, 1209; h) C. Y. He, S. L. Fan, X. G. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 12850; i) S. Potavathri, K. C. Pereira, S. I. Gorelsky, A. Pike, A. P. LeBris, B. DeBoef, *J. Am. Chem. Soc.* **2010**, *132*, 14676.
- [16] For reviews, see: a) A. Zapf, *Angew. Chem.* **2003**, *115*, 5552; *Angew. Chem. Int. Ed.* **2003**, *42*, 5394; b) J. D. Weaver, A. Recio, A. J. Grenning, J. A. Tunge, *Chem. Rev.* **2011**, *111*, 1846; c) L. J. Goossen, N. Rodríguez, K. Goossen, *Angew. Chem.* **2008**, *120*, 3144; *Angew. Chem. Int. Ed.* **2008**, *47*, 3100.
- [17] For selected examples on decarboxylative biaryl synthesis, see: a) L. J. Goossen, G. J. Deng, L. Levy, *Science* **2006**, *313*, 662; b) P. Forgiione, M. St-Onge, K. H. Thesen, M. D. Bailey, F. Bilofeu, *J. Am. Chem. Soc.* **2006**, *128*, 11350; c) L. J. Goossen, N. Rodríguez, B. Melzer, C. Linder, G. J. Deng, L. Levy, *J. Am. Chem. Soc.* **2007**, *129*, 4824; d) J. M. Becht, C. Catala, C. Drian, A. Wagner, *Org. Lett.* **2007**, *9*, 1781; e) L. J. Goossen, B. Melzer, *J. Org. Chem.* **2007**, *72*, 7473; f) L. J. Goossen, B. Zimmermann, T. Knauber, *Angew. Chem.* **2008**, *120*, 7211; *Angew. Chem. Int. Ed.* **2008**, *47*, 7103; g) L. J. Goossen, N. Rodríguez, C. Linder, *J. Am. Chem. Soc.* **2008**, *130*, 15248; h) L. J. Goossen, F. Rudolphi, C. Oppel, N. Rodríguez, *J. Am. Chem. Soc.* **2008**, *130*, 15240; i) A. Voutchkova, A. Coplin, N. E. Leadbeater, R. H. Crabtree, *Chem. Commun.* **2008**, 6312; j) C. Y. Wang, I. Piel, F. Glorius, *J. Am. Chem. Soc.* **2009**, *131*, 4194; k) W. Y. Yu, N. Sit, Z. Y. Zhou, A. S. C. Chan, *Org. Lett.* **2009**, *11*, 3174; l) M. Miyasaka, A. Fukushima, T. Satoh, K. Hirano, M. Miura, *Chem. Eur. J.* **2009**, *15*, 3674; m) R. Shang, Q. Xu, Y. Jiang, Y. Wang, L. Liu, *Org. Lett.* **2010**, *12*, 1000; n) K. Xie, Z. Yong, X. L. Zhou, X. J. Li, S. Z. Wang, Z. Tan, C. C. Guo, *Org. Lett.* **2010**, *12*, 1564; o) P. P. Lange, L. J. Goossen, P. Podmore, T. Underwood, N. Sciammetta, *Chem. Commun.* **2011**, *47*, 3628; p) H. Q. Zhao, Y. Wei, J. Xu, J. Kan, W. P. Su, M. C. Hong, *J. Org. Chem.* **2011**, *76*, 882.
- [18] a) J. Cornella, P. F. Lu, I. Larrosa, *Org. Lett.* **2009**, *11*, 5506; b) J. Zhou, P. Hu, M. Zhang, S. J. Huang, M. Wang, W. P. Su, *Chem. Eur. J.* **2010**, *16*, 5876.
- [19] a) S. R. Dubbaka, P. Vogel, *Angew. Chem.* **2005**, *117*, 7848; *Angew. Chem. Int. Ed.* **2005**, *44*, 7674; b) P. Page, *Organosulfur Chemistry: Stereochemical Aspects*, Academic Press, Inc., San Diego, **1998**; c) N. S. Simpkins, *Sulfones in Organic Synthesis*, Pergamon Press, Oxford, **1993**; d) X. Zhao, E. Dimitrijević, V. M. Dong, *J. Am. Chem. Soc.* **2009**, *131*, 3466.
- [20] For early investigations on desulfative reaction using sulfinic acid (salt), see: a) K. Garves, *J. Org. Chem.* **1970**, *35*, 3273; b) R. Selke, W. Thiele, *J. Prakt. Chem.* **1971**, *313*, 875; c) E. Wenkert, T. W. Ferreira, E. L. Michelotti, *J. Chem. Soc. Chem. Commun.* **1979**, 637; d) For high efficiency biaryl synthesis using sulfinic acid sodium salts and aromatic bromides, see: K. Sato, T. Okoshi, U.S. Patent 5,159,082, **1992**.
- [21] a) X. Y. Zhou, J. Y. Luo, J. Liu, S. M. Peng, G. J. Deng, *Org. Lett.* **2011**, *13*, 1432. A similar reaction was developed recently using copper(II) as the oxidant: b) G. W. Wang, T. Miao, *Chem. Eur. J.* **2011**, *17*, 5787.
- [22] a) J. Liu, X. Y. Zhou, H. H. Rao, F. H. Xiao, C. J. Li, G. J. Deng, *Chem. Eur. J.* **2011**, *17*, 7996. For other desulfative aryl ketone formation reactions, see: b) H. Yao, L. Yang, Q. Shuai, C. J. Li, *Adv. Synth. Catal.* **2011**, *353*, 1701; c) T. Miao, G. W. Wang, *Chem. Commun.* **2011**, *47*, 9501; d) M. Behrends, J. Särmarker, P. Sjöberg, M. Larhed, *ACS Catal.* **2011**, *1*, 1455.
- [23] In general, the ratio of C-2/C-3 arylation is >20:1 as determined by GC-MS and ¹H NMR methods.
- [24] The reaction might take a similar pathway as the direct alkenylation of indoles using a Pd/Cu catalytic system, see: a) N. Grimster, C. Gauntlett, C. Godfrey, M. J. Gaunt, *Angew. Chem.* **2005**, *117*, 3185; *Angew. Chem. Int. Ed.* **2005**, *44*, 3125; b) L. Djakovitch, P. Rouge, *J. Mol. Catal. A: Chem.* **2007**, *273*, 230; c) L. Djakovitch, P. Rouge, *Catal. Today* **2009**, *140*, 90.