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Diels−Alder Approach for the Construction of Halogenated, *o*-Nitro Biaryl Templates and Application to the Total Synthesis of the Anti-HIV Agent Siamenol

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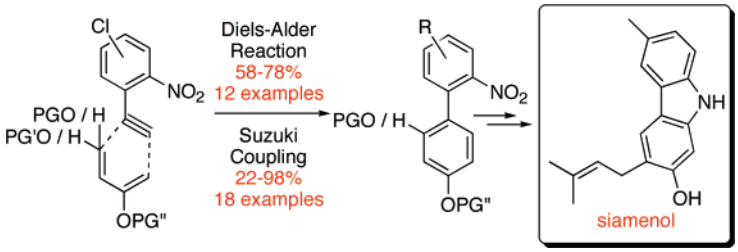

A rapid Diels−Alder approach to halogenated biaryl templates is described. These biaryl templates are available in two steps from the corresponding aromatic aldehydes. The scope of subsequent Suzuki couplings on the biaryl chlorides is explored. Good tolerance for both electron-donating and electron-withdrawing groups in the coupling process can be achieved. Further functionalization of the biaryl templates is described. Hydrogenation of the nitro moiety with concomitant removal of the benzyl ether yields the *o*-anilino, *o*-phenolic polyaryls. Selective reduction of the nitro group can be accomplished. Alternatively, the benzyl ether can be selectively removed under Lewis acidic conditions. The utilization of the Diels−Alder adducts for the synthesis of a series of chlorinated carbazoles via the Cadogan cyclization is also demonstrated. Finally, application of this technology to the total synthesis of siamenol, an anti-HIV agent, is reported.

Introduction

Biaryl compounds are ubiquitous in the chemical community—as pharmacophores for potential medicinal treatments[1,2] and ligands in metal catalysis.[3] Strategies for constructing this structural motif have primarily focused on metal-mediated couplings of two aryl precursors.[2,3] While this approach has proven useful, limitations to its abilities have been reported.[4] Documented reports of the significant cost of the necessary coupling partners (e.g., aryl halide or boronic acid) for traditional metal-mediated approaches to highly functionalized biaryls have made alternate strategies more attractive.[5] A corollary to the high cost of select coupling components is that the aryl halides

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(3) (a) Wallace, T. W. *Org. Biomol. Chem.* **2006**, *4*, 3197−210. (b) Shimizu, H.; Nagasaki, I.; Saito, T. *Tetrahedron* **2005**, *61*, 5405−32. (c) McCarthy, M.; Guiry, P. J. *Tetrahedron* **2001**, *57*, 3809−44.

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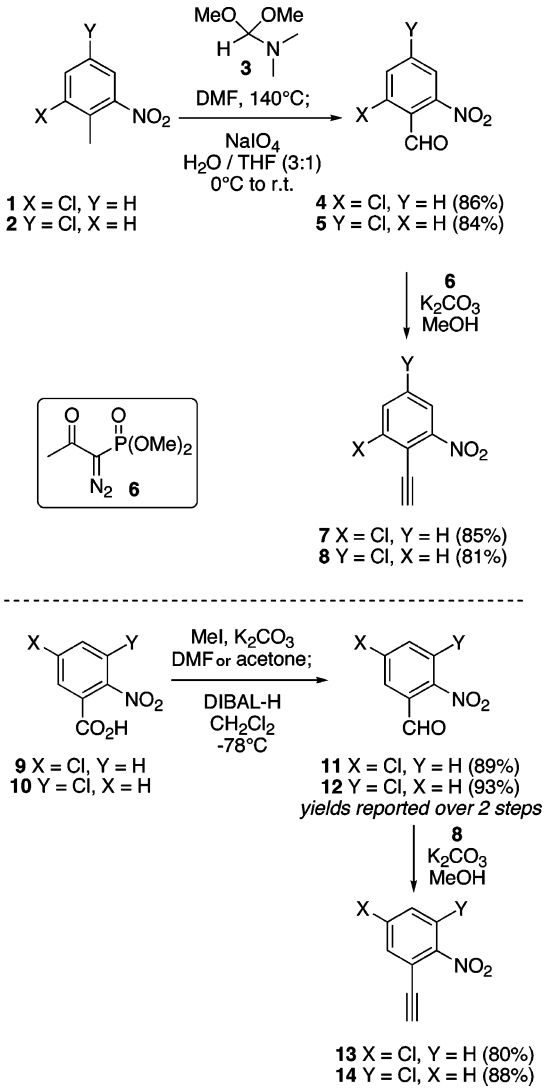
and/or aryl metallo species are not always readily available, as access to the proper substitution pattern has proven difficult to control.[6]

Recently, our laboratory reported a conceptually new method for the construction of biaryl compounds through the use of a Diels−Alder reaction[7] utilizing alkynes possessing *two* electron-withdrawing groups.[8] This Diels−Alder approach to biaryls (DAB) offers several advantages including the ability to incorporate orthogonal functionality within the biaryl template and to construct sterically congested biaryl linkages. In this article, we disclose our exploration into the utility of a *single* electron-withdrawing substituent (monosubstituted acetylenic haloarenes) as dienophiles with oxygenated dienes in the DAB strategy to yield polysubstituted biaryl templates. The functional group combinations accessible by DAB are not readily available from traditional cross-coupling strategies. We exploit this DAB technology in the rapid construction of a series of chlorinated carbazoles and for the total synthesis of the anti-HIV natural product siamenol.[9]

Results and Discussion

Alkyne Synthesis. The necessary dienophiles can be readily synthesized from commercially available reagents (Scheme 1). Inexpensive 2-chloro-6-nitrotoluene (**1**) and 4-chloro-2-nitrotoluene (**2**) could be converted to their corresponding benzaldehyde derivatives **4** and **5** via an oxidative protocol developed by Pfizer.[10] It should be noted that aldehyde **4** is also commercially available from the Sigma-Aldrich Corporation (Cat. No. 106,046). Subsequent alkyne formation with the Ohira−Bestmann reagent **6**[11] yielded the alkynes **7** and **8** in good yield. For the 3-chloro-2-nitro and 5-chloro-2-nitro substitution patterns, the preferred starting materials were the commercially available acids **9** and **10**. After a straightforward

SCHEME 1. Synthesis of Acetylenic Dienophiles



two-step protocol for conversion to aldehydes **11** and **12**,[12] synthesis of the necessary alkynes **13** and **14** was once again accomplished with diazophosphonate **6**. While aldehyde **12** is commercially available, we have found that the purity of this compound is less than optimal.

Diels−Alder Formation of Biaryls. With the alkynes in hand, we were prepared to explore the key Diels−Alder reaction. Due to the orthogonal orientation of the nitro moiety with respect to the aromatic ring in compound **14**, we suspected this dienophile might prove less reactive. For this reason, we first explored alkynes **7**, **8**, and **13** (Scheme 2). These dienophiles performed well in the key Diels−Alder reaction with dienes **15**, **19**, and **23**. In each case, the resultant phenol was protected as its benzyl ether and the yields were reported over two steps. Using Brassard's diene,[13] we initially employed TBAF for the aromatization of the initially formed Diels−Alder adduct. Under these conditions, low yields (30−50%) were routinely observed—despite the clean formation of the Diels−Alder adduct. We suspected that an alternate cleavage reagent might improve the efficiency of the aromatization step. After screening a range of

(7) Prior examples of using a Diels−Alder reaction to construct a biaryl: (a) Reed, J. A.; Schilling, C. L.; Tarvin, R. F.; Rettig, T. A.; Stille, J. K. *J. Org. Chem.* **1969**, *34*, 2188−92. (b) McDonald, E.; Suksamrarn, A.; Wylie, R. D. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1893−900. (c) Weinreb, S. M.; Basha, F. Z.; Hibino, S.; Khatri, N. A.; Kim, D.; Pye, W. E.; Wu, T.-T. *J. Am. Chem. Soc.* **1982**, *104*, 536−44. (d) Boger, D. L.; Panek, J. S.; Duff, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 5745−54. (e) Effenberger, F.; Ziegler, T. *Chem. Ber.* **1987**, *120*, 1339−46. (f) Sain, B.; Sandhu, J. S. *J. Org. Chem.* **1990**, *55*, 2545−46. (g) Smith, D. M.; Royles, B. J. L. *J. Chem. Soc., Perkin Trans. 1* **1994**, 355−58. (h) D'Auria, M. *Tetrahedron Lett.* **1995**, *36*, 6567−70. (i) Avenoza, A.; Busto, J. H.; Cativiela, C.; Peregrina, J. M. *Synthesis* **1995**, 671−74. (j) Balázs, L.; Kádas, I.; Tõke, L. *Tetrahedron Lett.* **2000**, *41*, 7583−87. (k) Watson, M. D.; Fechtenkotter, A.; Mullen, K. *Chem. Rev.* **2001**, *101*, 1267−300. (l) Min, S.-H.; Kim, Y.-W.; Choi, S.; Park, K. B.; Cho, C.-G. *Bull. Kor. Chem. Soc.* **2002**, *23*, 1021−22. (m) Hilt, G.; Smolko, K. I. *Synthesis* **2002**, 686−92. (n) Hilt, G.; Smolko, K. I.; Lotsch, B. V. *Synlett* **2002**, 1081−84. (o) Moore, J. E.; York, M.; Harrity, J. P. A. *Synlett* **2005**, 860−62. (p) Yamato, T.; Miyamoto, M.; Hironaka, T.; Miura, Y. *Org. Lett.* **2005**, *7*, 3−6. (q) Hilt, G.; Galbiati, F.; Harms, K. *Synthesis* **2006**, 3575−84.

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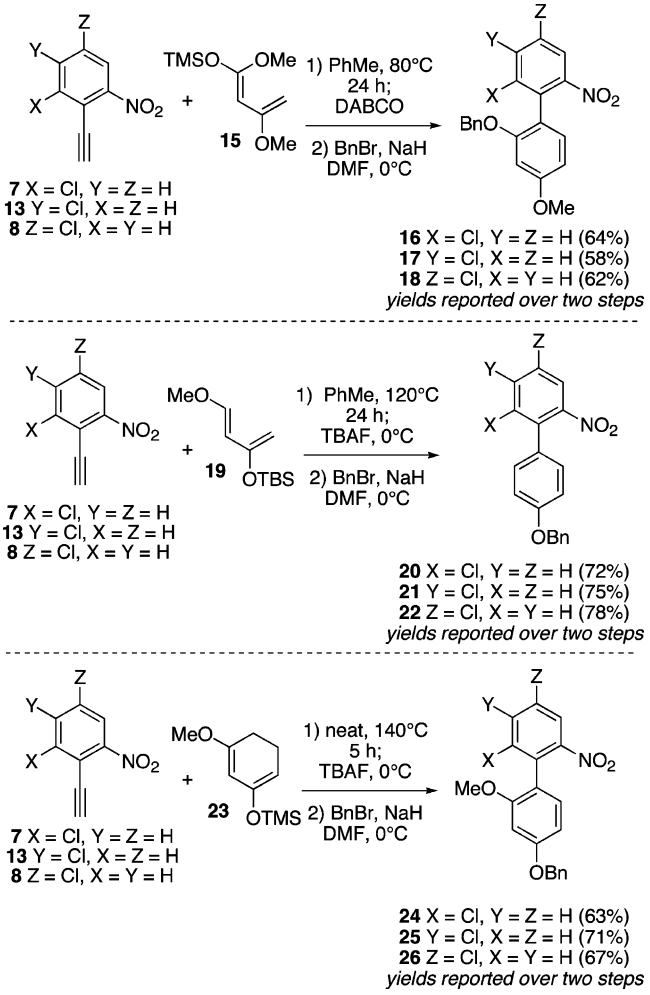
(10) (a) Vetlino, M. G.; Coe, J. W. *Tetrahedron Lett.* **1994**, *35*, 219−22. (b) Caron, S.; Vazquez, E.; Stevens, R. W.; Nahao, K.; Koike, H.; Murata, Y. *J. Org. Chem.* **2003**, *68*, 4104−07.

(11) (a) Ohira, S. *Synth. Commun.* **1989**, *19*, 561−4. (b) S. Müller, S.; Liepold, B.; Roth, G. J.; Bestmann, J. *Synlett* **1996**, 521−22. For preparation of **6**, see also: (c) Goundry, W. R. F.; Baldwin, J. E.; Lee, V. *Tetrahedron* **2003**, *59*, 1719−29. (d) Kitamura, M.; Tokynaga, M.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 2931−2.

(12) Liu, B.; Moffett, K. K.; Joseph, R. W.; Dorsey, B. D. *Tetrahedron Lett.* **2005**, *46*, 1779−1782.

(13) Savard, J.; Brassard, P. *Tetrahedron* **1984**, *40*, 3455−64.

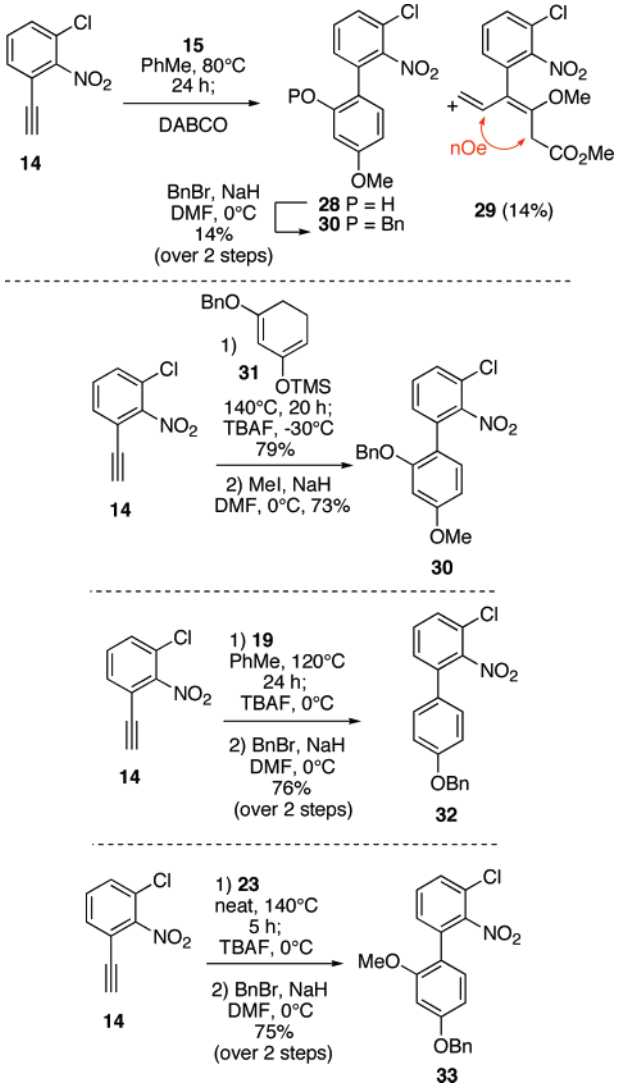
SCHEME 2. Diels–Alder Reactions with Oxygenated Dienes



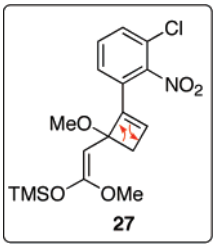
acids and bases, we found that DABCO gave the optimum results for aromatization—providing significant yield improvements over the original protocol. We are unsure of the exact mechanism for cleavage; however, one possible explanation is deprotonation of one of the methylene protons in the lower ring, inducing selective elimination of the methoxy moiety. An alternate mechanism would involve the attack of the silyl ether by methoxide and subsequent collapse to the biaryls **16**–**18**. The methoxide is likely formed from thermal decomposition of the excess Brassard diene during the Diels–Alder reaction. In contrast, TBAF is the preferred reagent for desilylation, elimination, and aromatization with the TBS-variant of Danishefsky's diene **19**. Cyclohexanedienes possessing two oxygen substituents (e.g., diene **23**[14]) were also effective in the synthesis of biaryl adducts—proceeding through an initial Diels–Alder cycloaddition to generate the [2.2.2] bicyclic adduct followed by ethylene extrusion to reveal the aromatic product. It should be noted that both oxygen substituents are required on the diene to achieve successful Diels–Alder reaction. Use of commercially available 1-methoxy-1,3-cyclohexanediene (alkyne **7**, neat, 180 °C) gave none of the expected product. This diene has proven effective on systems possessing an additional electron-withdrawing group on the alkyne.[8]

(14) (a) Freskos, J. N.; Morrow, G. W.; Swenton, J. S. *J. Org. Chem.* **1985**, *50*, 805–10. (b) Nicolaou, K. C.; Montagnon, T.; Vassilikogiznnakis, G.; Mathison, C. J. N. *J. Am. Chem. Soc.* **2005**, *127*, 8872–88.

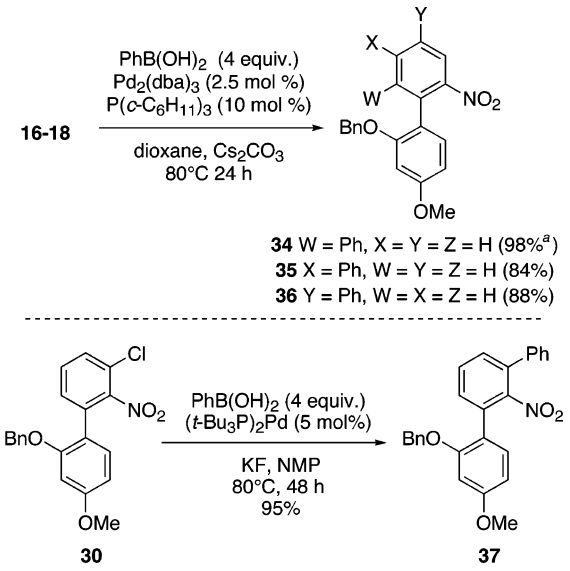
SCHEME 3. Diels–Alder Reactions of the *m*-Chloro Arenes with Oxygenated Dienes



With a solid understanding of the reactivity of the alkynes in the Diels–Alder process, we next chose to explore the 3-chloro series (Scheme 3). Reaction of the Brassard diene **15** with the (3-chloro-2-nitroaryl)alkyne **14** did cleanly yield a small amount of the expected aromatized product **30** after benzylation. In addition to this product, an interesting enol ether product **29** was also observed. We are unsure of an exact mechanism for the product **29** at this time; however, one possibility would involve an initial formation of [2+2] cycloaddition adduct **27** followed by ring opening. To access the desired substitution pattern in **30**, we found that the previously unknown diene **31** was an effective substitute for Brassard's diene. Diene **31** could be readily prepared from 1,3-cyclohexanedione in two steps[15]



SCHEME 4. Suzuki Couplings with Phenylboronic Acid



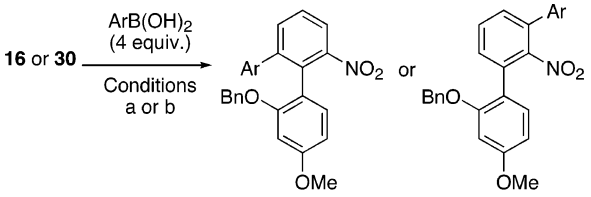
[a] Extended reaction time (48 h) was employed for this coupling.

[BnOH, PTSA (2.5 mol %), PhMe, Dean−Stark trap, reflux, 20 h, 86%; LDA, THF, −78 °C then TMSCl, 99%]. The Diels−Alder reaction was also performed with diene **19** to give the halogenated biaryl **32** in a reasonable yield. Finally, use of diene **23** gave the corresponding biaryl **33** after benzylation.

Suzuki Couplings. With a viable route developed for the synthesis of the halogenated biaryl compounds, their utility in Suzuki couplings was explored (Scheme 4). For the majority of the biaryl compounds, our optimized protocol employed in situ generation of the presumed Pd[P(*c*-C_6H_{11})$_3$]$_2$ catalyst from $Pd_2(dba)_3$ and P(*c*-C_6H_{11})$_3$.[16] The yields on these transformations were generally high (>80%) with only modest catalyst loading (5 mol % Pd). For the more challenging 3-chloro-2-nitroaryl series **30**, we observed incomplete conversion to the desired polyaryl product **37** with this catalyst system—even at high catalyst loading (20 mol %). Fortunately, use of the commercially available (*t*-$Bu_3P)_2Pd$ catalyst,[17] developed by the Fu laboratory,[18] allowed the reaction to proceed to completion by using reasonable catalyst loading (5 mol %). It should be noted that the 3-chloro-2-nitroaryl substitution pattern found in **30** is among the most challenging systems for accomplishing effective palladium couplings—due to the perpendicular orientation of the nitro moiety and the difficulty of insertion into carbon−chloride bonds.

We also chose to study a range of substitution patterns on the boronic acid in order to investigate the scope of this approach (Table 1). For this purpose, we only screened the most challenging substrates: biaryls **16** and **30**. With aryl chloride **16**, we observed that the electron-rich boronic acid coupled smoothly under the normal $Pd_2(dba)_3$/P(*c*-C_6H_{11})$_3$ conditions

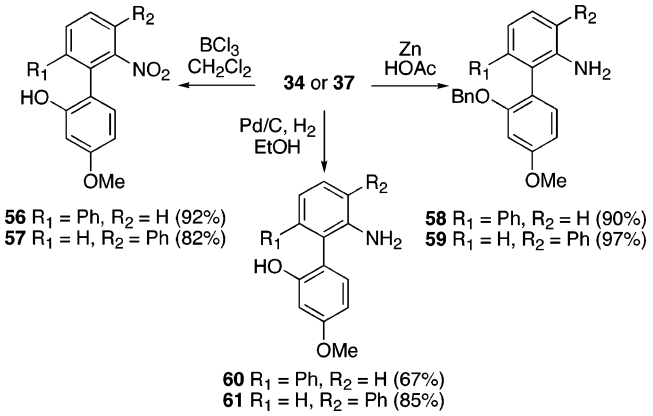
TABLE 1. Suzuki Couplings with Arylboronic Acids



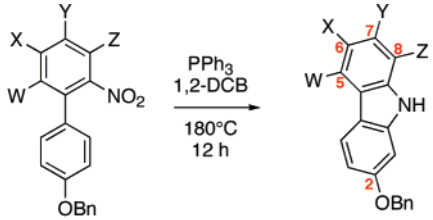
entry	halide	Ar	conditions[a]	% yield
1	**16**	4-OMe-C_6H_4-	a	90 (**38**)
2	**16**	3-OMe-C_6H_4-	a	91 (**39**)
3	**16**	2-OMe−C_6H_4-	a	80 (**40**)
4	**16**	2-Me-C_6H_4-	a	89 (**41**)
5	**16**	4-CN-C_6H_4-	b	80 (**42**)
6	**16**	C_6F_5-	b	0 (**43**)
7	**16**	4-CF_3-C_6H_4-	b[b]	N/A (**44**)
8	**16**	3-CF_3-C_6H_4-	b[b]	77 (**45**)
9	**16**	2-CF_3-C_6H_4-	b[b]	N/A (**46**)
10	**30**	4-OMe-C_6H_4-	b[b]	86 (**47**)
11	**30**	3-OMe-C_6H_4-	b[b]	64 (**48**)
12	**30**	2-OMe-C_6H_4-	b	44 (**49**)
13	**30**	2-Me-C_6H_4-	b[b]	34 (**50**)
14	**30**	4-CN-C_6H_4-	b	61 (**51**)
15	**30**	C_6F_5-	b	0 (**52**)
16	**30**	4-CF_3-C_6H_4-	b	60 (**53**)
17	**30**	3-CF_3-C_6H_4-	b[b]	71 (**54**)
18	**30**	2-CF_3-C_6H_4-	b	22 (**55**)

[a] Conditions: (a) $Pd_2(dba)_3$ (2.5 mol %), P(*c*-C_6H_{11})$_3$ (10 mol %), dioxane, Cs_2CO_3, 80 °C 24 h; (b) (*t*-$Bu_3P)_2Pd$ (5 mol %), KF, NMP, 80 °C, 24 h. [b] Extended reaction time (48 h) was employed for this coupling.

SCHEME 5. Selective Functionalization



SCHEME 6. Synthesis of Chlorinated Carbazoles



with good to excellent yields. Initial forays into electron-deficient boronic acids such as 4-cyanophenyl boronic acid did not perform well with use of the $Pd_2(dba)_3$/P(*c*-C_6H_{11})$_3$ conditions—with typical conversion rates of 40%. Use of the more active (*t*-$Bu_3P)_2Pd$ system allowed this transformation to

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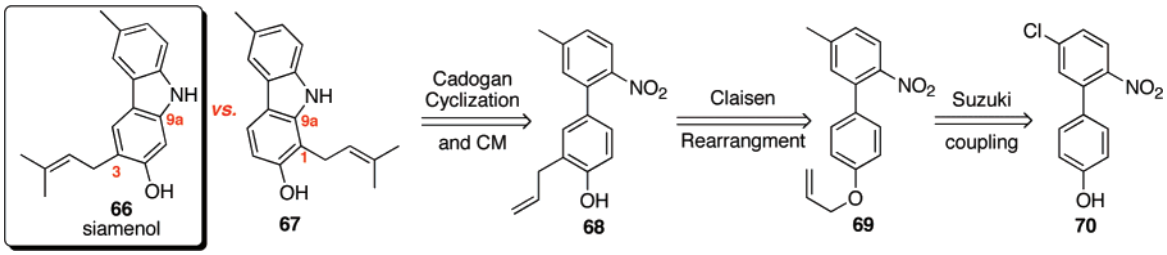
(16) (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176−211. (b) Minutolo, F.; Antonello, M.; Bertini, S.; Rapposelli, S.; Rossello, A.; Sheng, S.; Carlson, K. E.; Katzenellenbogen, J. A.; Macchia, M. *Bioorg. Med. Chem.* **2003**, *11*, 1247−57.

(17) Strem Catalog No. 46-0252.

(18) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020−28.

SCHEME 7. Retrosynthetic Analysis of Siamenol



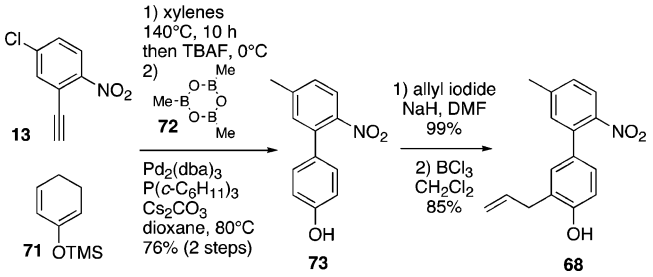
cleanly proceed to completion. It should be noted that the pentafluorophenyl boronic acid appears to be one limitation to this protocol (entry 6). In addition, the *p*-trifluoromethylphenyl boronic acid and the *o*-trifluoromethylphenyl boronic acid both proved capricious as significant amounts of dehalogenated product were observed along with incomplete conversion (entries 7 and 9). The *m*-trifluoromethylphenyl boronic acid was effective in the coupling process (entry 8). In the 3-chloro series **30**, we again found that electron-rich boronic acids coupled well. Electron-deficient boronic acids coupled with reasonable efficiencies; however, the use of pentafluorophenyl boronic acid again gave none of the desired product (entry 15). Use of alternative coupling conditions, such as Buchwald ligands[19] or PEPPSI,[20] was equally unsuccessful.

Further Functionalization. Selective manipulation of the nitro moiety and/or the benzylic phenol is possible (Scheme 5). On the basis of our previous work,[8] Zn/HOAc can be used to cleanly reduce the nitro group to the corresponding amine without deprotection of the benzyl phenol. A tandem reduction process to reveal both the phenol and aniline moieties is also possible via hydrogenation with Pd/C. Finally, selective removal of the benzyl moiety can be accomplished with BCl_3.[8]

Application to the Synthesis of Carbazoles. To demonstrate the utility of our DAB methodology, we have applied it to the rapid construction of chlorinated carbazoles (Scheme 6). Carbazoles have garnered considerable synthetic attention due to the diverse array of biologically active, carbazole natural products[21] and potential materials applications.[22] Using the biaryls **20**–**22** and **32**, we utilized the Cadogan cyclization[23] to provide the C_5–C_8 halogenated carbazoles **62**–**65**. These transformations proceeded cleanly with yields ranging between 65% and 87%. C_5-substituted carbazoles are of particular interest as they are difficult to construct via alternate methods.[24]

Siamenol. With an understanding of the utility of the Cadogan cyclization with our DAB methodology, we have applied it to the construction of the anti-HIV natural product siamenol (**66**) (Scheme 7).[9,25] This carbazole **66** has displayed significant anti-HIV activity (EC50 = 2.6 μg/mL) in the XTT-tetrazolium assay.

SCHEME 8. Synthesis of the Cadogan Precursor



Our biaryl template **70** should provide an excellent springboard for the synthesis of **66**. Key to our strategy is the selective introduction of the allyl group in the C_3 position. The selectivity for C_{9a} in the Cadogan cyclization has not been significantly explored (resulting in a C_3-allyl carbazole versus a C_1-allyl carbazole).[26] In addition, there appears to be little documented evidence on the effect of free phenols in Cadogan cyclizations.[23a]

Starting from the previously described alkyne **13**, Diels–Alder cycloaddition with the diene **71**[27] followed by in situ TBAF treatment cleanly generated the phenol **70** (Scheme 7). While the yields in the Diels–Alder process with use of the cyclohexadiene **71** and TBS-Danisfesky's diene were quite similar, the cyclic diene reaction proved easier to purify. For the Suzuki coupling, we employed our standard conditions with the boroxine **72** to give the methylated adduct **73** (Scheme 8). Next, the phenol **73** was converted to its corresponding allyl ether. We attempted to introduce the dimethylallyl substituent to directly give the prenyl sidearm after Claisen rearrangement; however, no ether formation was observed.[28] The key Claisen rearrangement could be accomplished by thermolysis of the allyl ether in dichlorobenzene (250 °C, sealed tube, 5 h) to induce a [3,3]-sigmatropic rearrangement to provide **68** in 62% yield. Alternatively, we found that treatment of the allyl ether with BCl_3 in CH_2Cl_2 led to rapid Claisen rearrangement at lower temperatures (25 °C) and in higher yield (85% yield of **68**).

Next, we set out to explore the utility of the Cadogan cyclization for the construction of the carbazole (Scheme 9). We first treated the allylated nitro phenol **68** under the standard conditions described previously in Scheme 6 (PPh_3, *o*-DCB, 180 °C). We were disappointed to find that the major product was the undesired C_1-allylated product **75** (51%) along with 32% yield of the desired isomer **74** and 11% yield of the aniline **76**.

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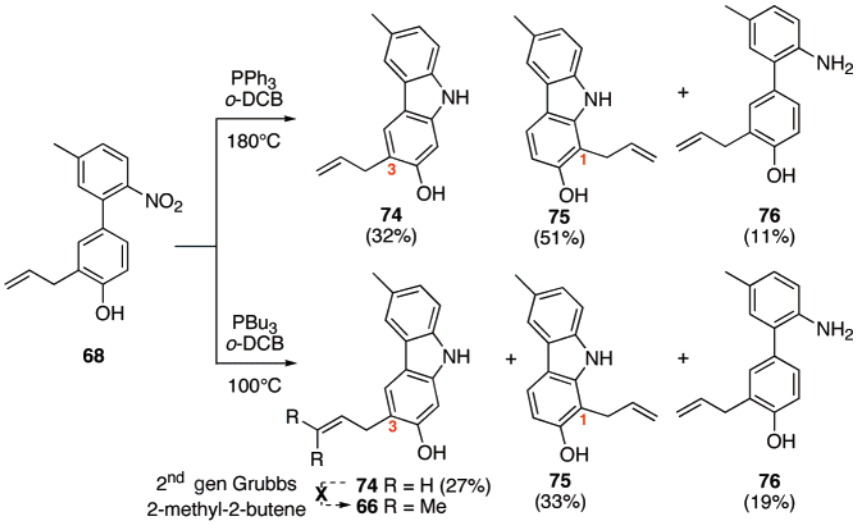
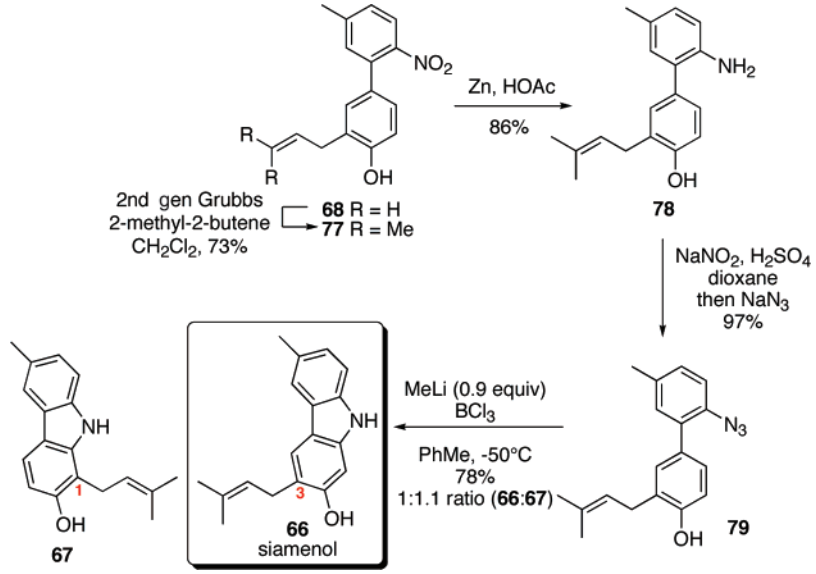
SCHEME 9. First Generation Strategy Toward Siamenol



SCHEME 10. Total Synthesis of Siamenol



Under these conditions, it appears that the electronic preference for the construction of a C_1-substituted carbazole overrides any steric bias. It should also be noted that a Claisen rearrangement of the requisite allyl ether carbazole is known to result in the placement of the allyl group in the more sterically congested C_1 position (e.g., compound **75**).[29] Use of lower temperatures (100 °C) and a more nucleophilic phosphine (Bu_3P) did provide an improved ratio of regioisomeric carbazoles (1:1.2, **74**:**75**) but at a reduced yield (60% overall) and with an increased amount of the aniline byproduct **76** (19%). With the desired regioisomer **74** in hand, we next turned our attention to cross metathesis of **74** under the conditions reported by Grubbs and Stoltz.[30] Unfortunately, treatment of **74** with second generation Grubbs catalyst in 2-methyl-2-butene gave only a trace of the desired natural product **66**. Grubbs has demonstrated a successful example of metathesizing an ortho-allylated phenol; however, the phenolic moiety was protected as its TBS-ether. That said, we suspected that the culprit functionality was the carbazole N−H bond and not the phenolic O−H moiety.

The successful construction of siamenol is shown in Scheme 10. We were pleased to find that our presumption about the culprit functionality in the cross metathesis proved correct; treatment of phenol **68** under the identical metathesis conditions [second generation Grubbs (1 mol %), 2-methyl-2-butene, CH_2Cl_2, rt, 18 h, 73% yield] cleanly provided the prenylated phenol **77**. To explore if the electronic bias for C_1 substitution in the carbazole formation could be overridden at lower temperatures, the nitro moiety was reduced with Zn/HOAc followed by diazotization and azide displacement to give compound **78**. Azides have been used to form carbazoles by treatment with a Lewis acid (usually BCl_3) at low temperatures;[31] however, we are unaware of any exploration of substituent effect (e.g., C_1 vs C_3 substitution) utilizing this approach. Treatment of the azide **79** with BCl_3 in toluene at

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−10 °C did induce cyclization to form the carbazoles **66** and **67**; however, the aniline byproduct **78** was again observed. One possible explanation for the unwanted aniline formation was the presence of the phenolic O−H bond. To address this issue, the phenol **76** was first treated with MeLi (0.9 equiv) followed by the addition of BCl_3 at −50 °C. Under these conditions, we observed clean conversion to the separable carbazoles **66** and **67** (1:1.1 ratio) in good overall yield (78%). Sodium hydride could also be used in the cyclization with similar results. Carbazole **66** was identical in all respects with the previously reported data for siamenol.[9,25] Alternatively, treatment of nitro phenol **77** with PBu_3 at 100 °C did provide the carbazoles **66** and **67** (70% overall yield, 1:1.5 ratio (**66**:**67**)) along with the aniline **78** (24%). Interestingly, addition of NaH to remove the phenolic O−H prior to treatment with PBu_3 completely supressed carbazole formation.

Conclusion

The DAB strategy has been developed for the synthesis of a range of halogenated biaryl templates. *This approach demonstrates for the first time the ability to construct biaryl compounds via a Diels−Alder reaction of oxygenated dienes with acetylenic dienophiles possessing only one electron-withdrawing substituent*. A series of cyclic and acyclic dienes were screened against the acetylenic dienophiles. Good tolerance of a range of oxygenated dienes was demonstrated in most cases. An unusual enol ether byproduct was observed when using Brassard's diene on the 3-chloro alkyne **14**; however, this side reaction can be overcome by use of oxygenated cyclohexadiene substrates. One particular attraction to this DAB strategy is the ability to place the halogen in each of the four possible positions in the nitro ring. Subsequent functionalization of the halogen, nitro moiety, and/or the benzylic phenol has been demonstrated. Finally, application to the synthesis of a series of carbazoles, including the total synthesis of carbazole natural product siamenol, has been accomplished.

Experimental Section

Representative Procedure for Alkyne Synthesis of 7, 8, 13, and 14. To a stirred solution of **4**, **5**, **11**, or **12** (1 mmol), K_2CO_3 (1.9 equiv), and MeOH (0.1 M) was added diazophosphonate reagent **6**[11] (1.3 equiv) at rt. After 2 h, the reaction was quenched with saturated aq $NaHCO_3$, and the MeOH was removed in vacuo. The reaction mixture was diluted with EtOAc and washed with saturated aq $NaHCO_3$, H_2O, and saturated aq NaCl. The dried extract ($MgSO_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5−20% EtOAc/hexanes, to give alkynes **7**, **8**, **13**, or **14** (80−88%) as a pale yellow solid.

7 (85%): mp 94−95 °C; IR (thin film) 3286, 1521, 1351, 808, 756, 736, 681 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.2, 1.1 Hz, 1H), 7.74 (dd, J = 8.2, 1.1 Hz, 1H), 7.47 (t, J = 8.2, 1H), 3.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 134.0, 129.6, 123.1, 117.6, 109.9, 91.7, 75.3; HRMS (CI^+) calcd for $C_8H_5NO_2Cl$ (M + H) 182.0009, found 182.0005.

8 (81%): mp 68−70 °C; IR (thin film) 3285, 1555, 1528, 1345, 891, 840, 791, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 2.0 Hz, 1H), 7.67 (dd, J = 8.4 Hz, 1H), 7.60 (dd, J = 8.4, 2.0, 1H), 3.59 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5, 136.4, 135.3, 133.1, 124.9, 115.9, 86.3, 77.6; HRMS (CI^+) calcd for $C_8H_5NO_2{}^{37}Cl$ (M + H) 183.9979, found 183.9980.

13 (80%): mp 70−73 °C; IR (thin film) 3286, 2112, 1599, 1559, 1516, 883, 834, 753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 8.7 Hz, 1H), 7.68 (d, J = 2.3 Hz, 1H), 7.49 (dd, J = 8.7, 2.3 Hz, 1H), 3.60 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.5, 139.5, 135.2, 129.6, 126.0, 119.2, 86.6, 77.5; HRMS (CI^+) calcd for $C_8H_5NO_2{}^{37}Cl$ (M + H) 183.9979, found 183.9977.

14 (88%): mp 42−43 °C; IR (neat) 3289, 3072, 1549 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, J = 1.4, 7.9 Hz, 1H), 7.54 (dd, J = 1.4, 7.9 Hz, 1H), 7.44 (dd, J = 7.9, 7.9 Hz, 1H), 3.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 132.0, 131.0, 130.7, 125.4, 117.1, 85.1, 75.8; HRMS (CI^+) calcd for $C_8H_4NO_2Cl$ (M + H) 182.0009, found 182.0001.

Representative Procedure for Biaryls 16−18. To a pressure vessel containing alkyne **7**, **8**, or **13** (1 mmol) and PhMe (0.5 M) was added diene **15**[13] (4 equiv) at rt. The mixture was heated at 80 °C. After 24 h, the reaction was cooled to 0 °C and DABCO (4 equiv) was added and the solution was gradually warmed to 40 °C over 30 min. After 1 h at 40 °C, the brown mixture was cooled to rt and quenched with aq HCl (1 M) until pH 2, diluted with EtOAc, and washed with H_2O and saturated aq NaCl. The dried (Na_2SO_4) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0−20% EtOAc/hexanes to give phenolic biaryl, which is used without additional purification. To a stirred solution of the purified phenolic biaryl and dry DMF (0.2 M) was added NaH (2 equiv, 60% dispersion in mineral oil) at 0 °C. To this dark red solution was added BnBr (10 equiv). After 10 min, the yellow solution was quenched with saturated aq NH_4Cl, diluted with EtOAc, and washed with H_2O and saturated aq NaCl (2 × 100 mL). The dried ($MgSO_4$) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 0−10% Et_2O/hexanes to give the benzylated biaryls **16**−**18** (58−64% over 2 steps) as a bright yellow crystalline solid.

16 (64% over 2 steps): mp 99−100 °C; IR (thin film) 2936, 1612, 1583, 1529, 1441 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.1, 1.2 Hz, 1H), 7.73 (dd, J = 8.1, 1.2 Hz, 1H), 7.443 (t, J = 8.1 Hz, 1H), 7.36−7.23 (m, 5H), 7.13 (d, J = 8.3 Hz, 1H), 6.63 (dd, J = 8.3, 2.3 Hz, 1H), 6.60 (d, J = 2.3 Hz, 1H), 5.05 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 156.6, 151.4, 136.8, 136.7, 133.4, 132.0, 130.7, 128.6, 128.4, 127.7, 126.8, 122.2, 116.2, 105.1, 100.3, 70.3, 55.3; HRMS (FAB^+) calcd for $C_{20}H_{16}NO_4Cl$ (M^+) 369.0768, found 369.0759.

17 (58% over 2 steps): mp 121−124 °C; IR (thin film) 2925, 2851, 1617, 1595, 1531, 1268, 1049 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, J = 0.3, 8.6 Hz, 1H), 7.45−7.39 (m, 2H), 7.37−7.33 (m, 3H), 7.27−7.22 (m, 3H), 6.65 (dd, J = 8.4, 2.4 Hz, 1H), 6.55 (d, J = 2.4 Hz, 1H), 5.00 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 156.2, 147.9, 138.6, 136.3, 135.1, 132.6, 130.2, 128.5, 127.9, 127.6, 127.2, 125.5, 119.2, 105.6, 100.3, 70.7, 55.4; HRMS (EI^+) calcd for $C_{20}H_{16}NO_4Cl$ (M^+) 369.0768, found 369.0776.

18 (62% over 2 steps): mp 126−128 °C; IR (thin film) 3032, 2925, 1608, 1527, 1260, 1050 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 2.2 Hz, 1H), 7.58 (dd, J = 8.3, 2.2 Hz, 1H), 7.44−7.20 (m, 7H), 6.63 (dd, J = 8.4, 2.4 Hz, 1H), 6.54 (d, J = 2.4 Hz, 1H), 5.00 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 156.1, 149.7, 136.3, 133.8, 133.3, 132.6, 131.7, 130.2, 128.5, 127.9, 127.1, 124.2, 119.2, 105.6, 100.3, 70.6, 55.4; HRMS (EI^+) calcd for $C_{20}H_{16}NO_4Cl$ (M^+) 369.0768, found 369.0766.

Representative Procedure for Palladium Coupling with $Pd_2(dba)_3$/(c-$C_6H_{11})_3P$: Synthesis of Triaryl 34. To a pressure vessel was added **16** (1.162 g, 3.141 mmol), $PhB(OH)_2$ (1.350 g, 11.07 mmol), Cs_2CO_3 (1.767 g, 5.245 mmol), $Pd_2(dba)_3$ (73.3 mg, 80.0 μmol), PCy_3 (76.6 mg, 0.273 mmol), and dry dioxane (5.80 mL). The solution was sealed under Ar and heated to 80 °C. After 48 h, the mixture was filtered over a pad of Celite, eluting with Et_2O (200 mL), and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 10% Et_2O/hexanes, to give **34** (1.267 g, 3.078 mmol, 98%) as a bright yellow crystalline solid. Mp 124−126 °C; IR (thin film) 3031, 2934, 1612, 1582, 1529, 1511, 1359, 1048 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, J = 8.0, 1.2 Hz, 1H), 7.63 (dd, J = 7.6, 1.6 Hz, 1H), 7.53 (t, J = 7.6, 1H), 7.37−7.25 (m, 3H), 7.25−7.17 (m, 5H), 7.10−

7.02 (m, 2H), 6.83 (d, J = 8.4 Hz, 1H), 6.40 (d, J = 2.4 Hz, 1H), 6.39 (dd, J = 8.4, 2.4 Hz, 1H), 4.99 (d, J = 12.4, 1H), 4.87 (d, J = 12.4, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 156.8, 151.2, 144.6, 140.1, 137.0, 133.9, 131.5, 131.1, 129.2, 128.4, 127.8, 127.7, 127.6, 127.0, 126.7, 122.5, 117.5, 104.8, 99.9, 70.0, 55.2; HRMS (FAB$^+$) calcd for $C_{26}H_{21}NO_4$ (M^+) 411.1471, found 411.1462.

Representative Procedure for Palladium Couplings with (t-Bu$_3$P)$_2$Pd: Synthesis of Triaryl 37. To a pressure vessel containing **30** (552 mg, 1.49 mmol) was sequentially added KF (783 mg, 13.5 mmol), $C_6H_5-B(OH)_2$ (732 mg, 6.00 mmol), (t-Bu$_3$P)$_2$Pd (38.4 mg, 0.0750 mmol), and NMP (15.0 mL). The solution was sealed under Ar and heated to 80 °C. After 48 h, the reaction was quenched with saturated aq NH_4Cl (15 mL), diluted with EtOAc (100 mL), and washed with H_2O (50 mL) and saturated aq NaCl (50 mL). The dried extract ($MgSO_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5−25% EtOAc/hexanes to give **37** (582 mg, 1.42 mmol, 95%) as a yellow crystalline solid. Mp 107−108 °C; IR (neat) 3063, 2930, 1608, 1534 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (t, J = 7.6 Hz, 1H), 7.46−7.42 (m, 7H), 7.37−7.30 (m, 5H), 7.22 (d, J = 8.0 Hz, 1H), 6.60−6.57 (m, 2H), 5.08 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 156.9, 150.4, 137.2, 137.0, 134.6, 131.8, 131.6, 130.9, 129.9, 129.7, 128.7, 128.5, 128.3, 128.1, 127.7, 126.8, 118.6, 105.3, 100.7, 70.5, 55.4; HRMS (FAB$^+$) calcd for $C_{26}H_{21}NO_4$ (M + H) 411.1471, found 411.1491.

Representative Procedure for Debenzylation with BCl_3. To a stirred solution of benzyl ether **34** or **37** (0.1 mmol) in CH_2Cl_2 (1.2 M) was added BCl_3 (5.45 equiv, 1.0 M in heptane) at 0 °C. After 4 h, the reaction was quenched with MeOH, concentrated in vacuo, and purified via flash chromatography over silica gel, eluting with 10−30% EtOAc/hexanes to give the phenol **56** or **57** (82−92%).

56 (92%): IR (neat) 3522, 1620, 1592, 1526, 1360, 1264, 1040, 877, 764 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 8.0, 1.4 Hz, 1H), 7.68 (dd, J = 8.0,1.4 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.28−7.21 (m, 3H), 7.19−7.12 (m, 2H), 6.77(d, J = 8.0 Hz, 1H), 6.41−6.32 (m, 2H), 4.95 (br, 1H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 154.0, 151.7, 145.2, 139.5, 134.1, 131.5, 129.7, 129.1, 128.5, 128.0, 127.4, 122.6, 115.0, 106.7, 101.7, 55.2; HRMS (EI$^+$) calcd for $C_{19}H_{15}NO_4$ 321.1001, found 321.0999.

57 (82%): mp 166−167 °C; IR (neat) 3409, 2921, 1617, 1530 cm^{-1}; ^{1}H NMR (400 MHz, MeOD) δ 7.62 (t, J = 7.7 Hz, 1H), 7.46−7.38 (m, 7H), 7.05 (d, J = 8.0 Hz, 1H), 6.50−6.47 (m, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, MeOD) δ 161.3, 155.6, 152.8, 150.5, 137.4, 134.4, 132.0, 131.5, 130.5, 129.5, 128.2, 127.9, 127.8, 116.6, 104.7, 101.0, 54.3; HRMS (EI$^+$) calcd for $C_{19}H_{15}NO_4$ (M + H) 321.1001, found 321.1004.

Representative Procedure for Nitro Reduction with Zn/HOAc. To a stirred solution of nitroarene **34** or **37** (0.1 mmol) in glacial HOAc (0.25 M) was added Zn dust (6.3 equiv) at rt. After 20 h, the mixture was quenched with saturated aq $NaHCO_3$, diluted with EtOAc, and washed with H_2O and saturated aq NaCl. The dried extract (Na_2SO_4) was concentrated in vacuo and purified via flash chromatography over silica gel, eluting with 15−25% EtOAc/hexanes to give the aniline **58** or **59** (90−97%).

58 (90%): IR (neat) 3471, 3379, 3058, 2835, 1609, 1580, 1266, 1044 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.13 (m, 11H), 7.01 (d, J = 9.0 Hz, 1H), 6.87 (dd, J = 8.0,1.1 Hz, 1H), 6.83 (dd, J = 8.0, 1.1 H, 1H), 6.54−6.41 (m, 2H), 5.02 (d, J = 12.8 Hz, 1H), 4.92 (d, J = 12.8 Hz, 1H), 3.76 (s, 3H), 3.52 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 157.2, 145.0, 143.2, 142.4, 137.4, 132.9, 129.3, 128.4, 128.1, 127.5, 127.4, 126.6, 126.0, 122.9, 120.2, 119.4, 114.3, 105.4, 100.6, 69.9, 55.3; HRMS (EI$^+$) calcd for $C_{26}H_{23}NO_2$ 381.1729, found 381.1721.

59 (97%): IR (neat) 3471, 3385, 3057, 2933, 1611, 1503, 1163 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.48 (m, 4H), 7.41 (dt, J = 1.5, 1.5, 7.2 Hz, 1H), 7.38−7.32 (m, 6H), 7.20 (dd, J = 1.2, 7.2 Hz, 2H), 6.93 (t, J = 7.5 Hz, 1H), 6.71−6.67 (m, 2H), 5.12 (s, 2H), 3.88 (s, 3H), 3.85 (broad s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 156.9, 142.0, 140.2, 137.2, 132.4, 130.7, 129.5, 129.4, 128.8, 128.5, 127.8, 127.7, 127.1, 126.9, 125.0, 122.0, 117.9, 106.0, 101.3, 70.7, 55.5; HRMS (EI$^+$) calcd for $C_{26}H_{23}NO_2$ (M + H) 382.1729, found 381.1728.

Representative Procedure for Hydrogenation with Pd/C. To a stirred solution of benzylated nitro arene **34** or **37** (0.1 mmol) and EtOH (0.28 M, absolute) was added Pd/C (475 mg/mmol, 10% Pd). After being stirred under an atmosphere of H_2 for 21 h, the mixture was filtered over a pad of Celite with EtOAc and concentrated in vacuo. The product was purified via flash chromatography over silica gel, eluting with 15−20% EtOAc/hexanes to give the anilino phenol **60** or **61** (67−85%).

60 (67%): IR (neat) 3472, 3382, 3187, 3057, 2959, 1621, 1573, 1265, 1161, 1039 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, J = 7.9 Hz, 1H), 7.25−7.10 (m, 5H), 6.95 (dd, J = 7.6, 1.0 Hz, 1H), 6.86 (dd, J = 8.0, 1.0 Hz, 1H), 6.80 (d, J = 8.5 Hz, 1H), 6.54 (d, J = 2.5 Hz, 1H), 6.38 (dd, 8.5, 2.5 Hz, 1H), 3.78 (s, 3H), 4.70−3.40 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 154.7, 144.7, 144.0, 141.3, 132.6, 129.1, 129.1, 127.7, 126.5, 121.4, 120.6, 115.9, 114.9, 107.3, 101.6, 55.2; HRMS (EI$^+$) calcd for $C_{19}H_{17}NO_2$ 291.1259, found 291.1251.

Phenol 61: mp 87−89 °C; IR (neat) 3394, 3301, 2921, 1731, 1617, 1160 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.50 (m, 4H), 7.45 (m, 1H), 7.29 (d, J = 2.0 Hz, 1H), 7.26 (dd, J = 1.6, 7.6 Hz, 1H), 7.23 (dd, J = 1.6, 8.4 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.69 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 154.9, 139.0, 138.9, 131.9, 131.1, 129.9, 129.8, 129.3, 129.1, 127.7, 126.3, 120.6, 118.8, 107.9, 103.1 55.4; HRMS (EI$^+$) calcd for $C_{19}H_{17}NO_2$ (M + H) 291.1259, found 291.126.

Representative Procedure Cadogan Cyclization with PPh_3. To a pressure vessel containing **20**, **21**, **22**, or **32** (0.1 mmol) and o-$C_6H_4Cl_2$ (0.5 M) was added PPh_3 (2.5 equiv) at rt. The mixture was heated to 180 °C. After 24 h, the reaction was cooled to rt and purified via flash chromatography over silica gel, eluting with 10−30% EtOAc/hexanes, and recrystalization affored the carbazole **62**, **63**, **64**, or **65** (65−89%) as an off-white solid.

62 (75%): mp 158−160 °C; IR (thin film) 3387, 1177 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 8.7 Hz, 1H), 8.02 (br s, 1H), 7.52 (d, J= 7.2 Hz, 2H), 7.45 (t, J = 7.2 Hz, 2H), 7.38 (t, J = 7.2 Hz, 1H), 7.33−7.18 (m, 3 H), 7.03 (dd, J = 8.7, 2.2 Hz, 1H), 6.97 (d, J = 0.9 Hz, 1H), 5.19 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 140.8, 140.6, 137.0, 128.7, 128.0, 127.8, 127.5, 125.0, 123.9, 120.9, 120.3, 116.4, 109.3, 108.6, 95.7, 70.4; HRMS (EI$^+$) calcd for $C_{19}H_{14}NOCl$ (M^+) 307.0764, found 307.0775.

63 (89%): mp 222−224 °C°C; IR (KBr) 3390, 2916, 1624, 1225, 1176, 1027, 816, 728 cm^{-1}; ^{1}H NMR (400 MHz, d_6-DMSO) δ 11.30 (s, 1H), 8.11 (s, 1H), 8.04 (d, J = 7.8 Hz, 1H), 7.68−7.19 (m, 7H), 7.08 (s, 1H), 6.89 (d, J = 7.8 Hz, 1H), 5.22 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 158.5, 142.2, 138.7, 137.7, 128.9, 128.3, 128.2, 124.5, 124.3, 123.4, 122.0, 119.4, 116.0, 112.5, 109.4, 96.2, 70.0; HRMS (EI$^+$) calcd for $C_{19}H_{14}NOCl$ (M^+) 307.0764, found 307.0764.

64 (84%): mp 235−238 °C; IR (KBr) 3396, 2923, 1605, 1016, 797 cm^{-1}; ^{1}H NMR (400 MHz, d_6-DMSO) δ 11.29 (s, 1H), 8.02 (d, J = 3.3 Hz, 1H), 8.00 (d, J = 3.7 Hz, 1H), 7.52 (d, J = 7.2 Hz, 2H), 7.46 (d, J = 1.8 Hz, 1H), 7.43 (t, J = 7.1 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.14 (dd, J = 8.3, 1.9 Hz, 1H), 7.09 (d, J = 2.3 Hz, 1H), 6.90 (dd, J = 8.6, 2.3 Hz, 1H), 5.21 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 158.3, 141.9, 140.9, 137.7, 129.0, 128.9, 128.3, 128.2, 122.0, 121.6, 121.1, 119.1, 116.2, 110.8, 109.4, 96.4, 70.0; HRMS (EI$^+$) calcd for $C_{19}H_{14}NOCl$ (M^+) 307.0764, found 307.0772.

65 (65%): mp 145−146 °C; IR 3419, 2911, 1419, 735; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.96 (d, J = 8.6 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 7.2 Hz, 2H), 7.45 (t, J = 7.1, 7.6 Hz, 2H), 7.38 (t, J = 7.2, 7.8 Hz, 2 H), 7.18 (t, J = 7.8 Hz, 1H), 7.07 (d, J = 2.0 Hz, 1H), 7.00 (dd, J = 2.2 Hz, 8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 140.5, 137.0, 136.7,

128.7, 128.1, 127.5, 125.0, 123.9, 121.6, 120.4, 117.9, 117.6, 115.8, 109.8, 96.2, 70.5; HRMS (FAB$^+$) calcd for $C_{19}H_{14}ClNO$ (M + H) 308.0842, found 308.0846.

Toluene 73. To a pressure vessel containing **13** (1.294 g, 7.126 mmol) and xylenes (14.0 mL) was added known diene **71**[27] (4.831 g, 28.70 mmol) at rt. The mixture was heated at 140 °C. After 10 h, the reaction was cooled to 0 °C and TBAF (29.0 mL, 29.0 mmol, 1 M in THF) was added. After 15 min, the brown mixture was quenched with saturated aq NH_4Cl (100 mL), diluted with EtOAc (200 mL), and washed with H_2O (2 × 50 mL) and saturated aq NaCl (2 × 50 mL). The dried (Na_2SO_4) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0−35% EtOAc/hexanes to give the phenol **70** (1.928 g) as an impure yellow oil. To a pressure vessel containing the impure phenol **70** (1.928 g) was added Cs_2CO_3 (4.637 g, 14.23 mmol), $Pd_2(dba)_3$ (35.8 mg, 39.1 mmol), PCy_3 (41.1 mg, 146 mmol), methyl boroxine (2.44 g, 2.70 mL, 19.4 mmol), and dioxane (20 mL). The solution was sealed under Ar and heated to 80 °C. After 10 h, the vessel was cooled to rt and filtered over a pad of Celite, eluting with EtOAc (150 mL), and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 0−20% EtOAc/PhMe, to give **73** (1.226 g, 5.348 mmol, 76% over two steps) as a bright yellow crystalline solid. Mp 94−97 °C; IR (thin film) 3407, 1612, 1517, 1350, 1216, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 1H), 7.29−7.19 (m, 4H), 6.93−6.87 (m, 2H), 4.96 (br s, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 146.9, 143.5, 136.2, 132.7, 129.9, 129.3, 128.3, 124.4, 115.7, 21.4; HRMS (EI$^+$) calcd for $C_{13}H_{11}NO_3$ (M$^+$) 229.0739, found 229.0732.

Phenol 77. To a stirred solution of **68** (43.2 mg, 160.4 μmol) in CH_2Cl_2 (500 μL) and 2-methyl-2-butene (596.0 mg, 0.90 mL, 8.49 mmol) was added Grubbs' second generation catalyst (4.0 mg, 4.7 μmol) at rt. After being stirred for 18 h, the mixture was concentrated in vacuo and purified directly via flash chromatography over silica gel, eluting with 0−10% EtOAc/PhMe, to give **77** (40.1 mg, 135.0 μmol, 73%) as a yellow oil. IR (neat) 3472, 1608, 1582, 1520, 1352, 824, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.8, Hz, 1H), 7.25 (d, J = 7.1 Hz, 2H), 7.09 (dd, J = 6.0, 2.1 Hz, 2H), 6.86 (d, J = 8.8 Hz, 1H), 5.48−5.31 (m, 2H), 3.41 (d, J = 7.1 Hz, 2H), 2.48 (s, 3H), 1.81 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 147.1, 143.1, 136.3, 135.2, 132.6, 130.0, 129.5, 128.1, 127.2, 127.1, 124.3, 121.4, 116.0, 29.7, 25.8, 21.4, 17.9; HRMS (EI$^+$) calcd for $C_{18}H_{19}NO_3$ (M$^+$) 297.1365, found 297.1364.

Aniline 78. To a stirred solution of **77** (196.7 mg, 660.4 μmol) in glacial HOAc (6.0 mL) was added Zn dust (314.2 mg, 4.803 mmol) at rt. After 3 h, the mixture was quenched with saturated aq $NaHCO_3$ (20 mL), diluted with EtOAc (100 mL), and washed with H_2O (10 mL) and saturated aq NaCl (2 × 20 mL). The dried extract (Na_2SO_4) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 0−40% EtOAc/hexanes, to give **78** (151.7 mg, 551.0 μmol, 86%) as an off white solid. Mp 126−132 °C; IR (thin film) 3363, 3276, 2920, 1604, 1431, 1279, 1233 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 2.0 Hz, 1H), 7.21 (dd, J = 8.3, 2.1 Hz, 1H), 7.00 (d, J = 9.1 Hz, 2H), 6.87 (d, J = 8.0 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 5.40 (tt, J = 5.9, 1.3 Hz, 1H), 4.18 (br s, 1H), 3.44 (d, J = 7.2 Hz, 2H), 2.32 (s, 3H), 1.83 (s, 3H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 140.9, 134.8, 131.9, 131.1, 130.7, 128.6, 128.1, 128.0, 128.0, 127.4, 121.7, 115.9, 115.9, 29.8, 25.9, 20.5, 17.9; HRMS (EI$^+$) calcd for $C_{18}H_{21}NO$ (M$^+$) 267.1623, found 267.1629.

Azide 79. To a stirred solution of **78** (150.2 mg, 562.1 μmol) and dioxane (2.00 mL) at −10 °C was added aq H_2SO_4 (5.60 mL, 1.98 M). After the solution had been stirred for 5 min at −10 °C, $NaNO_2$ (82.8 mg, 400 μL, 1.20 mmol, 3.00 M) was added via syringe. After 20 min at −10 °C, NaN_3 (117.0 mg, 600 μL, 1.80 mmol, 3.01 M) was added to the deep yellow solution and effervescence evolved. After 30 min, the mixture was warmed to rt and diluted with Et_2O (30 mL). The organic extract was washed with $NaHCO_3$ (3 × 15 mL) and saturated aq NaCl (2 × 10 mL). The dried extract (Na_2SO_4) was concentrated in vacuo to give **79** (114.0 mg, 542.8 μmol, 97%) as a brown oil and used without further purification. IR (thin film) 3419, 2115, 2068, 1608, 1296, 1263, 808 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.13 (m, 5H), 6.89 (d, J = 7.9 Hz, 1H), 5.41 (tt, J = 7.4, 1.3 Hz, 1H), 5.24 (d, J = 1.9 Hz, 1H), 3.45 (d, J = 7.2 Hz, 2H), 2.40 (s, 3H), 1.84 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ154.0, 135.0, 134.6, 134.3, 133.4, 131.8, 131.1, 130.8, 128.9, 128.6, 126.5, 121.7, 118.7, 115.5, 30.0, 25.8, 20.9, 17.9; HRMS (EI$^+$) calcd for $C_{18}H_{19}N_3O$ (M$^+$) 293.1528, found 293.1518.

Siamenol 66 and Carbazole 67. To a stirred solution of **74** (57.4 mg, 195.6 μmol), PhMe (1.96 mL), and 2-methyl-2-butene (300 μL) at −10 °C was added MeLi (160 μL, 216 μmol, 1.35 M in Et_2O). After 5 min, BCl_3 (600 μL, 600 μmol, 1 M in hexanes) was added to the red mixture, and slight effervescence was observed. After being stirred for 24 h at −10 °C, the mixture was quenched with MeOH (1 mL) at −10 °C, and then warmed to rt. The mixture was then diluted with CH_2Cl_2 (30 mL) and washed with saturated aq NH_4Cl (10 mL), H_2O (10 mL), and saturated aq NaCl (2 × 10 mL). The dried extract (Na_2SO_4) was concentrated in vacuo and purified via flash chromatography over silica gel, eluting with 0−20% EtOAc/hexanes, to give sequentially **67** (21.1 mg, 79.5 μmol, 41%) and **66** (19.2 mg, 72.3 μmol, 37%) as white solids. **66**: mp 140−143 °C; IR (thin film) 3406, 3252, 2920, 2852, 1636, 1617, 1465, 1319, 1210, 1014, 802 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (m, 3H), 7.27 (d, J = 8.0 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 6.86 (s, 1H), 5.44 (tt, J = 7.2, 1.2 H, 1H), 5.30 (s, 1H), 3.55 (d, J = 7.2 Hz, 2H), 2.54 (s, 3H), 1.88 (s, 3H), 1.85 (s, 3H); ^{1}H NMR (400 MHz, d_4-MeOD) δ 7.64 (dd, J = 1.6, 0.8 Hz, 1H), 7.60 (s, 1H), 7.19 (d, J = 8.2 Hz, 1H), 7.04 (dd, J = 8.1, 1.0 Hz, 1H), 6.79 (s, 1H), 5.43 (t-sept, J = 7.3, 1.4 Hz, 1H), 3.41 (d, J = 7.3 Hz, 2H), 2.45 (s, 3H), 1.78 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 139.9, 137.7, 134.7, 128.6, 125.7, 123.7, 122.6, 120.8, 119.4, 117.2, 109.9, 97.2, 30.5, 25.8, 21.4, 17.9; ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.16, 140.4, 138.5, 131.1, 127.3, 124.7, 124.0, 123.9, 120.5, 119.7, 118.5, 116.1, 109.7, 95.9, 28.5, 24.9, 20.4, 16.7; HRMS (EI$^+$) calcd for $C_{18}H_{19}NO$ 265.1467 (M$^+$), found 265.1471. **67**: mp 126−128 °C; IR (thin film) 3524, 3424, 3261, 2919, 2853, 1614, 1227, 1211, 1032, 802 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (br s, 1H), 7.78 (d, J = 1.0 Hz, 1H), 7.76 (d, J = 3.6 Hz, 1H), 7.31 (d, J = 8.2 Hz, 1H), 7.18 (dd, J = 8.4, 1.1 Hz, 1H), 6.76 (d, J = 8.3 Hz, 1H), 5.41 (d-quint, J = 6.9, 1.4 Hz, 1H), 5.11 (br s, 1H), 3.64 (d, J = 6.9 Hz, 2H), 2.54 (s, 3H), 1.94 (s, 3H), 1.82 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 140.4, 137.8, 134.9, 128.8, 125.8, 124.2, 121.5, 119.5, 118.6, 117.4, 110.1, 109.0, 108.3, 25.8, 24.4, 21.5, 18.1; HRMS (EI$^+$) calcd for $C_{16}H_{15}NO$ 237.1154 (M$^+$), found 237.1155.

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Supporting Information Available: Detailed experimental procedures for all new compounds not included in the Experimental Section, as well as ^{1}H and ^{13}C spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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