

Palladium Catalysis

Palladium-Catalyzed/Norbornene-Mediated C—H Activation/ N-Tosylhydrazone Insertion Reaction: A Route to Highly Functionalized Vinylarenes

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Abstract: A straightforward method for the synthesis of highly functionalized vinylarenes through palladium-catalyzed, norbornene-mediated C—H activation/carbene migratory insertion is described. Extension to a one-pot procedure is also developed. Furthermore, this method can also be used to generate polysubstituted bicyclic molecules. The reaction proceeds under mild conditions to give the products in satisfactory yields using readily available starting materials. This is a Catellani–Lautens reaction that incorporates different types of coupling partners. Additionally, this reaction is the first to demonstrate the possibility of combining Pdcatalyzed insertion of diazo compounds and Pd-catalyzed C–H activation.

Introduction

Multicomponent reactions (MCRs), which can create complex molecules in a single process from simple building blocks, have attracted significant attention over the past decades.^[1] Unlike stepwise processes, these reactions preclude the need for the synthesis of complex or prefunctionalized starting materials and these reactions are carried out in an efficient, atom economic way. For many years, palladium-catalyzed MCRs have been employed as one of the most reliable and powerful methods for the synthesis of complex organic compounds.^[2] Among them, palladium-catalyzed/norbornene mediated C-H activation, which was initially reported by Catellani and further developed by Lautens and others, have become more attractive because it is of fundamental importance in organic synthesis and because it offers a range of novel synthetic variations.^[3] The Catellani-Lautens reaction involves direct activation of an aromatic carbon-hydrogen bond and ortho-functionalization, followed by terminal cross-coupling processes for the formation of a diverse range of highly functionalized aromatic compounds. As shown in Scheme 1, the Catellani-Lautens reaction

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Scheme 1. Reaction mechanism of the Catellani-Lautens reaction.

starts with oxidative addition of an aryl halide to Pd⁰ to give palladium complex A, followed by carbopalladation of norbornene to form B. Next, C-H activation of the ortho position of the aryl halide and subsequent deprotonation delivers palladacycle C. This Pd^{II} complex reacts with a second alkyl halide, affording Pd^{V} complex **D**. Reductive elimination followed by deinsertion of norbornene through β -carbon elimination provides Pd^{\parallel} species **F**, which can further undergo palladium-catalyzed terminal cross-coupling reaction.^[4] In classic Catellani–Lautens reactions the type of coupling partners are often alkene or alkyne (Scheme 2, Eq. (1)),^[5]organometallic reagent (Scheme 2, Eq. (2)),^[6] nucleophile reagent (Scheme 2, Eq. (3)),^[7] hydrogen transfer reagent (Scheme 2, Eq. (4)),^[8] or heteroaromatics compound (Scheme 2, Eq. (5)).^[9] In view of the diverse requirements of synthetic organic chemistry, incorporation of different types of coupling partners in the reaction with terminal arylpalladium(II) species F is highly desired.

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Scheme 2. Terminal cross-coupling.

Recently, diazo compounds have been considered as a new type of cross-coupling partner in palladium-catalyzed reactions.^[10] In 2001, the first example of using stabilized trimethyl-silyldiazomethane as the coupling partner in palladium-catalyzed reactions was reported by Van Vranken.^[11] In 2007, Barluenga was the first to employ tosylhydrazones as a source of diazo compound in this unique reaction, which greatly expanded its scope.^[12] Over the past few years, significant advances have been made in the application of diazo compounds and tosylhydrazones as the coupling partner in this new class of reaction. However, most of these cross-couplings are still limited to oxidative addition and palladium carbene migratory insertion, followed by β -hydride elimination (Scheme 3).^[10] In-



Scheme 3. Traditional mechanism of Pd carbene migratory insertion.

corporation of the well-established chemistry of Pd concepts such as C-H activation, decarboxylative coupling, cascade reactions, oxidative cross-coupling reactions, and transmetallation, in this unique process would provide more novel transformations. Indeed, Wang and co-workers reported the first oxidative cross-coupling of boronic acids with α -diazocarbonyl compounds.^[13] Recently, the combination of transmetalation with palladium carbene migratory insertion has also been demonstrated by the same group.^[14] Van Vranken and co-workers developed a three-component cascade reaction of ethyl diazoacetate, vinyl halide, and secondary amine.^[15] We also reported a very interesting reaction that can be used to merge decarboxylation coupling with Pd carbene migratory insertion.[16] However, to our knowledge, incorporation of C-H activation in the palladium-catalyzed insertion of a diazo compound has not been explored.

In this paper, we report the first example of the use of *N*-tosylhydrazones as a coupling partner in the Catellani–Lautens reaction. We also demonstrate the possibility of combining Pdcatalyzed insertion of a diazo compound and Pd-catalyzed C– H activation.

Results and Discussion

At the outset, the three-component reaction of 1-iodo-2-methylbenzene (**1a**), 1-chloromethyl-4-methoxybenzene (**2a**), and *N*-tosylhydrazone **3a** was catalyzed by $Pd(OAc)_2$ (10 mol%)/ PPh₃ (20 mol%)/norbornene (3.0 equiv) in the presence of *t*BuOLi as base in dioxane at 90 °C for 15 h (Table 1, entry 1).^[17]



To our disappointment, none of the desired product **4a** was detected. A similar result was afforded when the base was changed to tBuOK, Na_2CO_3 , or K_2CO_3 (Table 1, entries 2–4). Gratifyingly, the desired product was isolated in 63% yield when Cs_2CO_3 was utilized as the base (Table 1, entry 5). With Cs_2CO_3 as the optimal base, we went on to evaluate other reaction parameters, such as solvent, additive, ligand and catalyst. Solvents such as 1,2-dichloroethane (DCE), CH₃CN, 2-methyltertrahydrofuran, and toluene were surveyed, but were found to be ineffective (Table 1, entries 6–9). We further investigated the effect of the additive. Barluenga and co-workers have

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shown that using water as additive in Pd-catalyzed cross-coupling with N-tosylhydrazone could significant improve the yield.^[18] Indeed, the yield could be further improved to 91% in the presence of 5.0 equiv. H₂O (Table 1, entry 10). To enhance the solubility of the sulfonylhydrazone salt, 2.0 equiv benzyl triethylammonium chloride (BTAC) was used as an additive, but this was found to be ineffective (data not shown). The use of 1.5 equiv of NEt₃ as co-base did not improve the yield (data not shown). No reaction occurred when [HPtBu₃]BF₄, Xphos, or Phen was used as the ligand, and a lower yield was obtained when the reaction was performed with tri(furan-2-yl)phosphine (TFP) (Table 1, entries 11-14). Employing dppb as the ligand gave moderate yields (Table 1, entry 15). For the palladium catalysts, various Pd^{II} and Pd^{0} were investigated, however, they were less efficient than Pd(OAc)₂ (Table 1, entries 16-20). Finally, a control experiment showed that the reaction did not proceed without palladium catalyst (Table 1, entry 21).

With the optimized reaction conditions established, the scope of this reaction was explored with a range of *N*-tosylhy-drazones **3**; the results are summarized in Table 2. It was found



that *N*-tosylhydrazones with electron-donating or electronwithdrawing groups on the aromatic ring worked smoothly to afford the desired product **4** in moderate to good yields. Notably, the NO₂ group was compatible with the reaction (Table 2, **4-12**). Additionally, *ortho*-substituted substrates also proceeded efficiently (Table 2, **4-13**, **4-14**, and **4-15**). It is worth noting that chloro- and bromo-substituents were tolerated under the Pd-catalyzed conditions, which allows further metal-catalyzed coupling reactions (Table 2, **4-5**, **4-6**, **4-10**, and **4-11**).

Next, a series of substituted benzyl chlorides were subjected to the optimized reaction conditions (Table 3). In all cases, the

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corresponding products were obtained in moderate to good yields. Both electron-withdrawing and electron-releasing groups on the aromatic ring were tolerated. The position of the substituent also did not noticeably affect the cross-coupling.

Finally, we tested the scope of the reaction with respect to aryl iodides under the standard conditions as shown in Table 2 and Table 3. Both electron-rich and electron-poor aryl iodides afforded the expected products **4** in moderate to good yields. Highly sterically hindered 1-iodo-2-isopropylbenzene successfully afforded the product **4-27** in 72% yield. 1-lodonaphthalene was also suitable for the reactions. According to previous reports, aryl iodides containing a substituent *ortho* to the C–H activation site are less reactive, which may be due to steric hindrance during the palladation of the C–H bond.^[9a,d,e] To our delight, the reaction proceeded efficiently and afforded the product in good yields (Table 4, **4-31**, **4-32**, and **4-33**).

The success of ortho-substituted aryl iodide in the C-H activation/carbene migratory insertion encouraged us to extend this methodology to prepare dibenzylated products by a double C-H activation of two ortho positions of aryl iodide. Indeed, dibenzylated products were obtained in moderate yields when aryl iodide was subjected to slightly modified standard reaction conditions. The reactions with meta- and para-substituted benzyl chloride all worked efficiently (Table 5, 4-35, 4-36, 4-37, 4-38, 4-39, and 4-40). For the aryl iodide, electronic effects of the substituent had a notable effect on the yield. Better results were obtained when the aryl iodide was substituted with an electron-rich group (Table 5, 4-41 and 4-42). A diminished yield was observed when the ring was substituted with an electron-poor group (Table 5, 4-45). The structure of 4-38 was confirmed by X-ray crystallographic analysis.[19]

Alkyl iodide was employed as the alkylating agent to further demonstrate the generality of this reaction. Various alkyl io-

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dides with substituents on the side chain reacted smoothly to afford the corresponding products in moderate to good yields. Chloride and oxygen atoms were tolerated, which could further undergo a variety of transformations (Table 6, **4-47** and **4-49**). Introduction of a CF₃ group was also accomplished, affording product **4-52** in 72% yield.

As summarized in Table 7, the three-component dialkylation/carbene migratory insertion cross-coupling could proceed smoothly with a wide range of alkyl iodide and *para*-substituted iodobenzene derivatives to give the products in moderate yields under the standard conditions.

We further extended the method to prepare polysubstituted bicyclic molecules. This coupling is more challenging because after intramolecular alkylation, the palladium species of substrate 1 s-v can react with itself instead of 2 k or 5 f. To our delight, when an excess of 2 k or 5 f was used, the desired product was isolated in moderate to good yields (Scheme 4). These results are consistent with a previous report.^[5f]

Taking into account that *N*-tosylhydrazone **3a** is readily formed by condensation of acetophenone with 4-methylbenzenesulfonohydrazide, we employed a one-pot reaction for the synthesis of product **4-1** and **4-51**. To our delight, when the reaction was performed directly from carbonyl compounds without the isolation of tosylhydrazone, a comparable yield was obtained to those observed for the twostep process (Scheme 5).

A plausible mechanism of ortho C-H activation/ carbene migratory insertion reaction is proposed in Scheme 6. Initial oxidative addition of Pd^0 to aryl iodide affords intermediate A, which undergoes carbopalladium of norbornene to give intermediate B. Insertion of Pd^{II} to the C–H bond followed by deprotonation generates intermediate C. Subsequently, reaction of alkyl or benzyl halides with this Pd^{II} species leads to octahedral Pd^{IV} intermediate **D**. Then reductive elimination takes place to form the Pd^{II} complex E. With steric stain of the two ortho substituents, extrusion of norbornene through β -carbon elimination occurs and the aryl palladium F is obtained, from which palladium carbene G is afforded by decomposition of diazo compound 3' (generated in situ from N-tosylhydrazone 3), followed by migratory insertion of the aryl group, and β -H elimination affords the product and regenerates the catalyst with the aid of base. Notably, for the Pd^{II} complex **E**, when R = H, a subsequent ortho C-H activation will occur to afford difunctionalized aryl palladium F.

Conclusion

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We have reported a Catellani–Lautens reaction with diazo compounds as a nucleophilic coupling partner in the termination steps for the synthesis of highly

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[a] Reaction conditions: **1a** (0.3 mmol, 1.0 equiv), **5** (0.75 mmol, 2.5 equiv), **3a** (0.6 mmol, 2.0 equiv), Pd(OAc)₂ (10 mol%), PPh₃ (20 mol%), norbornene (0.90 mmol, 3.0 equiv), H₂O (1.5 mmol, 5.0 equiv), Cs₂CO₃ (1.35 mmol, 4.5 equiv), dioxane (3 mL), 90 °C, 15 h under Ar. Yield of isolated product.



Scheme 4. Palladium-catalyzed sequential intramolecular alkylation/intermolecular alkylation/carbene migratory insertion reaction. Reaction conditions: 1 (0.3 mmol, 1.0 equiv), 2 k or 5 f (1.35 mmol, 4.5 equiv), 3 a (0.6 mmol, 2.0 equiv), Pd(OAc)₂ (10 mol%), PPh₃ (20 mol%), norbornene (0.90 mmol, 3.0 equiv), H₂O (1.5 mmol, 5.0 equiv), Cs₂CO₃ (1.65 mmol, 5.5 equiv), dioxane (3 mL), 90 °C, 15 h, under Ar. [a] The yield was determined by ¹H NMR spectroscopic analysis.





Scheme 5. One-pot synthesis of 4-1 and 4-51.

functionalized vinylarenes **4**. A one-pot procedure was also developed. This unique transformation, which involves a norbornene-mediated Pd-catalyzed C–H activation/carbene migratory insertion, was also the first example of incorporation of C–H activation in the Pd-catalyzed insertion of diazo compounds. The reaction has several potential advantages: 1) Two or three C–C bonds are formed in this process. 2) The reaction proceeds in moderate to good yield. 3) A wide range of functional groups could be compatible. 4) The starting materials are readily accessible. 5) Highly functionalized vinylarenes **4** are generated that are difficult to achieve by traditional methods.



Scheme 6. Proposed mechanism of *ortho* C–H activation/carbene migratory insertion reaction.

Experimental Section

Preparation of 4

General procedure: A dried Schlenk tube under an argon atmosphere was charged with aryl iodide 1, alkyl halides 2 or 5, *N*-tosyl-hydrazone 3, Pd(OAc)₂, PPh₃, norbornene, H₂O, Cs₂CO₃, and dioxane (3 mL). The mixture was stirred at RT for 15 min and then stirred at 90 °C for 15 h. The resulting mixture was cooled to RT and filtered through Celite with EtOAc as eluent. The solvents were evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel to afford pure **4**.

One-pot procedure for the preparation of 4-1 and 4-51: Acetophenone (0.66 mmol, 2.2 equiv) and 4-methylbenzenesulfonohydrazide (0.60 mmol, 2.0 equiv) were suspended in dioxane (1 mL) in a 10 mL Schlenk tube and the mixture was heated at 70 °C for 3 h. After cooling to RT, aryl iodide 1a (0.30 mmol, 1.0 equiv), alkyl halide 2a or 5 f (0.75 mmol, 2.5 equiv), $Pd(OAc)_2$ (10 mol%), PPh₃ (20 mol%), norbornene (0.90 mmol, 3.0 equiv), H_2O (0.9 mmol, 3.0 equiv), Cs_2CO_3 (1.35 mmol, 4.5 equiv), and dioxane (2 mL) were added. The Schlenk tube was fitted with an Ar balloon, the mixture was stirred at RT for 15 min, and then stirred at 90 °C for 15 h. The resulting mixture was cooled to RT and filtered through Celite with EtOAc as eluent. The solvents were evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel to afford pure 4-1 or 4-51.

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- [1] For selected books and reviews of MCR, see: a) A. Dömling, I. Ugi, Angew. Chem. 2000, 112, 3300; Angew. Chem. Int. Ed. 2000, 39, 3168; b) D. J. Ramón, M. Yus, Angew. Chem. 2005, 117, 1628; Angew. Chem. Int. Ed. 2005, 44, 1602; c) Multicomponent reactions, (Eds.: J. Zhu, H. Bienaymé),Wiley-VCH, Weinheim, 2005; d) D. Tejedor, F. García-Tellado, Chem. Soc. Rev. 2007, 36, 484; e) J. D. Sunderhaus, S. F. Martin, Chem. Eur. J. 2009, 15, 1300; f) B. B. Touré, D. G. Hall, Chem. Rev. 2009, 109, 4439; g) B. Ganem, Acc. Chem. Res. 2009, 42, 463; h) J. Yu, F. Shi, L.-Z. Gong, Acc. Chem. Res. 2011, 44, 1156; i) C. de Graaff, E. Ruijter, R. V. A. Orru, Chem. Soc. Rev. 2012, 41, 3969.
- [2] a) Handbook of Organopalladium Chemistry for Organic Synthesis (Eds.:
 E.-I. Negishi, A. de Meijere), Wiley, Hoboken, 2002; b) J. Tsuji, Palladium Reagents and Catalysts, Wiley, Chichester, 2004; c) Palladium in Organic Synthesis (Ed.: J. Tsuji), Springer, Berlin, 2005.
- [3] For selected reviews on Catellani–Lautens reaction, see: a) M. Catellani, Synlett 2003, 298; b) M. Catellani, Top. Organomet. Chem. 2005, 14, 21; c) M. Lautens, D. Alberico, C. Bressy, Y.-Q. Fang, B. Mariampillai, T. Wilhelm, Pure Appl. Chem. 2006, 78, 351; d) M. Catellani, E. Motti, N. Della Ca', Acc. Chem. Res. 2008, 41, 1512; e) P. Sehnal, R. J. K. Taylor, I. J. S. Fairlamb, Chem. Rev. 2010, 110, 824; f) A. Martins, B. Mariampillai, M. Lautens, Top. Curr. Chem. 2010, 292, 1; g) G. P. Chiusoli, M. Catellani, M. Costa, E. Motti, N. Della Ca', G. Maestri, Coord. Chem. Rev. 2010, 254, 456.
- [4] For selected references of mechanism studies, see: a) C.-S. Li, C.-H. Cheng, F.-L. Liao, S.-L. Wang, J. Chem. Soc. Chem. Commun. 1991, 710; b) M. Catellani, G. P. Chiusoli, J. Organomet. Chem. 1992, 425, 151; c) C.-S. Li, D.-C. Jou, C.-H. Cheng, Organometallics 1993, 12, 3945; d) C.-H. Liu, C.-S. Li, C.-H. Cheng, Organometallics 1994, 13, 18; e) M. Catellani, C. Mealli, E. Motti, P. Paoli, E. Perez-Carreño, P. S. Pregosin, J. Am. Chem. Soc. 2002, 124, 4336; f) D. J. Cárdenas, B. Martín-Matute, A. M. Echavarren, J. Am. Chem. Soc. 2006, 128, 5033; g) C. Amatore, M. Catellani, S. Deledda, A. Jutand, E. Motti, Organometallics 2008, 27, 4549; h) D. I. Chai, P. Thansandote, M. Lautens, Chem. Eur. J. 2011, 17, 8175; i) G. Maestri, E. Motti, N. Della Ca', M. Malacria, E. Derat, M. Catellani, J. Am. Chem. Soc. 2011, 133, 8574.
- [5] a) M. Catellani, M. C. Fagnola, Angew. Chem. 1994, 106, 2559; Angew. Chem. Int. Ed. Engl. 1994, 33, 2421; b) M. Catellani, F. Frignani, A. Rangoni, Anaew. Chem. 1997, 109, 142; Anaew. Chem. Int. Ed. Enal. 1997, 36, 119; c) M. Catellani, E. Motti, S. Baratta, Org. Lett. 2001, 3, 3611; d) M. Lautens, J.-F. Paguin, S. Piguel, M. Dahlmann, J. Org. Chem. 2001, 66, 8127; e) M. Lautens, J.-F. Paquin, S. Piguel, J. Org. Chem. 2002, 67, 3972; f) S. Pache, M. Lautens, Org. Lett. 2003, 5, 4827; g) F. Faccini, E. Motti, M. Catellani, J. Am. Chem. Soc. 2004, 126, 78; h) A. Martins, U. Marquardt, N. Kasravi, D. Alberico, M. Lautens, J. Org. Chem. 2006, 71, 4937; i) F. Jafarpour, M. Lautens, Org. Lett. 2006, 8, 3601; j) E. Motti, F. Faccini, I. Ferrari, M. Catellani, R. Ferraccioli, Org. Lett. 2006, 8, 3967; k) D. Alberico, A. Rudolph, M. Lautens, J. Org. Chem. 2007, 72, 775; I) N. Della Ca', E. Motti, M. Catellani, Adv. Synth. Catal. 2008, 350, 2513; m) K. M. Gericke, D. I. Chai, M. Lautens, Tetrahedron 2008, 64, 6002; n) K. M. Gericke, D. I. Chai, N. Bieler, M. Lautens, Angew. Chem. 2009, 121, 1475; Angew. Chem. Int. Ed. 2009, 48, 1447; o) P. Thansandote, C. Gouliaras, M.-O. Turcotte-Savard, M. Lautens, J. Org. Chem. 2009, 74, 1791; p) N. Della Ca', E. Motti, A. Mega, M. Catellani, Adv. Synth. Catal. 2010, 352, 1451; q) H. Liu, M. El-Salfiti, D. I. Chai, J. Auffret, M. Lautens, Org. Lett. 2012, 14, 3648; r) F. Jafarpour, N. Jalalimanesh, Tetrahedron 2012, 68, 10286; s) H. Liu, M. El-Salfiti, M. Lautens, Angew. Chem. 2012, 124, 9984; Angew. Chem. Int. Ed. 2012, 51, 9846; t) X. Sui, R. Zhu, G. Li, X. Ma, Z. Gu, J. Am. Chem. Soc. 2013, 135, 9318.
- [6] a) M. Catellani, E. Motti, M. Minari, *Chem. Commun.* 2000, 157; b) E. Motti, A. Mignozzi, M. Catellani, *J. Mol. Catal. A: Chem.* 2003, 204–205, 115; c) B. Mariampillai, D. Alberico, V. Bidau, M. Lautens, *J. Am. Chem. Soc.* 2006, 128, 14436; d) B. Mariampillai, J. Alliot, M. Li, M. Lautens, *J. Am. Chem. Soc.* 2007, 129, 15372; e) E. Motti, N. Della Ca', S. Deledda, E. Fava, F. Panciroli, M. Catellani, *Chem. Commun.* 2010, 46, 4291.
- [7] a) R. Ferraccioli, D. Carenzi, O. Rombolà, M. Catellani, Org. Lett. 2004, 6, 4759; b) P. Thansandote, M. Raemy, A. Rudolph, M. Lautens, Org. Lett. 2007, 9, 5255; c) D. A. Candito, M. Lautens, Angew. Chem. 2009, 121, 6841; Angew. Chem. Int. Ed. 2009, 48, 6713; d) G. Maestri, N. Della Ca', M. Catellani, Chem. Commun. 2009, 4892; e) P. Thansandote, E. Chong, K.-O. Feldmann, M. Lautens, J. Org. Chem. 2010, 75, 3495; f) G. Maestri, M.-H. Larraufie, E. Derat, C. Ollivier, L. Fensterbank, E. Lacôte, M. Malac-

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ria, Org. Lett. 2010, 12, 5692; g) M. Blanchot, D. A. Candito, F. Larnaud, M. Lautens, Org. Lett. 2011, 13, 1486.

- [8] a) S. Deledda, E. Motti, M. Catellani, *Can. J. Chem.* 2005, *83*, 741; b) T.
 Wilhelm, M. Lautens, *Org. Lett.* 2005, *7*, 4053; c) K. Mitsudo, P. Thansandote, T. Wilhelm, B. Mariampillai, M. Lautens, *Org. Lett.* 2006, *8*, 3939; d) A. Martins, M. Lautens, *Org. Lett.* 2008, *10*, 5095; e) Z. Dong, G. Dong, *J. Am. Chem. Soc.* 2013, *135*, 18350.
- [9] a) C. Bressy, D. Alberico, M. Lautens, J. Am. Chem. Soc. 2005, 127, 13148;
 b) C. Blaszykowski, E. Aktoudianakis, C. Bressy, D. Alberico, M. Lautens, Org. Lett. 2006, 8, 2043; c) A. Martins, D. Alberico, M. Lautens, Org. Lett. 2006, 8, 4827; d) C. Blaszykowski, E. Aktoudianakis, D. Alberico, C. Bressy, D. G. Hulcoop, F. Jafarpour, A. Joushaghani, B. Laleu, M. Lautens, J. Org. Chem. 2008, 73, 1888; e) B. Laleu, M. Lautens, J. Org. Chem. 2008, 73, 9164; f) A. Martins, M. Lautens, J. Org. Chem. 2008, 73, 8705;
 g) F. Jafarpour, H. Hazrati, Adv. Synth. Catal. 2010, 352, 363.
- [10] For reviews on using diazo compounds as coupling partner in palladium-catalyzed reaction, see: a) J. Barluenga, C. Valdés, Angew. Chem.
 2011, 123, 7626; Angew. Chem. Int. Ed. 2011, 50, 7486; b) N. M. G. Franssen, A. J. C. Walters, J. N. H. Reek, B. de Bruin, Catal. Sci. Technol. 2011, 1, 153; c) Y. Zhang, J. Wang, Eur. J. Org. Chem. 2011, 1015; d) Z. Shao, H. Zhang, Chem. Soc. Rev. 2012, 41, 560; e) Y. Zhang, J. Wang, Top. Curr. Chem. 2012, 327, 239; f) Q. Xiao, Y. Zhang, J. Wang, Acc. Chem. Res. 2013, 46, 236.
- [11] K. L. Greenman, D. S. Carter, D. L. Van Vranken, *Tetrahedron* **2001**, *57*, 5219.
- [12] J. Barluenga, P. Moriel, C. Valdés, F. Aznar, Angew. Chem. 2007, 119, 5683; Angew. Chem. Int. Ed. 2007, 46, 5587.
- [13] C. Peng, Y. Wang, J. Wang, J. Am. Chem. Soc. 2008, 130, 1566.

- [14] L. Zhou, F. Ye, Y. Zhang, J. Wang, J. Am. Chem. Soc. 2010, 132, 13590.
- [15] R. Kudirka, S. K. J. Devine, C. S. Adams, D. L. Van Vranken, Angew. Chem.
- 2009, 121, 3731; Angew. Chem. Int. Ed. 2009, 48, 3677.
 [16] Z.-S. Chen, X.-H. Duan, P.-X. Zhou, S. Ali, J.-Y. Luo, Y.-M. Liang, Angew. Chem. 2012, 124, 1399; Angew. Chem. Int. Ed. 2012, 51, 1370.
- [17] From the mechanism, norborene could theoretically be used in catalytic quantities. However, the reaction requires a large excess to favor norbornene insertion and C–H activation as the early step in the process instead of the palladium-catalyzed cross-coupling of the diazo compound with aryl iodide reaction. 10% of Pd(OAc)₂ was employed may be to match each step of the reaction. For selected references on Catellani–Lautens reaction and the use of excess norborene and 10% Pd(OAc)₂, see refs. [5d–5f, 5h, 5i, 5k, 5r, 5t, 6c, 6d, 7b, 7c, 7e, 7g, 8b, 8d, 9a–fl.
- [18] At this stage, the reason for the significantly improved yield with water is unknown, see: a) J. Barluenga, L. Florentino, F. Aznar, C. Valdés, Org. Lett. 2011, 13, 510; b) J. Barluenga, M. Escribano, F. Aznar, C. Valdés, Angew. Chem. 2010, 122, 7008; Angew. Chem. Int. Ed. 2010, 49, 6856.
- [19] The molecular structure of 4-38 was determined on the basis of X-ray crystallographic studies. CCDC-981521 contains 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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FULL PAPER

Palladium Catalysis

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Palladium-Catalyzed/Norbornene-Mediated C-H Activation/N-Tosylhydrazone Insertion Reaction: A Route to Highly Functionalized Vinylarenes

Activate and move! A novel method for the synthesis of highly functionalized vinylarenes through palladium-catalyzed, norbornene-mediated C—H activation/carbene migratory insertion is developed under mild reaction conditions with readily available starting materials (see scheme). This is a Catellani– Lautens reaction with diazo compound as a nucleophilic coupling partner. This unique transformation is also the first example of incorporation of C–H activation in the Pd-catalyzed insertion of a diazo compound.

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