JOC The Journal of Organic Chemistry

Article

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ortho-Bromo(propa-1,2-dien-1-yl)arenes: Substrates for Domino Reactions

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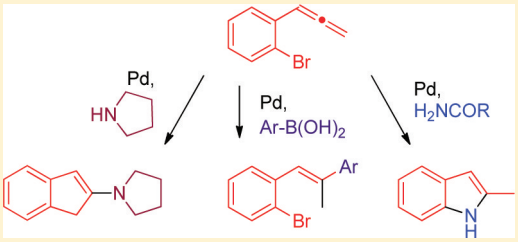
Supporting Information

ABSTRACT: *o*-Bromo(propa-1,2-dien-1-yl)arenes exhibit novel and orthogonal reactivity under Pd catalysis in the presence of secondary amines to form enamines (concerted Pd insertion, intramolecular carbopalladation, and terminative Buchwald–Hartwig coupling) and of amides to form indoles (addition, Buchwald–Hartwig cyclization, and loss of the acetyl group). The substrates for these reactions can be accessed in a reliable and highly selective two-step process from 2-bromoaryl bromides.

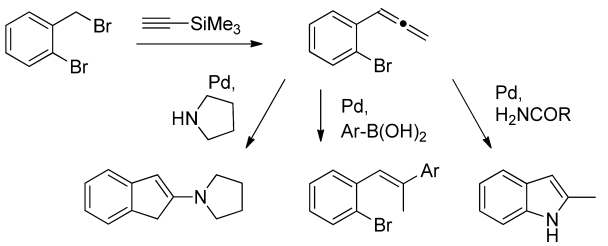


INTRODUCTION

The synthetic usage of allenes is currently a topic of interest.[1] Considerably more reactive than simple alkenes, allenes act as substrates with transition-metal catalysts in a variety of ways;[2] in particular, they are known to undergo facile carbopalladation processes. As part of our ongoing interest in Pd-catalyzed domino reactions,[3,4] we envisaged that 2-haloarylallenes (unknown in the literature)[5] present themselves as attractive substrates for transition-metal-catalyzed domino reactions: The aryl bromide serves as a functionality for Pd^0 insertion, while the allene could be a substrate to Pd^{II}-catalyzed carbopalladation. Domino reactions of allenes have hitherto predominantly involved the use of bifunctional substrates incorporating an organohalide/nucleophile unit in combination with an allene partner.[6] The alternative strategy, with the allene and organohalide as a bifunctional substrate, provides relatively fertile ground for exploration, despite the notable "zipper"-type reactions from Grigg and co-workers.[7]

We imagined that oxidative insertion of Pd^0 would be followed by a facile insertion of the π-system of the tethered allene (Scheme 1). The resulting 2-palladium(II) indenyl intermediates would then be treated with a variety of species for the achievement of reductive termination pathways: that is, the in situ presence of nucleophile or equivalent might result in a termination process to return Pd^0 catalyst. Specifically, the application of Pd catalysis with 2-halo-substituted arylallenes is predicted to give rise to, for example, amines or amides in the presence of base to effect Buchwald–Hartwig couplings,[8] stannanes to give Stille couplings,[9] or arylboronic acids to give Suzuki couplings,[10] each of which process would follow an initial intramolecular insertion of the alkene π-sytem to Ar–Pd^{II}–Br similar to that found in the Heck reaction.[11]

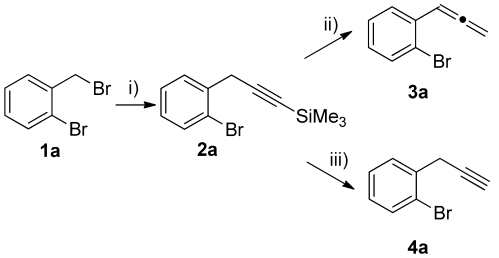
Scheme 1. Synthesis of, and Divergent Pd-Catalyzed Pathways from, *o*-Bromo(propa-1,2-dien-1-yl)arenes



RESULTS AND DISCUSSION

The initial coupling of 2-bromobenzyl bromide (**1a**) with trimethylsilylacetylene proved to be a surprisingly challenging reaction (Scheme 2, Table 1). The use of classical Sonogashira

Scheme 2. Conversion of 2-Bromo(bromo)methylbenzene (1a) to 2-Bromophenylprop-1,2-diene (3a) and 2-Bromophenylprop-2-yne (4a)



i) Trimethylsilylacetylene (2.00 equiv), CuI (1.00 equiv), Bu_4NI (1.00 equiv), Cs_2CO_3 (1.05 equiv), MeCN, 65 °C, 65 h, 66% (isolated); ii) TBAF (1.20 equiv), THF, rt, 0.7 h, 91% (isolated), or K_2CO_3, MeOH/THF, rt, 3 h, 80% (isolated); iii) $AgNO_3$ (1.5 equiv) EtOH/H_2O, 0.5 h; then KCN (1.00 equiv), 10 min, 87% (isolated).[15]

Received: September 2, 2011
Published: September 29, 2011

Table 1. Optimization of Step i: Conditions for the Alkynylation of 2-Bromobenzyl bromide[a]

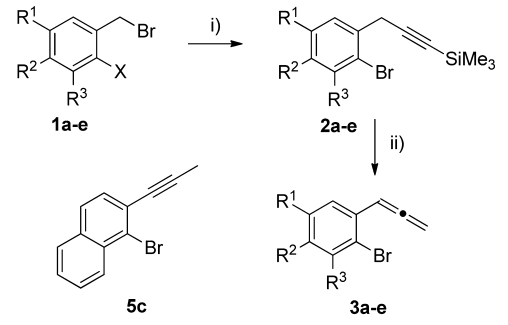
E	$M(L)_nX_n$	solvent	base	additive	T (°C)	time (h)	conv (%)
1	$Pd(PPh_3)_4$	THF	NEt_3	CuI	rt	48	16[b]
2	$Pd(PPh_3)_4$	THF	NEt_3	CuI	45	36	dec.[b]
3	CuI	MeCN	K_2CO_3	Bu_4NI	40	48	28[c]
4	CuI	MeCN	K_2CO_3	Bu_4NI	65	48	69
5	CuI	MeCN	K_2CO_3	Bu_4NI	65	72	71
6	CuI	MeCN	K_2CO_3	Bu_4NI	65	156	70
7	$Pd(PPh_3)_2Cl_2$	MeCN	K_2CO_3	CuI, Bu_4NI	45	108	100 [d]
8	Pd(XPhos)[e]	THF	Cs_2CO_3		65	48	0[f]
9	CuI	MeCN	Cs_2CO_3	Bu_4NI	65	65	100[g]

[a]Conversion determined by ^{1}H NMR analysis of the crude reaction mixtures. Several alternative methods including alkynyl Grignard and alkynyllithium·TMEDA complex substitution were attempted without success for this transformation: the use of Grignard methodology giving debrominated product exclusively and TMEDA–lithium acetylide giving a complex reaction mixture. Pd catalysts $Pd(PPh_3)_4$ and $Pd(PPh_3)_2Cl_2$ were used in 5 mol % and $Pd(OAc)_2$ in 2 mol % amounts, CuI was used in 1.00 equiv amount, except as an additive, where it was used in 20 mol % amount. Et_3N was used in 5.00 equiv, K_2CO_3 in 2.00 equiv, Cs_2CO_3 in 1.05 equiv, and Bu_4NI in 1.00 equiv amounts. [b]The use of triethylamine as base resulted in the generation of considerable amounts of benzyltrimethylammonium halide salts. [c]See ref 13. [d]Complete conversion of substrate, however, 70% NMR yield due to formation of a byproduct (30 mol %). [e]Formed in situ from $Pd(OAc)_2$ (2 mol %) and XPhos (6 mol %). [f]See ref 14. These conditions gave only 17% conversion to the aryl bromide coupled species. [g]Isolated yield 66%, scalable to 5 mmol.

conditions[12] did not deliver sufficient conversion (entry 1), and heating the reaction mixture gave the desired product and inseparable byproducts (entry 2). Pd-free reaction conditions with stoichiometric copper iodide, *n*-tetrabutylammonium iodide, and potassium carbonate as base in acetontirile, as employed by Wulff et al.,[13] gave cleaner reaction mixtures (entry 3), but complete conversion could not be achieved. Heating to 65 °C for 48 h improved the conversion to 69% (entry 4), but the conversion did not improve with further reaction time (entries 5 and 6). The addition of Pd catalysts to these latter reaction conditions led to complete consumption of the starting material, but with the generation of byproducts (entry 7). The use of conditions described by Buchwald et al.[14] gave aryl coupling (i.e., at the arene bromide moiety, entry 8). Lastly, the utilization of modified Wulff conditions (with cesium carbonate as base) gave complete conversion to the alkyne product (entry 9).

Application of the optimized conditions to the synthesis of substituted analogues of 2-bromobenzyl bromide (**1a–e**, Scheme 3)[16] proved to be generally applicable, giving good

Scheme 3. Conversion of *o*-Bromo(bromo)methylarenes 1b–d to *o*-Bromoarylallenes 3b–d[a]



a: X = Br, $R^1 = R^2 = R^3 = H$
b: X = Br, R^1-R^2 = -O-CH_2-O-, $R^3 = H$
c: X = Br, $R^1 = H$, R^2-R^3 = -CHCHCHCH-
d: X = Br, $R^1 = CO_2Me$, $R^2 = R^3 = H$
e: X = OMe, $R^1 = R^2 = R^3 = H$

[a]For conditions i and ii, see Scheme 2.

to excellent yields of the allene products in an efficient two-step process (see Scheme 3 and Table 2). The reaction sequence involving electron-deficient arene **1b** proved especially high yielding. In contrast, 1-bromonaphthalenyl substrate **1c** readily converted from trimethylsilylalkyne **2c** to alkyne **5c** in situ through a relatively facile desilylation/isomerization process. The desilylation of **2c** with TBAF led to allene **3c** alongside the same alkyne **5c**. The 2-bromomethylanisole **1e** also underwent the reaction sequence with high yields to **3e**.[17] The allenes were then tested under a variety of Pd-catalyzed reaction conditions.

First, the formal addition of (tethered) Ar and NRR′ across the allene π-system was accomplished using Buchwald–Hartwig amination conditions: $Pd(OAc)_2$, *rac*-BINAP, and an

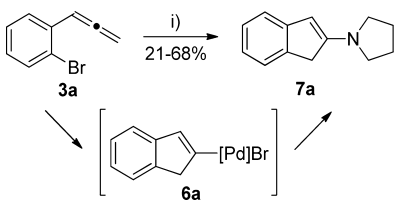
Table 2. Conversion of *o*-(Bromo)methylarenes 1 to Trimethylsilylalkynes 2 and then Allenes 3[a]

E	conditions	1x	2x	yield (%)	conditions	3x	yield (%)
1	i	**1a**	**2a**	66	ii	**3a**	91
2	i	**1b**	**2b**	94	ii	**3b**	87
3	i	**1c**	**2c**	46[b]	ii	**3c**	91[c]
4	i	**1d**	**2d**	67	ii	**3d**	90
5	i	**1e**	**2e**	87	ii	**3e**	99

[a]Isolated yield. [b]Allene **3c** as byproduct, 54%. [c]Only 1.0 equiv of Bu_4NF was used; otherwise, **5c** was obtained (45%).

excess of Cs_2CO_3 in toluene gave enamine **7a**, almost certainly by way of carbopalladate intermediate **6a** (Scheme 4).

Scheme 4. Buchwald–Hartwig Amination of 2-Bromoarylallene 3a[a]



[a]Key: (i) pyrrolidine (4.0 equiv), $Pd(OAc)_2$ (5 mol %), *rac*-BINAP (12 mol %), Cs_2CO_3 (2.0 equiv), toluene, 100 °C, 14 h, 21–68% yield.

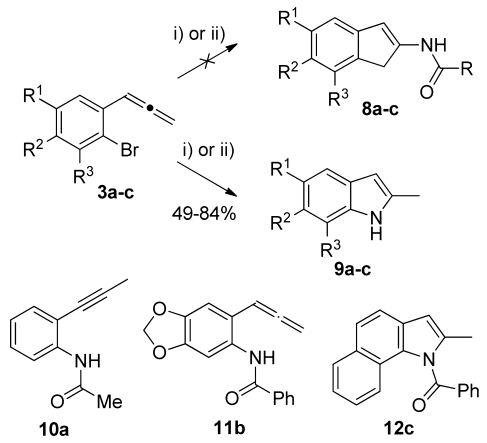
Unfortunately, the reaction proved capricious in terms of reproducibility (21–68% isolated yield); this is largely due to the nature of enamine **6a** as being easily hydrolyzed.

dx.doi.org/10.1021/jo201679s | J. Org. Chem. 2011, 76, 9060–9067

Application of other secondary amines (morpholine, bis-allylamine, diphenylamine) did not resolve this issue.

We sought to apply this methodology to the synthesis of indenylacetamides using the Buchwald–Hartwig amidation reaction;[8] however, under conditions previously reported for this reaction, an unexpected and selective indole synthesis was found to occur. Stirring the bromide with palladium acetate, Xantphos, cesium carbonate, and acetamide in dioxane at 100 °C[18] unexpectedly gave 2-methylindole **9a** as product in 40% yield, alongside alkyne **10a** (R^4 = Me, 29%), presumably an intermediate in the reaction (Scheme 5, Table 3). A marked

Scheme 5. Indole Formation under Buchwald–Hartwig Amidation Conditions[a]



[a]Both i and ii utilize $Pd(OAc)_2$ (5 mol %), Xantphos (12 mol %), Cs_2CO_3 (2.0 equiv), 1,4-dioxane (0.3 M), 100 °C, 19 h, in combination with (i) acetamide (1.30 equiv) and (ii) benzamide (1.30 equiv).

Table 3. Buchwald–Hartwig Amidation[a]

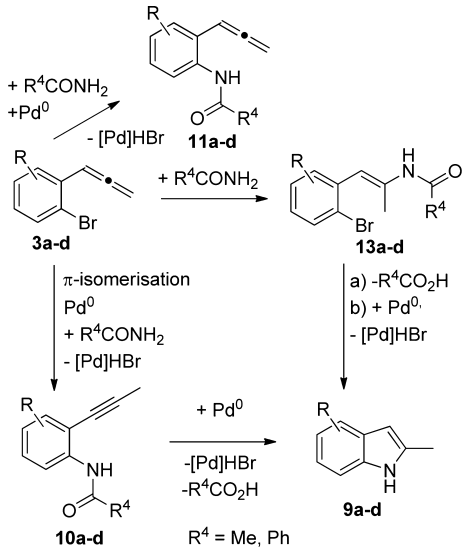
E	3x	conditions	9x	yield (%)	byproduct	yield (%)
1	**3a**	i	**9a**	40	**10a**	29
2	**3a**	ii	**9a**	84		
3	**3b**	ii	**9b**	49	**11b**	10
4	**3c**	ii	**9c**	54	**12c**	35
5	**3d**	ii	**9d**	58		
5	**5c**	ii	**9c**	43	**12c**	50

[a]Isolated yields.

increase in yield of **9a** (84%) resulted when benzamide was used as the amide coupling partner (Table 3). Under these conditions, notably clean reactions resulted in the generation of indole products **9a–c** that were both stable and isolable in fair to good yields; the major other species isolated from reaction mixtures were amide **11b** from bromide **3b** and amide **12c** from either allene **3c** or alkyne **5c**, which was also tested under the reaction conditions. While reactions involving the hydroamidation of allenes catalyzed by a variety of transition metals are known,[19] the one-pot or domino construction of indoles from separate aryl halide and amine components under Pd catalysis has not, to the best of our knowledge, been previously described.[20] Additionally, the use of benzamide or acetamide as ammonia surrogates in Pd-catalyzed reactions appears to not have been previously reported.[21,22]

A plausible pathway for the synthetic transformation from bromides **3a–d** and **5c** to the indole products **9a–d**, and which accounts for all of the observed byproducts in the various reactions, is presented below (Scheme 6). The initial

Scheme 6. Proposed Pathway of the Domino Addition, Buchwald–Hartwig Amidation, and Hydrolysis to Indoles 8 and Byproducts

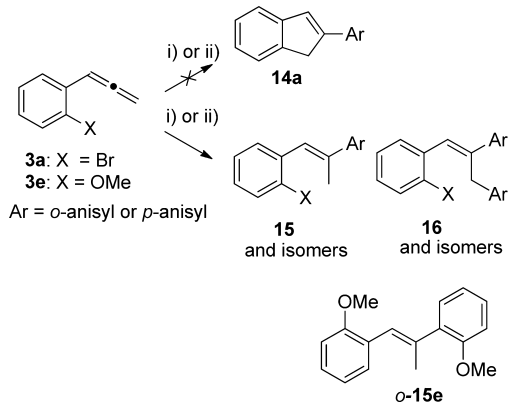


regioselective addition of amide across the allene gives vinyl amide **13a–d**, which then is hydrolyzed and undergoes intramolecular Buchwald–Hartwig coupling (steps a and b may also occur in the reverse order). Alternative reaction sequences involving initial Buchwald–Hartwig coupling would result in product **11b**, and a sequence of first π-isomerization[23] followed by Buchwald–Hartwig coupling would result in product **10b**. The cyclization of *o*-(acyl/benzyl)aminoalkynes of the type represented by **10a** is known.[24] The extent to which each pathway is active under these reaction conditions is highly substrate-dependent, as demonstrated by the byproduct generated in each case.

A domino carbopalladation–Suzuki reaction to deliver derivatives of the type **14a** was attempted under modified Suzuki conditions,[25,26] giving always complex product mixtures. For example, application of $Pd(dppf)Cl_2$ as catalyst with triethylamine as a base in a mixture of water and tetrahydrofuran, conditions reported by Banwell and co-workers,[26] gave mixtures too complex to characterize, so lower temperatures were used in an attempt to increase selectivity (40 °C). The reactivity of **3** to displayed at this temperature was orthogonal to that observed for the Buchwald–Hartwig amination and amidation conditions, in that the aryl bromide functionality stayed intact under the reaction conditions (i.e., the conversion from product does not involve oxidative insertion of Pd^0 at the aryl bromide functionality). Instead, the allene π-system was found to react in arylation processes delivering products with the net effect of addition across the allene π-system of ArH and 2Ar to give monoarylated and diarylated products (**15** and **16**, respectively, Scheme 7). Reaction mixtures were nonetheless quite complex, and only mixtures of mono- and diarylated isomers could be separated from one another.

dx.doi.org/10.1021/jo201679s | *J. Org. Chem.* 2011, 76, 9060–9067

Scheme 7. Addition of Ar-H and 2Ar to Allenes 3a and 3e, Respectively[a]



[a]Conditions i and ii: see Table 4.

The ratio of these products depended on the nature of the arylboronic acid used (Table 4, entries 1 and 2). It was found that the use of 2-methoxyphenylboronic acid gave both a higher overall reactivity and relative amount of the diaryl-addition product relative to arylhydride addition in comparison to 4-methoxyphenylboronic acid under identical conditions. The 2-methoxyphenylallene **3e** was exposed to the same reaction conditions, under which it reacted in an analogous manner with addition of ArH and 2Ar across the allene π-system (entries 3 and 4). In the case of the reaction with 2-methoxyphenylboronic acid, isolation of the *trans*-stilbene addition product ***o*-15e** was possible in 32% yield (stereochemistry determined by NOESY). Such a process has been previously reported for the reaction of allenes and boronic acids in the presence of Pd-catalyst and acid.[27]

Table 4. Hydroarylation of Allenes

E	3x	Ar-X	conditions[a]	compd 15	yield[b] (%)	compd 16	yield (%)
1	3a	Br	i	*o*-15a	57	*o*-16a	30
2	3a	Br	ii	*p*-15a	49	*p*-16a	8
3	3e	OMe	i	*o*-15e	51	*o*-16e	12
4	3e	OMe	ii	*p*-15e	28	*p*-16e	9

[a]See Scheme 7. Key: (i) 2-methoxyphenylboronic acid (2.0 equiv), $Pd(dppf)Cl_2$ (6 mol %), $Et_3N/H_2O/THF$ (5:2:18), 40 °C, 48 h; (ii) as with i, but with 4-methoxyphenylboronic acid (2.0 equiv). [b]Yields determined from separation of products into groups of double-bond isomers and regioisomers.

The further investigation of these multitalented substrates is currently underway in our laboratories, and we will report further on their application in other Pd-catalyzed domino reactions in due course.

EXPERIMENTAL SECTION

Example Procedure A: Coupling of Trimethylsilylacetylene with *o*-Heteroatom-Substituted Aryl Bromides (2a). 2-Bromobenzyl bromide (**1a**, 500 mg, 2.00 mmol), cuprous iodide (381 mg, 2.00 mmol), tetra-*n*-butylammonium iodide (739 mg, 2.00 mmol), cesium carbonate (684 mg, 2.10 mmol), and acetonitrile (HPLC grade, 3.0 mL) were sealed in a 20 mL reaction vial with a stirring bar and degassed (3 × vacuum and backfill with argon while stirring vigorously) via a needle through the septum. Trimethylsilylacetylene (296 mg, 405 μL, 3.00 mmol) was then added by syringe, and the reaction mixture stirred in an aluminum heating block at 65 °C for 72 h, with daily shaking to loosen up cesium carbonate deposits on the walls of the reaction vessel. After this time, the magenta suspension was diluted with diethyl ether (10 mL) and filtered through a Celite pad. The tetra-*n*-butylammonium iodide subsequently crystallized, and a second filtration was made through a cotton wool plug. The crude was reduced of volatiles on the rotary evaporator (care was taken, as the products can be volatile at low pressures). The resulting crude was subjected to column chromatography [silica gel, ethyl acetate/cyclohexane (1:160)] to yield (3-(2-bromophenyl)prop-1-yn-1-yl)trimethylsilane (**2a**) as a colorless oil (353 mg, 1.32 mmol, 66%).

Example Procedure B: Desilylation/Allene Formation (3a). (3-(2-Bromophenyl)prop-1-yn-1-yl)trimethylsilane (**2a**, 335 mg, 1.25 mmol) was dissolved in tetrahydrofuran (5.0 mL) and then stirred at room temperature. A solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran (1.00 M, 1.50 mL, 1.50 mmol) was added dropwise by syringe at room temperature, and the resulting black solution was stirred for 0.5 h. After this time, the reaction was quenched with a saturated solution of ammonium chloride (10 mL) and extracted with diethyl ether (2 × 15 mL). The organic layers were combined, washed with saturated sodium hydrogen carbonate solution (20 mL) and saturated brine (20 mL), dried over sodium sulfate, filtered, and reduced of volatiles on the rotary evaporator (care was taken, as the products can be volatile at low pressures). The resulting crude was subjected to column chromatography (silica gel, pentane) to give 1-bromo-2-(propa-1,2-dien-1-yl)benzene (**3a**) as a colorless volatile oil (221 mg, 1.14 mmol, 91%).

Procedure C: Domino Carbopalladation Buchwald–Hartwig Amination To Form 1-(1*H*-Inden-2-yl)pyrrolidine (7a). 1-Bromo-2-(propa-1,2-dien-1-yl)benzene (**3a**, 97.6 mg, 0.50 mmol), cesium carbonate (164 mg, 0.50 mmol), palladium acetate (2.8 mg, 0.013 mmol), *rac*-BINAP (18.7 mg, 0.03 mmol), and toluene (1.00 mL) were combined together with a stirring bar in a 20 mL vial, which was then sealed and degassed (3 × vacuum and backfill with argon while stirring vigorously) via a needle through the septum. Pyrrolidine (71.0 mg, 1.00 mmol) was then added, and the reaction mixture was stirred in an aluminum heating block at 80 °C for 14 h, after which time it was cooled and diluted with dichloromethane (5 mL) and the suspension filtered through a small plug of Celite. The crude was reduced of volatiles on the rotary evaporator (care was taken, as the products can be volatile at low pressures) and then crystallized by slow evaporation from the crude in ethyl acetate (**7a**) as a pale brown crystalline solid (61.5 mg, 0.34 mmol, 68%). Mp: 117–118 °C.

Example Procedure D: Domino Buchwald–Hartwig Amidation/Allene Amidation To Form Indoles 9a–c. 1-Bromo-2-(propa-1,2-dien-1-yl)benzene (**3a**, 74.0 mg, 0.38 mmol), benzamide (60.6 mg, 0.50 mmol), cesium carbonate (248 mg, 0.76 mmol), palladium acetate (2.2 mg, 0.010 mmol), Xantphos (13.9 mg, 0.024 mmol), and dioxane (1.00 mL) were combined together with a stirring bar in a 20 mL vial, which was then sealed and degassed (3 × vacuum and backfill with argon while stirring vigorously) via a needle through the septum. The reaction mixture was stirred in an aluminum heating block at 100 °C for 19 h, after which time it was cooled and diluted with dichloromethane (5 mL) and the suspension filtered through a small plug of Celite. The crude was reduced of volatiles on the rotary evaporator (care was taken, as the products can be volatile at low pressures) and then subjected to column chromatography [silica gel, ethyl acetate/cyclohexane (1:9)] to yield 2-methylindole (**9a**) as a brown-purple crystalline solid (42.3 mg, 0.32 mmol, 84%). Mp: 51–52 °C.

General Methods. Unless otherwise specified, chemicals were purchased from commercial suppliers and used without further purification. All reactions involving moisture-sensitive reactants were executed under an argon atmosphere using oven-dried glassware. All solvents were used as commercially available (AR grade), with the exception of tetrahydrofuran, which was refluxed with sodium/potassium alloy under argon atmosphere.

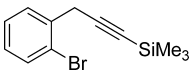
All reactions were monitored by thin layer chromatography (TLC) (silica gel 60 on aluminum plate, fluorescence indicator F_{254}, 0.25 mm

dx.doi.org/10.1021/jo201679s | J. Org. Chem. 2011, 76, 9060–9067

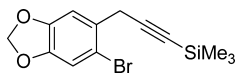
layer thickness). An ultraviolet lamp as well as the Seebach reagent (phosphomolybdic acid (12 g), cerium(IV) sulfate tetrahydrate (5 g), concentrated sulfuric acid (30 mL) and ethanol (250 mL)) and vanillin (vanillin (15 g), concentrated sulfuric acid (2.5 mL) in ethanol (250 mL)) were used for detection. The separation and the purification of products from mixtures was performed by means of column chromatography according to the Stille procedure. Silica gel 60 was used as stationary phase, and eluent system mixtures were previously distilled.

^{1}H NMR spectra were recorded on either an AC 250 MHz or AM 400 MHz spectrometer. Chemical shifts are reported in parts per million (δ (ppm)) downfield from tetramethylsilane (TMS), with $CHCl_3$ or acetone as an internal standard ($CHCl_3$: 7.26 ppm; acetone: 2.05 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets, ddd = doublet of dd, dt = doublet of triplets, ddt = doublet of dt, m_c = centered multiplet), integration, and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a 63 or 101 MHz NMR spectrometer. Chemical shifts are reported in ppm with $CHCl_3$ or acetone as an internal standard ($CHCl_3$: 77.2 ppm; acetone: 29.8 ppm). The signal structure was analyzed by DEPT and is described as follows: C = quaternary C-atom (no DEPT signal), CH = tertiary C-atom (positive DEPT signal), CH_2 = secondary C-atom (negative DEPT signal) and CH_3 = primary C-atom (positive DEPT signal). MS: The molecular fragments are quoted as the relation between mass and charge (m/z), the intensities as a percentage value relative to the intensity of the base signal (100%). The abbreviation $[M]^+$ refers to the molecular ion.

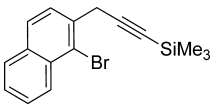
Compounds and Characterization Data. *(3-(2-Bromophenyl)-prop-1-yn-1-yl)trimethylsilane (**2a**).* After reaction of benzyl bromide **1a** (500 mg, 2.00 mmol) through example procedure A, silane **2a** was isolated as a colorless oil (353 mg, 1.32 mmol, 66% yield): ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.64 (ddd, J = 7.8, 0.07, 0.07 Hz, 1H), 7.53 (dd, J = 8.0, 1.2 Hz, 1H), 7.32 (ddd, J = 7.6, 7.6, 1.2, 1H), 7.12 (ddd, J = 8.0, 7.9, 1.7, 1H), 3.72 (s, 2H), 0.21 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 135.7 (C), 132.4 (CH), 129.5 (CH), 128.2 (CH), 127.5 (CH) 123.8 (C), 102.9 (C), 88.3 (C), 21.2 (CH_2), 0.4 (CH_3); EI-MS m/z 266.1 (50) [M^+], 251.1 (100) [$(C_{11}H_{12}SiBr)^+$]; EI-HRMS calcd for $C_{12}H_{15}SiBr$ 266.0126, found 266.0128. Data are consistent with the literature: Kuno, A.; Saino, N.; Kamachi, T.; Okamoto, S. *Tetrahedron Lett.* **2006**, *47*, 2591–2594.



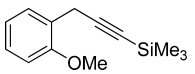
*(3-(6-Bromobenzo[d][1,3]dioxol-5-yl)prop-1-yn-1-yl)-trimethylsilane (**2b**).* After reaction of benzyl bromide **1b** (584 mg, 2.00 mmol) through example procedure A, silane **2b** was isolated as a pale orange solid (588 mg, 1.88 mmol, 94% yield): mp 37 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.14 (s, 1H), 6.99 (s, 1H), 5.97 (s, 2H), 3.62 (s, 2H), 0.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 147.4 (C), 147.1 (C), 128.8 (C), 113.8 (C), 112.4 (CH), 109.5 (CH), 103.1 (C), 101.6 (CH_2), 88.1 (C), 26.9 (CH_2), 0.00 (CH_3); EI-MS m/z 310.0 (100) [M^+], 295 (38) [$(C_{12}H_{12}BrO_2Si)^+$], 173.1 (56) [$(C_{12}H_{12}BrO_2Si)^+$]; EI-HRMS calcd for $C_{13}H_{15}BrO_2Si$ 310.0025, found 310.0027.



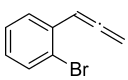
*(3-(1-Bromonaphthalen-2-yl)prop-1-yn-1-yl)trimethylsilane (**2c**).* After reaction of benzyl bromide **1c** (600 mg, 2.00 mmol) through example procedure A, silane **2c** was isolated as a colorless crystalline solid (293 mg, 0.92 mmol, 46% yield), alongside allene **3c** (264 mg, 1.07 mmol, 54% yield; see below): mp 51–53 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.30 (d, J = 8.8 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.95 (d, J = 8.1 Hz, 1H), 7.74 (d, J = 8.5 Hz, 1H), 7.69 (ddd, J = 8.5, 6.9, 1.4 Hz, 1H), 7.60 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 4.02 (s, 2H), 0.17 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 135.9 (C), 135.4 (C), 133.9 (C), 130.0 (CH), 129.7 (CH), 129.5 (CH), 128.7 (CH), 128.3 (CH), 128.2 (CH), 124.4 (C), 104.8 (C), 88.7 (C), 28.5 (CH_2), 0.8 (CH_3); EI-MS m/z 316.1 (31) [M^+], 303 (14) [$(C_{15}H_{14}BrSi)^+$], 165.1 (100) [$(C_{13}H_9)^+$]; EI-HRMS calcd for $C_{16}H_{17}BrSi$ 316.0283, found 316.0282.



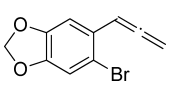
*(3-(2-Methoxyphenyl)prop-1-yn-1-yl)trimethylsilane (**2e**).* After reaction of benzyl bromide **1e** (402 mg, 2.00 mmol) through example procedure A, silane **2e** was isolated as a pale yellow oil (378 mg, 1.74 mmol, 87% yield): ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.53 (d, J = 7.4 Hz, 1H), 7.21–7.25 (m, 1H), 6.95–6.99 (m, 1H), 6.83 (d, J = 8,0 Hz, 1H), 3.83 (s, 3H), 3.62 (s, 2H), 0.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 156.5 (C), 128.6 (CH), 127.6 (CH), 124.6 (C), 120.3 (CH), 109.8 (CH), 104.3 (C), 86.8 (C), 55.2 (CH_3), 20.3 (CH_2), 0.00 ($SiCH_3$); EI-MS m/z 218.2 (89) [M^+], 203.2 (100) [$(C_{12}H_{15}OSi)$]; EI-HRMS calcd for $C_{13}H_{18}OSi$ 218.1126, found 218.1127.



*1-Bromo-2-(propa-1,2-dien-1-yl)benzene (**3a**).* After reaction of substrate **2a** (330 mg, 1.23 mmol) through example procedure B above, allene **3a** was isolated as a pale yellow oil (222 mg, 1.14 mmol, 92% yield): ^{1}H NMR ($(CD_3)_2CO$, 400 MHz) δ = 7.60 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.16 (t, J = 7.4 Hz, 1H), 6.59 (t, J = 6.9 Hz, 1H), 5.29 (d, J = 6.9 Hz, 2H); ^{13}C NMR ($(CD_3)_2CO$, 100 MHz) δ = 212.2 (C), 135.2 (C), 134.8 (CH), 130.5 (CH), 130.2 (CH), 129.7 (CH), 123.6 (C), 94.2 (CH), 80.5 (CH_2); EI-MS m/z 194.0 (23) [M^+], 115.0 (100) [$(C_9H_7)^+$]; EI-HRMS calcd for C_9H_7Br 193.97311, found 193.9729.

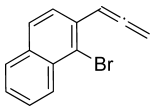


*5-Bromo-6-(propa-1,2-dien-1-yl)benzo[d][1,3]dioxole (**3b**).* After reaction of silane **2b** (1.81 g, 5.82 mmol) through example procedure B above, allene **3b** was isolated as a pale yellow solid (1.21 g, 5.04 mmol, 87% yield): mp 42 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 6.97 (s, 1H), 6.94 (s, 1H), 6.56 (t, J = 6.8 Hz, 1H), 5.98 (s, 2H), 5.17 (d, J = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 210.1 (C), 147.6 (C), 147.4 (C), 126.7 (C), 112.9 (C), 112.6 (CH), 107.4 (CH), 101.7 (CH_2), 93.2 (CH), 79.3 (CH_2); EI-MS m/z 238.0 (100) [M^+], 159.1 (40) [$(C_{10}H_7O_2)^+$]; EI-HRMS calcd for $C_{10}H_7O_2Br$ 237.9630, found 237.9628.

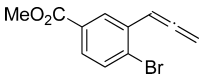


*1-Bromo-2-(propa-1,2-dien-1-yl)naphthalene (**3c**).* After reaction of silane **2c** (400 mg, 1.26 mmol) through example procedure B above, using only 1.00 equivalents of Bu_4NF, allene **3c** was isolated as a pale yellow solid (281 mg, 1.15 mmol, 91% yield). Also, after reaction of bromide **1c** (600 mg, 2.00 mmol) through standard procedure A above, allene **3c** was isolated as a yellow solid (264 mg, 1.07 mmol, 54% yield). Note: This allene isomerizes to alkyne **5c** readily and is optimally used directly after preparation: mp 41 °C; ^{1}H NMR ($(CD_3)_2CO$, 400 MHz) δ = 8.29 (d, J = 8.40 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.89 (d, J = 8.6 Hz, 1H) 7.69–7.54 (m_c, 3H), 6.95 (t, J = 6.8 Hz, 1H), 5.38 (d, J = 6.8 Hz, 2H); ^{13}C NMR ($(CD_3)_2CO$, 100 MHz) δ = 213.4 (C), 135.8 (C), 134.7 (C), 133.5 (C), 130.4 (CH), 130.1 (CH), 130.0 (CH), 129.2 (CH), 128.7 (CH), 127.2 (CH), 123.0 (C), 95.8 (CH), 81.0 (CH_2); EI-MS m/z 244.0 (7) [M^+], 234.0 (100) [$(C_{12}H_{11}Br)^+$]; EI-HRMS calcd for $C_{13}H_9Br$ 243.9888, found 243.9890.

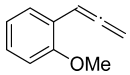
dx.doi.org/10.1021/jo201679s | *J. Org. Chem.* 2011, 76, 9060–9067



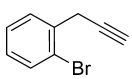
*Methyl 4-Bromo-3-(propa-1,2-dien-1-yl)benzoate (**3d**).* After reaction of silane **2d** (326 mg, 1.00 mmol) through example procedure B, allene **3d** was isolated as a pale yellow oil (227 mg, 0.90 mmol, 90% yield): ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.15 (d, J = 1.7 Hz, 1H), 7.94 (dd, J = 8.2, 1.7 Hz, 1H), 7.61 (d, J = 8.2 Hz, 1H), 6.64 (t, J = 6.8, 6.8 Hz, 1H), 5.38 (d, J = 6.8 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 213.2 (C), 166.7 (C), 140.2 (C), 135.6 (CH), 132.1 (C), 130.3 (CH), 130.1 (CH), 123.3 (C), 93.9 (CH), 81.8 (CH_2), 53.7 (CH_3); EI-MS m/z 252.0 (93) [M^+], 243.1 (100) [$(x)^+$]; EI-HRMS calcd for $C_{11}H_9O_2Br$: 251.9786, found 251.9789.



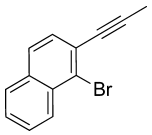
*1-Methoxy-2-(propa-1,2-dien-1-yl)benzene (**3e**).* After reaction of silane **2e** (355 mg, 1.63 mmol) through example procedure B above, allene **3e** was isolated as a yellow oil (235 mg, 1.62 mmol, 99% yield): ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.40 (dd, J = 7.6, 1.5 Hz, 1H), 7.20 (ddd, J = 8.3, 7.5, 1.5 Hz, 1H), 6.93 (ddd, J = 7.5, 7.6, 0.8 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 6.57 (t, J = 6.9 Hz, 1H), 5.11 (d, J = 6.9 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 210.4 (C), 156.0 (C), 128.2 (CH), 128.0 (CH), 122.6 (C), 121.1 (CH), 111.2 (CH), 88.1 (CH), 78.3 (CH_2), 55.9 (CH_3); EI-MS m/z 146.1 (11) [M^+], 135.1 (100) [$(x)^+$]; EI-HRMS calcd for $C_{10}H_{10}O$ 146.0732, found 146.0734. Data are consistent with the literature: Benoit, B.; Odabachian, Y.; Gagosz, F. *J. Am. Chem. Soc.* **2010**, *132*, 7294−7296.



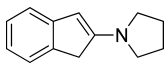
*1-Bromo-2-(prop-2-yn-1-yl)benzene (**4a**).* Following the procedure of Jung and Hagenah,[15] silane **2a** (202 mg, 0.76 mmol) was dissolved in 4 mL of ethanol, to which a solution of silver nitrate (193 mg, 1.13 mmol) dissolved in 0.3 mL of water and 0.7 mL of ethanol was added dropwise. During the addition, a gumlike oil separated from the solution. Stirring was continued at room temperature for an additional 30 min. At this time, a solution of potassium cyanide (523 mg, 7.56 mmol) in 3 mL of water was added. This mixture was stirred until the oil dissolved, then the solution was diluted with 25 mL of diethyl ether. The organic layer was washed with water (1 × 10 mL) and brine (1 × 10 mL), dried over Na_2SO_4, and concentrated in vacuo to give a crude gum (152 mg). Column chromatography followed with pentane and then dichloromethane/pentane delivered the product as a pale yellow oil (128 mg, 0.66 mmol, 87% yield): ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.61 (d, J = 7.7 Hz, 1H), 7.56 (dd, J = 7.6, 1.2 Hz, 1H), 7.35 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.18 (ddd, J = 7.7, 7.6, 1.2 Hz, 1H), 3.64 (d, J = 2.8 Hz, 2H), 2.68 (t, J = 2.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 137.9 (C), 134.6 (CH), 131.8 (CH), 130.8 (CH), 130.0 (CH), 125.4 (C), 82.4 (C), 74.2 (CH), 27.3 (CH_2); EI-MS m/z 194.0 (89) [M^+], 115.1 (100) [$(C_9H_7)^+$]. Data are consistent with the literature: Curran, D. P.; Liu, H.; Josien, H.; Ko, J.-B. *Tetrahedron* **1996**, *52*, 11385−11404.



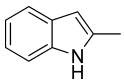
*1-Bromo-2-(prop-1-yn-1-yl)naphthalene (**5c**).* After reaction of silane **2c** (600 mg, 2.00 mmol) through example procedure B above, alkyne **5c** was isolated as a pale yellow solid (219 mg, 0.90 mmol, 45% yield): mp 37 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.05 (d, J = 8.5 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.33−7.37 (m, 2H), 7.24−7.28 (m, 1H), 1.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 133.4 (C), 132.2 (C), 129.4 (CH), 128.2 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH), 126.8 (CH), 125.9 (C), 124.2 (C), 92.0 (C), 79.9 (C), 4.9 (CH_3); EI-MS m/z 244.0 (97) [M^+], 165.1 (100) [$(C_{13}H_9)^+$]; EI-HRMS calcd for $C_{13}H_9Br$ 243.9888, found 243.9890.



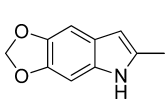
*1-(1H-Inden-2-yl)pyrrolidine (**7a**).* After reaction of allene **3a** (110 mg, 0.50 mmol) through example procedure C, enamine **7a** was isolated as a pale brown crystalline solid (61.5 mg, 0.34 mmol, 68%): mp 117−118 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.18 (d, J = 7.26 Hz, 1H), 7.09 (t, J = 7.47 Hz, 1H), 6.98 (d, J = 7.45 Hz, 1H), 6.79 (td, J = 7.36, 1.04 Hz, 1H), 5.19 (s, 1H), 3.37 (br s, 2H), 3.24 (m_c, 4H), 1.96 (m_c, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 155.5 (C), 148.6 (C), 136.9 (C), 127.0 (CH), 123.0 (CH), 119.5 (CH), 116.8 (CH), 95.3 (CH), 48.9 (CH_2), 38.3 (CH_2), 25.8 (CH_2); Data are consistent with the literature: ^{13}C NMR: Edlund, U. *Chem. Scripta* **1975**, V7, *2*, 85−89. Preparation (mp 120−121 °C): Blomqvuist, A. T.; Morricone, E. J. *J. Org. Chem.* **1961**, *26*, 3761.



*2-Methyl-1H-indole (**9a**).* After the reaction of bromide **3a** (74 mg, 0.038 mmol) with benzamide according to example procedure D, indole **9a** was isolated as a brown-purple crystalline solid (42.3 mg, 0.322 mmol, 84% yield): mp 52 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.82 (br s, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 7.07−7.15 (m, 2H), 6.23−6.24 (m, 1H), 2,45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 136.1 (C) 135.1 (C), 129.1 (C), 120.9 (CH), 119,7 (2 × CH), 110.3 (CH), 100.4 (CH), 13.7 (CH_3). Data are consistent with the literature: Kasaya, Y.; Hoshi, K.; Terada, Y.; Nishida, A.; Shuto, S.; Arisawa, M. *Eur. J. Org. Chem.*, **2009**, *27*, 4606−4613.

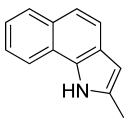


*6-Methyl-5H-[1,3]dioxolo[4,5-f]indole (**9b**).* After the reaction of bromide **3b** (91 mg, 0.038 mmol) with benzamide according to example procedure D, indole **9b** was isolated as a purple crystalline solid (32.8 mg, 0.187 mmol, 49% yield): mp 118 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.71 (brs, 1H), 6.91 (s, 1H), 6.76 (s, 1H), 6.09 (s, 1H), 5.91 (s, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 143.9 (C), 142.0 (C), 133.6 (C), 130.6 (C), 122.7 (C), 100.6 (CH), 100.4 (CH_2), 98.0 (CH), 91.0 (CH), 13.7 (CH_3); EI-MS m/z 175.1 (100) [M^+], 174.1 (47) [$(C_{10}H_8NO_2)^+$]; EI-HRMS calcd for $C_{10}H_9NO_2$ 175.0633, found 175.0632. Data are consistent with the literature: Fleming, I.; Woolias, M. *J. Chem. Soc., Perkin Trans. 1* **1979**, *3*, 829−837.

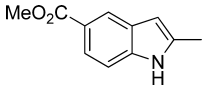


*2-Methyl-1H-benzo[g]indole (**9c**).* After the reaction of bromide **3c** (83 mg, 0.38 mmol) with benzamide according to example procedure D, indole **9c** was isolated as a purple crystalline solid (38 mg, 0.20 mmol, 54% yield): mp 131−132 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.59 (brs, 1H), 7.37−7.95 (m, 6H), 6.38 (s, 1H), 2.55 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 133.3 (C), 130.4 (C), 130.2 (C), 128.9 (CH), 125.3 (CH), 125.1 (C), 123.5 (CH), 121.6 (C), 120.7 (CH), 120.5 (CH), 119.3 (CH), 102.5 (CH), 13.8 (CH_3); EI-MS m/z 181.1 (100) [M^+], 153.1 (21) [$(C_{10}H_8NO_2)^+$]; EI-RMS

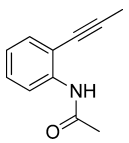
calcd for $C_{13}H_{11}N$ 181.0895, found 181.0891. Data are consistent with the literature: Gassman, P. G. *J. Org. Chem.* **1977**, *42*, 3240−3243.



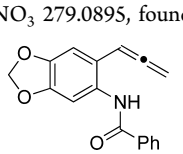
*Methyl 2-methyl-1H-indole-5-carboxylate (**9d**).* After the reaction of bromide **3d** (126 mg, 0.50 mmol) with benzamide according to example procedure D, indole **9d** was isolated as a pale beige solid (55 mg, 0.20 mmol, 58% yield): ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.38 (br s, 1H), 8.07 (s, 1H), 7.77 (dd, J = 8.3, 1.4 Hz), 7.51 (d, J = 8.3 Hz, 1H), 6.86 (br s, 1H), 3.93 (s, 3H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 168.5 (C), 138.8 (C), 136.7 (C), 135.3 (CH), 133.0 (C), 122.3 (CH), 120.8 (CH), 119.0 (CH), 112.5 (C), 100.9 (C), 51.8 (CH_3), 13.8 (CH_3); EI-MS m/z 189.1 (100) [M^+], 158.1 (98) [$(C_{10}H_8NO)^+$]; EI-RMS calcd for $C_{11}H_{11}NO_2$ 189.0790, found 189.0788. Data are consistent with the literature: Ambrogio, I.; Cacchi, S.; Fabrizi, G.; Prastaro, A. *Tetrahedron* **2009** 65, 8916−8929.



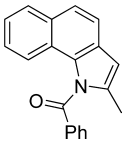
*N-(2-(Prop-1-yn-1-yl)phenyl)acetamide (**10a**).* After reaction of bromide **3a** (74 mg, 0.38 mmol scale) with acetamide through example procedure D above, amide **9e** was isolated (alongside **8a**, see above) as a pale brown crystalline solid (19.5 mg, 0.11 mmol, 29% yield): mp 75 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.37 (d, J = 8.3 Hz, 1H), 7.91 (brs, 1H), 7.35 (dd, J = 7.7, 1.1 Hz, 1H), 7.28 (m, 1H), 7.00 (dd, J = 7.5, 7.5 Hz, 1H), 2.22 (s, 3H), 2.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 168.2 (C), 138.9 (C), 131.7 (CH), 128.9 (CH), 123.2 (CH), 119.1 (CH), 112.5 (C), 93.2 (C) 75.1 (C), 25.0 (CH_3), 4.6 (CH_3); EI-MS m/z 173.1 (95) [M^+], 131.1 (100) [$(C_9H_9N)^+$], 130.0 (98)) [$(C_9H_8N)^+$]; EI-HRMS calcd for $C_{11}H_{11}NO$ 173.0841, found 173.0838. Data are consistent with the literature: Miyagi, T. *Tetrahedron Lett.* **2004**, *45*, 6303−6305.



*N-(6-(Propa-1,2-dien-1-yl)benzo[d][1,3]dioxol-5-yl)benzamide (**11b**).* After reaction of bromide **3b** (91 mg, 0.038 mmol) through example procedure D above, amide **10b** was isolated as a beige solid (11.0 mg, 0.039 mmol, 10% yield): mp 129−135 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.79 (d, J = 7.6 Hz, 2H), 7.51−7.42 (m, 3H), 6.86 (s, 1H), 6.74 (s, 1H), 6.60 (brs, 1H), 5.96 (s, 2H), 5.92 (s, 1H), 5.11 (s, 1H), 4.19 (s, 1H) ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 200.4 (C), 167.5 (C═O), 147.1 (C), 141.5 (C), 137.9 (C), 134.1 (C), 131.7 (CH), 128.6 (CH), 128.6 (C), 127.0 (CH), 104.7 (CH), 100.9 (CH), 100.8 (CH), 100.0 (CH_2), 77.2 (CH_2); EI-MS m/z 279.1 (70) [M^+], 174.1 (75) [$(C_{10}H_8NO_2)^+$], 105.0 (100) [$(C_7H_5O)^+$]; EI-HRMS calcd for $C_{17}H_{13}NO_3$ 279.0895, found 279.0893.



*(2-Methyl-1H-benzo[g]indol-1-yl)(phenyl)methanone (**12c**).* After reaction of bromide **5c** (83 mg, 0.38 mmol) through example procedure D above, amide **12c** was isolated as a pale brown gum (55 mg, 0.19 mmol, 50% yield): ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.87 (d, J = 8.3 Hz, 1H), 7.74 (J = dd, 8.3, 1.2 Hz, 2H), 7.68−7.59 (m, 3H), 7.57 (m_c, 1H), 7.39 (dd, J = 7.8, 7.8 Hz, 2H), 7.29 (ddd, J = 8.01, 8.0, 1.1 Hz, 1H), 7.21 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 6.54 (d, J = 0.9 Hz, 1H), 2.38 (d, J = 0.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 172.5 (C═O), 136.0 (C), 134.3 (C), 134.0 (CH), 131.2 (C), 131.0 (C), 130.5 (CH), 128.8 (CH), 128.8 (CH), 126.0 (C), 125.2 (CH), 123.4 (CH), 123.2 (CH), 121.8 (C), 121.5 (CH), 119.5 (CH), 105.9 (CH), 14.2 (CH_3); EI-MS m/z 285.1 (55) [M^+], 166.1 (100) [$C_{13}H_{10}^{+\bullet}$]; EI-HRMS calcd for $C_{20}H_{15}NO$ 285.1154, found 285.1152.



■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR data for compounds. This material is available free of charge via the Internet at http://pubs.acs.org/.

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■ ACKNOWLEDGMENTS

K.-S.M. acknowledges the generous funding and support provided by the Alexander von Humboldt Foundation.

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