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Efficient Synthesis of Aryl Vinyl Ethers Exploiting 2,4,6-Trivinylcyclotriboroxane as a Vinylboronic Acid Equivalent

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The synthesis of functionalized aryl vinyl ether derivatives can be readily achieved utilizing a room-temperature copper(II) acetate mediated coupling of substituted phenols with 2,4,6-trivinylcyclotriboroxane−pyridine complex in the presence of a suitable base. The scope of the procedure was demonstrated by the generation of an array of substituted aryl vinyl ethers. The reaction was seen to be tolerant of a diverse range of functional groups yielding products in high isolated yields. We have shown that one role of an amine base in the reaction sequence is the in situ generation of an amine coordinated boroxine ring. An X-ray crystal structure and low temperature ^{11}B NMR study of 2,4,6-trivinylcyclotriboroxane−pyridine complex demonstrated the nature of the tetracoordinate boron species, which may have a key role to play within the reaction sequence.

Introduction

Recently we described the pyridine complex of 2,4,6-trivinylcyclotriboroxane **1** as a bench-stable synthetic equivalent of unstable vinylboronic acid (Figure 1). Cyclodehydration of vinyl boronic acid into its corresponding trivinyl boroxine did not impede its reactivity in palladium-catalyzed Suzuki−Miyaura cross-coupling reactions with substituted aryl halides facilitating the generation of substituted styrenes in high yields.[1]

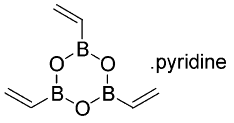

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FIGURE 1. 2,4,6-Trivinylcyclotriboroxane−pyridine complex.

We now report a further important synthetic utilization of this reagent in a carbon−oxygen bond-forming reaction for the generation of aryl vinyl ethers. Aryl vinyl ethers have wide synthetic applications and are employed as key synthetic intermediates for the generation of new polymeric materials,[2] as dienophiles for cycloaddition reactions,[3] in cyclopropanations,[4] in hydroformylations,[5] and in natural product analogue synthesis.[6] Traditional methods for their generation require an elimination under basic conditions from α-bromo ethers to generate the double bond.[7] The base-catalyzed reaction of phenols with acetylene under high temperature and pressure conditions was the first method developed which used an unsaturated carbon−carbon bond as the vinyl source.[8] As a result of these harsh conditions there has been a recent resurgence in the development of improved methods. The new methods are based upon the coupling of various vinyl sources with phenols in conjunction with a metal catalyst. The use of vinyl acetate in an iridium-catalyzed reaction with phenols in toluene at 100 °C has been shown to be a viable route to this class of compound.[9] Tetravinyltin has also been shown to effectively react with phenols in a room-temperature copper(II) acetate mediated reaction in acetonitrile under an atmosphere of oxygen.[10] But the requirement of stoichiometric amounts of the tetravinyltin reagent and the known high toxicity of the tin byproducts could be considered disadvantageous for this methodology. Our aim was to develop **1** as a viable reagent for the generation of aryl vinyl ethers exploiting mild copper-mediated coupling conditions. The reaction conditions used for this coupling are based on those developed by Evans, Chan, and Lam for the coupling of arylboronic acids with phenols or amines.[11] Recently, copper-mediated coupling of *trans*-1-hexenylboronic acid with 3,5-di-*tert*-butylphenol has been reported in a 52% yield.[12]

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(1) (a) Kerins, F.; O'Shea, D. F. *J. Org. Chem.* **2002**, *67*, 4968. (b) Matteson, D. S. *J. Org. Chem.* **1962**, *27*, 3712. (c) Coleman, C. M.; O'Shea, D. F. *J. Am. Chem. Soc.* **2003**, *125*, 4054.

(2) Kojima, K.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1989**, *22*, 1552.

(3) (a) Savinov, S. N.; Austin, D. J. *Chem. Commun.* **1999**, 1813. (b) Marko, I. E.; Evans, G. R.; Declercq, J.-P. *Tetrahedron* **1994**, *50*, 4557. (c) El-Nabi, H. A. A. *Tetrahedron* **1997**, *53*, 1813.

(4) (a) Maligres, P. E.; Waters, M. M.; Lee, J.; Reamer, R. A.; Askin, D.; Ashwood, M. S.; Cameron, M. *J. Org. Chem.* **2002**, *67*, 1093. (b) Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Sanchez, E. L. *J. Am. Chem. Soc.* **1983**, *105*, 2021.

(5) Lyle, F. R. U.S. Patent 5 973 257, 1985; *Chem. Abstr.* **1985**, *65*, 2870.

(6) Ahrendt, K. A.; Bergman, R. G.; Ellman, J. A. *Org. Lett.* **2003**, *5*, 1301.

(7) Maligres, P. E.; Waters, M. M.; Lee, J.; Reamer, R. A.; Askin, D. *J. Org. Chem.* **2002**, *67*, 1093.

(8) Reppe, W. *Ann.* **1956**, *601*, 84.

(9) Okimoto, Y.; Sakaguchi, S.; Ishii, Y. *J. Am. Chem. Soc.* **2002**, *124*, 1590.

(10) Blouin, M.; Frenette R. *J. Org. Chem.* **2001**, *66*, 9043.

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SCHEME 1. Synthesis of Aryl Vinyl Ethers

TABLE 1. Investigation of Coupling Reaction Conditions

entry	phenol	solvent	equiv of Cu	equiv of **1**	equiv of pyridine	conversion[a,b] (%)
1	4-Ph	CH_2Cl_2	1	1	10	99
2	4-Ph	CH_2Cl_2	1	0.66	10	95
3	4-Ph	CH_2Cl_2	1	0.33	10	70
4	4-Ph	CH_2Cl_2	0.75	0.66	10	95
5	4-Ph	CH_2Cl_2	0.50	0.66	10	94
6	4-Ph	CH_2Cl_2	0.25	0.66	10	44
7	4-Ph	CH_2Cl_2	0.10	0.66	10	18
8	4-Ph	CH_3CN	0.75	0.66	10	85
9	4-Ph	THF	0.75	0.66	10	27
10	4-Cl	CH_2Cl_2	1	1	10	99
11	4-Cl	CH_2Cl_2	1	0.66	10	91
12	4-Cl	CH_2Cl_2	0.75	0.66	10	68
13	4-Ph	CH_2Cl_2	0.50	0.66	10	90[c]
14	4-Ph	CH_2Cl_2	0.25	0.66	10	83[c]
15	4-Ph	CH_2Cl_2	1	0.66	10	33[d]
16	4-Ph	CH_2Cl_2	1	1	0	52
17	4-Cl	CH_2Cl_2	1	1	0	51
18	4-Ph	CH_2Cl_2	1	0.66	0	50[e]
19	4-Ph	CH_2Cl_2	1	0.66	0	86[f]
20	4-Ph	CH_2Cl_2	1	0.66	0	100[g]
21	4-Cl	CH_2Cl_2	1	0.66	0	100[g]

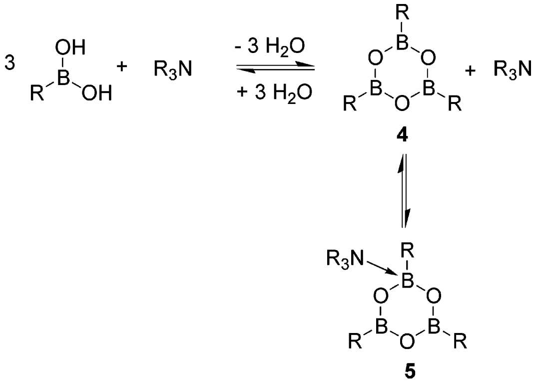
[a] Room temperature, 24 h (reaction times are not minimized). [b] Average of two runs. [c] Reaction conducted under oxygen. [d] Reaction conducted under nitrogen. [e] 1 molar equiv of Na_2CO_3 added. [f] 1 molar equiv of K_2CO_3 added. [g] 1 molar equiv of Cs_2CO_3 added.

Results and Discussion

Optimization of Coupling Conditions. For our preliminary investigation to determine the optimal reaction conditions we chose 4-phenyl- and 4-chlorophenol as our test substrates, which we anticipated would give us an indication of the phenol reactivity range for the reaction. To test the suitability of **1** for this transformation, a study of varying reaction conditions was undertaken. The first conditions attempted were an equal stoichiometric ratio of phenol, $Cu(OAc)_2$ and **1** (formally 3 molar equiv of $H_2C{=}CH{-}B{-}O$), with 10 molar equiv of pyridine in dry dichloromethane, at room temperature, for 24 h (Scheme 1).

Encouragingly, the reagent **1** effectively participated in the reaction to give complete conversion to the desired product as determined by GC, GC–MS, and ^1H NMR (Table 1, entries 1 and 10). We next examined the effect of lowering the molar equivalents of **1** to 0.66, effectively 2 molar equiv of $H_2C{=}CH{-}B{-}O$. For both phenol substrates the reaction conversion remained above 90% (entries 2 and 11). Upon lowering the molar ratio of **1** to 0.33, the reactions failed to achieve a satisfactory conversion (70%) for 4-phenylphenol (entry 3). As a result, we chose a 0.66 molar ratio of reagent **1** for our optimal reaction conditions. Examination of required levels of copper for the reaction showed that reduction of the $Cu(OAc)_2$ molar ratio to 0.75 with 0.66 molar ratio of **1** maintained high product conversion for 4-phenylphenol (95%) but not 4-chlorophenol (68%) (entries 4 and 12).

SCHEME 2. Generation of Amine-Complexed Trisubstituted Boroxine Rings



Further reduction in copper levels below the 0.75 molar ratio gave rise to inefficient coupling (entries 5 and 6), which led us to conclude that a stoichiometric quantity of copper would be required to develop a general set of reaction conditions.

A survey of other reaction solvents, acetonitrile and THF, showed that acetonitrile is an effective solvent for the reaction but THF was not (entries 8 and 9) from which we decided that dichloromethane would be our solvent of choice for the reaction. An examination of the benefit of an oxidant within the reaction sequence showed that the reaction was improved if carried out under an atmosphere of oxygen.[11a,d,12] When using 0.25 molar equiv of $Cu(OAc)_2$ the conversion was improved from 44% to 83% but the reaction did not reach completion (compare entries 6 and 14). In contrast, when the reaction was carried out under an atmosphere of nitrogen using a stoichiometric equivalent of $Cu(OAc)_2$ the reaction conversion was significantly reduced to 33% (entry 15).

It has been previously reported that the addition of molecular sieves to the reaction was beneficial in the coupling of arylboronic acids with phenols.[11a,13] Improved yields were attributed to the prevention of the copper-mediated reaction of boronic acid with water which gave rise to phenols which further reacted with remaining boronic acid to generate their subsequent coupled byproducts. One possible source of this water would be from the in situ generation of trisubstituted boroxines **4** from cyclodehydration of three molecules of boronic acid (Scheme 2).

As we start with a preformed boroxine ring already complexed with 1 mol of pyridine, we anticipated that the inclusion of molecular sieves in the reaction would be unnecessary and that it would facilitate an investigation of the role of the base in the reaction sequence. Although **1** already has one molecule of pyridine associated with it, omitting additional pyridine from the

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(11) (a) Evans, D. A.; Katz, J. L.; West, T. R.; *Tetrahedron Lett.* **1998**, *39*, 2937. (b) Chan, D. M. T.; Monaco, K. L.; Wang, R.-P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933. (c) Lam P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett.* **1998**, *39*, 2941. (d) Lam, P. Y. S.; Vincent, G.; Clark, C. G.; Deudon, S.; Jadhav, P. K. *Tetrahedron Lett.* **2001**, *42*, 3415. (e) Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 1381. (f) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400 (review).

(12) Lam, P. Y. S.; Vincent, G.; Bonne, D.; Clark, C. G. *Tetrahedron Lett.* **2003**, *44*, 4927.

(13) Sagar, A. D.; Tale, R. H.; Adude, R. N. *Tetrahedron Lett.* **2003**, *44*, 7061.

TABLE 2. Parallel Generated Array of Aryl Vinyl Ethers

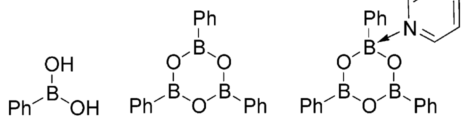
entry	phenol	R	product	conversion[a] (%)	yield[a] (%)
1	**2a**	*p*-Ph	**3a**	93	85
2	**2b**	*p*-Cl	**3b**	96	76
3	**2c**	*o*-Br	**3c**	90	83
4	**2d**	*m*-I	**3d**	91	76
5	**2e**	*p*-CO_2CH_3	**3e**	78	68
6	**2f**	*m*-CN	**3f**	90	92
7	**2g**	*p*-CHO	**3g**	86	84
8	**2h**	*p*-OCH_3	**3h**	99	90
9	**2i**	*o*-OCH_3	**3i**	99	70
10	**2j**	*p*-*t*-Bu	**3j**	99	67
11	**2k**	*m*-$N(CH_3)_2$	**3k**	98	88
12	**2l**	*o*-$NHCOCH_3$	**3l**	94	80

[a] Average of two runs.

reaction reduced by half the product conversions for both 4-phenyl and 4-chlorophenol (entries 16 and 17). A study of inorganic bases revealed a synthetic alternative to organic bases such as pyridine. The use of 1 molar equiv of sodium, potassium, or cesium carbonate gave improved conversions in comparison to the conditions that contained no additional pyridine base, but only cesium carbonate resulted in a complete reaction conversion (entries 18−21). Thus cesium carbonate could be utilized as an alternative to an amine base if the amine coordinated boroxine ring is preformed.

Synthesis of Aryl Vinyl Ethers. We have tested the scope of the reaction with a range of electronically and functionally diverse phenols **2a**−**l** in order to examine the substituent tolerance of the reaction procedure (Table 2).

The optimized set of conditions employed for the reactions were as follows: 1.0 molar equiv of phenol and $Cu(OAc)_2$, 0.66 molar equiv of **1** (2 molar equiv of $H_2C{=}CH{-}B{-}O$), and 10 molar equiv of pyridine, in dichloromethane, at room temperature, for 24 h. For ease of synthetic applicability we considered it advantageous if the reactions were not carried out under an oxygen atmosphere, though they were exposed to ambient air through a calcium chloride drying tube. The reactions were carried out in parallel using a manual parallel synthesizer. Upon reaction completion individual reactions were worked up by washing with aqueous ammonium acetate followed by analysis with GC, GC−MS, and ^1H NMR. The reaction was successful for each phenol derivative examined with nine derivatives giving product conversions higher that 90% (Table 2). We discovered that as with the coupling of arylboronic acid to phenols, this reaction was tolerant of a wide range of sensitive functional groups such as halo, formyl, nitrile, ester, amino and amide. The reaction tolerated both electron-donating and -withdrawing substituents giving good conversions, though substrates with electron-withdrawing groups were marginally lower (Table 2, entries 5 and 6). The steric hindrance of the ortho-substituted phenol derivatives **2c**, **2i**, and **2l** did not appear to significantly impede the reaction with *o*-bromo, methoxy, and amidophenol giving high conversions and yields (entries 3, 9, and 12). The reaction was also tolerant of halo-substituted phenols with neither the bromo of **2c** or the iodo of **2d** participating in a cross-coupling reaction (entries 3 and 4).



6 **7** **8**

FIGURE 2. Phenylboronic acid **6**, triphenylboroxine **7**, and triphenylboroxine pyridine complex **8**.

To demonstrate individual reactions on a larger scale we chose four phenols, 4-phenyl- **2a**, 2-bromo- **2c**, 3-iodo- **2d**, and 4-*tert*-butylphenol **2j**, from the library and remade their corresponding vinyl ethers. The reactions were carried out on a 0.5 g scale of substituted phenol under conditions identical to those used in the parallel synthesis. The isolated purified product yields from each reaction were excellent with the vinyl ethers **3a**, **3c**, and **3d** above 90% and **3j** at 80%. **3a** was also re-synthesized on the same scale using an equivalent of cesium carbonate as base, which resulted in a comparable yield (93%) as that obtained from the pyridine base reaction conditions.

Role of the Base in the Reaction Sequence. It has been shown that the coupling of arylboronic acids with phenols fails in the absence of an amine base. Two proposed roles of the base are as a ligand for coordination to organocopper intermediates and/or to function as a proton acceptor, though the exact role(s) of base within the reaction sequence remain unclear.[11a] We sought to investigate an additional possible role of the base in regard to the boronic acid species within the reaction. The synthesis of monoamine adducts of substituted boroxine rings **5** has been previously described for a wide range of amines and substituted boronic acids (Scheme 2).[14,15] Typical reaction conditions for the formation of **5** would be stirring at room temperature in an organic solvent with an equimolar quantity of amine base.[15a−d] These mild reaction conditions indicate that amine adducts of boroxine rings could be readily formed in situ from boronic acids under the typical copper mediated coupling conditions utilized for this class of reaction.[16]

To demonstrate this role of the base, we carried out a study of the reaction of phenylboronic acid **6**, triphenylboroxine **7**, and the pyridine complex of triphenylboroxine **8** with the phenol **2a** (Figure 2).

Compounds **7** and **8** were synthesized by literature methods[14a,15a] and chosen as the model reagents due to the synthetic inaccessibility of vinylboronic acid.[1a] The

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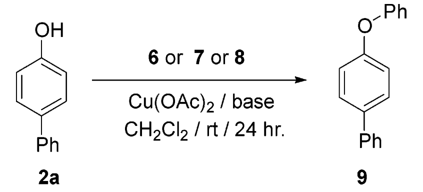
(14) (a) Burg, A. B. *J. Am. Chem. Soc.* **1940**, *62*, 2228. (b) Snyder, H. R.; Konecky, M. S.; Lennarz, W. J. *J. Am. Chem. Soc.* **1958**, *80*, 3611.

(15) (a) Beckmann, J.; Dakternieks, D.; Duthie, A.; Lim, A. E. K.; Tiekink, E. R. T. *J. Organomet. Chem.* **2001**, *633*, 149. (b) Yalpani, M.; Boese, R. *Chem. Ber.* **1983**, *116*, 3347. (c) Beckett, M. A.; Brassington, D. S.; Owen, P.; Hursthouse, M. B.; Light, M. E.; Malik, K. M. A.; Varma, K. S. *J. Organomet. Chem.* **1999**, *585*, 7. (d) Beckett, M. A.; Strickland, G. C.; Varma, K. S.; Hibbs, D. E.; Hursthouse, M. B.; Malik, K. M. A. *J. Organomet. Chem.* **1997**, *535*, 33. (e) Beckett, M. A.; Strickland, G. C.; Varma, K. S.; Hibbs, D. E.; Hursthouse, M. B.; Malik, K. M. A. *Polyhedron* **1995**, *14*, 2623. (f) Ferguson, G.; Lough, A. J.; Sheehan, J. P.; Spalding, T. R. *Acta Crystallogr. Sect. C* **1990**, *46*, 2390. (g) Yalpani, M.; Köster, R. *Chem. Ber.* **1988**, *121*, 1553. (h) Das, M. K.; Mariategui, J. F.; Niedenzu, K. *Inorg. Chem.* **1987**, *26*, 3114. (i) Wu, Q. G.; Wu, G.; Brancaleon, L.; Wang, S. *Organometallics* **1999**, *18*, 2553.

(16) The possible in situ formation of triarylboroxines **4** has been proposed; see ref 11a.

TABLE 3. Coupling of 4-Phenylphenol with 6, 7, and 8[a]



entry	reagent (equiv)	base (equiv)	conversion[b] (%)
1	**6** (2)		7
2	**6** (2)	Cs_2CO_3 (1)	35
3	**7** (0.66)		5
4	**7** (0.66)	Cs_2CO_3 (1)	60
5	**8** (0.66)		93
6	**8** (0.66)	Cs_2CO_3 (1)	99

[a] Reaction conditions of 1 molar equivalence of **2a** and copper acetate in dichloromethane at rt for 24 h. [b] Average of two runs.

reaction of **6** in the absence of base with substrate 4-phenylphenol **2a** gave a very low 7% conversion to 4-phenylbiphenyl ether **9** (Table 3, entry 1). The product conversion improved to 35% when 1 equiv of cesium carbonate was used in the reaction (entry 2). Similarly, **7** gave poor conversion to **9** (5%) in the absence of base and yielded a moderate conversion of 60% when an equivalent of cesium carbonate was employed in the reaction (entries 3 and 4). In comparison, the reaction of **8** in the absence of base gave a good product conversion (93%) and when the reaction was carried out using cesium carbonate the reaction reached completion (entries 5 and 6).

These results suggest that the amine-coordinated boroxine rings **5** have a role to play in the reaction sequence (Scheme 2).

Solution- and Solid-State Structure of 1. In solution, amine complexes of boroxines have been reported to undergo rapid ligand dissociation−recombination process at rt.[15b−e] The ^{11}B NMR (300K, CD_2Cl_2) of **1** gave a single signal with a chemical shift of 17.7 ppm implying the magnetic equivalence of the boron centers at that temperature and indicating a significant degree of amine interaction with the boroxine ring. As comparison, the chemical shifts of triphenylboroxine **7** and triphenylboroxine pyridine complex **8** have been reported to be 30.4 and 20.5 ppm, respectively, at room temperature.[15b] In an attempt to obtain limiting slow-exchange spectra of **1** we carried out low-temperature ^{11}B NMR (193 K), which resulted in significant broadening of the signal with a peak shoulder to a lower chemical shift, but we were unable to resolve the peaks into two definitive signals (Supporting Information). The ^{1}H NMR (303K) of **1** gave pyridine signals that were downfield by 0.21−0.34 ppm in comparison to pyridine (Supporting Information). These results are consistent with an amine ligand exchange process, which appears to be general for this class of compound.

X-ray diffraction study of a colorless crystal of **1** obtained by the slow evaporation of a toluene solution confirmed the trivinyl-substituted boroxine ring as a monopyridine adduct. The molecular structure revealed the six-membered boroxine ring with one boron atom coordinated to the nitrogen of pyridine with a distorted tetrahedral geometry and two boron atoms with trigional geometry (Figure 3, view A).

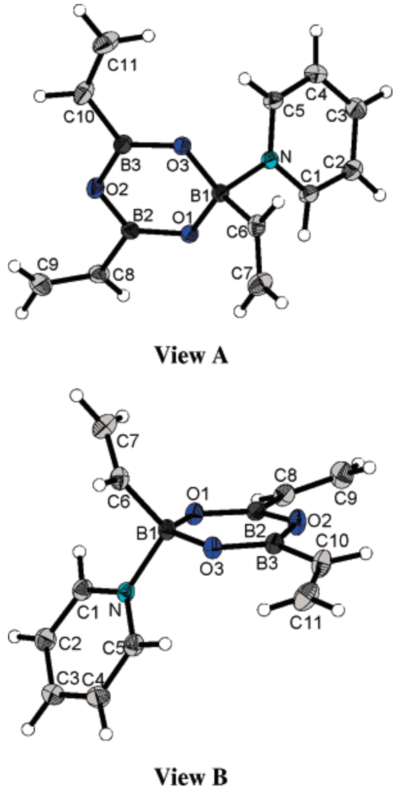


FIGURE 3. Views of 2,4,6-trivinylcyclotriboroxane−pyridine complex **1** with the atomic numbering scheme. Thermal ellipsoids drawn at 50% probability level.

TABLE 4. Selected Bond Lengths and Angles for 1

bond length	Å	bond length	Å
B(1)−N	1.643	B(3)−O(2)	1.385
B(1)−O(1)	1.463	B(3)−O(3)	1.350
B(1)−O(3)	1.458	B(1)−C(6)	1.599
B(2)−O(1)	1.348	B(2)−C(8)	1.561
B(2)−O(2)	1.390	B(3)−C-10)	1.561
bond angle	**deg**	**bond angle**	**deg**
C(6)−B(1)−O(1)	113.43	N−B(1)−C(6)	106.54
C(6)−B(1)−O(3)	112.70	N−B(1)−O(1)	104.59
O(1)−B(1)−O(3)	113.20	N−B(1)−O(3)	105.4

The sum of the internal angles of boroxine ring was 719.2° indicating planarity for the ring system (sum 720°). The pyridine nitrogen to boron bond length of 1.643 Å is comparable to other reported structurally related triaryl and trialkyl boroxine derivatives.[15] The structural consequences of the amine coordinating to a single boron atom of the boroxine are distinct. Two of the boron centers form a trigonal planar geometry with bond angles ranging from 118.4° to 121.1° whereas the other is a distorted tetrahedron with the bond angles about B(1) varying from 104.6° to 113.4° (Table 4). An estimate of percentage tetrahedral character of B(1) was calculated from its six bond angles to give a value of 75%.[17] Comparison of the average B−O bond lengths of the tetrahedral B(1) and trigonal boron atoms B(2), B(3) show that they are longer for the tetrahedral boron. Similarly the boron to carbon bond length for tetrahedral boron

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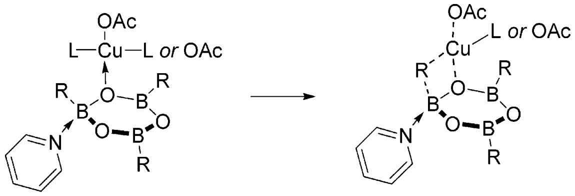
(17) Höpfl, H. *J. Organomet. Chem.* **1999**, *581*, 129.



10 **11**

FIGURE 4. Possible mode of transmetalation.

B(1)−C(6) is considerably longer at 1.599 Å compared to B(2)−C(8) and B(3)−C(10) at 1.561 Å (Table 4).

From the solid- and solution-state characteristics of **1**, which are common to all substituted boroxine amine complexes, we could speculate that the structural consequences of the amine to boron coordination could predispose such compounds to a transmetalation process. It is known that tetracoordinate boron species are key to a successful transmetalation step for a number of other boronic acid coupling reactions including the Suzuki−Miyaura[18] and the thiol ester coupling[19] reactions. As such the tetrahedral boron atom of **1** could indicate a possible reaction site with copper (Figure 3, view B). Increased B(1)−O and B(1)−C bond lengths and reduced C−B(1)−O bond angles around the tetrahedral boron could facilitate an oxygen to boron coordination generating **10** which could be envisaged to possibly give rise to an intermediate of type **11** (Figure 4).

Due to the complicated dimeric or oligmeric nature of many copper complexes and the fact that it is as yet unclear if a copper(I) or copper(II) species is the one which initially reacts, this may be an oversimplified view of the pathway. As alternative reaction pathways could also be proposed, further speculation at this time is not justified but investigations are ongoing to attempt to further resolve the mechanistic issues of this reaction class.

Conclusions

In summary, we have described a diversity tolerant synthetic methodology for the generation of synthetically important aryl vinyl ethers exploiting a bench stable vinylboronic acid equivalent as the key reagent. The role of the organic base has been investigated and we have shown that one equivalent of an organic amine base is required to generate the boroxine ring, but the additional base required can be provided by either organic amine base or an inorganic base such as cesium carbonate. Solid-state and solution evidence of a tetravalent boron species is provided which could play a role in facilitating the key steps of this reaction.

Experimental Section

Materials. All commercially available solvents and reagents were used as supplied unless otherwise stated. Copper(II) acetate was used without any modification. Pyridine was supplied as anhydrous and used without any modification. Dichloromethane was dried over calcium chloride and distilled from calcium hydride.

Analysis. ^{1}H and ^{13}C NMR were recorded on a 300 MHz instrument and were referenced to tetramethylsilane (TMS). Melting points are uncorrected.

Parallel Library Procedure. Compound **1** (0.51 mmol), phenol (0.77 mmol), pyridine (7.7 mmol), and copper(II) acetate (0.77 mmol) were added to individual reaction vessels in the parallel synthesizer and stirred at room temperature in anhydrous dichloromethane (8 mL) for 24 h, under a calcium chloride drying tube. Each reaction mixture was treated with 3 M aqueous ammonium acetate (2 × 10 mL) and stirring continued for a further 30 min. Organic layers were separated and dried over sodium sulfate, solvent was evaporated, and the product was analyzed by GC, GC−MS, and ^{1}H and ^{13}C NMR. If required, further purification by column chromatography on alumina, eluting with CH_2Cl_2 was performed.

Individual Procedures. 4-Vinyloxybiphenyl (3a). $Cu(OAc)_2$ (0.54 g 2.94 mmol) was stirred at room temperature in dry CH_2Cl_2 (20 mL) for 10 min. Compound **1** (0.47 g, 1.96 mmol), 4-phenylphenol (0.50 g 2.94 mmol), and pyridine (2.4 mL, 29.4 mmol) were added, and the reaction was stirred at room temperature for 24 h. The reaction solution was passed through an alumina column eluting with CH_2Cl_2 yielding the product as a white solid (0.57 g, 98%). Mp: 52−53 °C. ^{1}H NMR ($CDCl_3$) δ: 4.45 (dd, J = 1.8, 6.2 Hz, 1H), 4.78 (dd, J = 1.8, 13.8 Hz, 1H), 6.65 (dd, J = 6.2, 13.8 Hz, 1H), 7.05−7.10 (m, 2H), 7.29−7.57 (m, 7H). ^{13}C NMR ($CDCl_3$) δ: 95.4, 117.4, 126.9, 127.1, 128.4, 128.8, 136.2, 140.5, 148.1, 156.2. IR (KBr disk) cm^{-1}: 1643, 1602. EI-MS: m/z 196.3.

4-Vinyloxybiphenyl (3a). $Cu(OAc)_2$ (0.54 g 2.94 mmol) was stirred at room temperature in dry CH_2Cl_2 (20 mL) for 10 min. Compound **1** (0.47 g, 1.96 mmol), 4-phenylphenol (0.50 g 2.94 mmol), and Cs_2CO_3 (0.96 g, 29.4 mmol) were added and the reaction stirred at room temperature for 24 h. The reaction solution was passed through an alumina column eluting with CH_2Cl_2 yielding the product as a white solid 0.54 g, 93%.

1-Bromo-2-vinyloxybenzene (3c). $Cu(OAc)_2$ (0.53 g, 2.93 mmol) was stirred at room temperature in dry CH_2Cl_2 (20 mL) for 10 min. Compound **1** (0.47 g, 1.92 mmol), 2-bromophenol (0.50 g, 2.93 mmol), and pyridine (2.4 mL, 29.3 mmol) were added, and the reaction was stirred at room temperature for 24 h. The reaction mixture was washed with 3 M aqueous ammonium acetate (2 × 40 mL), and the aqueous layers were extracted with ethyl acetate (3 × 40 mL). The organic layers were combined, washed with brine (2 × 40 mL), dried over sodium sulfate, and concentrated to 20 mL. (Note: evaporation to dryness can lead to lower yields.) The solution was diluted with CH_2Cl_2 (20 mL) and passed through an alumina column eluting with CH_2Cl_2 yielding the product as an oil (0.55 g, 95%). ^{1}H NMR (DMSO-d_6) δ: 4.55 (dd, J = 1.9, 6.2 Hz, 1H), 4.69 (dd, J = 1.9, 13.6 Hz, 1H), 6.81 (dd, J = 6.2, 13.6 Hz, 1H), 7.05−7.11 (m, 1H), 7.18−7.21 (m, 1H), 7.37−7.43 (m, 1H), 7.65−7.68 (m, 1H). ^{13}C NMR (DMSO-d_6) δ: 96.4, 113.7, 118.7, 125.5, 129.8, 133.9, 148.8, 153.6. IR (neat) cm^{-1}: 1644, 1584. EI-MS: m/z 198.0. Anal. Calcd for C_8H_8BrO: C, 48.28; H, 3.54. Found: C, 48.58; H, 3.68.

1-Iodo-3-vinyloxybenzene (3d). $Cu(OAc)_2$ (0.41 g, 2.27 mmol) was stirred at room temperature in dry CH_2Cl_2 for 10 min. Compound **1** (0.55 g, 2.27 mmol), 3-iodophenol (0.50 g, 2.27 mmol), and pyridine (1.8 mL, 22.7 mmol) were added, and the reaction was stirred at room temperature for 24 h. The reaction mixture was washed with 3 M aqueous ammonium acetate (2 × 40 mL), and the aqueous layers were extracted with ethyl acetate (2 × 40 mL). The organic layers were combined, washed with brine (2 × 40 mL), dried over sodium sulfate, and reduced to dryness. The residue was diluted with CH_2Cl_2 (30 mL) and passed through an alumina column eluting with CH_2Cl_2 yielding the product as an oil (0.53 g, 95%). ^{1}H NMR ($CDCl_3$) δ: 4.47 (dd, J = 1.8, 6.2 Hz, 1H), 4.78

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(18) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972. (c) Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095. (d) Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461.

(19) (a) Liebeskind, L. S.; Srogl, J. *Org. Lett.* **2002**, *4*, 979. (b) Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, *122*, 11260.

(dd, $J = 1.8$, 13.8 Hz, 1H), 6.55 (dd, $J = 6.2$, 13.8 Hz, 1H), 6.95−7.06 (m, 2H), 7.35−7.43 (m, 2H). ^{13}C NMR (CDCl$_3$) δ: 96.3, 116.6, 126.2, 127.4, 131.0, 132.2, 147.5, 158.1. IR (KBr disk) cm^{-1}: 1643, 1580. EI-MS: m/z 246.2. Anal. Calcd for C_8H_7IO: C, 39.05; H, 2.87. Found: C, 38.98; H, 2.88.

1-*tert*-Butyl-4-vinyloxy-benzene (3j). Cu(OAc)$_2$ (0.60 g, 3.33 mmol) was stirred at room temperature in dry CH_2Cl_2 for 10 min. Compound **1** (0.53 g, 2.21 mmol), 4-*tert*-butylphenol (0.50 g, 3.33 mmol), and pyridine (2.7 mL, 33.3 mmol) were added, and the reaction was stirred at room temperature for 24 h. The reaction mixture was washed with 3 M aqueous ammonium acetate (2 × 40 mL), and the aqueous layers were extracted with ethyl acetate (2 × 40 mL). The organic layers were combined, washed with 1 M HCl (2 × 25 mL) and brine (2 × 25 mL), dried over sodium sulfate, and reduced to dryness yielding the product as an oil 0.47 g, 80%. ^{1}H NMR (CDCl$_3$) δ: 1.30 (s, 9H), 4.37 (dd, $J = 1.5$, 6.0 Hz, 1H), 4.70 (dd, $J = 1.5$, 13.6 Hz, 1H), 6.60 (dd, $J = 6.0$, 13.6 Hz, 1H), 6.91−6.96 (m, 2H), 7.31−7.36 (m, 2H). ^{13}C NMR (CDCl$_3$) δ: 31.5, 34.2, 94.1, 116.7, 126.5, 127.4, 148.3, 154.4. IR (neat) cm^{-1}: 1643, 1503. EI-MS: m/z 176.3.

Analytical data for the new compounds in Table 2.

4-Vinyloxybenzaldehyde (3g). ^{1}H NMR (CDCl$_3$) δ: 4.62 (dd, $J = 1.8$, 6.0 Hz, 1H), 4.92 (dd, $J = 1.8$, 13.6 Hz, 1H), 6.67 (dd, $J = 6.0$, 13.6, 1H), 7.09−7.14 (m, 2H), 7.85−7.90 (m, 2H), 9.93 (s, 1H). ^{13}C NMR (CDCl$_3$) δ: 98.4, 116.9, 131.8, 132.2, 146.5, 161.8, 190.9. IR (KBr disk) cm^{-1}: 1705, 1644. EI-MS: m/z 148.1. Anal. Calcd for $C_9H_8O_2$: C, 72.96; H, 5.44. Found: C, 72.63; H, 5.46.

1-Methoxy-2-vinyloxybenzene (3i). ^{1}H NMR (CDCl$_3$) δ: 3.80 (s, 3H), 4.30 (dd, $J = 1.7$, 6.0 Hz, 1H), 4.60 (dd, $J = 1.7$, 13.8 Hz, 1H), 6.50 (dd, $J = 6.0$, 13.8 Hz, 1H), 6.85−7.19 (m, 4H). ^{13}C NMR (CDCl$_3$) δ: 56.2, 94.2, 112.8, 118.9, 121.2, 124.5, 145.8, 149.5, 150.5. IR (KBr disk) cm^{-1}: 1639. EI-MS: m/z 150.3. Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.64; H, 6.70.

Dimethyl(3-vinyloxyphenyl)amine (3k). ^{1}H NMR (CDCl$_3$) δ: 2.94 (s, 6H), 4.37 (dd, $J = 0.7$, 6.0 Hz, 1H), 4.72 (dd, $J = 0.7$, 13.3, 1H), 6.35−6.46 (m, 3H), 6.63 (dd, $J = 6.0$, 13.3 Hz, 1H), 7.13−7.19 (m, 1H). ^{13}C NMR (CDCl$_3$) δ: 40.7, 94.7, 101.8, 104.9, 107.9, 130.1, 148.7, 152.2, 158.3. IR (KBr disk) cm^{-1}: 1607. EI-MS: m/z 163.3. Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.28; H, 7.96; N, 8.61.

4-Phenylbiphenyl Ether (9). Cu(OAc)$_2$ (0.14 g, 0.77 mmol) was stirred at room temperature in dry CH_2Cl_2 for 10 min. Triphenylboroxine−pyridine complex **8** (0.20 g, 0.51 mmol), 4-phenylphenol (0.13 g, 0.77 mmol), and pyridine (0.60 mL, 7.70 mmol) were added, and the reaction was stirred at room temperature for 24 h. The reaction mixture was washed with 3 M aqueous ammonium acetate (2 × 40 mL), and the aqueous layers were extracted with ethyl acetate (2 × 40 mL). The organic layers were combined, washed with brine (2 × 25 mL), dried over sodium sulfate, and reduced to dryness yielding a brown solid. The solid was washed through a short plug of alumina with dichloromethane and the filtrate reduced to yield the product as white solid (0.17 g, 91%). Mp: 67−68 °C. ^{1}H NMR (CDCl$_3$) δ: 6.99−7.15 (m, 5H), 7.31−7.46 (m, 5H), 7.53−7.58 (m, 4H). ^{13}C NMR (CDCl$_3$) δ: 118.0, 122.4, 125.9, 126.0, 127.4, 127.8, 128.8, 135.3, 139.5, 155.8, 156.1. EI-MS: m/z 246.30.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for new compounds **3d**,**g**,**i**,**k**. Literature references for known compounds. Variable-temperature ^{11}B NMR spectra of **1** and room-temperature comparison with pyridine. X-ray crystallographic data of **1** as a CIF file with a view of the crystal packing. This material is available free of charge via the Internet at http://pubs.acs.org.

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