JOC Article

Cross Coupling of Bromo Sydnones: Development of a Flexible Route toward Functionalized Pyrazoles

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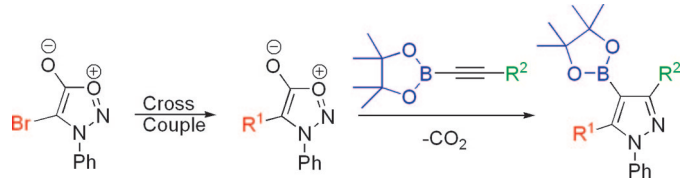


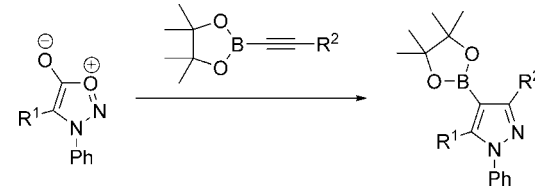
The application of a Suzuki cross coupling approach to a range of *C*-4 substituted sydnones from a 4-bromosydnone is described. Moreover, the potential of this approach to prepare a diverse range of pyrazoles is demonstrated.

Introduction

The presence of pyrazoles as key motifs in biologically active compounds has grown rapidly in the past decade. Both the pharmaceutical[1] and agrochemical[2] industries employ this diazole as a central building block for the synthesis of compound libraries. In this context, we have recently discovered that pyrazole boronic esters can be efficiently synthesized by the cycloaddition of sydnones[3] and alkynylboronates (Scheme 1).[4] While this approach allowed the ready introduction of a range of substituents at two positions of the pyrazole via the alkynylboronate, the substituent at *C*-5 ultimately originated from the sydnone substrate (R^1 in Scheme 1). Although in principle a range of suitably substituted sydnones could be prepared from the corresponding amino acids,[5] this would represent a rather linear approach and would be of limited practical use for the rapid generation of pyrazole libraries.

In an effort to address this issue, we set out to develop a Pd-catalyzed cross-coupling technique for the synthesis of an array of *C*-4 substituted sydnones derived from a late-stage intermediate, *N*-phenyl-4-bromosydnone **2**. We report herein our observations.

SCHEME 1



Results and Discussion

Despite significant interest in this mesoionic scaffold,[6] their elaboration via cross-coupling methods has received relatively little attention. Kalinin et al.[7] demonstrated that a lithiated sydnone can be transmetalated to palladium via a cuprate, resulting in a cross-coupled product. However, to the best of our knowledge this chemistry has not been revisited since the advent of modern palladium methods.[8]

Our studies commenced with the large-scale preparation of **2**. Synthesis of the sydnone precursor **1** was accomplished on a 50-g scale in two steps from *N*-phenylglycine by using a modified method of Thoman and Voaden.[9] Halogenation of **1** is well-documented,[10] particularly bromination,[11] and we were pleased to find that treatment of **1** with bromine in the presence

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(1) Singh, P.; Paul, K.; Holzer, W. *Bioorg. Med. Chem.* **2006**, *14*, 5061, and references cited therein.
(2) Lamberth, C. *Heterocycles* **2007**, *71*, 1467.
(3) For general overviews of the chemistry of sydnones see: (a) Baker, W.; Ollis, W. D. *Q. Rev. (London)* **1957**, *11*, 15. (b) Stewart, F. H. C. *Chem. Rev.* **1964**, *64*, 129.
(4) Browne, D. L.; Helm, M. D.; Plant, A.; Harrity, J. P. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8656.
(5) Applegate, J; Turnbull, K. *Synthesis* **1988**, 1011.
(6) As well as being of synthetic interest,[3] sydnones have shown biological activity with potential applications as antineoplastic, antibacterial, and antihypertensive agents: Turnbull, K.; Gross, K. C.; Hall, T. A. *Synth. Commun.* **1998**, *28*, 931, and references cited therein.
(7) (a) Kalinin, V. N.; Min, S. F. *J. Organomet. Chem.* **1988**, *352*, C34. (b) Tullis, S. A.; Turnbull, K *Synth. Commun.* **1990**, *20*, 3137.
(8) Sonogashira cross couplings have been reported recently: Turnbull, K.; Krein, D. M.; Tullis, S. A. *Synth. Commun.* **2003**, *33*, 2209.
(9) Thoman, C. J.; Voaden, D. J. *Org. Synth.* **1965**, *45*, 96.

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SCHEME 2

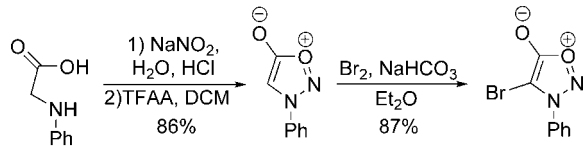
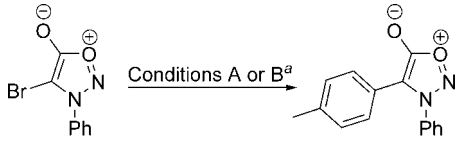


TABLE 1. Optimization of Palladium Catalyst for the Suzuki Reaction



entry	conditions[a]	catalyst	yield[b] (%)
1	A	$Pd(OAc)_2$, PPh_3	77
2	A	$Pd(OAc)_2$, $^tBu_3P.HBF_4$	55
3	A	$Pd(OAc)_2$, Dppe	70
4	A	$Pd(OAc)_2$, Dppp	62
5	A	$Pd(OAc)_2$, Dppf	67
6	A	$Pd(OAc)_2$, XanthPHOS	46 (67)[c]
7	A	$Pd(OAc)_2$, S-PHOS	75
8	B	$PdCl_2(PPh_3)_2$	81
9	B	$PdCl_2$(dppf)·DCM	80
10	B	$Pd(PPh_3)_4$	80
11	B	PEPPSI-^{i}Pr	80

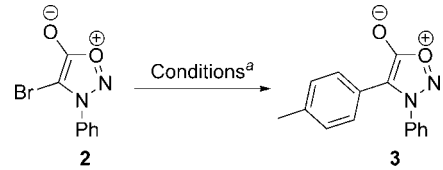
[a] Conditions A: $Pd(OAc)_2$ (5 mol %), ligand (10 mol %), K_3PO_4 (3 equiv), *p*-TolB$(OH)_2$ (1.5 equiv), DME:H_2O (1:1), 130 °C, microwave, 30 min. Conditions B: Pd complex (5 mol %), K_3PO_4 (3 equiv), *p*-TolB$(OH)_2$ (1.5 equiv), DME:H_2O (1:1), 130 °C, microwave, 30 min. [b] Isolated yield after flash chromatography. [c] Yield in parentheses based on recovered starting material. S-PHOS: 2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl. PEPPSI-^{i}Pr: [1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride.

of a mild base furnished the key intermediate in 75% yield over the three steps (Scheme 2).

Having secured a route to multigram quantities of the required intermediate, attention was turned to the investigation of the Suzuki−Miyaura coupling reaction.[12] In an effort to rapidly uncover an effective metal/ligand combination, microwave-promoted cross-coupling conditions[13] were employed with a selection of readily available ligands and palladium acetate, or preformed complexes, in the presence of K_3PO_4 in a DME/H_2O solvent mixture. *p*-Tolylboronic acid was chosen as the cross-coupling partner and our results are depicted in Table 1.

Gratifyingly, the desired cross-coupled sydnone product was obtained from the outset. Indeed, the catalyst screening study suggests that the palladium/ligand combination is not crucial for reaction success, as all combinations studied furnished the desired biaryl product. However, it is interesting that in general the commercially available palladium complexes performed better than the in situ generated species under these conditions (compare entries 1−7 and 8−11).

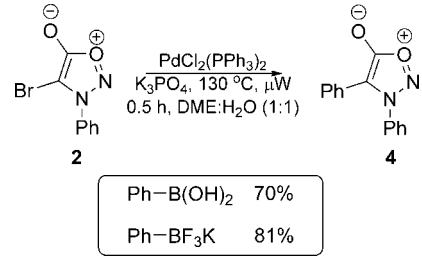
TABLE 2. Solvent/Base Optimization



entry	solvent	base	yield[b] (%)
1	DME:H_2O (1:1)	K_3PO_4	81
2	DME	K_3PO_4	72
3	H_2O	K_3PO_4	50
4	toluene	K_3PO_4	62
5	1,4-dioxane	K_3PO_4	58
6	DMF	K_3PO_4	73
7	DME:H_2O (1:1)	Cs_2CO_3	88
8	DME:H_2O (1:1)	CsF	93
9	DME:H_2O (1:1)	K_2CO_3	81
10	DME:H_2O (1:1)	LiOH	45
11	DME:H_2O (1:1)	KHF_2	91

[a] $PdCl_2(PPh_3)_2$ (5 mol %), base (3 equiv), *p*-TolB$(OH)_2$ (1.5 equiv), solvent, 130 °C, microwave, 30 min. [b] Isolated yield after flash chromatography.

SCHEME 3

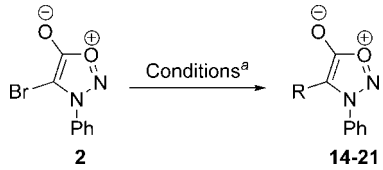


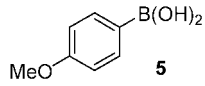
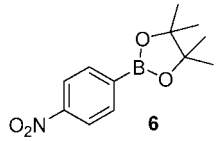
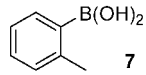
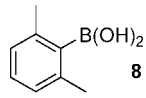
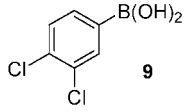
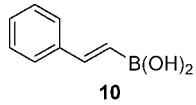
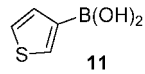
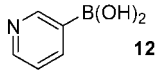
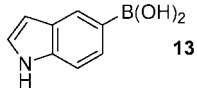
Further optimization revealed that the existing solvent system (DME:H_2O, 1:1) was optimal for K_3PO_4 base (Table 2, entries 1−6). However, and importantly, if water-sensitive functional groups are to be employed in this chemistry, the process was shown to be effective in a range of organic solvents in the absence of water. A screen of common bases (or more precisely, boron activating agents) demonstrated that cesium carbonate and cesium fluoride resulted in more efficient activation of the boronic acid than tripotassium phosphate (entries 7−10). Interestingly, we also found that potassium hydrogendifluoride promoted the cross-coupling reaction with very high efficiency. To the best of our knowledge this is the first reported example of *a Suzuki−Muyaura coupling employing KHF_2 as the activating species.*[14] This result suggested that aryltrifluoroborates would also function as competent reaction partners in this process.[15] Indeed, and as outlined in Scheme 3, phenyltrifluoroborate underwent cross coupling in excellent yield and with greater efficiency than the corresponding boronic acid under these conditions.

Next, employing the optimal conditions, a concise range of boron coupling partners were used to investigate the scope of the newly developed process, and our results are shown in Table 3. Pleasingly, both electron-rich and electron-poor boronic acid derivatives **5** and **6** were found to couple in high yield (entries 1 and 2). Coupling of the *o*-tolyl boronic acid **7** also proceeded relatively smoothly (entry 3); however, the more encumbered 2,6-dimethylphenyl boronic acid **8** failed to yield any product,

(10) Dumitraşcu, F.; Mitan, C. I.; Dumitrescu, D.; Drăghici, C.; Căproiu, M. T. *ARKIVOC* **2002**, 80.
(11) Kato, H.; Ohta, M. *Bull. Chem. Soc. Jpn.* **1957**, *30*, 210.
(12) (a) Miura, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2201. (b) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (c) Suzuki, A. *Pure Appl. Chem.* **1994**, *66*, 213.
(13) Leadbeater, N. E. *Chem. Commun.* **2005**, 2881.
(14) Aqueous solutions of KHF_2 are acidic and this reaction therefore represents an unusual acid-mediated Suzuki coupling reaction.
(15) For an overview of the cross-coupling reactions of organotrifluoroborates see: Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275.
(16) Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 2768.

TABLE 3. Scope of the Cross-Coupling Reaction



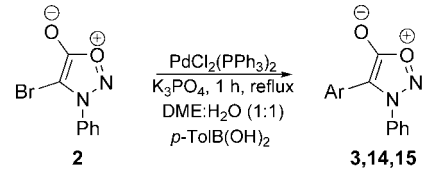
entry	organoboron	yield
1	 5	**14**; 71%
2	 6	**15**; 86%
3	 7	**16**; 56% (69%)[b]
4	 8	0% (0%)[b]
5	 9	**17**; 69%[c] (83%)[d]
6	 10	**18**; 79%
7	 11	**19**; 75%
8	 12	**20**; 78%
9	 13	**21**; 82%

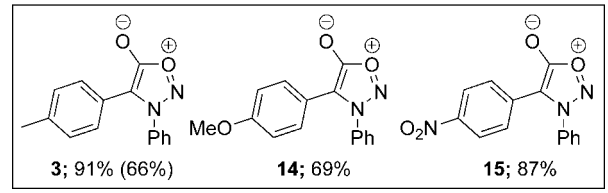
[a] $PdCl_2(PPh_3)_2$ (5 mol %), CsF (3 equiv), $RB(OR)_2$ (1.5 equiv), DME:H_2O (1:1), 130 °C, microwave, 30 min. [b] Values in parentheses represent yield when PEPPSI-^{i}Pr was employed as catalyst. [c] Boronic acid loading reduced to 1 equiv. [d] Values in parentheses represent yield when $Pd(PPh_3)_4$ was employed as catalyst and boronic acid loading was reduced to 1 equiv.

even when the highly active isopropyl-PEPPSI catalyst[16] was employed (entry 4). The employment of chloroaryl derivative **9** resulted in the isolation of a significant amount of polyaromatic material when 1.5 equiv of **9** was used; this issue was circumvented by simply reducing the boronic acid stoichiometry to 1 equiv.[17] Styrylboronic acid was coupled in excellent yield as were thiophene-, pyridine-, and indole-based boronic acids (entries 6−9), demonstrating that this process can be extended to vinyl and heteroaromatic partners.

(17) It appears that **17** undergoes further cross coupling to **9** at a slower rate than the reaction of **2** and **9**.

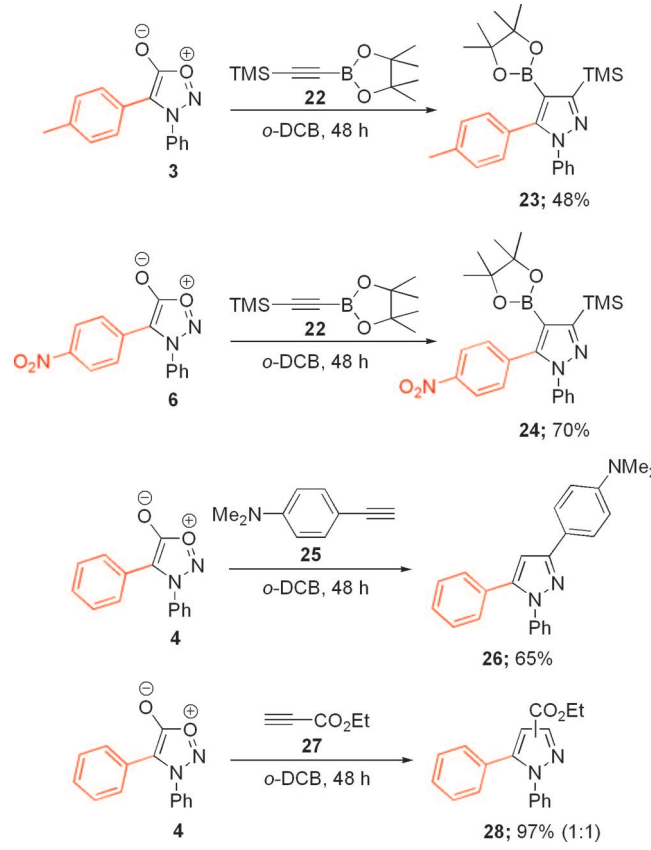
SCHEME 4[a]





[a] Yield in parentheses is for reaction conducted at rt over 24 h with 5% $Pd(OAc)_2$ and 10% S-Phos.

SCHEME 5



Finally, we wished to confirm that these cross-coupling reactions would proceed efficiently under traditional thermal conditions (i.e., in the absence of microwave irradiation) and also the potential of the product sydnones to function as substrates for pyrazole formation. Accordingly, as shown in Scheme 4, the thermally promoted cross coupling of **2** and three representative boronic acids delivered the desired products in high yield after 1 h at reflux, confirming that microwave irradiation is not essential for efficient reaction. In the context of cycloaddition chemistry, we were able to demonstrate that these more heavily substituted 1,3-dipoles could undergo cycloaddition (Scheme 5). The trimethylsilyl-substituted alkynylboronate[4] **22** gave pyrazoles **23** and **24**, respectively, as single regioisomers (scheme 5). In addition, to highlight the potential of this methodology to generate 1,3,5-trisubstituted pyrazoles

we carried out the cycloaddition of simple terminal alkynes. Specifically, 4-ethynyl-*N*,*N*-dimethylaniline **25** provided **26** in 65% yield as a single regioisomer, while ethylpropiolate **27** underwent a highly efficient cycloaddition that resulted in an inseparable mixture of ethylcarboxylate pyrazole isomers **28** with no regiocontrol.

Conclusion

In conclusion, we have demonstrated that boronic acids, esters, and trifluoroborates readily participate in Pd-catalyzed cross-coupling reactions with sydnone **2**, thus providing a convenient means for the generation of a diverse array of these compounds, and ultimately, a range of pyrazole products. Notably, these processes are extremely robust and simple to perform. Indeed, these reactions were carried out with commercial grade nondegassed solvents, using Pd-salts and ligands directly as received.

Experimental Section

General Procedure for the Microwave-Promoted Suzuki Coupling of Bromosydnone 2. To a microwave vial was added base (1.2 mmol), bromosydnone **2**[11] (0.4 mmol), and the boronic acid derivative (0.6 mmol) followed by either palladium catalyst (0.05 equiv) or palladium salt (0.05 equiv) with ligand (0.1 equiv). To this mixture was added dimethoxyethane and water (1:1, 2 mL). The vial was sealed after addition of a stirrer bar. The microwave reactor was set for high absorption, 30 min at 130 °C with 60 s prestirring and a fixed hold time. The crude reaction mixture was poured straight into a round-bottomed flask and concentrated onto silica gel, packed onto a dry loading cartridge, and purified by an ISCO automated chromatography system (gradient running from 0 to 45% ethyl acetate in hexane over 30 min). The relevant fractions were evaporated to dryness yielding the products.

Procedure for the Suzuki Coupling of Bromosydnone 2 under Thermal Conditions As Applied to the Synthesis of 3-Phenyl-4-*p*-tolyl-1,2,3-oxadiazol-3-ium-5-olate (3). To a 10 mL round-bottomed flask was added bromosydnone **2** (0.4 mmol, 100 mg), *p*-tolylboronic acid (0.6 mmol, 82 mg), CsF (1.2 mmol, 182 mg), and $PdCl_2(PPh_3)_2$ (0.02 mmol, 14 mg). The mixture was dissolved in a 1:1 DME/H_2O mixture (2 mL) and heated at reflux for 1 h. The crude reaction mixture was dry loaded onto silica gel and purified by flash chromatography (stepwise gradient; starting with petroleum ether and finishing with 20% EtOAc in petroleum ether).

3-Phenyl-4-*p*-tolyl-1,2,3-oxadiazol-3-ium-5-olate (3). 3 was isolated as an off-white solid (94 mg, 93%), mp 144−146 °C. ^{1}H (400 MHz, $CDCl_3$) δ 2.31 (s, 3 H), 7.07−7.11 (m, 2 H),7.15−7.19 (m, 2 H), 7.46−7.50 (m, 2 H), 7.55−7.60 (m, 2 H), 7.63−7.68 (m, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.1, 138.9, 134.7, 132.0, 130.1, 129.4, 127.2, 124.8, 121.4, 108.0, 21.2; FTIR (CH_2Cl_2) 1741 (s), 1533 (m), 1471 (w), 1262 (s), 1006 (s), 968 (m) cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{15}H_{13}N_2O_2$ 253.0977, found 253.0989.

3,4-Diphenyl-1,2,3-oxadiazol-3-ium-5-olate (4).[7a] **4** was isolated as a dark brown solid (79 mg, 81%), mp 189−191 °C (lit.[3] mp 189−192 °C). ^{1}H (400 MHz, $CDCl_3$) δ 7.45−7.50 (m, 4 H), 7.53−7.61 (m, 4 H), 7.67−7.72 (m, 2 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.1, 134.5, 132.1, 130.1, 128.7 (2C), 127.3, 124.7, 124.3, 107.8; FTIR (CH_2Cl_2) 1751 (s), 1735 (s), 1598 (w), 1516 (m), 1454 (w), 1265 (s), 1006 (m), 965 (m), cm^{-1}.

4-(4-Methoxyphenyl)-3-phenyl-1,2,3-oxadiazol-3-ium-5-olate (14).[7a] **14** was isolated as a brown solid (76 mg, 71%), mp 146−148 °C dec (lit.[3] mp 146−148 °C). ^{1}H (400 MHz, $CDCl_3$) δ 3.78 (s, 3 H), 6.79−6.84 (m, 2 H), 7.19−7.25 (m, 2 H), 7.46−7.51 (m, 2 H), 7.56−7.61 (m, 2 H), 7.63−7.66 (m, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.2, 159.7, 134.6, 131.9, 130.0, 128.9, 124.8, 116.5, 114.2, 108.1, 55.2. FTIR (CH_2Cl_2) 1731 (s), 1606 (m), 1528 (s), 1297 (s), 1245 (s), 1177 (s), 1000 (m), 966 (m) cm^{-1}.

4-(4-Nitrophenyl)-3-phenyl-1,2,3-oxadiazol-3-ium-5-olate (15).[7a] **15** was isolated as a yellow solid (97 mg, 86%), mp 166−168 °C (lit.[3] mp 167−170 °C). ^{1}H (400 MHz, $CDCl_3$) δ 7.47−7.54 (m, 4 H), 7.65−7.70 (m, 2 H), 7.74−7.79 (m, 1 H), 8.11−816 (m, 2 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.3, 146.7, 134.2, 132.9, 130.8, 130.7, 126.9, 124.8, 123.9, 105.7; FTIR (CH_2Cl_2) 1760 (s), 1739 (s), 1591 (m), 1512 (s), 1344 (s), 1331 (s), 1269 (s), 1004 (S), 964 (m), 852 (s) cm^{-1}.

3-Phenyl-4-*o*-tolyl-1,2,3-oxadiazol-3-ium-5-olate (16). 16 was isolated as an off-white solid (69 mg, 69%), mp 165−167 °C. ^{1}H (400 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.95−7.00 (m, 1 H), 7.07−7.12 (m, 1 H), 7.22−7.30 (m, 2 H), 7.34−7.38 (m, 2 H), 7.43−7.48 (m, 2 H), 7.54 (m, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.0, 138.7, 134.5, 131.7, 131.1, 130.8, 129.9, 129.8, 126.1, 123.9, 123.4, 107.9, 19.8. FTIR (CH_2Cl_2) 1733 (s), 1468 (m), 1275 (m), 1004 (m), 969 (m) cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{15}H_{13}N_2O_2$ 253.0977, found 253.0978.

4-(3,4-Dichlorophenyl)-3-phenyl-1,2,3-oxadiazol-3-ium-5-olate (17). 17 was isolated as an off-white solid (102 mg, 83%), mp 115−117 °C. ^{1}H (400 MHz, $CDCl_3$) δ 7.01−7.08 (m, 1 H), 7.32 (d, J = 8.5 Hz, 1 H), 7.44−7.52 (m, 3 H), 7.61−7.68 (m, 2 H), 7.72−7.77 (m, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.4, 134.1, 133.1, 132.7, 130.6, 130.4, 128.5, 128.4, 125.8, 124.7, 124.3, 105.6. FTIR (CH_2Cl_2) 1732 (s), 1509 (m), 1250 (m), 1027 (m), 1014 (s), 974 (w) cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{14}H_9{}^{35}Cl_2N_2O_2$ 307.0041, found 307.0038.

(*E*)-3-Phenyl-4-styryl-1,2,3-oxadiazol-3-ium-5-olate (18).[7a] 18 was isolated as a yellow solid (83 mg, 79%), mp 177−179 °C (lit.[3] mp 179−181 °C). ^{1}H (400 MHz, $CDCl_3$) δ 6.58 (d, J = 16.0 Hz, 1 H), 7.22−7.32 (m, 3 H), 7.34−7.37 (m, 2 H), 7.58−7.63 (m, 2 H), 7.67−7.77 (m, 4 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.0, 136.2, 133.4, 132.3, 131.2, 130.2, 128.7, 128.5, 126.6, 125.0, 109.7, 108.6; FTIR (CH_2Cl_2) 1725 (s), 1475 (m), 1245 (S), 1073 (w), 954 (m) cm^{-1}.

3-Phenyl-4-(thiophen-3-yl)-1,2,3-oxadiazol-3-ium-5-olate (19). 19 was isolated as a biege solid (73 mg, 75%), mp 134−136 °C dec. ^{1}H (400 MHz, $CDCl_3$) δ 5.94−5.98 (m, 1 H), 7.30−7.35 (m, 1 H), 7.55−7.59 (m, 2 H), 7.65−7.70 (m, 2 H), 7.73−7.78 (m, 2 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.7, 134.4, 132.4, 130.2, 126.2, 125.2, 124.5, 124.4, 123.3, 106.1; FTIR (CH_2Cl_2) 1720 (s), 1475 (m), 1388 (m), 1243 (s), 1213 (s), 1016 (m), 907 (m) cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{12}H_9N_2O_2S$ 245.0385, found 245.0381.

3-Phenyl-4-(pyridin-3-yl)-1,2,3-oxadiazol-3-ium-5-olate (20). 20 was isolated as a orange solid (75 mg, 78%), mp 128−130 °C. ^{1}H (400 MHz, $CDCl_3$) δ 7.25−7.31 (m, 1 H), 7.49−7.54 (m, 2 H), 7.60−7.64 (m, 2 H), 7.68−7.74 (m, 1 H), 7.77−7.83 (m, 1 H), 8.36−8.40 (m, 1 H), 8.47−8.51 (m, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.6, 149.1, 147.5, 134.2, 134.0, 132.5, 130.5, 124.6, 123.4, 121.2, 104.9; FTIR (CH_2Cl_2) 1734 (s), 1512 (m), 1470 (m), 1265 (m), 1119 (w), 1028 (m), 968 (m) cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{13}H_9N_3O_2$ 240.0773, found 240.0777.

4-(1*H*-Indol-5-yl)-3-phenyl-1,2,3-oxadiazol-3-ium-5-olate (21). 21 was isolated as a yellow solid (91 mg, 82%), mp 135−137 °C. ^{1}H (400 MHz, $CDCl_3$) δ 6.41−6.45 (m, 1 H), 6.92−6.96 (m, 1 H), 7.17−7.25 (m, 2 H), 7.45−7.53 (m, 4 H), 7.57−7.65 (m, 2 H), 8.66 (br s, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.8, 135.7, 134.9, 131.7, 129.9, 127.9, 125.5, 124.8, 121.7, 121.0, 115.5, 111.6, 109.7, 103.1; FTIR (CH_2Cl_2) 3356 (m) 1709 (s), 1465 (w), 1233 (m), 1012 (m), 890 (m) cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{16}H_{12}N_3O_2$ 278.0930, found 278.0926.

Synthesis of 1-Phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-*p*-tolyl-3-(trimethylsilyl)-1*H*-pyrazole (23). Sydnone **3** (126 mg, 0.5 mmol), alkynyl boronate **19** (224 mg, 1 mmol), and *o*-dichlorobenzene (0.5 mL) where heated at reflux for 48 h under nitrogen. The crude reaction mixture was purified by flash

column chromatography (eluent starting with petroleum ether and finishing with 10% ethyl acetate in petroleum ether). Compound **20** was isolated as an off-white solid (104 mg, 48%), mp 133−135 °C. ^{1}H (400 MHz, $CDCl_3$) δ 0.45 (s, 9H), 1.27 (s, 12H), 2.40 (s, 3H), 7.06−7.10 (m, 2H), 7.13−7.17 (m, 2H), 7.22−7.29 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 159.7, 149.9, 140.2, 137.7, 130.5, 128.5, 128.3, 128.2, 126.8, 125.4, 83.0, 24.9, 21.4, −0.5; FTIR (CH_2Cl_2) 2978 (m) 2598 (w), 1495 (s), 1418 (m), 1308 (m), 1244 (m), 1143 (s), 1044 (s), 844 cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{25}H_{34}BN_2O_2Si$ 433.2483, found 433.2476.

Synthesis of 5-(4-Nitrophenyl)-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(trimethylsilyl)-1*H*-pyrazole (24). Sydnone **7** (142 mg, 0.5 mmol), alkynyl boronate **19** (224 mg, 1 mmol), and *o*-dichlorobenzene (0.5 mL) were heated at reflux for 48 h under nitrogen. The crude reaction mixture was purified by flash column chromatography (eluent starting with petroleum ether and finishing with 10% ethyl acetate in petroleum ether). Compound **21** was isolated as a yellow solid (162 mg, 70%), mp 178−181 °C. ^{1}H (400 MHz, $CDCl_3$) δ 0.46 (s, 9H), 1.27 (s, 12H), 7.18−7.22 (m, 2H), 7.27−7.34 (m, 3H), 7.43−7.47 (m, 2H), 8.13−8.17 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 160.6, 147.6, 147.4, 139.5, 138.2, 131.6, 129.0, 127.6, 125.4, 122.7, 83.4, 24.9, −0.6; FTIR (CH_2Cl_2): 2978 (m) 2599 (m), 1522 (s), 1500 (m), 1409 (m), 1345 (s), 1244 (m), 1142 (s), 1043 (s), 854 cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{24}H_{31}BN_3O_4Si$ 464.2177, found 464.2196.

Synthesis of 4-(1,5-Diphenyl-1*H*-pyrazol-3-yl)-*N*,*N*-dimethylaniline (26). Sydnone **4** (119 mg, 0.5 mmol), alkyne **22** (145 mg, 1 mmol), and *o*-dichlorobenzene (0.5 mL) where heated at reflux for 48 h under nitrogen. The crude reaction mixture was purified by flash column chromatography (eluent starting with petroleum ether and finishing with 20% ethyl acetate in petroleum ether). Compound **23** was isolated as an orange solid (110 mg, 65%), mp 140−143 °C. ^{1}H (400 MHz, $CDCl_3$) δ 3.04 (s, 6H), 6.80 (s, 1H), 6.82−6.86 (m, 2H), 7.30−7.44 (m, 10H), 7.84−7.89 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.4, 150.4, 144.1, 140.4, 131.0, 128.9, 128.8, 128.5, 128.2, 127.1, 126.8, 125.3, 121.5, 112.5, 104.6, 40.6; FTIR (CH_2Cl_2) 3418 (br), 2801 (w), 2360 (m), 1615 (s), 1533 (m), 1500(s), 1434 (m), 1356 (m), 1164 (w), 764 (s) cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{23}H_{22}N_3$ 340.1814, found 340.1808.

Synthesis of Ethyl 1,5-Diphenyl-1*H*-pyrazole-4-carboxylate and Ethyl 1,5-Diphenyl-1*H*-pyrazole-3-carboxylate Mixture (28). Sydnone **4** (119 mg, 0.5 mmol), ethyl propiolate **24** (98 mg, 1 mmol), and *o*-dichlorobenzene (0.5 mL) where heated at reflux for 48 h under nitrogen. The crude reaction mixture was purified by flash column chromatography (eluent starting with petroleum ether and finishing with 30% ethyl acetate in petroleum ether). Compounds **25** were isolated as an inseparable mixture appearing as a yellow oil (142 mg, 97%). ^{1}H (400 MHz, $CDCl_3$) δ 1.23 (t, J = 7.0 Hz, 3H), 1.44 (t, J = 7.0 Hz, 3H), 4.22 (q, J = 7.0 Hz, 2H), 4.47 (q, J = 7.0 Hz, 2H), 7.07 (s, 1H), 7.20−7.37 (m, 20H), 8.21 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.0, 162.4, 145.4, 144.6, 144.4, 142.4, 139.6, 139.3, 130.5, 129.6 (2C), 129.1, 129.0, 128.8, 128.7, 128.6, 128.4, 128.0, 127.9, 125.7, 125.3, 113.9, 109.9, 61.1, 60.1, 14.4, 14.2; FTIR (CH_2Cl_2): 2981 (w), 2360 (w), 1719 (s), 1596 (m), 1501 (m), 1447 (m), 1228 (s), 1128 (m), 1023 (m), 959 (w) cm^{-1}; HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{18}H_{17}N_2O_2$ 293.1290, found 293.1284.

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

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