ORGANIC
LETTERS

2004
Vol. 6, No. 21
3739−3741

Synthesis of Carbazoles and Dibenzofurans via Cross-Coupling of *o*-Iodoanilines and *o*-Iodophenols with Silylaryl Triflates

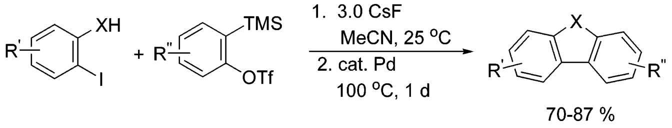
Zhijian Liu and Richard C. Larock*

Department of Chemistry, Iowa State University, Ames, Iowa 50011

larock@iastate.edu

Received July 23, 2004

ABSTRACT



X = O, NH, NCH_3, CH_3SO_2N, NCO_2Et

An efficient route to synthesize a variety of carbazoles and dibenzofurans has been developed. It involves the reaction of *o*-iodoanilines or *o*-iodophenols with silylaryl triflates in the presence of CsF to afford the N- or O-arylated products, which are subsequently cyclized using a Pd catalyst to carbazoles and dibenzofurans in good to excellent yields. This chemistry tolerates a variety of functional groups.

Carbazoles[1] and dibenzofurans[2] are important heteroaromatic compounds, which display a wide variety of biological activities. Carbazole derivatives are also widely used as building blocks for potential electroluminescent materials,[3] polymers with useful electrical[4] and thermal properties,[5] and host materials for triplet emitters in organic light-emitting diodes.[6] The dibenzofuran-containing phytoalexins show manifold biological activities, eliciting a strong interest from chemists and biologists.[7] Considerable effort has been devoted to the development of efficient methods for the construction of these ring systems.[8] For example, very recently Wu has utilized anionic cycloaromatization to synthesize 5-substituted dibenzofurans and carbazoles.[9] While there are presently a number of useful synthetic procedures to prepare these compounds, there remain several limitations as well. (1) Most of the present procedures involve several steps, and the overall yields usually are not very good. (2) The starting materials are often not very readily available.[8] (3) Harsh reaction conditions are usually needed. One

---

(1) (a) Chakraborty, D. P. In *The Alkaloids*; Bossi, A., Ed.; Academic Press: New York, 1993; Vol. 44, p 257. (b) Gallagher, P. T. *Science of Synthesis*; Thieme: Stuttgart, 2000; Vol. 10, pp 693−744. (c) Omura, S.; Sasaki, Y.; Iwai, Y.; Takeshima, H. *J. Antibiot.* **1995**, *48*, 535−548. (d) Knölker, H. J. In *Advances in Nitrogen Heterocycles*; Moody, C. J., Ed.; JAI: Greenwich, 1995; Vol. 1, p 173. (e) Moody, C. J. *Synlett* **1994**, 681−688. (f) Bergman, J.; Pelcman, B. *Pure Appl. Chem.* **1990**, *62*, 1967−1976.

(2) (a) Abe, H.; Uchiyama, M.; Tanaka, Y.; Saitô, H. *Tetrahedron Lett.* **1976**, *17*, 3807−3810. (b) Morris, H. R.; Taylor, G. W.; Masento, M. S.; Jermyn, K. A.; Kay, R. R. *Nature* **1987**, *328*, 811−814. (c) Hogberg, H.-E.; Hjalmarsson, M. *Tetrahedron Lett.* **1978**, *19*, 5215−5218. (d) Kokubun, T.; Harborne, J. B.; Eagles, J.; Waterman, P. G. *Phytochemistry* **1995**, *39*, 1039−1042.

(3) Justin Thomas, K. R.; Lin, J. T.; Tao, Y.-T.; Ko, C.-W. *J. Am. Chem. Soc.* **2001**, *123*, 9404−9411.

(4) Biswas, M.; Das, S. K. *Polymer* **1982**, *23*, 1713−1725.

(5) (a) Biswas, M.; Mishra, G. C. *Makromol. Chem.* **1981**, *182*, 261−264. (b) Biswas, M.; Das, S. K. *Eur. Polym. J.* **1981**, *17*, 1245−1251.

(6) Van Dijken, V.; Bastiaansen, J. J. A. M.; Kiggen, N. M. M.; Langeveld, B. M. W.; Rothe, C.; Monkman, A.; Bach, I.; Stössel, P.; Brunner, K. *J. Am. Chem. Soc.* **2004**, *126*, 7718−7727.

(7) (a) Konijn, T. M.; Van de Meene, J. G. C.; Bonner, J. T.; Barkley, D. S. *Biochemistry* **1967**, *6*, 1152−1154. (b) Wang, S.; Hall, J. E.; Tanious, F. A.; Wilson, W. D.; Partick, D. A.; McCurdy, D. R.; Bender, B. C.; Tidwell, R. R. *Eur. J. Med. Chem.* **1999**, *34*, 215−224.

(8) (a) Knölker, H.-J.; Reddy, K. R. *Chem. Rev.* **2002**, *102*, 4303−4427. (b) Pindur, U.; Erfanian-Abdoust, H. *Chem. Rev.* **1989**, *89*, 1681−1689. (c) Boese, R.; Van Sickle, A. P.; Vollhardt, K. P. C. *Synthesis* **1994**, 1374−1382. (d) Yamato, T.; Hideshima, C.; Prakach, G. K. S.; Olah, G. A. *J. Org. Chem.* **1991**, *56*, 3192−3194. (e) Gray, A. P.; Dipinto, V. M.; Solomon, I. J. *J. Org. Chem.* **1976**, *41*, 2428−2434. (f) Akermark, B.; Eberson, L.; Jonsson, E.; Petterson, E. *J. Org. Chem.* **1975**, *40*, 1365−1367.

(9) (a) Lee, C.-Y.; Lin, C.-F.; Lee, J.-L.; Chiu, C.-C.; Lu, W.-D.; Wu, M.-J. *J. Org. Chem.* **2004**, *69*, 2106−2110. (b) Wu, M.-J.; Lee, C.-Y.; Lin, C.-F. *Angew. Chem., Int. Ed.* **2002**, *41*, 4077−4079.

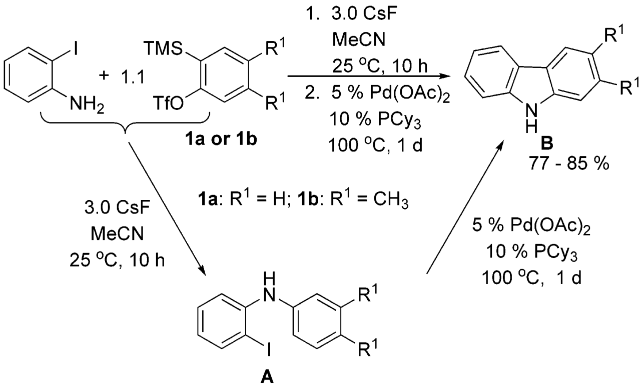
10.1021/ol048564l CCC: $27.50

simple, efficient, and general method to synthesize both the carbazole and dibenzofuran ring systems would be quite attractive, because of the growing interest in these compounds.[10]

Considerable work has been reported on the synthesis of indoles and benzofurans by the cross-coupling of *o*-haloanilines or *o*-halophenols with alkynes by palladium chemistry.[11] Nobody has studied the cross-coupling of *o*-haloanilines or *o*-halophenols with arynes or their synthetic equivalents, which, if successful, could afford a very direct route to carbazoles and dibenzofurans.

Recently, silylaryl triflate **1a**[12] has been employed to generate benzyne, which can easily undergo a variety of electrophilic and nucleophilic reactions,[13] under very mild reaction conditions. Herein, we report a simple, economical, and efficient one-pot, two-step procedure to synthesize the carbazole and dibenzofuran ring systems in good to excellent yields through the cross-coupling of *o*-iodoanilines or *o*-iodophenols with the silylaryl triflates **1a**/**1b**, followed by palladium-catalyzed intramolecular cyclization. The essential aspects of our approach are shown in Scheme 1. *o*-Iodoaniline first reacts with silylaryl triflate **1a** or **1b** to afford the N-arylated *o*-iodoaniline (**A**), which subsequently undergoes intramolecular palladium-catalyzed arylation in the same pot to produce the carbazole derivatives **B** in good yields.

Scheme 1



Preliminary studies focused on optimization of the intramolecular arylation step (**A**→**B**). A range of palladium catalysts was employed. We found that $Pd(OAc)_2$ was the best catalyst. All other palladium catalysts [$PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, $Pd(dba)_2$] examined afforded either comparable or lower yields. The ligand added to the reaction did not make much difference. Thus, the ligands dppe, dppm, and PCy_3 all worked well in our system. After our optimization work was complete, we settled on the following standard two-step procedure. The iodoaniline (0.25 mmol), the silylaryl triflate (1.1 equiv), and CsF (3.0 equiv) were allowed to react at room temperature for 10 h in acetonitrile (4.0 mL) under air. Then, $Pd(OAc)_2$ (3.1 mg, 5 mol %) and PCy_3 (7.0 mg, 10 mol %) were added and the reaction mixture was heated to 100 °C for 1 day under argon.

The results using this method are summarized in Table 1. A variety of *o*-iodoanilines react with silylaryl triflate **1a** or **1b** to afford high yields of the desired carbazoles (entries 1−7, Table 1). A slight excess of the silylaryl triflate **1a** has been allowed to react with *o*-iodoaniline (entry 1) to afford a 77% yield of the desired carbazole after cyclization under our standard reaction conditions. Similarly, 2,4-dichloro-6-iodoaniline reacts with 1.1 equiv of silylaryl triflate **1a** to afford 1,3-dichlorocarbazole in an 87% yield (entry 2). The presence of the two chlorines does not appear to interfere with the overall process. When silylaryl triflate **1b** was employed with this same iodoaniline, we obtained the desired product in an 85% yield. Approximately a 5% yield of the isomeric product 1,2-dimethyl-6,8-dichlorocarbazole was also observed as detected by GC/MS (entry 3). *N*-Methylcarbazole was also readily obtained in an 85% yield when *N*-methyl-2-iodoaniline was employed as the substrate (entry 4). *N*-(2-Iodophenyl)methanesulfonamide and *N*-(ethoxycarbonyl)-2-iodoaniline also reacted well with silylaryl triflate **1a** or **1b** to afford high yields of the corresponding products (entries 5−7); again only about 5% of a product isomeric with the product shown in entry 6 was observed by GC/MS analysis. One can also start with *N*-(2-iodobenzyl)methanesulfonamide and produce the desired six-membered ring product in a 66% yield (entry 8).

We have also investigated the use of *o*-iodophenols in this process. Thus, *o*-iodophenol and methyl 4-hydroxy-3-iodobenzoate react with silylaryl triflate **1a** to afford the corresponding dibenzofurans in 70 and 80% yields, respectively (entries 9 and 10). Here, we needed to use 1.2 equiv of silylaryl triflate **1a** and 3.5 equiv of CsF to get the yields specified. It is noteworthy that the presence of an electron-withdrawing ester moiety presented no difficulties and, in fact, gave a higher yield of the desired product.

In summary, we have developed a simple and efficient one-pot, two-step procedure to synthesize the carbazole and dibenzofuran ring systems by the cross-coupling of *o*-iodoanilines or *o*-iodophenols with arynes, followed by palladium-catalyzed intermolecular arylation. The starting materials are commercially available or can be easily made. The yields are good to excellent. Several new and multisubstituted carbazoles and dibenzofurans have been synthesized. Further studies into the scope and limitations of this process are currently underway in our laboratories.

---

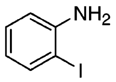
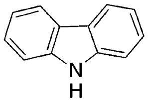
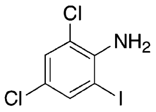
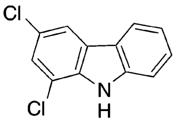
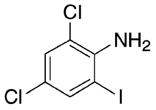
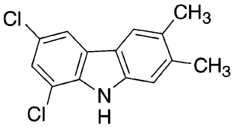
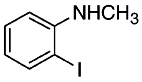
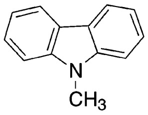
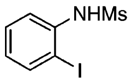
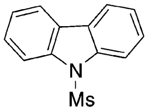
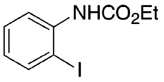
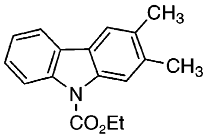
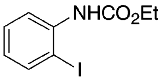
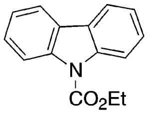
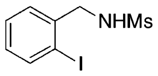
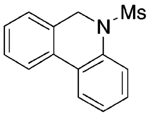
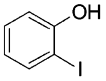
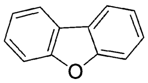
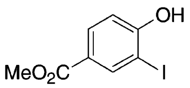
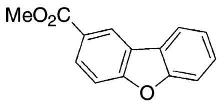
[10] (a) Istvan, E. J.; Ling, Y.; Kassoum, N.; Tork, T.; Wu, X.; Cao, Y.; Guo, R.; Li, B.; Zhu, X.; Huang, Y.; Long, Y. Q. *J. Med. Chem.* **2001**, *44*, 4313−4324. (b) Yasuo, K.; Yutaka, A.; Takeshi, S. *J. Org. Chem.* **2001**, *66*, 8612−8615. (c) Silvere, A.; Edwige, N.; Mireille, L.; Cecile, M.; Cao, W.; Kiefer, D. W.; Sheila, C.; Gerard, L.; Patrice, F. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 209−212.

[11] (a) Pal, M.; Subramanian, V.; Yeleswarapu, K. R. *Tetrahedron Lett.* **2003**, *44*, 8221−8225. (b) Dai, W.-M.; Lai, K. W. *Tetrahedron Lett.* **2002**, *43*, 9377−9380. (c) Bates, C. G.; Saejueng, D.; Murphy, J. M.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 4727−4729. (d) Larock, R. C.; Yum, E. K. *J. Am. Chem. Soc.* **1991**, *113*, 6689−6690. (e) Larock, R. C.; Yum, E. K.; Doty, M. J.; Sham, K. K. *J. Org. Chem.* **1995**, *60*, 3270−3271.

[12] Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211−1214.

[13] (a) Yoshida, H.; Honda, Y.; Shirakawa, E.; Hiyama, T. *Chem. Commun.* **2001**, 1880−1881. (b) Yoshida, H.; Shirakawa, E.; Honda, Y.; Hiyama, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 3247−3249. (c) Liu, Z.; Larock, R. C. *Org. Lett.* **2003**, *5*, 4673−4675. (d) Liu, Z.; Larock, R. C. *Org. Lett.* **2004**, *6*, 99−102.

Table 1. Synthesis of Carbazole, Dibenzofuran, and Related Molecules[a]

entry	substrate		aryl triflate (equiv)	CsF (equiv)	product		% isolated yield
1		**(1)**	**1a** (1.1)	3.0		**(2)**	77
2		**(3)**	**1a** (1.1)	3.0		**(4)**	87
3		**(3)**	**1b** (1.1)	3.0		**(5)**	85
4		**(6)**	**1a** (1.1)	3.0		**(7)**	82
5		**(8)**	**1a** (1.1)	3.0		**(9)**	85
6		**(10)**	**1b** (1.1)	3.0		**(11)**	85
7		**(10)**	**1a** (1.1)	3.0		**(12)**	85
8		**(13)**	**1a** (1.1)	3.0		**(14)**	66
9		**(15)**	**1a** (1.2)	3.5		**(16)**	70
10		**(17)**	**1a** (1.2)	3.5		**(18)**	80

[a] Reaction conditions: 0.25 mmol of aryl iodide were allowed to react with the number of equiv of aryl triflates and CsF shown in the Table and 4.0 mL of MeCN as the solvent at room temperature for 10 h, followed by the addition of 5 mol % $Pd(OAc)_2$ and 10 mol % PCy_3 and heating for 1 day at 100 °C.

Acknowledgment. We are grateful to the Petroleum Research Fund, administered by the American Chemical Society, for their generous financial support and Johnson Matthey, Inc., and Kawaken Fine Chemicals Co. for providing the palladium salts.

Supporting Information Available: Detailed experimental procedures and characterization data for all previously unknown products. This material is available free of charge via the Internet at http://pubs.acs.org.

OL048564L