Regioisomeric and substituent effects upon the outcome of the reaction of 1-borodienes with nitrosoarene compounds.

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Abstract

A study of the reactivity of 1-borodienes with nitrosoarene compounds has been carried out showing an outcome that differs according to the hybridization state of the boron moiety. Using an \( sp^2 \) boron substituent, a one-pot hetero-Diels-Alder/ring contraction cascade occurred to afford \( N \)-arylpyrroles with low to good yield depending on the electronic properties of the substituents on the borodiene. Whereas, an \( sp^3 \) boron substituent led to the formation of stable boro-oxazines.
with high regioselectivity in most of cases, in moderate to good yield. $^1$H and $^{11}$B NMR studies on two boro-oxazine regioisomers showed that selective deprotection can be performed. Formation of either the pyrrole or furan derivative is pH and regioisomer-structure dependent. The results obtained, together with previous B3LYP calculations, support mechanistic proposals which suggest that pyrrole, or furan formation, proceeds \textit{via} oxazine formation, followed by a boryl rearrangement and an intramolecular addition-elimination sequence.

\textbf{Introduction}

The hetero Diels-Alder reaction between a nitroso hetero dienophile and a diene is a useful tool in organic chemistry. Since 1947 and the pioneering work of Wichterle,$^1$ this reaction has been widely studied and numerous nitroso and diene partners have been used to enlarge its scope and efficiency. A large range of nitroso reagents, including acylnitroso, nitrosoarene and chloronitroso etc., have been used, as well as substituted acyclic, cyclic and heterocyclic dienes to provide 3,6-dihydro-1,2-oxazine scaffolds.$^2$ The resulting oxazine skeleton is a key intermediate in the synthesis of natural products, such as alkaloids derivatives,$^3$ heterocycles$^4$ and saccharide mimetics.$^5$ However, the modest regioselectivity encountered with some types of unsymmetric dienes can constitute an important limitation for applications in organic synthesis. The nitroso [4+2]-cycloaddition can provide two regioisomers; the distal isomer (major substituent close to the nitrogen of the oxazine cycloadduct) and the proximal isomer (major substituent close to the oxygen of the oxazine cycloadduct) (Scheme 1). Several studies on the regiocontrol of this reaction have shown that it results from a combination of both steric and electronic effects on both the nitroso and diene partners. For example, Houk \textit{et al.} examined monosubstituted dienes and their addition to numerous nitroso derivatives$^6$ and established a
correlation between regioselectivity and: 1) the properties and position of substituents on the diene; 2) the nature of the nitroso compound. More recently, Kouklovsky et al. examined 1,2-disubstituted dienes and their reaction with Boc-nitroso compounds to derive nitroso Diels-Alder cycloadducts with high regioselectivity. To predominantly obtain the distal isomer, it is necessary for the diene to bear a bulky substituent at C$_1$ and an electron donating group at the C$_2$ position. For the proximal isomer, a non-bulky substituent at C$_1$ and an electron-withdrawing group at C$_2$ are required. Nevertheless, regioselectivity is also dependent upon the nature of the nitroso compound.

Scheme 1. Regioselectivity of nitroso Diels-Alder reaction with mono- and di-substituted dienes.

Despite the synthetic utility of borodienes, especially in multicomponent and cascade processes, no investigation of the reaction of borodienes has been carried out with nitroso compounds until our recent preliminary communication which focused on the reaction of 1,3-dienylboronic esters 1 (Scheme 1, R$^1$ = Bpin) with aryl nitroso derivatives 2. In addition to the possible post-functionalisation of the resulting cycloadducts, we expected that tuning of the electronic properties of the boronated group through the introduction of various substituents on boron would provide an insight into the control of the regioselectivity of the [4+2] cycloaddition.
reaction, and therefore, the subsequent transformation of the resulting cycloadducts. Herein, we report the full details of these studies, especially the impact of varying the nature of both the borodiene and dienophile substituents upon the reaction outcome, and hence, discuss the mechanistic implications of the results.

Results and Discussion

Reaction 1-dienylboronate pinacolate esters with nitrosoarene compounds

As reported previously, initial investigations into the reaction between the dienyl boronate 1 and nitrosobenzene 2 resulted in the formation of the unexpected N-phenylpyrrole 3a instead of a mixture of regioisomeric oxazine cycloadducts (Scheme 2). Given that such reactions tend to lack high regiocontrol, the efficiency of the pyrrole formation was intriguing and clearly required further study and explanation. Indeed, even when the reaction was followed by $^1$H NMR, only 3-methyl-1-phenyl-pyrrole 3a, together with some azoxybenzene 4, was identified. There was a notable absence of any oxazine cycloadducts and the reaction was complete after 5 h to afford 3a in 82% isolated yield (Table 1, Entry 3).

Scheme 2. N-Phenylpyrrole formation from the reaction of boronated diene 1 and nitrosobenzene 2.
Further studies to address the scope of this reaction were conducted, the results of which are summarized in Table 1.

Table 1. Pyrrole formation from the reaction of nitrosoarenes with diene 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Nitroso compound</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1[a]</td>
<td>C₆H₅NO</td>
<td>3a</td>
<td>67</td>
</tr>
<tr>
<td>2[b]</td>
<td>C₆H₅NO</td>
<td>3a</td>
<td>61</td>
</tr>
<tr>
<td>3[c]</td>
<td>C₆H₅NO</td>
<td>3a</td>
<td>82</td>
</tr>
<tr>
<td>4[c]</td>
<td>p-Me-C₆H₄NO</td>
<td>3b</td>
<td>60</td>
</tr>
<tr>
<td>5[c]</td>
<td>p-Cl-C₆H₄NO</td>
<td>3c</td>
<td>68</td>
</tr>
<tr>
<td>6[c]</td>
<td>p-Br-C₆H₄NO</td>
<td>3d</td>
<td>65</td>
</tr>
<tr>
<td>7[c]</td>
<td>p-EtO₂C₆H₄NO</td>
<td>3e</td>
<td>57</td>
</tr>
<tr>
<td>8[c]</td>
<td>p-MeO-C₆H₄NO</td>
<td>3f</td>
<td>77</td>
</tr>
<tr>
<td>9[c]</td>
<td>o-Me-C₆H₄NO</td>
<td>3g</td>
<td>69</td>
</tr>
</tbody>
</table>

[a] Reaction with 1.5 eq of ArNO in MeOH at RT for 5 h.
[b] Reaction with 1.5 eq of ArNO in DCM at RT for 48 h.
[c] Reaction with 2.5 eq of ArNO in MeOH at RT for 5 h.
Differently substituted nitrosoarene compounds were reacted with borodiene 1 to afford \(N\)-arylpyrroles 3 in moderate to good yields. Use of either a protic solvent (MeOH) or an aprotic solvent (DCM), had no significant effect (Entries 1 and 2, Table 1). Due to the formation of the azoxybenzene by-product, an excess of nitrosoarene reagent (2.5 eq) was used in order to increase the isolated yield, for example, by 15% in the cases of comparing Entries 1 and 3 (Table 1). Modification of the nature or the location of the aromatic ring substituent on the nitrosoarene moiety showed no notable effect on the formation of the \(N\)-arylpyrrole products 3a-g, which were isolated in 52 to 82% yields (Entries 4-9, Table 1). Other dienes, prepared according to literature procedures,\(^{11}\) were also examined, as summarised in Table 2.

**Table 2. Reaction of dienes 5-7 with nitrosobenzene**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^{[a]})</td>
<td>5</td>
<td><img src="image" alt="Product Image" /></td>
<td>78</td>
</tr>
<tr>
<td>2(^{[b]})</td>
<td>6</td>
<td><img src="image" alt="Product Image" /></td>
<td>16</td>
</tr>
<tr>
<td>3(^{[b]})</td>
<td>7</td>
<td><img src="image" alt="Product Image" /></td>
<td>34</td>
</tr>
</tbody>
</table>

\(^{[a]}\) Reaction with 2.5 eq of ArNO in MeOH at RT for 5 h.  
\(^{[b]}\) Reaction with 2.5 eq of ArNO in MeOH at RT for 16 h.
Unsubstituted 1-borobutadiene 5 reacted efficiently with nitrosobenzene to give the corresponding pyrrole 3h in 78% yield (Entry 1, Table 2). However, there was a major decrease in yield observed in the case of the more substituted and cyclic borodiene 6 (Entry 2, Table 2). The acyclic, 2-substituted diene 7 also resulted in a reduced yield (Entry 3, Table 2), though the yield was not quite as low as for cyclic diene 6. The corresponding pyrroles were nevertheless isolated in only 34% and 16% yields respectively, and despite the extended reaction times.

Next, the influence of substituents on the borodiene were examined, possessing aromatic or electron withdrawing groups in position 4. Diene 8 was prepared via a 3 step pathway, involving a Sonogashira reaction of β-bromostyrene with trimethylsilylacetylene, followed by protodesilylation, to give 4-phenyl-3-buten-1-yne as an E/Z mixture (91/9). Hydroboration using pinacolborane and Schwartz’ catalyst11a provided the desired diene 8 as a mixture of two stereoisomers (E,E:E,Z = 91:9) in a 56% overall yield. The subsequent reactions of diene 8 with nitrosobenzene are shown in Table 3.

**Table 3. Study of the reactivity of diene 8 with nitrosobenzene**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Conversion (Isolated yield) (%)</th>
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<tbody>
<tr>
<td>1[a]</td>
<td>MeOH</td>
<td>rt</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>2[a]</td>
<td>Toluene</td>
<td>rt</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>3[a]</td>
<td>MeOH</td>
<td>reflux</td>
<td>5</td>
<td>50</td>
</tr>
</tbody>
</table>
In the presence of nitrosobenzene, no reaction of diene 8 was observed at room temperature in either toluene or MeOH (Entries 1 and 2, Table 3). Heating triggered reaction according to \(^1\)H NMR in both MeOH and toluene (Entries 3 and 4, Table 3), and the starting nitrosobenzene was fully consumed after an extended 22 h reaction time, resulting in 72% conversion of diene 8 (Entry 5, Table 3). No further improvement was observed if the nitrosobenzene was added in portions in an attempt to decrease azo-by-product formation (1 eq at the outset - 1 eq after 4 h - 0.5 eq after 4 h), or by slowly addition of a MeOH solution by syringe pump (see Entries 6 and 7, Table 3). Finally, the use of 3.5 eq of nitrosobenzene (Entry 8, Table 3) was required in order to achieve the complete conversion of both stereoisomers of diene 8, resulting in the formation pyrrole 3k and a 36% isolated yield.

The introduction of an electron withdrawing group (methyl carboxylate function) in position 4 of the borodiene was next examined. Diene 9 was, therefore, synthesized by a Wittig route from an ester-stabilised ylide and \(\beta\)-borylacrolein pinacol ester, resulting in a mixture of three stereoisomers \((E,E;E,Z;Z,E = 83:10:7)\) in an unoptimized 30% overall yield.\(^{13}\) The subsequent reactions of diene 9 are shown in Table 4.

**Table 4. Study of the reactivity of diene 9 with nitrosobenzene**
Diene 9 proved even less reactive than diene 8, and longer reaction times and higher temperatures were required to give an improved conversion (see Table 4, Entries 1-5). In order to form the pyrrole 3l, 5 equivalents of nitrosobenzene and a 128 h reaction time was required in toluene at reflux, and only the E,E-stereoisomer reacted. Indeed, even under longer reaction times, the other isomers were still unreacted and present in the reaction mixture (Entry 5, Table 4). Nevertheless, 26% of the corresponding pyrrole 3l was isolated after silica gel chromatography (Entry 5, Table 4).

**Reaction of tetracoordinated 1-borodienes to nitrosoarene compounds**

Since the various 1-borodienes with pinacol esters all resulted in reactions in which the oxazine was not observed, our attention was turned our attention to the study of the influence of boron
substituents that might result in the oxazine cycloadducts being isolated. The impact of replacing the pinacol ester of boronate 1 by diethanolamine was studied, as outlined in Scheme 3.

**Scheme 3. Reactivity of dienyl diethanolamine esters 10 with nitrosobenzene.**

Reaction of 1-borodiene 10 with nitrosobenzene resulted in the identification of the [4+2]-cycloadduct 11 in the $^1$H NMR spectrum of the crude mixture. After 2 h, all the diene 10 was consumed and the intermediate boro-1,2-oxazine 11 had also disappeared, resulting in only pyrrole 3a formation, together with small amounts of azoxybenzene 4 (Scheme 3). This cycloaddition (Scheme 4) was notably faster with this tetracoordinated boron substituent (50% conversion after 5 min at room temperature compared with 5 h for complete conversion of the corresponding pinacol ester (Table 1, Entry 3).

Indeed, this increased reactivity was confirmed by the reaction of cyclic diene 12 which provided pyrrole 3i after only 2 h and in a 46% yield as shown in Equation 1 (compared with 16% over 16 h for the corresponding pinacol ester derivative, Entry 2, Table 2).
Most interestingly of course, the observation of the transient [4+2]-hetero-Diels-Alder cycloadduct 11 (Scheme 3) confirms the key role of the oxazine cycloadduct in the subsequent formation of the pyrrole. Diethanolamine esters are known for their facile hydrolysis or methanolysis to regenerate the corresponding boronic acid or ester,\textsuperscript{17} however, simply the reversibility of B-N chelation could be responsible for allowing the facile rearrangement to the pyrrole (\textit{vide infra}). We can also observe in these results, the beneficial effect of the tetracoordinated boronate ester, which is presumably less electron withdrawing than a pinacol ester, and therefore, more reactive towards the electron deficient dienophile.

Prompted by these results, we therefore examined the behavior of corresponding MIDA (\textit{N}-methyliminodiacetic)borodiene derivatives. Because of their high stability towards air and moisture, these compounds have been used as flexible scaffolds for the synthesis of a wide range of functionalized small molecules.\textsuperscript{18} It was our expectation that such dienes would make it possible to isolate and study the intermediate oxazine cycloadducts. The presence of an sp\textsuperscript{3}-\textit{versus} a sp\textsuperscript{2}-hybridized borodiene would also be expected to be a useful tool to examine the regioselectivity of the cycloaddition reaction. The scope of the reaction of the MIDA diene 13 was, therefore, examined with various nitrosoarene compounds, as outlined in Table 5. Reactions were carried out in AcOEt for a better solubility of the diene B-MIDA 13.
Table 5. Reactivity of MIDA-substituted diene 13 with nitrosoarene compounds

![Chemical structures](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Nitroso compound</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₆H₅NO</td>
<td><img src="image" alt="Structure 14a" /></td>
<td>64</td>
</tr>
<tr>
<td>2</td>
<td>p-MeO-C₆H₄-NO</td>
<td><img src="image" alt="Structure 14b" /></td>
<td>47</td>
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<tr>
<td>3</td>
<td>o-Me-C₆H₄-NO</td>
<td><img src="image" alt="Structure 14c" /></td>
<td>56</td>
</tr>
<tr>
<td>4</td>
<td>p-Cl-C₆H₄-NO</td>
<td><img src="image" alt="Structure 14d" /></td>
<td>77</td>
</tr>
</tbody>
</table>
The reaction of the MIDA-borodiene 13 provided the corresponding oxazine cycloadducts in moderate to good yields with the different nitrosoarene compounds, without obvious electronic effects from the aryl substituent. However, single regioisomeric products were obtained, as exemplified by the formation of the stable [4+2]-cycloadduct 14a, obtained from reaction of diene 13 with nitrosobenzene and isolated in 64% yield (Entry 1, Table 5). Only the boron-oxygen 1,2 related regioisomer (in red in Table 5) was observed and its structure was assigned by NOESY NMR by correlation between the o-phenyl Hs and one of the NCHs on the oxazine ring. The introduction of different nitrosoarene substituents, i.e. electron donating and withdrawing groups in positions 2 and 4, did not change the resulting regiochemical outcome (Entries 2-5, Table 5) and yields ranged between 47 to 77%. It is also noteworthy that little or no dimerization of the nitrosoarene took place during these reactions, reflecting the short reaction times and more reactive diene, reducing the potential for competitive by-product formation from the nitroso compound.

The impact of different MIDA borodiene substituents was then examined, i.e. dienes 15-18, which were synthesized by Stille or Suzuki-Miyaura couplings of (E)-(2-bromovinyl)-MIDA boronate with either vinyltributyltin (72%), (E)-hex-1-ene boronic acid (79%), (1-bromovinyl)benzene (68%) or 1-phenylvinylboronic acid (76%), respectively. The resulting nitroso addition reactions are summarised in Table 6.
Table 6. Reactivity of MIDA-substituted dienes 15-18 with nitrosobenzene

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>Product</th>
<th>Yield (%)</th>
<th>(Isomer ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1[a]</td>
<td><img src="image" alt="Diene 15" /></td>
<td><img src="image" alt="Product 19" /></td>
<td>43</td>
<td>(100/0)</td>
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<tr>
<td>2[a]</td>
<td><img src="image" alt="Diene 16" /></td>
<td><img src="image" alt="Product 20" /></td>
<td>68</td>
<td>(100/0)</td>
</tr>
<tr>
<td>3[a]</td>
<td><img src="image" alt="Diene 17" /></td>
<td><img src="image" alt="Product 21" /></td>
<td>78</td>
<td>(100/0)</td>
</tr>
<tr>
<td>4[b]</td>
<td><img src="image" alt="Diene 18" /></td>
<td><img src="image" alt="Product 22" /></td>
<td>89</td>
<td>(40/60)</td>
</tr>
</tbody>
</table>

[a] Reaction with 2.5 eq of nitrosobenzene in AcOEt at rt for 6 h.
[b] Reaction with 5 eq of nitrosobenzene AcOEt at reflux for 24 h.

Similar to the results observed with the MIDA derivative 13, the first three dienes (15-17) gave the same single regioisomeric boron-oxygen 1,2-related products at room temperature (in red in
Table 6), with the boron occupying the α-position relative to the ring oxygen of the oxazine (Entries 1-3, Table 6). The introduction of a phenyl group at C₄ noticeably reduced the reactivity of the borodiene 18 with reaction only occurring at reflux in EtOAc over 24 h. In addition, a mixture of regioisomers 22 and 22' (ratio 40:60) was isolated in an 89% combined yield (Entry 4, Table 6). The structure of the major boron-oxygen 1,3-related regioisomer 22' (in blue in Table 6) was secured by single crystal X-ray structure analysis (see SI), confirming the cis-stereochemistry of the boron and phenyl ring substituents. Both steric and electronic effects of the phenyl ring can explain this observed preferred regiochemistry (as discussed by Houk et al. for 1-phenylbutadiene compared with penta-1,3-diene²⁰).

Mechanistic aspects of the reaction 1-borodienes with nitrosoarene compounds

The mechanism which was hypothesized and subsequently supported by DFT calculations⁹ to rationalize the observed formation of pyrroles 3a-l is shown in Scheme 4, which involves a [4+2]-Diels–Alder cycloaddition intermediate 23 or 24, followed by rearrangement of the resulting oxazine. Consequently, borodienes 1, 5-9 and dienyl diethanolamine esters 10, 12 react with the nitroso compounds to afford the corresponding 3,6-dihydro-1,2-oxazines 24 and 23 respectively. The subsequent boryl rearrangement would give 26 followed by an intramolecular aza-boryl addition to the aldehyde generating 27 and finally, borate elimination provides the pyrrole 3a-l.

Scheme 4. Proposed mechanism for the formation of pyrroles from the reaction of 1-borodienes with nitrosoarene compounds.
Further investigations into this process to support our supposition and DFT calculations\(^9\) have now been provided by experimental investigations. Therefore, the replacement of the boronate pinacol ester on the diene component by diethanolamine (\textit{vide supra}) resulted in the identification of the [4+2]-cycloadduct in the \(^1\)H NMR spectrum of the crude mixture.\(^{14}\) Reacting diene 10 or 12 with nitrosobenzene for 2 hours, resulted in complete diene consumption and even the boronate 1,2-oxazine 11 had totally disappeared to afford only pyrrole 3a with only small amounts of azoxybenzene 4 (Scheme 4) produced. The pyrrole formation under these conditions can be explained by an facile equilibrium between the dioxazaborocane 23 and the corresponding methyl ester 24 due to solvolysis.\(^{17}\) This equilibrium releases the vacant orbital on boron, and consequently, the subsequent rearrangement occurs to access the pyrrole (Scheme 4). The enhanced reactivity of the borodiene possessing a diethanolamine ester (50\% conversion after 5 min at rt for 10 vs. 5 h for complete conversion for 1, Table 1, Entry 1) is consistent with similar
observations already reported in the literature,\textsuperscript{17} \textit{i.e.} a more electron rich diene, reacting with an electron deficient nitroso compound, in a 'normal' electron, frontier-orbital-controlled [4+2]-cycloaddition reaction. It is noteworthy that even diene 12 provided a 48\% yield of pyrrole 3i after 2 h at rt (\textit{c.f.} 16\% in 16 h, Entry 2, Table 2) which further demonstrates the advantages of the more electron rich diene. Indeed, these conclusions are further supported by the MIDA boronate ester derivatives, as outlined in Scheme 5.

\textbf{Scheme 5. Proposed reaction sequence for the formation of pyrrole 3k from MIDA boronate oxazine derivative 22}

The reaction of nitrosobenzene with the MIDA boronate 18 results in the formation of the two regioisomers 22 and 22' (\textit{vide supra}). Under the same conditions (Scheme 5), regioisomer 22 reacted cleanly to give the pyrrole 3k, whereas the other regioisomer 22' gave a mixture of unidentified products. It was, therefore, decided to test another method to deprotect the MIDA boronate ester function of these types of oxazine cycloadducts. Hence, under acidic conditions (DCI 1M, 1 eq) in acetone-$d_6$, 2-phenylfuran 31 was cleanly and quantitatively produced after 15 minutes at room temperature from regioisomer 22', as shown in Equation 2. Under the same acidic conditions, the regioisomer 22 did not lead to the formation of the pyrrole 3k. Instead, only the hydrochloride salt of the MIDA system was clearly identified. Thus, it is possible to
selectively, and cleanly deprotect, each regioisomer depending on the conditions. Pyrrole formation requires a regioisomer like 22, and to be released in a basic medium, whereas furan formation requires a regioisomer like 22' and an acidic medium.

Moreover, the by-product 36 was isolated by extracting the reaction mixture with DCM (see Scheme 6) in 25% yield, whose structure was established by $^1$H, $^{13}$C and $^{11}$B NMR, and mass spectroscopy. These experimental observations are in agreement with the proposed mechanism outlined in Scheme 4. In addition, a preliminary and essential protonation of the nitrogen atom of the MIDA boronate 22' results in the de-coordination of the nitrogen from boron, leading to the intermediate 32. Formation of this BX$_2$ moiety 32 enables the facile boryl rearrangement 33-35 to take place, and in this case, to form the furan 31 (Scheme 6).
Scheme 6. Proposed mechanism for the formation of furan 31 from 22’

Transformations of boro-1,6-dihydro-1,2-oxazine derivatives

To explore the synthetic importance of B-MIDA oxazine derivatives, we decided to carry out a Suzuki-Miyaura coupling with the cycloadduct 14a as a model substrate. Under classical experimental conditions for this class of reaction, $^1$H NMR of the crude reaction mixture (see ESI) shows a full conversion of the starting material into the pyrrole 3a that showed that 14a is not stable enough to survive under Suzuki-Miyaura coupling conditions (Scheme 7).
Scheme 7. Reactivity of oxazine 14a and iodobenzene under Suzuki-Miyaura coupling conditions

To confirm that this is indeed the location of the boronated group that is responsible for this failure, the diene 37 was synthesized from (1-bromovinyl)-MIDA boronate and 1-bromostyrene. The reaction with nitrosobenzene regioselectively provided the cycloadduct 38 in a 73% isolated yield with only traces of the second isomer. To confirm the structure of the major regioisomer, it was engaged in a Suzuki-Miyaura cross-coupling with 1-bromotoluene in the presence of palladium acetate and SPhos (Scheme 8). The 2,4,5-trisubstituted dihydrooxazine 39 was isolated in a 71% yield. A NOESY NMR experiment (correlation between Hs of the methyl group of the toluene moiety and Hs on the oxazine ring at C₆) established the structure of this compound and consequently the orientation of the first cycloaddition. No ring contraction product was observed in this case.
Scheme 8. Synthesis of triarylated oxazine 39 from the nitrosobenzene cycloadduct 38 after Suzuki-Miyaura cross-coupling reaction sequence

Conclusions
This study revealed that hetero Diels Alder cycloadditions of nitroso compounds and boronated dienes can afford either pyrrole derivatives or oxazine cycloadducts. The most critical parameter to guide these reactions remains the ability of the boron to keep, or not, its sp³ hybridization state, the presence of a boronate function α to the oxygen or the nitrogen atom of the oxazine ring being responsible of the fate of the ring contraction. Different experimental observations led us to propose a mechanism to rationalize these results, also in agreement with previous theoretical investigations. In the case of 2-MIDA borodienes, the formation of the corresponding [4+2]-cycloadduct is highly regioselective, and notably, these more electron rich dienes react faster with the nitrosoarene compounds. Indeed, this increased reactivity directly results in a decrease in the amount of nitrosoarene compound which can competitively degrade to azo by-products. No decomposition of the oxazine ring was observed during a Suzuki-Miyaura coupling. A 2,4,5-triaryl-3,6-dihydro-1,2-oxazine was isolated in good yield, thus showing the interest of this
approach to prepare these class of heterocycles with complete control of the position of the different substituents.

EXPERIMENTAL SECTION

General information and materials.
Reagents and solvents were used as received from the supplier, unless specified. When specified, dried solvents were used; THF and toluene were distillate on sodium, benzophenone and DCM on P$_2$O$_5$. Reactions were monitored by TLC analysis using Silica Gel 60 F$_{254}$ plates. Purifications on silica gel were carried out on silica gel 0.060-0.200 mm, 60 Å. NMR Spectra were recorded on apparatus at 300, 400 or 500 MHz for 1H, 75, or 101 MHz for $^{13}$C and 96 MHz for $^{11}$B. $^1$H and $^{13}$C NMR chemical shifts were referenced to Me$_4$Si as internal reference, and $^{11}$B NMR chemical shifts to external BF$_3$.OEt$_2$ (0.0 ppm). Deuterated chloroform CDCl$_3$ and acetone-$d_6$ were used for NMR spectra. NMR data are reported as; chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dt = doublet of triplet, m = multiplet, b = broad), coupling constant J (Hz) and integration. High-resolution mass spectra (HMRS) were obtained on a Q-TOF instrument and measured using either electrospray ionization (ESI) or electron impact (EI). Melting points were measured and reported in °C.

General procedure for pyrrole synthesis.
To a solution of diene (1 eq) (pinacol boronate or diethanolamine esters) in the solvent was added nitrosoarene compound (2.5 to 5 eq). The reaction mixture was stirred at the temperature
indicated in the experimental procedure. The solvent was evaporated and the crude product was purified by silica gel chromatography.

**Characterization and experimental procedure of compound 3a-j.** 9

**1,2-Diphenyl-1H-pyrrole 3k.** 27

To a solution of diene 8 (65 mg, 0.25 mmol) in MeOH (1 mL) was added nitrosobenzene (94.9 mg, 0.76 mmol). The reaction mixture was heated to boiling and stirred for 22 h. The solvent was evaporated and the crude product was purified by silica gel chromatography (cyclohexane/toluene 98/2, R_f = 0.3) to give compound 3k (19.7 mg, 36%). ^1^H NMR (400 MHz, CDCl_3) δ ppm 7.33 -7.31 (m, 2H), 7.28 - 7.26 (m, 1H), 7.21-7.14 (m, 7H), 6.99 (dd, J = 2.7, 1.8 Hz, 1H), 6.47 (dd, J = 3.4, 1.8 Hz, 1H), 6.41 (dd, J = 3.4, 3.0 Hz, 1H); ^13^C NMR (101 MHz, CDCl_3) δ ppm 140.7, 134.0, 133.1, 129.1, 128.4, 128.2, 126.7, 126.4, 125.9, 124.5, 110.8, 109.4.

**Methyl-1-phenyl-1H-pyrrole-2-carboxylate 3l.** 28

To a solution of diene 9 (65 mg, 0.25 mmol) in MeOH (0.5 mL) was added nitrosobenzene (94.9 mg, 0.76 mmol). The reaction mixture was heated to boiling and stirred for 22 h. The solvent was evaporated and the crude product was purified by silica gel chromatography (cyclohexane/toluene 98/2, R_f = 0.3) to give compound 3l (15 mg, 26%). ^1^H NMR (400 MHz, CDCl_3) δ ppm 7.45 – 7.29 (m, 5H), 7.10 (dd, J = 3.9, 1.8 Hz, 1H), 6.95 (dd, J = 2.7, 1.8 Hz, 1H), 6.29 (dd, J = 3.9, 2.7 Hz, 1H), 3.71 (s, 3H); ^13^C NMR (101 MHz, CDCl_3) δ ppm 161.1, 140.6, 130.0, 128.7, 128.0, 126.5, 119.1, 109.3, 51.3.

*(E,E)-1,3-Butadienyl-(4-butyl)-1-boronic MIDA ester 16.*
Compound 16 was synthesized using procedure Burke et al. procedure\textsuperscript{15}. M.p = 122°C; \textsuperscript{1}H NMR (400 MHz, acetone-\textit{d}_6) δ ppm 6.53 (dd, \textit{J} = 17.5, 10.2 Hz, 1H), 6.18 – 6.07 (m, 1H), 5.81 – 5.72 (m, 1H), 5.54 (d, \textit{J} = 17.5 Hz, 1H), 4.19 (d, \textit{J} = 16.8 Hz, 2H), 4.01 (d, \textit{J} = 16.8 Hz, 2H), 2.98 (s, 3H), 2.09 (q, \textit{J} = 6.9 Hz, 2H), 1.45 – 1.27 (m, 4H), 0.89 (t, \textit{J} = 7.2 Hz, 3H); \textsuperscript{13}C NMR (101 MHz, acetone-\textit{d}_6) δ ppm 169.1, 143.7, 136.4, 133.6, 62.2, 47.3, 32.9, 32.1, 22.9, 14.1 (boron-carbon bound was not visible); \textsuperscript{11}B NMR (96 MHz, acetone-\textit{d}_6) δ ppm 10.8; HRMS (ESI) calcd. for C\textsubscript{16}H\textsubscript{22}N [M+H]\textsuperscript{+}: 265.1485 found: 265.1484.

**General procedure for [4+2] cycloaddition of B-MIDA dienes to nitrosoarene compounds.**

To a solution of diene (1 eq) (MIDA ester) in AcOEt was added aryl nitroso (2.5 eq). The reaction mixture was stirred at room temperature or in reflux conditions. The solvent was evaporated and the crude product was purified by silica gel chromatography.

**For oxazine 14a, see reference 9.**

**Oxazine 14b.**

To a suspension of diene 13 (50 mg, 0.22 mmol) in AcOEt (2 mL), was added 4-methoxynitrosobenzene (61.5 mg, 0.45 mmol). The reaction mixture was stirred at room temperature overnight. The solvent was evaporated and the crude product was purified by solid phase silica gel chromatography. (Et\textsubscript{2}O:MeCN 8/2, \textit{R}_f = 0.4). \textit{14b} (37.2 mg, 47%). M.p. = 164 °C; \textsuperscript{1}H NMR (400 MHz, acetone-\textit{d}_6) δ ppm 7.09-7.05 (m, 2H), 6.87-6.83 (m, 2H), 5.71 (ddd, \textit{J} = 3.2, 1.7, 1.6 Hz, 1H), 4.47 (bs, 1H), 4.26 (dd, \textit{J} = 16.8, 6.8 Hz, 2H), 4.01 (dd, \textit{J} = 33.6, 16.8 Hz, 2H), 3.75 (s, 3H) 3.74-3.69 (m, 1H), 3.57-3.51 (m, 1H), 3.27 (s, 3H), 1.79 (s, 3H); \textsuperscript{13}C NMR (101 MHz, acetone-\textit{d}_6) δ ppm 168.8, 168.5, 156.4, 145.6, 129.6, 122.3, 119.1, 114.8, 63.19, 63.17,
57.1, 55.7, 55.0, 46.8, 20.6 (boron-carbon bound was not visible); \(^{11}\)B NMR (96 MHz, acetone-
\(d_6\)) \(\delta\) ppm 9.9; HRMS (ESI) calcd. for [M+Na]\(^+\)(C\(_{17}\)H\(_{21}\)N\(_2\)O\(_6\)\(^{11}\)BNa): 383.1385 found: 383.1382.

**Oxazine 14c.**

To a suspension of diene 13 (60 mg, 0.27 mmol) in AcOEt (2 mL), was added 2-nitrosotoluene
(48.9 mg, 0.40 mmol). The reaction mixture was stirred at room temperature overnight. The
solvent was evaporated and the crude product was purified by solid phase silica gel chromatography. (Et\(_2\)O/MeCN 8/2, \(R_f = 0.5\)). 14c (52 mg, 56%). M.p. = 169 \(°C\); \(^1\)H NMR (400 MHz, acetone-
\(d_6\)) \(\delta\) ppm 7.23 (m, 1H), 7.16 (m, 2H), 7.15 (m, 1H), 5.74 (s, 1H), 4.51 (bs, 1H),
4.21 (dd, \(J = 16.8, 11.1\) Hz, 2H), 3.94 (dd, \(J = 19.5, 16.8\) Hz, 2H), 3.69-3.65 (m, 1H) 3.45-3.41
(m, 1H), 3.17 (s, 3H), 2.30 (s, 3H), 1.80 (s, 3H); \(^{13}\)C NMR (101 MHz, acetone-
\(d_6\)) \(\delta\) ppm 168.7, 168.6, 149.7, 133.6, 131.4, 130.2, 127.1, 125.7, 122.2, 119.0, 63.21, 63.16, 56.7, 46.8, 20.6, 18.5
(boron-carbon bound was not visible); \(^{11}\)B NMR (96 MHz, acetone-
\(d_6\)) \(\delta\) ppm 9.9; HRMS (ESI) calcd. for [M+Na]\(^+\)(C\(_{17}\)H\(_{21}\)N\(_2\)O\(_5\)\(^{11}\)BNa): 367.1436 found: 367.1439.

**Oxazine 14d.**

To a suspension of diene 13 (50 mg, 0.22 mmol) in AcOEt (2 mL), was added 4-
chloronitrosobenzene (47.6 mg, 0.34 mmol). The reaction mixture was stirred at room
temperature overnight. The solvent was evaporated and the crude product was purified by solid
phase silica gel chromatography. (Et\(_2\)O:MeCN 8/2, \(R_f = 0.5\)). 14d (61 mg, 77%). M.p. = 224 \(°C\);
\(^1\)H NMR (400 MHz, acetone-
\(d_6\)) \(\delta\) ppm 7.31 – 7.23 (m, 2H), 7.16 – 7.08 (m, 2H), 5.74 (s, 1H),
4.51 (bs, 1H), 4.29 (dd, \(J = 16.8, 0.7\) Hz, 2H), 4.05 (dd, \(J = 20.8, 16.8\) Hz, 2H), 3.94-3.89 (m, 1H),
3.62 – 3.54 (m, 1H), 3.29 (s, 3H), 1.81 (s, 3H); \(^{13}\)C NMR (101 MHz, acetone-
\(d_6\)) \(\delta\) ppm 168.7, 168.5, 150.6, 129.4, 129.3, 126.9, 122.3, 118.1, 63.24, 63.23, 55.9, 46.9, 20.5 (boron-
carbon bound was not visible); $^{11}$B NMR (96 MHz, acetone-$d_6$) $\delta$ ppm 9.9; HRMS (ESI) calcd. for [M+Na]$^+$\((C_{16}H_{18}N_2O_5^{35}C^11)\text{BNa})$: 387.0889 found: 367.0888.

**Oxazine 14e.**

To a suspension of diene 13 (30 mg, 0.13 mmol) in AcOEt (1 ml), was added 4-nitrosobenzoate (33.9 mg, 0.19 mmol). The reaction mixture was stirred at room temperature overnight. The solvent was evaporated and the crude product was purified by solid phase silica gel chromatography. (Et$_2$O:MeCN 8/2, $R_f$ = 0.4). 14e (31.9 mg, 61%). M.p. = 210 °C; $^1$H NMR (400 MHz, acetone-$d_6$) $\delta$ ppm 7.93-7.90 (m, 2H), 7.17-7.14 (m, 2H), 5.76 (s, 1H), 4.56 (bs, 1H), 4.35-4.29 (dd, $J = 16.8, 0.8$ Hz, 2H), 4.29 (q, $J = 7.1$ Hz, 2H), 4.14-4.04 (dd, $J = 16.8, 10.1, 1.1$ Hz, 2H), 4.12-4.05 (m, 1H), 3.70-3.65 (m, 1H), 3.33 (s, 3H), 1.83 (s, 3H), 1.33 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, acetone-$d_6$) $\delta$ ppm 168.7, 168.5, 166.5, 155.0, 131.4, 129.1, 123.6, 122.2, 114.9, 63.28, 63.25, 60.9, 54.6, 47.0, 20.4, 14.7 (boron-carbon bound was not visible); $^{11}$B NMR (96 MHz, acetone-$d_6$) $\delta$ ppm 10.0; HRMS (ESI) calcd. for [M+Na]$^+$\((C_{19}H_{23}N_2O_7^{11})\text{BNa})$: 425.1490 found: 425.1491.

**Oxazine 19.**

To a suspension of diene 15 (40.0 mg, 2.21 mmol) in AcOEt (2 ml), was added nitrosobenzene (59.1 mg, 5.52 mmol). The reaction mixture was stirred at room temperature for 6 h. The solvent was evaporated and the crude product was purified by solid phase silica gel chromatography. (Et$_2$O:MeCN 8/2, $R_f$ = 0.4). 19 (28 mg, 43%). M.p. = 161 °C; $^1$H NMR (400 MHz, acetone-$d_6$) $\delta$ ppm 7.29-7.25 (m, 2H), 7.12-7.08 (m, 2H), 6.96-6.92 (m, 1H), 6.06 (dd, $J = 10.1, 2.4, 1.7, 1.6$ Hz, 1H), 5.93 (dd, $J = 10.1, 5.2, 2.8, 1.7$ Hz, 1H), 4.61(bs, 1H), 4.29 (dd, $J = 16.8, 0.7$ Hz, 2H), 4.10-4.04 (m, 1H), 4.06 (dd, $J = 22.6, 16.8$ Hz, 2H), 3.70-3.64 (m, 1H), 3.32 (s, 3H); $^{13}$C NMR
(101 MHz, acetone-$d_6$) δ ppm 168.7, 168.5, 152.0, 129.6, 127.9, 122.6, 122.2, 116.5, 63.2, 52.6, 46.9 (boron-carbon bound was not visible); $^{11}$B NMR (96 MHz, acetone-$d_6$) δ ppm 9.9; HRMS (ESI) calcd. for [M+Na]$^+$($C_{15}H_{17}N_2O_5^{11}$BNa): 339.1128 found: 339.1125.

**Oxazine 20.**

To a suspension of diene 16 (63 mg, 0.24 mmol) in AcOEt (3 mL), was added nitrosobenzene (64 mg, 0.60 mmol). The reaction mixture was stirred at room temperature for 6 h. The solvent was evaporated and the crude product was purified by solid phase silica gel chromatography (Et₂O:MeCN 8/2, $R_f = 0.7$). 20 (61 mg, 68%). M.p. = 188 °C; $^1$H NMR (400 MHz, acetone-$d_6$) δ ppm 7.28 – 7.21 (m, 2H), 7.02 (m, 1H), 6.86 (m, 1H), 6.06 (ddd, $J = 10.3, 5.2, 2.8$ Hz, 1H), 5.91 (dt, $J = 10.3, 1.4$ Hz, 1H), 4.37 (bd, $J = 1.4$ Hz, 1H), 4.31 (dd, $J = 19.2, 16.9$ Hz, 2H), 4.10 (dd, $J = 16.9, 10.7$ Hz, 2H), 4.10 – 4.07 (m, 1H), 3.35 (s, 3H), 1.68 – 1.62 (m, 2H), 1.44 – 1.21 (m, 4H), 0.85 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (101 MHz, acetone-$d_6$) δ ppm 169.0, 168.1, 149.9, 129.6, 127.6, 126.3, 121.4, 116.8, 69.6, 63.2, 58.1, 46.8, 31.9, 23.4, 14.3; $^{11}$B NMR (96 MHz, acetone-$d_6$) δ ppm 10.2; HRMS (ESI) calcd. for [M+H]$^+$($C_{19}H_{25}N_2O_5^{11}$B): 373.1935 found: 373.1933.

**Oxazine 21.**

To a suspension of diene 17 (30 mg, 0.11 mmol) in AcOEt (2 mL), was added nitrosobenzene (23 mg, 0.21 mmol). The reaction mixture was stirred at room temperature for 6 h. The solvent was evaporated and the crude product was purified by silica gel chromatography. (Et₂O:MeCN 8/2, $R_f = 0.4$). 21 (32 mg, 78%). M.p. = 207 °C; $^1$H NMR (400 MHz, acetone-$d_6$) δ ppm 7.59-7.57 (m, 2H), 7.40-7.36 (m, 2H), 7.33-7.23 (m, 5H), 7.00-6.96 (m, 1H), 6.51 (m, 1H), 4.74 (bs, 1H), 4.57 (ddd, $J = 15.8, 2.8, 1.8$ Hz, 1H), 4.33 (d, $J = 16.8$ Hz), 4.10 (dd, $J = 26.0, 16.8$ Hz) 4.01 (ddd, $J = 15.8, 2.8, 1.1$ Hz, 1H), 3.36 (s, 3H); $^{13}$C NMR (101 MHz, acetone-$d_6$) δ ppm 169.8, 169.6, 152.7,
140.4, 133.5, 130.6, 130.4, 129.2, 126.6, 126.2, 123.8, 118.0, 64.3, 54.8, 48.0 (boron-carbon bound was not visible); $^{11}$B NMR (96 MHz, acetone-$d_6$) \( \delta \) ppm 10.2; HRMS (ESI) calcd. for [M+H]$^+$($C_{21}H_{21}N_2O_5^{11}$B): 393.1622 found: 393.1618.

**Oxazine 22 and 22’.**

To a suspension of diene 18 (50 mg, 0.18 mmol) in AcOEt (2 mL), was added nitrosobenzene (38 mg, 0.35 mmol). The reaction mixture was stirred under reflux during 24 h. The solvent was evaporated and the crude product was purified by solid phase silica gel chromatography. (Et$_2$O:MeCN 8/2, \( R_f = 0.4 \)). 22 + 22’ (40/60) (62.8 mg, 89%). The mixture of isomer was solubilised in the minimum amount of CHCl$_3$, and left overnight in a fridge at +5 °C. The precipitate was filtered, washed with Et$_2$O and recrystallized in MeOH to afford pure isomer 22’ as white crystals. The filtrate was evaporated and diluted in CHCl$_3$ (1 mL). Aqueous HCl (1M) (0.5 mL) was added and heterogeneous mixture was vigorously stirred for 24 h to decompose the residual 22’. The organic phase was separated, dried over MgSO$_4$, filtered and concentrated under vacuum. After purification by silica gel chromatography, 22 was obtained as a pale yellow solid.

Isomer 22: M.p. = 174 °C; $^1$H NMR (400 MHz, acetone-$d_6$) \( \delta \) ppm 7.44-7.40 (m, 2H), 7.17-7.09 (m, 5H), 7.00-6.95 (m, 2H), 6.81-6.75 (m, 1H), 6.17 (dd, \( J = 10.0, 1.7, 1.6 \) Hz, 1H), 6.04 (ddd, \( J = 10.0, 5.2, 2.9 \) Hz, 1H) 5.24 (ddd, \( J = 4.8, 2.9, 1.7 \) Hz, 1H), 4.59 (m, 1H), 4.36 (dd, \( J = 29.6, 16.9 \) Hz, 2H), 4.10 (dd, \( J = 39.7, 16.9 \) Hz, 2H), 3.33 (s, 3H); $^{13}$C NMR (101 MHz, acetone-$d_6$) \( \delta \) ppm 169.1, 167.9, 150.1, 139.1, 130.5, 129.2, 128.4, 127.9, 127.8, 125.9, 121.9, 117.3, 72.8, 64.3, 63.21, 63.16, 46.7; $^{11}$B NMR (96 MHz, acetone-$d_6$) \( \delta \) ppm 10.3; HRMS (ESI) calcd. for [M+H]$^+$($C_{21}H_{22}N_2O_5^{11}$B): 393.1622 found: 393.1624.
Isomer 22*: M.p. = 152 °C; $^1$H NMR (400 MHz, acetone-$d_6$) δ ppm 7.60-7.58 (m, 2H), 7.37-7.31 (m, 5H), 7.22-7.20 (m, 2H), 6.98-6.94 (m, 1H), 6.19 (ddd, $J = 10.5, 4.8, 2.4$ Hz, 1H), 5.68 (ddd, $J = 10.5, 1.7, 1.5$ Hz, 1H), 5.11 (m, 1H), 4.19 (dd, $J = 88.8, 16.9$ Hz, 2H), 4.11 (dd, $J = 54.0, 16.9$ Hz, 2H), 4.11-4.07 (m, 1H), 3.13 (s, 3H); $^{13}$C NMR (101 MHz, acetone-$d_6$) δ ppm 169.4, 167.8, 149.9, 139.9, 130.2, 129.6, 129.1, 129.0, 127.0, 125.1, 122.1, 117.1, 72.8, 63.08, 63.03, 49.8, 47.3, 45.4; $^{11}$B NMR (96 MHz, acetone-$d_6$) δ ppm 10.6; HRMS (ESI) calcd. for [M+H]$^+$($C_{21}H_{22}N_2O_5^{11}$B): 393.1622 found: 393.1632.

**Conversion of 22 to 1,2-diphenyl-1H-pyrrole 3k under basic conditions.**

Oxazine 22 (6.0 mg, 0.015 mmol) was dissolved in acetone-$d_6$ (0.4 mL). NaOD (1M in water, 15 µL, 0.015 mmol) was then added and the reaction was directly followed by $^1$H and $^{11}$B NMR. After one night, a 32% conversion was observed with no further evolution if the reaction was left longer at room temperature. NaOD (1M, 30 µL, 0.030 mmol) was finally added to observe complete consumption of the starting oxazine, followed by DCI (1M in D$_2$O, 15 µL, 0.015 mmol). After 15 min, a full conversion into the corresponding pyrrole was observed. The reaction mixture was poured into DCM (2 mL), and water (1 mL) was added. The aqueous layer was extracted with DCM (3 x). The organic phase was dried over MgSO$_4$, and filtered over a pad of silica gel and eluted with DCM to give pyrrole 3k (2.8 mg, 85%).

**Conversion of 22’ to 2-phenylfuran 31 under acidic conditions**

Oxazine 22’ (6.8 mg, 0.017 mmol) was dissolved in acetone-$d_6$ (0.4 mL). DCI in D$_2$O (1M, 18 µL, 0.018 mmol). After full conversion of the starting oxazine, reaction mixture was poured into DCM (1 mL). NaOH (1M, 0.2 mL) was added. The aqueous layer was extracted with DCM (3 x),
dried over MgSO$_4$, filtered and purified over a pad of silica (DCM). Furan 31 was isolated. (2.4 mg, quantitative)

**Isolation of by-product 36**

Oxazine 22* (25.2 mg, 0.064 mmol) was dissolved in acetone-$d_6$ (0.7 mL). DCl (1M in D$_2$O, 64 µL, 0.064 mmol) was then added and the reaction was followed by $^1$H and $^{11}$B NMR. After full conversion of the starting oxazine, the reaction mixture was extracted with DCM (3 x), dried over MgSO$_4$, filtered and concentrated. The crude yellow solid was suspended in CHCl$_3$ (0.5 mL) and filtered. The resulting solid was washed with CHCl$_3$ (3 x). (4 mg of 36, 25%).

**2-Phenylfuran 31.**$^{29}$

$^1$H NMR (400 MHz, CDCl$_3$) δ ppm $^1$H NMR (400 MHz, CDCl$_3$) δ \(7.71 - 7.66\) (m, 2H), \(7.48\) (dd, \(J = 1.8, 0.7\) Hz, 1H), \(7.42 - 7.36\) (m, 2H), \(7.27\) (m, 1H), \(6.66\) (dd, \(J = 3.4, 0.7\) Hz, 1H), \(6.48\) (dd, \(J = 3.4, 1.8\) Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ ppm 154.1, 142.2, 131.0, 128.8, 127.5, 123.9, 111.8, 105.1.

**6-Methyl-2-(phenylamino)-1,3,6,2-dioxazaborocane-4,8-dione 36.**

$^1$H NMR (400 MHz, acetone-$d_6$) δ ppm \(7.07\) (m, 2H), \(6.85\) (d, \(J = 7.7\) Hz, 2H), \(6.62\) (m, 1H), \(4.74\) (bs, 1H), \(4.25\) (d, \(J = 17.2\) Hz, 2H), \(4.09\) (d, \(J = 17.2\) Hz, 2H), \(3.01\) (s, 3H); $^{13}$C NMR (101 MHz, acetone-$d_6$) δ ppm 167.6, 147.2, 129.0, 117.4, 116.2, 62.1, 45.8, boron-carbon bound was not visible; $^{11}$B NMR (96 MHz, acetone-$d_6$) δ ppm 9.9; HRMS (ESI) calcd. for [M+H]$^+$\((C_{11}H_{14}N_{2}O_{4})^{11}\)B): 249.1047 found: 249.1042.
Synthesis and Suzuki-Miyaura coupling of boronated oxazine MIDA ester 38 with 2-bromotoluene

To a suspension of diene 37 (229 mg, 0.80 mmol) in AcOEt (10 mL), was added nitrosobenzene (221 mg, 2.06 mmol). The reaction mixture was stirred at 50 °C for 22 h. The solvent was evaporated and the crude product was purified by solid phase silica gel chromatography (Et₂O:MeCN 8/2, Rₐ = 0.4). 38 (229 mg, 73%). M.p. = 153 °C; ¹H NMR (400 MHz, acetone-d₆) δ ppm 7.40 – 7.25 (m, 7H), 7.17 (m, 2H), 6.94 (m, 1H), 4.67 (t, J = 2.4 Hz, 2H), 3.97 (t, J = 2.4 Hz, 2H), 3.94 (d, J = 16.8 Hz, 2H), 3.43 (d, J = 16.8 Hz, 2H), 3.07 (s, 3H); ¹³C NMR (101 MHz, acetone-d₆) δ ppm 168.2, 151.5, 144.4, 141.9, 129.7, 129.5, 129.4, 128.2, 122.5, 116.2, 72.2, 63.0, 58.3, 47.3 (boron-carbon bound was not visible); ¹¹B NMR (96 MHz, acetone-d₆) δ ppm 10.4; HRMS (ESI) calcd. for [M+H]+ ([C₂₁H₂₂N₂O₅]⁺): 393.1618 found: 393.1622.

In a flask under an inert atmosphere was added oxazine 38 (41 mg, 0.10 mmol), Pd(OAc)₂ (1.2 mg, 0.0053 mmol), SPhos (4.3 mg, 0.010 mmol) and 2-bromotoluene (14 µL, 0.11 mmol) in dioxane (2 mL). An aqueous solution of K₃PO₄ (3M, 190 mL, 0.57 mmol) previously degassed with Ar for 15 min was then added. The orange reaction mixture was stirred at 60 °C overnight. Et₂O (5 mL) and NaOH (1M, 5 mL) were added in the reaction mixture. Aqueous phase was extracted with Et₂O (3 x) and the organic layer was dried over MgSO₄, filtered and concentrated under vacuum. Crude compound was purified by silica gel chromatography (hexane/AcOEt 95/5, Rₐ = 0.4). 39 (27 mg, 71%). M.p. = 161 °C; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.40 – 6.83 (m, 14H), 4.58 (s, 2H), 4.12 (s, 2H), 2.00 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ ppm 150.2, 138.9, 137.1, 136.1, 134.1, 131.0, 130.3, 130.0, 129.1, 128.2, 128.1, 127.6, 127.2, 125.8, 122.8, 116.2, 72.0, 55.4, 19.7; HRMS (ESI) calcd. for [M+H]+ ([C₂₃H₂₂NO]⁺): 328.1689 found: 328.1701.

ASSOCIATED CONTENT
Supporting Information

Spectral data of all pyrrole and oxazine compounds; X-ray structural data of 22'. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES


(14) The cycloadduct 11 was identified (NMR experiment, D$_6$-Me$_2$CO by comparison of its $^1$H spectrum with that of the corresponding MIDA cycloadduct 14a).


