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Synthesis of *N*-Vinylcarbazoles via Dehydrogenative Coupling of *N*-H Carbazoles with Alkenes under Palladium Catalysis

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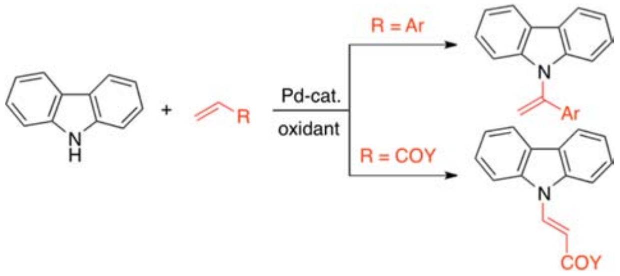
ABSTRACT



The synthesis of *N*-vinylcarbazoles was achieved by the palladium-catalyzed aza-Wacker reaction of *N*-H carbazoles with styrenes. In this reaction, Markovnikov adducts were exclusively produced. In contrast, the reaction with electron-deficient alkenes such as acrylates and acrylamides gave only anti-Markovnikov adducts.

N-Vinylcarbazoles have been recognized to be an important class of monomers for the production of poly(vinylcarbazole)s.[1] Polymers and oligomers containing carbazole moieties are now widely utilized in organic electroluminescence (EL) devices, photocopiers, and nonlinear optical (NLO) systems, etc.[1,2] However, their conventional preparation methods are problematic because of their multistep procedures and low selectivity and efficiency. Recently, the palladium- and copper-catalyzed coupling reactions of *N*-H carbazoles with vinyl bromides have been developed for the simple preparation of *N*-vinylcarbazoles.[3] From the atom- and step-economical points of view, a more attractive approach is the oxidative coupling of *N*-H carbazoles with alkenes. In this kind of intermolecular aza-Wacker reaction, however, the nucleophiles are so far limited to amides and carbamates.[4]

[†] Osaka University.

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(1) Selected examples: (a) Yomogida, T.; Watanabe, M.; Takeshima, M.; Aoki, S. Jpn. Kokai Tokkyo Koho. JP 201241387, 2012. (b) Angiuli, M.; Ciardelli, F.; Colligiani, A.; Greco, F.; Romano, A.; Ruggeri, G.; Tombari, E. *Appl. Opt.* **2006**, *45*, 7928. (c) Brustolin, F.; Castelvetro, V.; Ciardelli, F.; Rugger, G.; Colligiani, A. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 253. (d) Park, S.-H.; Ogino, K.; Sato, H. *Synth. Met.* **2000**, *113*, 135. (e) Trofimov, B. A.; Mikhaleva, A. I.; Morozova, L. V. *Russ. Chem. Rev.* **1985**, *54*, 609.

(2) Selected examples: (a) Jiang, W.; Duan, L.; Qiao, J.; Dong, G.; Zhang, D.; Wang, L.; Qui, Y. *J. Mater. Chem.* **2011**, *21*, 4918. (b) Albrecht, K.; Yamamoto, K. *J. Am. Chem. Soc.* **2009**, *131*, 2244. (c) Watanabe, S.; Okada, H. Jpn. Kokai Tokkyo Koho. JP 200418787, 2004. (d) Kawakami, T.; Sonoda, N. *Appl. Phys. Lett.* **1993**, *62*, 2167.

(3) (a) Liao, Q.; Wang, Y.; Zhang, L.; Xi, C. *J. Org. Chem.* **2009**, *74*, 6371. (b) Dehli, J. R.; Legros, J.; Bolm, C. *Chem. Commun.* **2005**, 973. (c) Lebedev, A. Y.; Izmer, V. V.; Kazyul'kin, D. N.; Beletskaya, I. P.; Voskoboynikov, A. Z. *Org. Lett.* **2002**, *4*, 623. See also reviews concerning catalytic C–N coupling reactions of organic halides with amines: (d) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805. (e) Hartwig, J. F. *Acc. Chem. Res.* **1998**, *31*, 852.

(4) (a) Liu, X.; Hii, K. K. *Eur. J. Org. Chem.* **2010**, 5181. (b) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 6328. (c) Lee, J. M.; Ahn, D.-S.; Jung, D. Y.; Lee, J.; Do, Y.; Kim, S. K.; Chang, S. *J. Am. Chem. Soc.* **2006**, *128*, 12954. (d) Timokhin, V. I.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 17888. (e) Brice, J. L.; Harang, J. E.; Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 2868. (f) Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2003**, *125*, 12996. (g) Hosokawa, T.; Takano, M.; Kuroki, Y.; Murahashi, S.-I. *Tetrahedron Lett.* **1992**, *33*, 6643. See also a review: (h) Kotov, V.; Scarborough, C. C.; Stahl, S. S. *Inorg. Chem.* **2007**, *46*, 1910.

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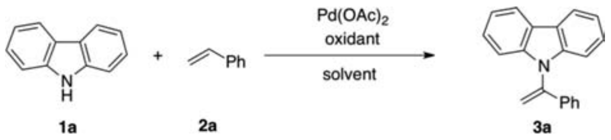
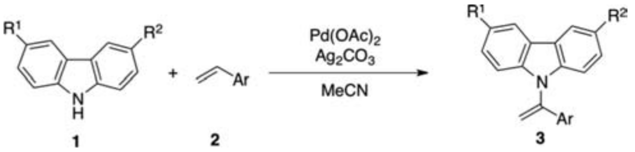
Table 1. Reaction of Carbazole (**1a**) with Styrene (**2a**)^a

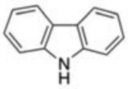
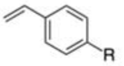
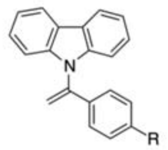
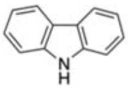
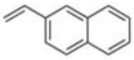
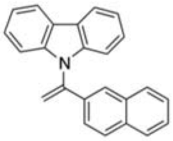
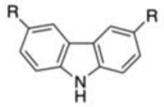
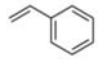
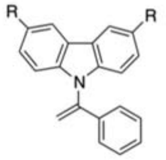
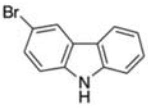
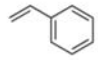
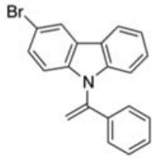


entry	oxidant (mmol)	solvent	yield of **3a**^{b} (%)
1	AgOAc (0.4)	MeCN	84
2	AgOAc (0.4)	*o*-xylene	49
3	AgOAc (0.4)	dioxane	54
4	AgOAc (0.4)	diglyme	39
5	AgOAc (0.4)	DME	48
6	AgOAc (0.4)	DMF	58
7^c	Ag_2CO_3 (0.2)	MeCN	>99 (85)
8	$Cu(OAc)_2 \cdot H_2O$ (0.4)	MeCN	53
9^d	$Cu(OAc)_2 \cdot H_2O$ (0.04)	MeCN	57
10^e	$Cu(OAc)_2 \cdot H_2O$ (0.04)	MeCN	39

^{a} Reaction conditions: [**1a**]/[**2a**]/[$Pd(OAc)_2$] = 0.2:1:0.02 (in mmol), in solvent (2 mL) at 100 °C for 6 h under N_2, unless otherwise noted. ^{b} GC yield based on the amount of **1a** used. Value in parentheses indicates yield after purification. ^{c} For 3 h. ^{d} Under O_2. ^{e} Under air.

Table 2. Reaction of Carbazoles **1** with Styrenes **2**^{a}



entry	**1**	**2**	**3**, yield (%)^b
			
1	**1a**	**2b**: R = Me	**3b**: R = Me, >99 (98)
2		**2c**: R = OMe	**3c**: R = OMe, >99 (98)
3		**2d**: R = Cl	**3d**: R = Cl, 80 (80)
			
4	**1a**	**2e**	**3e**, 92 (92)
			
5	**1b**: R = ^{t}Bu	**2a**	**3f**: R = ^{t}Bu, 89 (86)
6^c	**1c**: R = Cl		**3g**: R = Cl, 79 (69)
7^{c,d}	**1d**: R = Br		**3h**: R = Br, 69 (61)
			
8^c	**1e**	**2a**	**3i**, 51 (51)

^{a} Reaction conditions: [**1**]/[**2**]/[$Pd(OAc)_2$]/[Ag_2CO_3] = 0.2:1:0.02:0.2 (in mmol), in MeCN (2 mL) at 100 °C for 3 h under N_2, unless otherwise noted. ^{b} GC yield based on the amount of **1** used. Value in parentheses indicates yield after purification. ^{c} For 1 d. ^{d} At 120 °C.

Although one exception using anilines has been known,[5] there is, to our knowledge, no report of the reactions of azoles.[6] In the context of our studies of the palladium-catalyzed oxidative coupling of nitrogen-containing heteroarenes,[7] we succeeded in finding that the novel aza-Wacker-type dehydrogenative coupling of carbazoles with alkenes can be realized under palladium catalysis to produce *N*-vinylated carbazole derivatives.[8] Depending on the identities of alkenes, Markovnikov- or anti-Markovnikov adducts can be exclusively obtained. These new findings are described herein.

In an initial attempt, carbazole (**1a**) (0.2 mmol) was treated with an excess amount of styrene (**2a**) (1 mmol) in the presence of $Pd(OAc)_2$ (0.02 mmol) and AgOAc (0.4 mmol) as catalyst and oxidant, respectively, in MeCN (2 mL) at 100 °C for 6 h under N_2. As a result, the dehydrogenative coupling effectively proceeded to afford a Markovnikov adduct, 9-(1-phenylethenyl)-9*H*-carbazole (**3a**) in 84% yield, along with a small amount (ca. 5%) of an isomer (entry 1 in Table 1). The reaction was somewhat sluggish in other solvents such as *o*-xylene, dioxane, diglyme, DME, and DMF (entries 2−6). Interestingly, the use of Ag_2CO_3 (0.2 mmol) in place of AgOAc promoted effectively to produce **3a** quantitatively within 3 h (entry 7). The reaction also proceeded even under O_2 atmosphere in the presence of a catalytic amount of $Cu(OAc)_2 \cdot H_2O$ (0.04 mmol) to give **3a** in a moderate yield (entry 9). Under air, however, the product yield was reduced further (entry 10).

The reactions of various carbazoles **1** with styrenes **2** were next examined. Under optimized conditions in Table 1 (entry 7), a series of *para*-substituted styrenes **2b**−**d** underwent coupling with **1a** to afford the corresponding 9-[1-(*p*-substituted phenyl)ethenyl]-9*H*-carbazoles **3b**−**d** in good yields (entries 1−3 in Table 2). 2-Vinylnaphthalene (**2e**) could also be employed in place of styrenes

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(5) Bozell, J. J.; Hegedus, L. S. *J. Org. Chem.* **1981**, *46*, 2561.

(6) Baran and co-workers recently reported the palladium-catalyzed *N*-*tert*-prenylation of indoles: Luzung, M. R.; Lewis, C. A.; Baran, P. S. *Angew. Chem., Int. Ed.* **2009**, *48*, 7025.

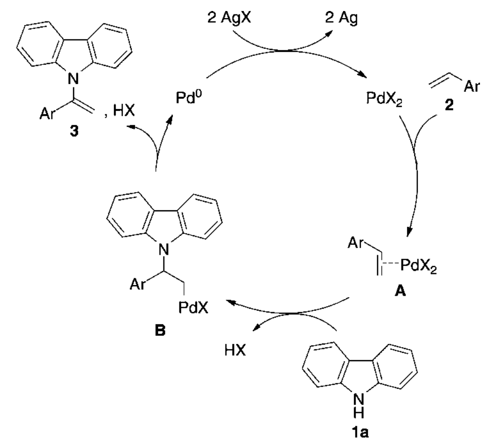
(7) (a) Miyasaka, M.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2010**, *75*, 5421. (b) Yamashita, M.; Horiguchi, H.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 7481. (c) Yamashita, M.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2009**, *11*, 2337. (d) Maehara, A.; Tsurugi, H.; Satoh, T.; Miura, M. *Org. Lett.* **2008**, *10*, 1159.

(8) During the preparation of this manuscript, Jiang, Wang, and co-workers reported the palladium-catalyzed oxidative coupling of azoles with alkynes: (a) Wang, L.; Huang, J.; Peng, S.; Liu, H.; Jiang, X.; Wang, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 1768. For a related reaction of carbon nucleophiles with alkynes, see: (b) Wang, L.; Peng, S.; Wang, J. *Chem. Commun.* **2011**, *47*, 5422.

(entry 4). Under similar conditions, 3,6-di-*tert*-butylcarbazole (**1b**) reacted efficiently with **2a** to form an aza-Wacker product **3f** (entry 5). In contrast, the reactions of relatively electron-poorer carbazoles such as 3,6-dichloro- and 3,6-dibromocarbazoles **1c** and **1d** were sluggish. After 1 d, the corresponding products **3g** and **3h** were obtained in 79 and 69% yields, respectively (entries 6 and 7). Especially in the latter case, heating at 120 °C was required. 3-Monobromocarbazole (**1e**) also underwent the reaction, albeit with moderate efficiency (entry 8).

A plausible mechanism for the reaction of carbazole (**1a**) with styrene **2** is illustrated in Scheme 1, in which neutral ligands are omitted. Coordination of **2** to a Pd^{II} center and subsequent nucleophilic attack on the resulting intermediate **A** by **1** take place to form an alkylpalladium intermediate **B**, accompanied by C−N bond formation. Finally, β-hydrogen elimination may occur to release **3**. The Pd^{II} species seems to be regenerated by Ag^{I}. Similar Markovnikov regioselectivity has also been observed in the palladium-catalyzed aza-Wacker reaction of styrenes with amides.[4d,f]

Scheme 1



It should be noted that the bromo moieties in substrates are tolerable under the present Pd^{II}/Pd^{0} catalysis.[9] These moieties can be employed in further functionalization. As a preliminary trial, we examined the palladium-catalyzed amination of the C−Br bonds.[3d,e] Treatment of **3h**, produced in the reaction of **1d** with **2a** (entry 7 in Table 2), with carbazole (**1a**) in the presence of $Pd(OAc)_2$, P^tBu_3, and ^tBuONa as catalyst, ligand, and base, respectively, gave a double-aminated product **4** in 72% yield (Scheme 2). This kind of carbazole trimer is known to be utilizable as host material for phosphorescent devices.[2a,c]

Scheme 2

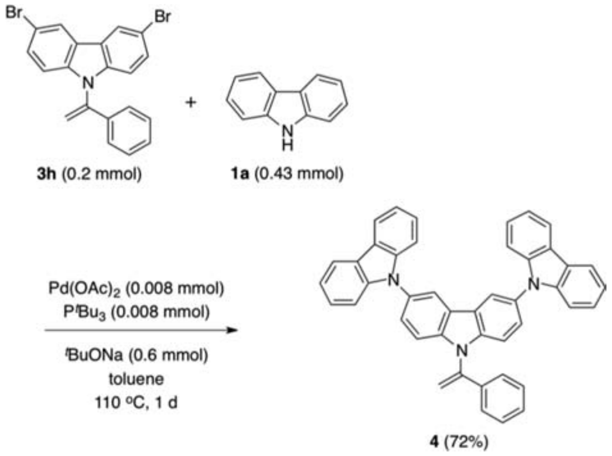
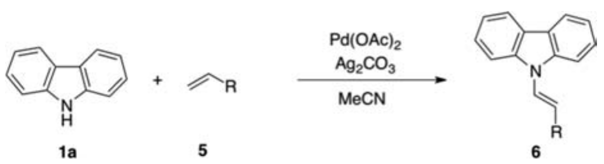


Table 3. Reaction of Carbazole **1a** with Acrylates or Acrylamides **5**[a]



entry	5	temp (°C)	time	6, yield[b] (%)
1	**5a**: R = $CO_2{}^nBu$	100	6 h	**6a**: R = $CO_2{}^nBu$, 63
2[c]	**5a**: R = $CO_2{}^nBu$	100	6 h	**6a**: R = $CO_2{}^nBu$, 25
3[d,e]	**5a**: R = $CO_2{}^nBu$	100	6 h	**6a**: R = $CO_2{}^nBu$, 22
4	**5a**: R = $CO_2{}^nBu$	80	6 h	**6a**: R = $CO_2{}^nBu$, 72
5	**5a**: R = $CO_2{}^nBu$	60	6 h	**6a**: R = $CO_2{}^nBu$, 48
6	**5a**: R = $CO_2{}^nBu$	60	1.5 d	**6a**: R = $CO_2{}^nBu$, 90 (85)
7	**5a**: R = $CO_2{}^nBu$	rt	8 d	**6a**: R = $CO_2{}^nBu$, 72 (72)
8	**5b**: R = $CO_2{}^iBu$	60	1.5 d	**6b**: R = $CO_2{}^iBu$, 90 (77)
9	**5c**: R = CO_2Cy[f]	60	1.5 d	**6c**: R = CO_2Cy, 87 (86)
10	**5d**: R = $CONMe_2$	100	1 d	**6d**: R = $CONMe_2$, >99 (98)
11	**5e**: R = $CONH^tBu$	100	1 d	**6e**: R = $CONH^tBu$, 87 (86)

[a] Reaction conditions: [**1a**]/[**5**]/[$Pd(OAc)_2$]/[Ag_2CO_3] = 0.2:1:0.02:0.2 (in mmol), in MeCN (2 mL) under N_2, unless otherwise noted. [b] GC yield based on the amount of **1a** used. Value in parentheses indicates yield after purification. [c] $Cu(OAc)_2 \cdot H_2O$ (0.4 mmol) was used in place of Ag_2CO_3. [d] $Cu(OAc)_2 \cdot H_2O$ (0.04 mmol) was used in place of Ag_2CO_3. [e] Under air. [f] Cy = cyclohexyl.

In contrast to the reaction of styrenes, it has been known that the aza-Wacker reactions of electron-deficient alkenes such as acrylates with amides give anti-Markovnikov adducts selectively.[4a,c,g] The same trend was also observed in the reaction with carbazoles. Thus, treatment of *n*-butyl acrylate (**5a**) with **1a** under standard conditions using $Pd(OAc)_2$ (10 mol %) and Ag_2CO_3 (1 equiv) in MeCN at 100 °C for 6 h exclusively gave (*E*)-*n*-butyl 3-(9*H*-carbazol-9-yl)acrylate (**6a**) in 63% yield, no regioisomer being detected by GC and GC−MS (entry 1 in Table 3). Under conditions using a stoichiometric amount of $Cu(OAc)_2 \cdot H_2O$ (entry 2) or a catalytic amount of $Cu(OAc)_2 \cdot H_2O$ under air (entry 3) as oxidant in place of Ag_2CO_3, the product yield considerably decreased. Decreasing reaction temperature was found to enhance the yield. Thus, **6a** was

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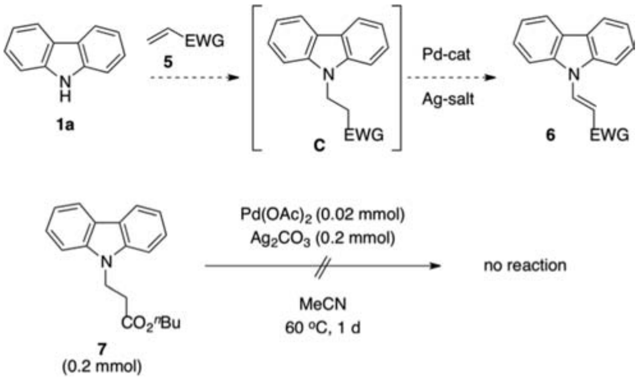
[9] Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094.

Scheme 3



obtained in 72% yield at 80 °C (entry 4). Moreover, although the reaction was retarded at 60 °C, the yield of **6a** reached 90% after 1.5 d (entry 6). Even at room temperature, **6a** was obtained in 72% yield upon treatment for 8 d (entry 7). At 60 °C, **1a** also coupled with isobutyl and cyclohexyl acrylates **5b** and **5c** to give **6b** and **6c** in good yields (entries 8 and 9). Acrylamides **5d** and **5e** could also be employed for the anti-Markovnikov addition to produce **6d** and **6e** efficiently (entries 10 and 11).

Since carbazole is known to readily add to electron-deficient alkenes under mild conditions even in the absence of any catalyst,[10] it is possible that **6** was produced through the initial nucleophilic addition of **1a** to **5** to form an intermediate **C** and subsequent its dehydrogenation (Scheme 3). However, the dehydrogenation of separately synthesized **7** did not proceed at all under standard conditions: **7** being completely intact even after 1 d. Therefore, the stepwise route involving the intermediary formation of **7** can be ruled out.

In summary, we have demonstrated that the palladium-catalyzed aza-Wacker reaction of carbazoles with alkenes proceeds efficiently to give the corresponding *N*-vinylated carbazoles. Markovnikov- and anti-Markovnikov adducts could be exclusively prepared in the reactions with styrenes and acrylates, respectively.

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Supporting Information Available. Standard experimental procedure and characterization data of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Ferorelli, S.; Abate, C.; Colabufo, N. A.; Niso, M.; Inglese, C.; Berardi, F.; Perrone, R. *J. Med. Chem.* **2007**, *50*, 4648.

The authors declare no competing financial interest.