DOI: 10.1002/adsc.200800162

Suzuki–Miyaura Cross-Coupling of 2-Nitroarenediazonium Tetrafluoroborates: Synthesis of Unsymmetrical 2-Nitrobiphenyls and Highly Functionalized Carbazoles

Jeffrey T. Kuethe[a,*] and Karla G. Childers[a]

[a] Department of Process Chemistry, Merck & Co., Inc., P.O Box 2000, Rahway, New Jersey 07065, USA
Fax: (+1)-732-594-5170; e-mail: Jeffrey_Kuethe@merck.com

Received: March 17, 2008; Published online: June 13, 2008

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: The Suzuki–Miyaura cross-coupling of 2-nitrodiazonium tetrafluoroborate salts with substituted boronic acids is an effective and efficient means of preparing highly functionalized 2-nitrobiphenyls in modest to excellent yield under extremely mild reaction conditions. Cross-coupling of 2-nitrodiazonium tetrafluoroborate salts with *ortho*-methoxy- and benzyloxyphenylboronic acids was also demonstrated leading to the *ortho-ortho*-2-nitrobiphenyls. Reductive cyclization of the 2-nitrobiphenyl products allows for the overall three-step synthesis of uniquely substituted carbazoles from readily available 2-nitroanilines. The methodology was further highlighted by the short total synthesis of the carbazole alkaloids clausine V, N, C, and glycoborine.

Keywords: carbazoles; cross-coupling; natural products; 2-nitrodiazonium tetrafluoroborates; 2-nitrophenyls; Suzuki–Miyaura reaction

Introduction

The palladium-catalyzed cross-coupling between aryl halides or sulfonates and arylboronic acids (the Suzuki–Miyaura coupling) is arguably the most versatile and widely utilized transformation in modern synthetic chemistry. It is often the method of choice for the preparation of both symmetrical and unsymmetrical biaryls, which constitute the core skeleton of a number of natural products, pharmaceuticals, agrochemicals, optically active ligands, conducting polymers, molecular wires, and liquid crystals.[1] Since the pioneering work of Suzuki and Miyaura,[2] numerous studies have emerged aimed at the development of new catalysts, ligands, and cross-coupling partners. The reaction continues to attract the attention of both academic and industrial researchers as new applications are uncovered.[3] The use of arenediazonium tetrafluoroborate salts in Suzuki–Miyaura cross-coupling reactions, developed independently by Genêt[4] and Sengupta,[5] has recently surfaced as a highly efficient synthetic tool for carbon-carbon bond formation.[6] Arenediazonium tetrafluoroborate salts are easily prepared in high yield from inexpensive and readily available anilines, and are often more reactive than aryl halides in palladium-catalyzed reactions when oxidative addition is the rate-determining step. Arenediazonium tetrafluoroborate salts have successfully been coupled with both aryl- and alkenylboronic acids,[4,5,7] potassium trifluoroborates,[8] and vinylsilanes[9] in the presence of catalytic amounts of palladium in a number of solvent systems (MeOH, THF, and 1,4-dioxane being the most common). The reaction is typically carried out under extremely mild reaction conditions (0 to 50 °C) in the absence of added base, salt additives, or ligands, which allows for the preparation of substrates possessing sensitive functional groups. While the use of phosphine ligands has been reported to be detrimental in these reactions due to decomposition of the arenediazonium salts, several groups have successfully demonstrated that imidazolium carbenes[10] and a C_2-symmetrical thiourea[11] are effective ligands for Suzuki–Miyaura cross-coupling reactions. However, the full potential of this interesting reaction has remained academic since applications have been limited to the preparation of relatively simple biaryl compounds.

Carbazoles are an important class of nitrogen heterocycles found in many biologically active natural products and medicinal agents.[12] Carbazole derivatives often serve as organic materials due to their photoconducting[13] and semiconducting properties,[14] as well as their high thermal and charge-transport properties.[15] Significant efforts have been devoted to

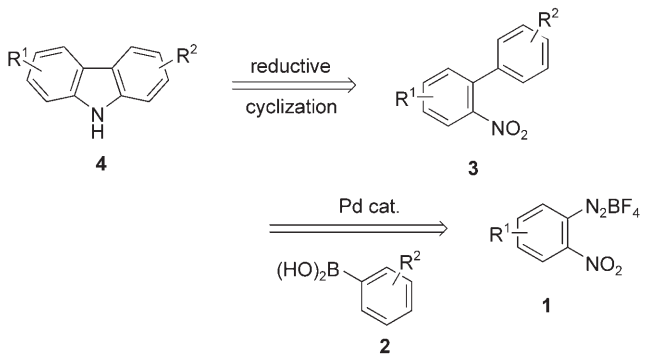
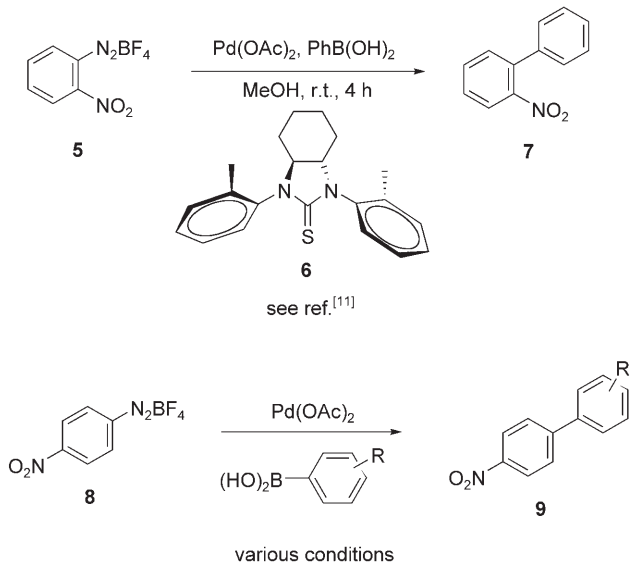


Figure 1.

the preparation of carbazoles since funtionalization of the parent carbazole nucleus is limited to certain positions of the ring at which electrophiles can be introduced. When more highly functionalized carbazoles are required, preparation of the carbazole ring bearing the appropriate substituents is necessary. The choice of method employed for the synthesis of carbazoles is often dictated by functional groups present within the starting materials. Perhaps the most commonly employed method for carbazole synthesis is the reductive cyclization of 2-nitrobiphenyl derivatives due to functional group tolerance, increased substrate scope, and regiocontrol of the functional groups within the carbazole product. For the preparation of biologically active biaryls and carbazoles, the selectivity and potency of these compounds depends on the nature of the substituents about each ring systems. In order to fully define biological profiles, strategies which allow for the rapid assembly of both functionalized biaryls and carbazoles continue to offer significant advantages. Reactions leading to increasing molecular complexity are important synthetic tools, and we reasoned that a combination of Suzuki–Miyaura cross-coupling of 2-nitrobenzenediazonium salts **1** with arylboronic acids **2** to give 2-nitrobiphenyls **3** followed by reductive cyclization would allow for the preparation of a unique set of carbazoles **4** possessing a range of functionality and substitution patterns not accessible through current methodology (Figure 1). In this paper, we document the realization of this strategy and present a complete account of our investigations in this area.

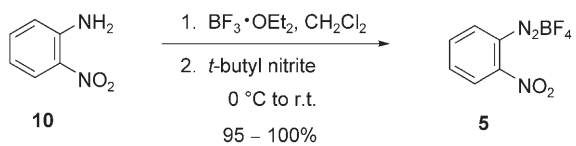
Results and Discussion

The coupling of 2-nitrobenzenediazonium tetrafluoroborate salts **1** with arylboronic acids **2** has remained an unexplored landscape since the initial disclosure by Sengupta who reported that the reaction failed in the presence of 10 mol% $Pd(OAc)_2$ in refluxing methanol.[5] A single example employing the C_2-symmetrical thiourea ligand **6** developed by Yang and co-workers has been reported describing the preparation of *o*-nitrobiphenyl **7** from 2-nitrobenzenediazonium tetrafluoroborate salt **5** (Scheme 1).[1] Recently, Felpin and Fouquet have also reported the coupling of **5** with boronic acids in the presence of Pd(0)/barium carbonate in MeOH.[16] While the use of commercially available 4-nitrobenzenediazonium salt **8** is well documented providing the 4-nitrobiphenyls of type **9**,[4b,7a,e,8a–c,11] the failure of 2-nitrobenzenediazonium tetrafluoroborate salts **1** to participate in Suzuki–Miyaura cross-coupling reactions has been attributed to high redox-potentials and a preference for homolytic dediazotization pathways.[17] The *o*-nitro group can function as an electron-withdrawing group and chelate the oxidative addition intermediate.[18] These factors would seem to favor the coupling of these reaction partners since numerous couplings of 2-halogen-1-nitrobenzenes with boronic acids have been reported.[19] It was with this background in mind that we began our investigations.



Scheme 1.

Our investigations began with the preparation of the prerequisite 2-nitrobenzenediazonium tetrafluoroborate salts **1** which were prepared *via* the Doyle protocol (Scheme 2).[20] For example, treatment of 2-nitroaniline **10** with $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at 0 °C followed by the dropwise addition of *tert*-butyl nitrite furnished **5** which crystallized from the reaction mix-

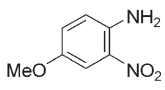
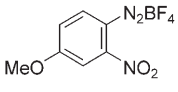
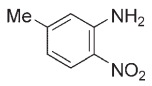
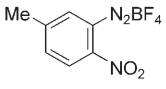
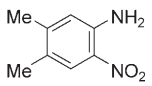
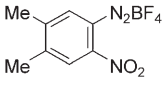
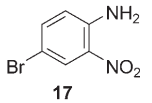
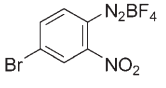
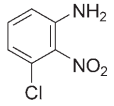
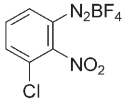
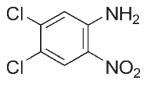
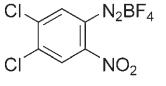
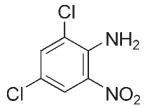
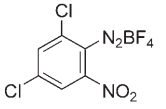
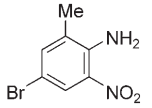
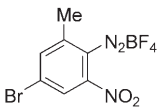


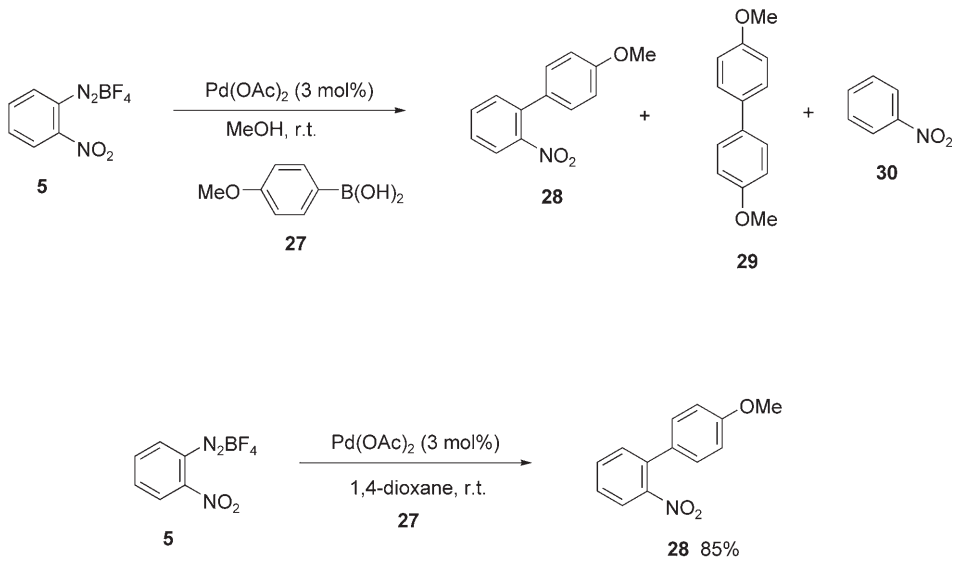
Scheme 2.

ture and was isolated in 95% yield. This general sequence allowed for the preparation of a number of structurally intriguing 2-nitrobenzenediazonium tetrafluoroborate salts in good to excellent yield as shown in Table 1. The salts depicted in Table 1 were stable at room temperature for at least 24 h, but decomposition was observed after several days. However, they can be stored indefinitely in the freezer (−20 °C) without any degradation.

With an array of 2-nitrobenzenediazonium tetrafluoroborate salts in hand, our attention turned to examination of appropriate conditions to affect Suzuki–Miyaura cross-coupling. Initial experiments were carried out between **5** and 4-methoxyphenylboronic acid **27** (Scheme 3). As part of our initial experimental design, we elected to only examine ligand-free conditions employing catalytic $Pd(OAc)_2$. As various solvents have been used in these types of couplings, a simple solvent screen served as the starting point. For example, addition of 5 mol% $Pd(OAc)_2$ to a mixture of **5** (1 equiv.) and **27** (1 equiv.) in MeOH at room temperature resulted in an immediate reaction and rapid release of nitrogen, with palladium black being deposited within one minute. After allowing the reaction mixture to cool to room temperature, the crude reaction mixture was filtered through Celite and concentrated. Examination of the residue by NMR revealed the formation of the desired product **28** in approximately 50% yield. Also detected in the crude reaction mixture was 4,4′-dimethoxybiphenyl **29** (27%) resulting from homocoupling of **27** and nitrobenzene **30** (15%) arising from homolytic cleavage of **5**. When the reaction was performed in anhydrous THF at room temperature, little conversion to **28** was observed even after stirring at room temperature for 24 h. The low solubility of **5** in THF may contribute to the low conversion. On the other hand, treatment of **5** and **27** with 5 mol% $Pd(OAc)_2$ in 1,4-dioxane under the identical reaction conditions provided **28** in just one hour in 75% isolated yield. Under these conditions, only trace amounts of **29** (~5%) and **30** (<5%) were observed in the crude NMR. These minor by-products were easily removed by silica gel chromatography. While **5** appeared to have little solubility in 1,4-dioxane, we speculate that a delicate balance between solubility and reactivity leads to the high yield of the desired product. In addition, 1,4-dioxane is an aprotic solvent which appears to effectively suppress the homolytic cleavage of **5** leading to **30**. When MeOH was used as the solvent, both **5** and **27** were soluble leading to multiple reaction pathways and the rapid formation of **28**, **29**, and **30**. The use of 1,4-dioxane as the optimal solvent for these reactions has also been reported by Genêt.[4] With 1,4-dioxane as the solvent of choice, the reaction was optimized in terms of catalyst and reagent charges. After extensive experimentation it was discovered that the optimal conditions employed 3 mol% $Pd(OAc)_2$, 1.1 equiv. of **5**, and 1.0 equiv. of **27** in 1,4-dioxane for 2 h at room temperature which provided **28** in 85% isolated yield. Although homocoupling of **27** could never be completely suppressed, the formation of **29** was minimized to <5% and the formation of **30** was <5%. These reaction conditions proved general, allowing for the preparation of a diverse array of 2-nitrobiphenyls in modest to excellent yield (Table 2). The results in Table 2 demonstrate that both electron-poor and electron-rich boronic acids participate equally as well in the coupling reaction. In addition, substitution about the diazonium salts was well tolerated providing 2-nitrobiphenyls of increasing molecular complexity (entries 5–11). We also examined the identical conditions for the preparation of the isomeric 4-nitro analogues (entries 12 and 13) which gave the expected products

Table 1.

Entry	2-Nitroaniline	2-Nitrodiazonium tetrafluoroborate salt	Yield
1	 **11**	 **12**	97%
2	 **13**	 **14**	94%
3	 **15**	 **16**	88%
4	 **17**	 **18**	97%
5	 **19**	 **20**	99%
6	 **21**	 **22**	89%
7	 **23**	 **24**	97%
8	 **25**	 **26**	99%



Scheme 3.

in excellent yield. The excellent chemoselectivity of Suzuki–Miyaura cross-couplings that can be achieved with halogen-containing boronic acids and arenediazonium salts, in conjunction with the mild reaction conditions, furnished 2-nitrobiphenyls having suitable handles for further manipulation.

The effect of steric hindrance about both the 2-nitrodiazonium tetrafluoroborate salts and boronic acids was next probed. It has been reported that *ortho* substitutions on the diazonium component are generally well tolerated with both electron-donating and electron-withdrawing groups readily participating in cross-coupling reactions. However, it has also been reported that *ortho* substitution on the boronic acid counterpart results in significant erosion in the isolated yields (0–30%) of the biphenyl products regardless of the method employed.[4,5,7,8] Despite these reported limitations, we elected to investigate the coupling of

Table 2.

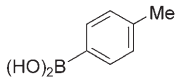
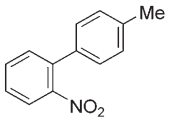
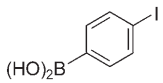
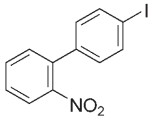
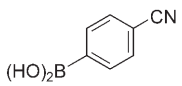
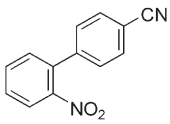
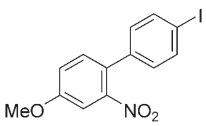
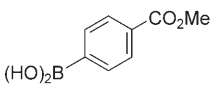
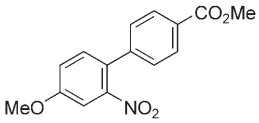
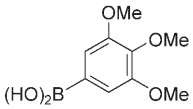
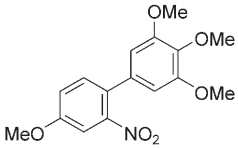
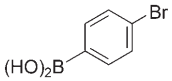
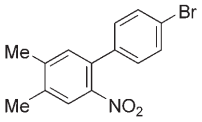
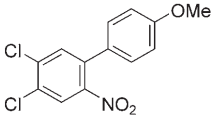
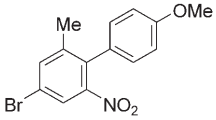
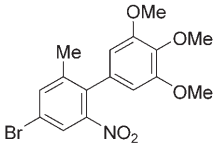
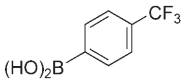
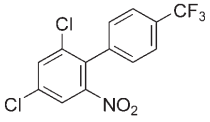
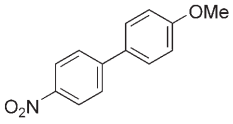
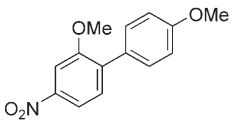
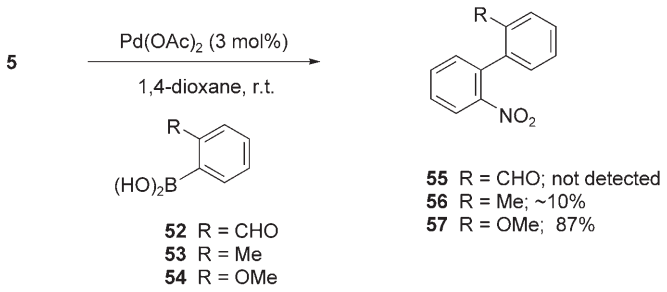
Entry	Diazonium salt	Boronic acid	2-Nitrobiphenyl	Yield
1	**5**	 **31**	 **32**	93%
2	**5**	 **33**	 **34**	85%
3	**5**	 **35**	 **36**	85%
4	**12**	**33**	 **37**	77%

Table 2. (Continued)

Entry	Diazonium salt	Boronic acid	2-Nitrobiphenyl	Yield
5	**12**	 **38**	 **39**	81%
6	**12**	 **40**	 **41**	83%
7	**16**	 **42**	 **43**	91%
8	**22**	**27**	 **44**	78%
9	**26**	**27**	 **45**	77%
10	**26**	**40**	 **46**	57%
11	**24**	 **47**	 **48**	65%
12	**8**	**27**	 **49**	70%
13	Fast Red B[a] **50**	**27**	 **51**	88%

[a] Fast Red B tetrafluoroborate salt **50** (2-methoxy-4-nitrobenzenediazonium tetrafluoroborate) is commercially available.

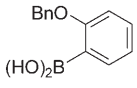
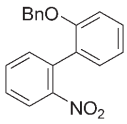
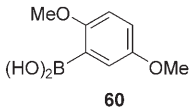
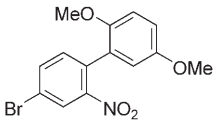
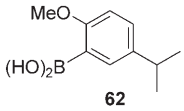
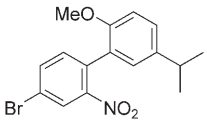
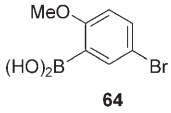
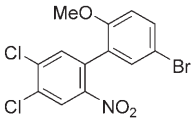
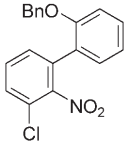
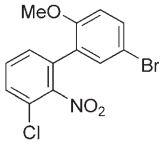
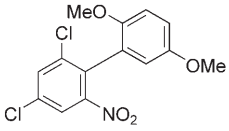
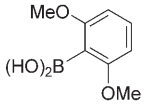
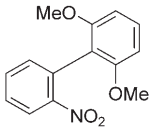
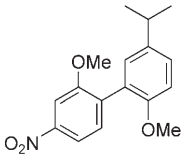


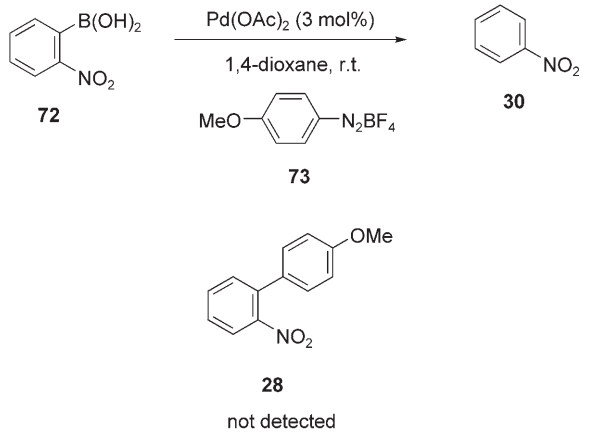
Scheme 4.

2-nitrobenzenediazonium salts with *ortho*-substituted boronic acids. We speculated that the electronic nature of the *ortho*-substituent on the boronic acid may actually override steric interactions leading to successful cross-coupling. To this end, we explored the cross-coupling of **5** with boronic acids **52** (electron-deficient), **53** (moderately electron-donating), and **54** (strongly electron-donating) (Scheme 4). Cross-coupling of **5** with **52** under our optimized conditions resulted in no detectable amounts of **55** being formed with the only identifiable reaction product being **30** resulting from homolytic cleavage of **5**. Cross-coupling of **5** with **53** gave similar results and the desired product **56** was only obtained in ~10% yield. The mass balance of this reaction was **30** and homocoupling of **52**. On the other hand, cross-coupling of **5** with **54** under the identical reaction conditions provided **57** in 85% yield. From these results it was apparent that boronic acids possessing strongly electron-donating groups in the *ortho*-position were particularly reactive. This extremely gratifying result prompted us to further explore the coupling of various diazonium tetrafluoroborate salts with boronic acids bearing an alkoxy substituent in the *ortho* position. The results are shown in Table 3 which illustrates that *ortho*-methoxy- and benzyloxyphenylboronic acids readily participate in Suzuki–Miyaura cross coupling reactions with diazonium tetrafluoroborate salts providing an interesting array of highly functionalized 2-nitrobiphenyls in good to excellent yield. Only in the cases where either the diazonium salt (entry 7) or the boronic acid (entry 8) presented significant steric hurdles did the reaction perform poorly. Entry 9 illustrates that preparation of isomeric *ortho*-*ortho*′-4-nitro derivatives (Fast Red B) was also possible and 4-nitrobiphenyl **71** was isolated in high yield.

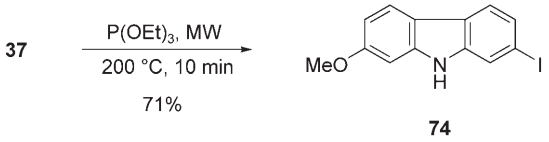
We briefly examined the reverse coupling of 2-nitrophenylboronic acid **72** with 4-methoxybenzenediazonium tetrafluoroborate salt **73** (Scheme 5). Reaction of **72** with **73** under the optimized conditions described above did not afford any detectable amounts of **28** in the crude reaction mixture. The only identifiable product was nitrobenzene **30**. Since it is an established fact that the presence of an electron-withdraw-

Table 3.

Entry	Diazonium salt	Boronic acid	Nitrobiaryl	Yield
1	**5**	 **58**	 **59**	85%
2	**18**	 **60**	 **61**	84%
3	**18**	 **62**	 **63**	89%
4	**22**	 **64**	 **65**	81%
5	**20**	**58**	 **66**	72%
6	**20**	**64**	 **67**	48%
7	**24**	**60**	 **68**	23%
8	**5**	 **69**	 **70**	0%
9	**50**	**62**	 **71**	90%



Scheme 5.



Scheme 6.

ing nitro group in the *ortho*-position of a carbon-boron bond makes it susceptible to proto-deboronation, this result was not completely surprising.[21]

With a wealth of 2-nitrobiaryl compounds in hand, we next turned our attention to the formation of the corresponding carbazoles. Although elegant palladium-catalyzed cyclization strategies employing CO-induced C–H activation have been developed,[22] the Cadogan–Sundberg cyclization[23] employing phosphite reagents, or the recently developed PPh_3-mediated reductive cyclization by Freeman and co-workers,[24] remain the methods of choice for the rapid preparation of carbazoles from 2-nitrobiphenyls. Due to the relatively harsh reaction conditions utilized in the PPh_3-mediated protocol (refluxing dichlorobenzene, 2.5 equiv. of PPh_3) and the long reaction times typically required when employing $P(OEt)_3$ as solvent and reductant, we became intrigued with the recently reported microwave-enhanced Cadogan–Sundberg cyclization reported by Dehaen and co-workers.[25] Microwave irradiation has emerged as a valuable synthetic tool since dramatic rate enhancements and superior yields are often obtained under focused microwave irradiation.[26] The microwave-enhanced Cadogan–Sundberg cyclization conditions reported by Dehaen involved reaction of 2-nitrobiaryls in dilute $P(OEt)_3$ (0.08 molar) at 210 °C for 10–20 min at a maximum irradiation power of 300 W. We briefly probed the Dehaen conditions and settled on a slight modification of the reaction conditions that involved running the reaction at 200 °C for 10 min in $P(OEt)_3$ (0.5 M) at a maximum irradiation power of 350 W. For example, microwave irradiation of **37** under these conditions furnished carbazole **74** which was isolated in 71% yield (Scheme 6). These conditions were extended to selected 2-nitrobiaryls allowing for the preparation of a range of structurally diverse carbazoles in modest to good yield as shown in Table 4. Mono-, di-, tri-, tetra-, and pentasubstituted carba-

Table 4.

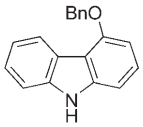
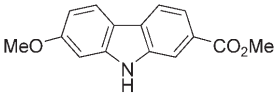
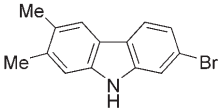
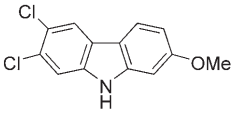
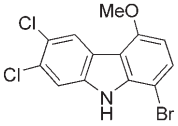
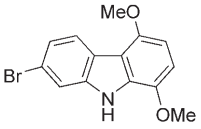
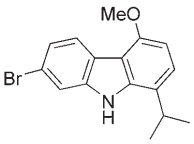
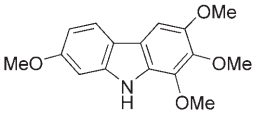
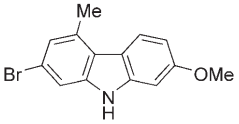
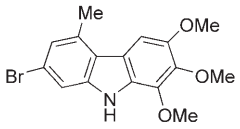
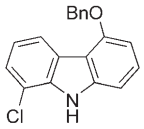
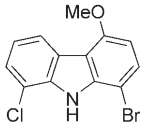
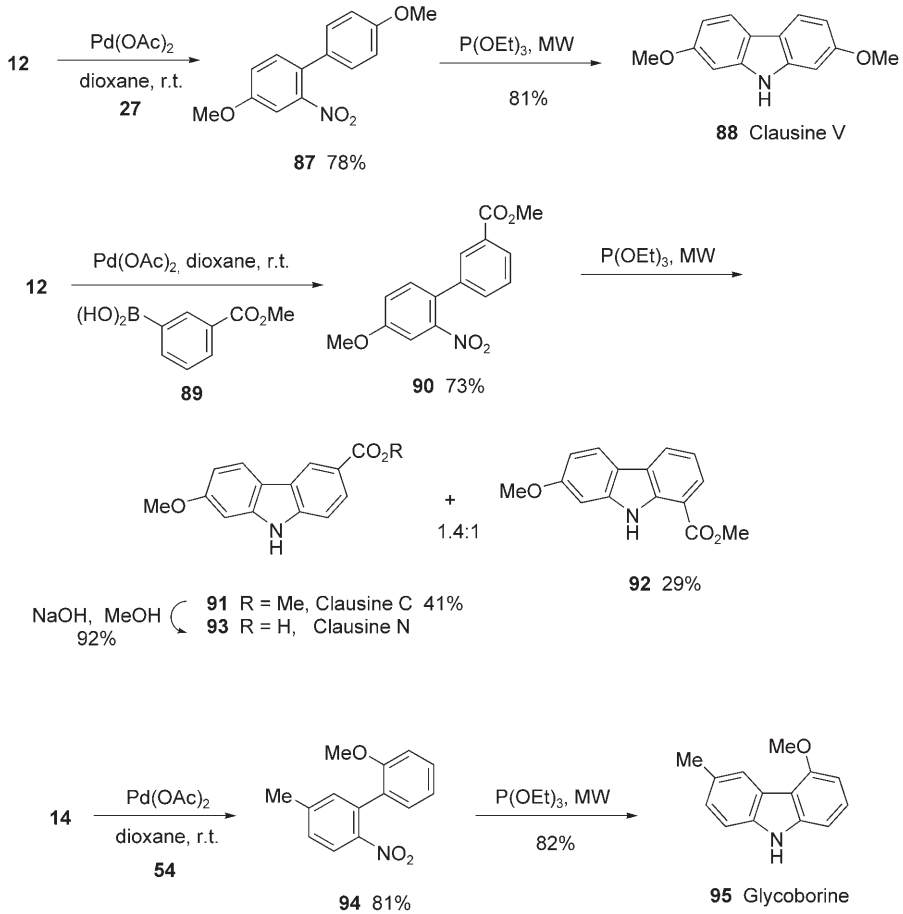
Entry	2-Nitrobiphenyl	Carbazole	Yield
1	**59**	 **75**	63%
2	**39**	 **76**	62%
3	**43**	 **77**	59%
4	**44**	 **78**	73%
5	**65**	 **79**	81%
6	**61**	 **80**	85%
7	**63**	 **81**	86%
8	**41**	 **82**	66%
9	**45**	 **83**	83%

Table 4. (Continued)

Entry	2-Nitrobiphenyl	Carbazole	Yield
10	**46**	 **84**	85%
11	**66**	 **85**	63%
12	**67**	 **86**	41%

zoles bearing functional handles for further manipulation were rapidly prepared in just three synthetic steps from readily available starting materials.

The facility with which 2-nitrobenzenediazonium salts readily undergo Suzuki–Miyaura cross-coupling to give 2-nitrobiphenyls followed by reductive cyclization to carbazoles was further highlighted by the short total synthesis of the carbazole natural products clausine V **88**, clausine C **91**, clausine N **93**, and glycoborine **95** (Scheme 7). The clausine alkaloids have been isolated from the stem bark and roots of *Clausena excavate*,[27] a wild plant which has been claimed to be useful in folk medicine as a detoxification agent and for the treatment of snake bites.[28] Clausine V **88** has been utilized in the preparation of a number of carbazole polymers having interesting electrochemical, conductive, and magnetic properties.[29] The preparation of clausine V **88**, which closely parallels previous syntheses, involved the Suzuki–Miyaura cross coupling of **12** with boronic acid **27** in the presence of $Pd(OAc)_2$ and provided **87** in 78% yield.[26] Reductive cyclization of **87** under microwave irradiation in $P(OEt)_3$ gave clausine V **88** in 81% yield. For the preparation of clausine C **91**, coupling of **12** with boronic acid **89** under the optimized reaction conditions gave **90** in 73% yield. Reductive cyclization of **90** afforded a 1.4:1 mixture of clausine C **91** (41%) and the regioiso-



Scheme 7.

meric carbazole **92** (29%) which were easily separated from one another by silica gel chromatography. Saponification of **91** in aqueous NaOH/MeOH gave clausine N **93** in 92% yield and represents the first reported total synthesis of clausine N **93**. The three-step total synthesis of glycoborine **95**, isolated from *Glycosmis arborea*,[30] began with the cross-coupling of **14** with boronic acid **54** to give 2-nitrobiphenyl **94** in 81% yield. Reductive cyclization of **94** furnished glycoborine **95** (82%) which was identical in all regards to that reported for natural glycoborine.[29]

Conclusions

In conclusion, we have outlined an efficient protocol for Suzuki–Miyaura cross-coupling of 2-nitrodiazonium tetrafluoroborate salts with boronic acids under extremely mild reaction conditions providing highly functionalized 2-nitrobiphenyls in modest to excellent yield. Cross-coupling of 2-nitrodiazonium tetrafluoroborate salts with *ortho*-methoxy- and benzyloxyphenylboronic acids was also demonstrated where strongly electron-donating boronic acids provide increased reactivity, despite steric interactions. Reductive cyclization of 2-nitrobiphenyls allows for the three-step preparation of uniquely substituted carbazoles from readily available 2-nitroanilines. This sequence was further highlighted by the short synthesis of the carbazole natural products clausine V, clausine N, clausing C, and glycoborine.

Experimental Section

Characterization data of all compounds is available in the Supporting Information.

General Procedure for the Preparation of 2-Nitrobenzenediazonium Tetrafluoroborate Salts

To a solution of the appropriately substituted 2-nitroaniline (10 mmol, 1.0 equiv.) in 100 mL of CH_2Cl_2 at 0 °C was added $BF_3{\cdot}OEt_2$ (12 mmol, 1.2 equiv.) followed by *tert*-butyl nitrite (15 mmol, 1.5 equiv.). The resulting reaction mixture was allowed to warm to room temperature and the slurry of the product was stirred at this temperature for 30–60 min and filtered. The crude product was washed with 25 mL of CH_2Cl_2 and dried under vacuum/N_2 sweep for 2 h to give the 2-nitrobenzenediazonium tetrafluoroborate salt in $>95\%$ yield.

General Procedure for Palladium-Catalyzed Cross-Coupling of Nitrobenzenediazonium Tetrafluoroborate Salts with Boronic Acids

To a slurry of the appropriate nitrobenzenediazonium tetrafluoroborate salt (11.0 mmol, 1.1 equiv.) and the appropriate boronic acid (10.0 mmol, 1.0 equiv.) in 25 mL of 1,4-dioxane was added $Pd(OAc)_2$ (67 mg, 0.3 mmol, 0.03 equiv.). The resulting mixture was stirred at room temperature for 1–3 h and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give the 2-nitrobiaryl product.

General Procedure for the Preparation of N-H Carbazoles

In a 10-mL glass vial was placed the appropriately substituted 2-nitrobiaryl (2.50 mmol) and 5 mL of triethyl phosphite. The reaction was irradiated at a maximum power of 300 W for 10 min at a temperature of 200 °C and allowed to cool to room temperature. The homogeneous solution was diluted with 35 mL of EtOAc and added to a solution of 50 mL of 6 N HCl. The layers were well mixed for 20 min and separated. The aqueous layer was back-extracted with 20 mL of EtOAc. The combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was concentrated under reduced pressure and the residue was purified by silica gel chromatography to afford the pure carbazole.

Acknowledgements

The authors wish to thank Dr. Michael Palucki, Dr. Greg Beutner, and Dr. Nobuyoshi Yasuda for helpful discussions during the preparation of this manuscript.

References

[1] For leading references, see: a) J. Hassan, M. Sévignon, C. Gozzi, E. Shulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359–1470; b) C. Bolm, J. P. Hildebrand, K. Muñiz, N. Hermanns, *Angew. Chem.* **2001**, *113*, 3382–3407; *Angew. Chem. Int. Ed.* **2001**, *40*, 3284–3308.

[2] N. Miyaura, T. Yanagi, A. Suzuki, *Synth. Commun.* 1981, 11, 513–519.

[3] For recent reviews, see: a) N. Miyaura, A. Suzuki *Chem. Rev.* **1995**, *95*, 2457–2483; b) N. Miyaura, in: *Advances in Metal-Organic Chemistry*, Vol. 6, (Ed.: L. S. Liebeskind), JAI Press, London, **1998**, pp 187–243; c) A. Suzuki, in: *Metal-Catalyzed Cross-Coupling Reactions*, (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, New York, **1998**, chaper 2; d) A. Suzuki *J. Organomet. Chem.* **1999**, *576*, 147–168; e) N. Miyaura, in: *Topics in Current Chemistry*, Vol. 219, (Ed.: N, Miyaura), Springer-Verlag, Berlin, **2002**, p 11; f) S. Kotha, K. Lahiri, D. Kashinath, *Tetrahedron* **2002**, *58*, 9633–9695; g) A. Suzuki, *J. Organomet. Chem.* **2002**, *653*, 83–90; h) N. Miyaura, *J. Organomet. Chem.* **2002**, *653*, 54–57; i) F. Bellina, A. Carpita, R. Rossi, *Synthesis* **2004**, 2419–2440; j) N. T. S. Phan, M. Van Der Sluys, C. W. Jones *Adv. Synth. Catal.* **2006**, *348*, 609–679.

[4] a) S. Darses, T. Jeffery, J.-P. Genêt, *Tetrahedron Lett.* **1996**, *37*, 3857–3860; b) S. Darses, T. Jeffrey, J. L. Brayer, J. P. Demoute, J. P. Genét, *Bull. Soc. Chim. Fr.* **1996**, *133*, 1095–1102.

[5] S. Sengupta, S. Bhattacharyya, *J. Org. Chem.* **1997**, *62*, 3405–3406.

[6] For a recent review on palladium-catalyzed cross-couplings, see: A. Roglans, A. Pla-Quintana, M. Moreno-Mañas, *Chem. Rev.* **2006**, *106*, 4622–4643.
[7] a) R. H. Taylor, F.-X. Felpin *Org. Lett.* **2007**, *9*, 2911–2914; b) V. Gallo, P. Mastrorilli, C. F. Nobile, R. Paolillo, N. Taccardi, *Eur. J. Inorg. Chem.* **2005**, 582–588; c) J. Jo, C. Chi, S. Höger, G. Wegner, D. Y. Yoon, *Chem. Eur. J.* **2004**, *10*, 2681–2688; d) M. L. Nelson, M. Y. Ismail, L. McIntyre, B. Bhatia, P. Viski, P. Hawkins, G. Rennie, D. Andorsky, D. Messersmith, K. Stapleton, J. Dumornay, P. Sheahan, A. K. Verma, T. Warchol, S. B. Levy, *J. Org. Chem.* **2003**, *68*, 5838–5851; e) D. M. Willis, R. M. Strongin, *Tetrahedron Lett.* **2000**, *41*, 6271–6274; f) S. Sengupta, S. K. Sadhukhan, *Tetrahedron Lett.* **1998**, *39*, 715–718.
[8] a) H.-J. Frohn, N. Y. Adonin, V. V. Bardin, V. F. Starichenko, *J. Fluorine Chem.* **2002**, *117*, 115–120; b) S. Darses, G. Michaud, J.-P Genêt, *Eur. J. Org. Chem.* **1999**, 1875–1883; c) S. Darses, G. Michaud, J.-P. Genêt, *Tetrahedron Lett.* **1998**, *39*, 5045–5048; d) S. Darses, J.-P. Genêt, *Tetrahedron Lett.* **1997**, *38*, 4393–4396.
[9] F. Babudri, G. M. Farinola, F. Naso, D. Panessa, *J. Org. Chem.* **2000**, *65*, 1554–1557.
[10] a) M. B. Andrus, Y. Ma, Y. Zang, C. Song, *Tetrahedron Lett.* **2002**, *43*, 9137–9140; b) K. Selvakumar, A. Zapf, A. Spannenberg, M. Beller, *Chem. Eur. J.* **2002**, *8*, 3901–3906; c) M. B. Andrus, C. Song, *Org. Lett.* **2001**, *3*, 3761–3764.
[11] M. Dai, B. Liang, C. Wang, J. Chen, Z. Yang, *Org. Lett.* **2004**, *6*, 221–224.
[12] For recent reviews, see: a) H.-J. Knölker, K. R. Reddy, *Chem. Rev.* **2002**, *102*, 4303–4427; b) H.-J. Knölker *Top. Curr. Chem.* **2005**, *244*, 115–148; c) D. P. Chakraborty, in: *The Alkaloids*, (Ed.: A. Bossi), Academic Press, New York, **1993**, Vol. 44, p 257; d) P. T. Gallagher, in: *Science of Synthesis*, Thieme, Stuttgart, **2000**, Vol 10, p 693; e) S. Omura, Y. Sasaki, Y. Iwai, H. Takeshima, *J. Antibiot.* **1995**, *48*, 535–548; f) H.-J. Knölker, in: *Advances in Nitrogen Heterocycles*, (Ed. C. J. Moody), JAI Press, Greewich, **1995**, Vol. 1, p 173; g) C. J. Moody, *Synlett* **1994**, 681–688; h) J. Bergman, B. Pelcman, *Pure Appl. Chem.* **1990**, *62*, 1967–1976; i) K. Sakano, K. Ishimaru, S. Nakamura, *J. Antibiot.* **1980**, *33*, 683–689; j) K. C. Das, D. P. Chakraborty, P. K. Bose, *Experientia* **1965**, *21*, 340.
[13] a) T. Ganguly, L. Farmer, W. Li, J. Y. Bergeron, D. Gravel, G. Durocher *Macromolecules* **1993**, *26*, 2315–2322; b) T. Ganguly, J. Y. Bergeron, L. Farmer, D. Gravel, G. J. Durocher, *J. Lumin.* **1994**, *59*, 247–256.
[14] J. Bouchard, S. Wakim, M. Leclerc, *J. Org. Chem.* **2004**, *69*, 5705–5711.
[15] a) M. Biswas, S. K. Das, *Eur. Polym. J.* **1981**, *17*, 1245–1251; b) M. Biswas, G. C. Mishra, *Makromol. Chem.* **1981**, *182*, 261–264; c) M. Biswas, S. K. Das, *Polymer* **1982**, *23*, 1713–1725; d) K. R. Justin Thomas, J. T. Lin, Y.-T. Tao, C.-W. Ko, *J. Am. Chem. Soc.* **2001**, *123*, 9404–9411.
[16] F.-X. Felpin, E. Fouquet, *Adv. Synth. Catal.* **2008**, *350*, 863–868.
[17] a) S. Yasui, M. Fujii, C. Kawano, Y. Nishimura, K. Shioji, A. Ohno, *J. Chem. Soc. Perkin Trans. 2* **1994**, 177–183; b) S. Yasui, M. Fujii, C. Kawano, Y. Nishimura, A. Ohno, *Tetrahedron Lett.* **1991**, *32*, 5601–5604.
[18] For leading references discussing 2-nitro-palladium complexes, see: a) J. Vicente, M. T. Chicote, J. Martín,, M. Artigao, X. Solans, M. Font-Altaba, Aguiló, *J. Chem. Soc. Dalton Trans.* **1988**, 141–147, and references cited therein; b) D. A. Widdowson, R. Wilhelm, *Chem. Commun.* **2003**, 578–579.
[19] For a few leading references, see: a) M. R. Naffziger, B. O. Ashburn, J. R. Perkins, R. G. Carter, *J. Org. Chem.* **2007**, *72*, 9857–9865; b) J.-H. Li, W.-J. Liu, *Org. Lett.* **2004**, *6*, 2809–2811; c) J. Liu, Z. Diwu, W.-Y. Leung, Y. Lu, B. Patch, R. P. Haugland *Tetrahedron Lett.* **2003**, *44*, 4355–4359; d) A. Arcadi, G. Cerichelli, M. Chiarini, M. Correa, D. Zorzan, *Eur. J. Org. Chem.* **2003**, 4080–4086; e) J. T. Manka, F. Guo, J. Huang, H. Yin, J. M. Farrar, M. Sienkowska, V. Benin, P. Kaszynski, *J. Org. Chem.* **2003**, *68*, 9574–9588; f) T. Iihama, J. M. Fu, M. Bourguignon, V. Snieckus, *Synthesis* **1989**, 184–188; g) A. Suzuki, *J. Organomet. Chem.* **1999**, *576*, 147–168; h) J. C. Anderson, H. Namli, C. A. Roberts, *Tetrahedron* **1997**, *53*, 15123–15134.
[20] M. P. Doyle, W. J. Bryker, *J. Org. Chem.* **1979**, *44*, 1572–1574.
[21] L. G. Monovich, Y. LeHuérou, M. Rönn, G. A. Molander, *J. Am. Chem. Soc.* 2000, 122, 52–57 and references cited therein.
[22] J. H. Smitrovich, I. W. Davies, *Org. Lett.* **2004**, *6*, 533–535.
[23] a) J. I. G. Cadogan, M. Cameron-Wood, *Proc. Chem. Soc.* **1962**, 361; b) J. I. G. Cadogan, R. K. Mackie, M. J. Todd, *J. Chem. Soc. Chem. Commun.* **1966**, 491; c) R. J. Sundberg, *J. Org. Chem.* **1965**, *30*, 3640–3650.
[24] A. W. Freeman, M. Urvoy, M. E. Criswell, *J. Org. Chem.* **2005**, *70*, 5014–5019.
[25] P. Appukkuttan, E. Van der Eycken, W. Dehaen, *Synlett* **2005**, 127–133.
[26] For leading references, see: a) D. Adam, *Nature* **2003**, *421*, 571–572; b) N, Kaval, J. Van der Eychken, J. Caroen, W. Dehaen, G. A. Strohmeier, C. O. Kappe, E. van der Eycken, *J. Comb. Chem.* **2003**, *5*, 560–568; c) A. Lew, P. O. Krutzik, M. E. Hart, R. A. Chamerlin, *J. Comb. Chem.* **2002**, *4*, 95–105; d) C. O. Kappe, *Curr. Opin. Chem. Biol.* **2002**, *6*, 314–320; e) P. Lidström, J. Westman, A. Lewis, *Comb. Chem. High Throughput Screening* **2002**, *5*, 441–458; f) E. Van der Eycken, P. Appukkuttan, W. De Borggraeve, W. Dehaen, D. Dallinger, C. O. Kappe, *J. Org. Chem.* **2002**, *67*, 7904–7907.
[27] a) T.-S. Wu, S.-C. Huang, P.-L. Wu, *Phytochemistry* **1996**, *43*, 1427–1429; b) T.-S. Wu, S.-C. Huang, P.-L. Wu, C.-S. Kuoh *Phtochemistry* **1999**, *52*, 523–527.
[28] S. Sasaki, in: *Khoyo Taiwan Minkan Yakyo Shokubutsu Shi*, Taipei, Khobunkan, **1924**, p 36.
[29] For leading references, see: a) B. R. Hsieh, M. H. Litt, *Macromolecules* **1985**, *18*, 1388–1394; b) G. Zotti, G. Schiavon, S. Zecchin, J.-F. Morin, M. Leclerc, *Macromolecules* **2002**, *35*, 2122–2128.
[30] A. K. Charkravarty, T. Sarkar, K. Masuda, T. Takey, H. Doi, E. Kotani, K. Shiojima, *Indian J. Chem. Sec B.* **2001**, *40*, 484–489.

