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Copper-Promoted *N*-Arylations of Cyclic Imides within Six-Membered Rings: A Facile Route to Arylene-Based Organic Materials

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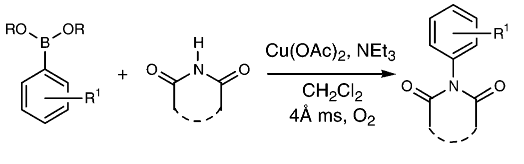

Cyclic imides within six-membered rings are shown to undergo efficient *N*-arylation using various arylboronic esters mediated by copper(II) acetate in the presence of an amine base and oxygen atmosphere with gentle heating. Until now, the synthesis of *N*-arylated cyclic imides having six-membered rings was restricted largely to strongly heating anilines in the presence of anhydrides. This reaction is applicable to the synthesis of new organic materials based on arylene imide and bis(imide) dyes, such as perylene-3,4:9,10-bis(dicarboximide)s.

Molecules that contain multiple imide linkages have a variety of scientific and industrial applications, including polymers, organic semiconductors, photovoltaics, OLEDS, fluorescent tags, dyes, etc.[1−5] Current interest includes developing molecules that mimic light harvesting and photoinduced charge separation within photosynthetic proteins. Quite often, these molecules contain redox active chromophores that utilize $\pi-\pi$ interactions to self-assemble into supramolecular arrays.[6−12] Many of these macromolecules are constructed with imide linkages, which have a large influence on the photophysical and conformational properties of the molecules.[13,14] However, an important synthetic challenge is the efficient formation of imide bonds that connect the various components of these target molecules under conditions sufficiently mild to prevent the alteration of other functional groups within the molecules. *N*-Aryl imide bond formation frequently requires the low-yielding condensation of an arylamine with a free anhydride at high temperatures for extended periods of time. Additional complications can include the air sensitivity of many amines as well as the insolubility and hydrolytic susceptibility of the anhydrides. Herein, we report that cyclic imides and arylboronic esters undergo efficient *N*-arylation reactions in the presence of copper(II) acetate.

Transition metal-catalyzed cross-coupling reactions have revolutionized organic synthesis over the last several decades. There have been a number of recent advances in the field of transition metal-promoted C−N cross-coupling reactions, most notably by Buchwald and Hartwig.[15−22] We desired a mild and efficient method to *N*-arylate cyclic imides within six-membered rings from the corresponding free imide and aryl boronic ester. Although copper-promoted heteroatom coupling reactions between various amines, amides, thiols, and boronic acids have been reported,[23−37] the use of imides as coupling

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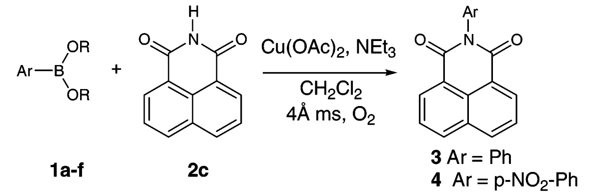
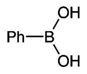
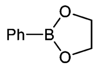
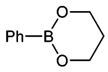
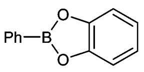
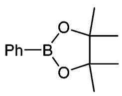
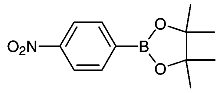
TABLE 1. Variation of Aryl Coupling Partner



entry	ester/acid	product	imide/ester/Cu/base[b]	temp (°C)	yield (%)[b]
1	 **1a**	**3**	1:3:2:3	r.t.	78[c]
2	 **1b**	**3**	1:3:3:3	55	71
3	 **1c**	**3**	1:3:2:3	55	94
4	 **1d**	**3**	1:2:2:3	47	32
5	 **1e**	**3**			no reaction
6	 **1f**	**4**	1:2:2:3	r.t.	43[c]

[a] All reactions were carried out for approximately 20 h with the exception of entry 1, which was reacted for 44 h. [b] Yields are obtained via HPLC using **3** as an external standard. [c] Isolated yield via column chromatography.

partners in these processes is rare and has been restricted to cyclic imides within five-membered rings.[26,29,37,38]

The general reaction conditions were optimized utilizing naphthalimide (**2c**) as the imide and varying the aryl boron species (Table 1). Gratifyingly, moderate to excellent yields are obtained when 1 equiv of imide, 2−3 equiv of boronic ester, 2−3 equiv of copper(II) acetate, and 3 equiv of triethylamine are employed in methylene chloride with moderate heating. Various copper sources in addition to copper(II) acetate were explored in this reaction including copper(II) fluoride, copper(II) chloride, and copper(II) triflate (not shown). Both the chloride and fluoride salts were ineffective, yielding little to no product. Copper(II) triflate promoted the desired reaction (43% yield of imide **3**), but the need to use stoichiometric quantities of Cu(II) in this reaction focused our attention on optimizing the results for the most economical reagent, copper(II) acetate. All reactions were performed under an oxygen atmosphere (*caution!*) utilizing an oxygen balloon and stirred with 4 Å molecular sieves to prevent the boronic esters from hydrolyzing. Interestingly, reactions employing pyridine instead of triethylamine as the base in this reaction afforded poor yields of the desired compounds. In addition, reactions in ambient air also resulted in lower yields overall.

Although phenylboronic acids have recently been demonstrated to be active coupling partners with select five-membered ring cyclic imides, such as succinimide and phthalimide,[26,29,37,38] we desired a general method applicable to naphthalimides because they are an important structural analogue to the aromatic dyes we employ in efforts to prepare photofunctional organic materials. We thought that the use of arylboronic esters would be especially appealing since these compounds are generally stable, easy to handle and purify, and simple to synthesize.[39−44] Additionally, previous reports have suggested that it is not the boronic acid, but the cyclic boroxine, which is the reactive coupling species.[45] Accordingly, various arylboron species were assessed for their coupling propensity (Table 1). Reaction conditions were optimized utilizing HPLC and an external standard to calculate yields for this survey; however, isolated yields were not obtained until favorable conditions were applied to a variety of imide substrates and extended aromatic systems discussed later in this paper. The coupling of the arylboronic ester derived from 1,3-propanediol (**1c**) generated the desired imide **3** in 94% yield (entry 3), while the ethylene glycolate afforded a satisfactory 71% yield of **3**. However, the phenyl boron catecholate (**1d**) gave a disappointing 32% yield of **3**, possibly due to decomposition of the boronic ester upon addition of the copper(II) acetate.[45] Surprisingly, the phenyl boron pinacolate (**1e**) does not react with naphthalimide, even upon heating (entry 5). This is consistent with previous reports of low yields when the boronic ester is coupled with a phenol, amine, and cyclic amide,[45] presumably due to steric hindrance around the boron. However, we do obtain a 43% yield of imide **4** when the electron-deficient boronic ester **1f** is reacted with naphthalimide (**2c**), suggesting that electronic factors as well as steric interactions are important (entry 6).

With an efficient *N*-arylation system for cyclic imide **3** in hand, we decided to expand the scope of this reaction by exploring a variety of imide substrates (Table 2). Since the 1,3-propanediol-derived phenylboronic ester (**1c**) provided optimal yields in Table 1, we decided to utilize this boronic ester under standard conditions in these experiments. The reaction proceeds with both maleimide

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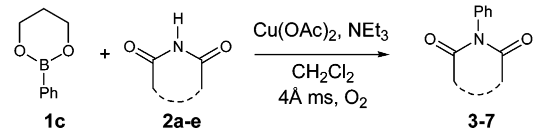
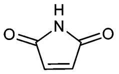
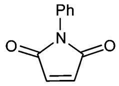
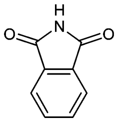
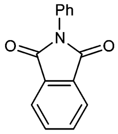
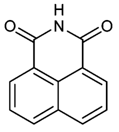
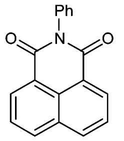
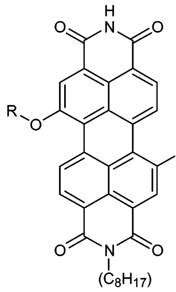
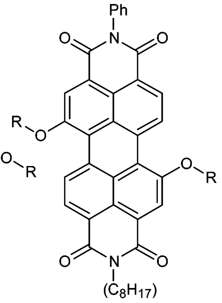
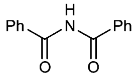
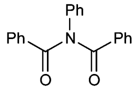
TABLE 2. Survey of Imide Substrates

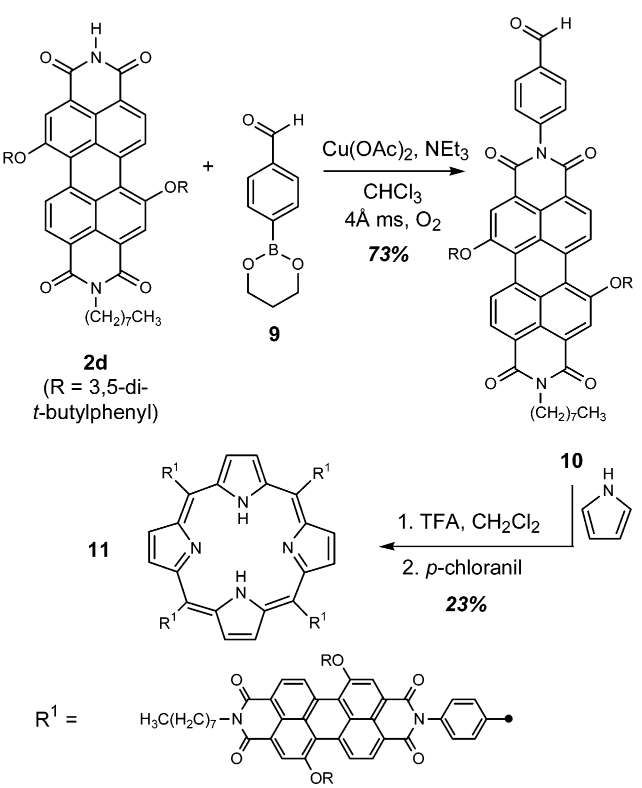


entry	imide	product	yield (%)[a]
1	 **2a**	 **5**	43
2	 **2b**	 **6**	97
3	 **2c**	 **3**	70[b]
4	 **2d**	 **7**	74[c, d]
5	 **2e**	 **8**	no reaction

[a] Standard reaction conditions involve a 1:3:3:3 ratio of imide/ester/Cu/base stirred in CH$_2$Cl$_2$ for 19−20 h at 45 °C. Yields are obtained via column chromatography. [b] 1:3:2:3 ratio of imide/ester/Cu/base stirred at 55 °C. [c] R = 3,5-di-*tert*-butylphenyl. [d] Reaction stirred for 48 h at 40 °C in CHCl$_3$.

(entry 1, 43% yield) and phthalimide (entry 2, 97% yield), with the lower yield of **2a** accompanied by significant amounts of side products. Six-membered cyclic imides afford good yields of the desired *N*-arylated products (entries 3 and 4), even when accompanied with extended π-systems. Interestingly, the cyclic imides are necessary for this reaction to proceed. For example, no reaction is observed when dibenzamide (**2e**) is employed (entry 5). It is possible that under the reaction conditions, imide **2e** chelates the copper(II) metal center, since its carbonyl groups can adopt a parallel, coplanar conformation similar to an acetylacetonate ligand. Chelation of the copper may prevent the active copper species from participating in the reaction and/or may attenuate the reactivity of the imide. Since this conformation is unavailable to the *cyclic* imide coupling partners in this study that successfully undergo *N*-arylation, we conclude that the scope of this reaction may be limited to cyclic imides.

SCHEME 1. Construction of a Stacking Porphyrin Precursor



Last, we have employed this chemistry to prepare a precursor useful for the synthesis of photofunctional chromophoric arrays.[6] This is accomplished by coupling perylenebis(imide) **2d** with 4-formylphenylboronic ester **9** shown in Scheme 1. Synthesis of this precursor via the traditional route of coupling an anhydride with arylamine would require protection of the aldehyde to avoid imine formation by self-condensation or the condensation of *p*-aminobenzyl alcohol with the anhydride, followed by oxidization of the alcohol to the aldehyde. Another drawback includes the difficult recovery of the perylene monoimide−monoanhydride due to hydrolysis. By utilizing the copper(II)-mediated coupling reaction, aldehyde **10** is obtained in good yield (73%). An added benefit of the gentle copper-promoted conditions is any unreacted bis(imide) **2d** that does not undergo coupling can be completely recovered and reused in subsequent reactions. Employing Lindsey's conditions for porphyrin synthesis,[46] the treatment of aldehyde **10** with pyrrole and trifluoroacetic acid, followed by oxidation with *p*-chloranil yields porphyrin **11** in a respectable 23% yield. Conditions previously used in our laboratory to synthesize porphyrins analogous to **11** are harsh, requiring several days of reflux in pyridine to promote imide condensation of 5,10,15,20-tetrakis(*p*-aminophenyl)porphyrin with an excess of perylene monoimide-monoanhydride (PIA).[47]

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In conclusion, we have developed a mild and efficient method to couple cyclic imides with arylboronic esters using copper(II) acetate, which is cost-effective and easy to handle without the need for an inert atmosphere. The overall process avoids thermal condensation of anhydrides and arylamines at high temperatures, thereby accessing the desired functionalized imides in much higher yields with much less degradation of the starting materials. Further applications of this *N*-arylation methodology toward the construction of large chromophoric arrays as well as studies to render the reaction catalytic in copper(II) are ongoing and will be reported in due course.

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Supporting Information Available: Compounds **1b**−**f**, **2e**, **3**−**6**, and **9** have previously been reported.[6,47−54] Compounds **1a** and **2a**−**c** are commercially available. General experimental details and spectroscopic data for compounds **2d**, **7**, **10**, and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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