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Access to Fused Pyrroles from Cyclic 1,3-Dienyl Boronic Esters and Arylnitroso Compounds

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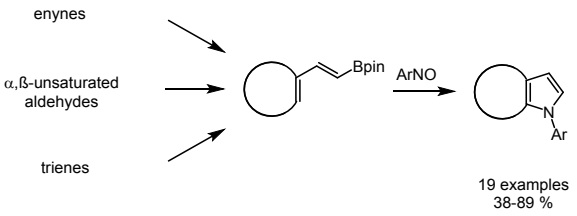
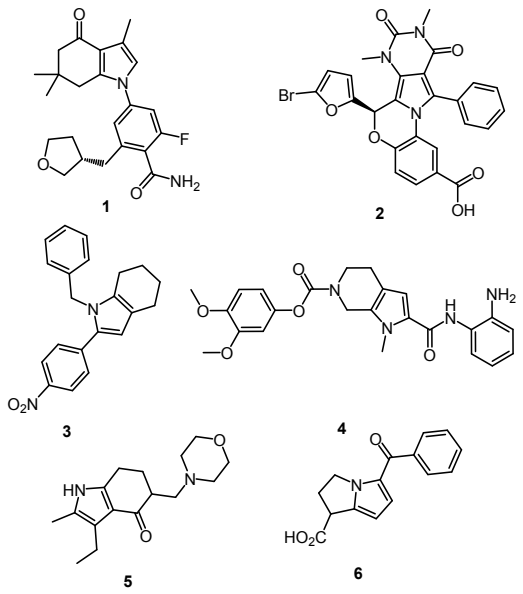


ABSTRACT. Complimentary to classical hydroboration and boron-Wittig reactions, a new, efficient access to cyclic 1,3-dienyl boronic esters has been developed *via* diene or triene metathesis. Subsequently, fused pyrroles were synthesized with a broad substrate scope from the reaction of cyclic 1,3-dienyl boronic esters with arylnitroso compounds using a one-pot hetero-Diels−Alder/ring contraction sequence.

INTRODUCTION

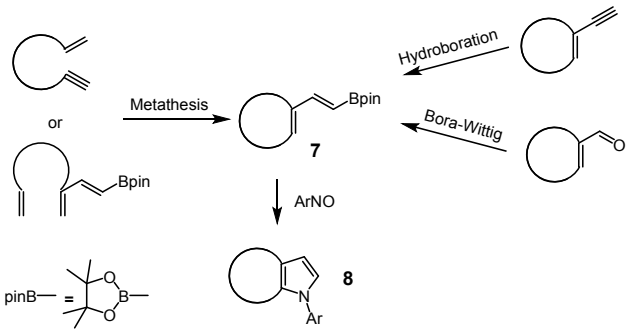
Nitrogenous heterocycles are one of the most commonly investigated and essential families of organic compounds, mainly due to their presence in many important molecules used in various fields ranging from life to materials sciences. Pyrroles and their derivatives in particular occupy a prominent place in this family, for example, as basic structural units in many natural products,[1] such as the porphyrins of heme, the constituents of hemoglobins and oxygen-carrying myoglobins, and chlorophyll, a pigment essential to life. They are also found in vitamin B12 and in many alkaloids isolated from marine organisms such as lamellarins [2] or spongiacidin B.[3] In addition to natural products, many pyrrole derivatives of synthetic origin have remarkable biological activities, including anticancer, anti-inflammatory, antibiotic, anti-HIV, anti-tuberculosis, antimalarials, fungicides, etc. Some of them are used for medicinal purposes, such as atorvastatin and tolmetin, or for plant treatments, such as chlorfenapyr.[4]

Among all the molecules of interest having a pyrrole core, a number of them have also a cyclic structure juxtaposed with this moiety. While benzofused derivatives, as indoles, isoindoles and carbazoles, are the most prominent examples of this family, other compounds for which the adjacent ring is not aromatic also exhibit remarkable biological activities. This includes, in particular, **1** which acts as an inhibitor of the HSP90 protein for regulation of the dopaminergic pathway in Parkinson's disease,[5] **2** which blocks CFTR protein for the treatment of severe diarrhea,[6] **3** for the prevention of cellular replication of hepatitis C virus (HCV),[7] and **4**, an inhibitor of histone deacetylases that play an important role in the regulation of gene expression.[8] Also, ketorolac **5** is a nonsteroidal anti-inflammatory drug with analgesic activity [9] and molindone **6** (Moban) has been used in the United States as an antipsychotic for the treatment of schizophrenia.[10]



The synthesis of differently substituted pyrroles has been the subject of a great deal of work and there are numerous reviews describing various strategies.[11,4c] In addition to the named, classical, methods and their variants, including Hantzsch,[12] Knorr,[13] Paal-Knorr [14] reactions, or the more recently reported van Leussen [15] and Barton-Zard syntheses,[16] a number of other original strategies based on multicomponent [17] and (or) transition metal catalyzed processes [18] have also been developed, as has the use of 3,6-dihydro-1,2-oxazines as precursors.[19] Indeed, some of these approaches have been applied to fused pyrroles.[20] We recently proposed a new mild synthesis of *N*-aryl pyrroles from dienyl pinacol boronic esters and nitrosoarenes [21] and, in this paper, we expand the scope of this methodology to the preparation of fused pyrroles **8** (Scheme 1) [22] and also include new metathesis reactions to access cyclic precursors **7**, which complements the classical routes usually employed for the synthesis of these valuable building blocks.[23]

Scheme 1. Synthesis of cyclic dienyl boronic esters 7 and their conversion to fused pyrroles 8.

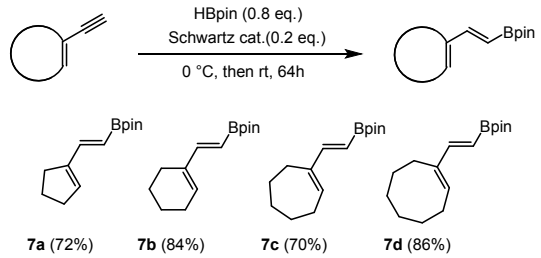


RESULTS AND DISCUSSION

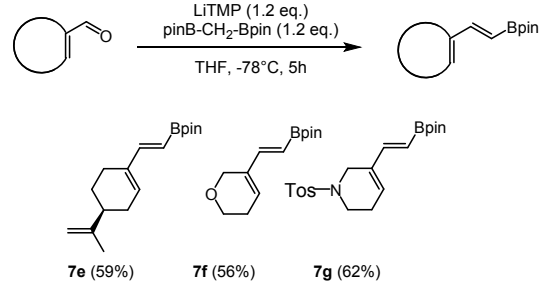
1,3-Dienyl boronic esters **7a-d** were first prepared in 70-86% yields by hydroboration of the corresponding 1,3-enynes with pinacolborane in the presence of the Schwartz′ reagent (Scheme 2).[24] In parallel, an *(E)*-stereoselective boron-Wittig reaction between bis[(pinacolato)boryl] methane and α,β-unsaturated aldehydes with lithium tetramethylpiperidide as base furnished **7e-g** in good yields.[25]

Scheme 2. Synthesis of cyclic dienyl boronic esters 7a-g by hydroboration and boron-Wittig reactions.

A. *Hydroboration*

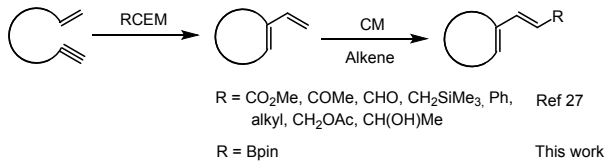


B. *Boron-Wittig reaction*

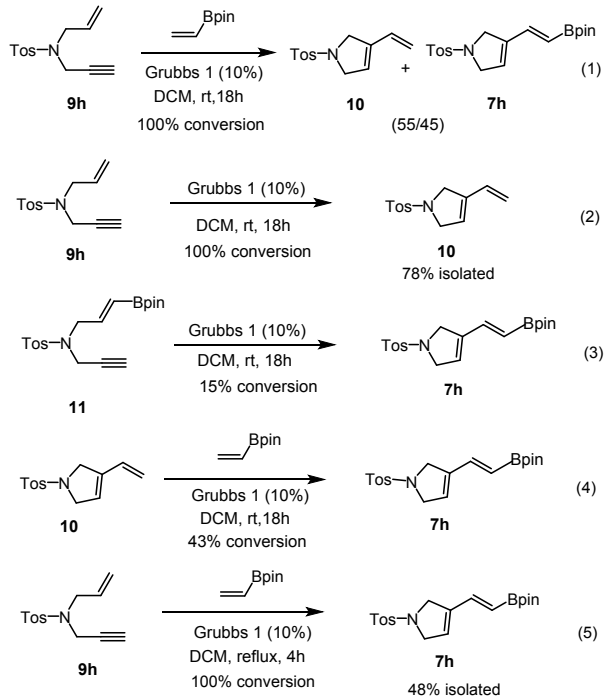


To increase the range of cyclic dienyl boronic esters, we then turned our attention to another approach, i.e. the ring closing enyne metathesis (RCEM), a powerful tool for the synthesis of 1,3-diene.[26] Such a reaction could be followed by a cross-metathesis reaction (CM) that then allowed the post-functionalization of the initial dienyl structure. The reactants used in this second step were generally mono-substituted alkenes, whether activated or not.[27] Although 2-vinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (vinyl-Bpin) has been used occasionally as a metathesis partner with dienes,[28] to our knowledge, it has been never involved in a one-pot, two-step sequence, making such an approach both attractive and useful to access a wider range of boronate-substituted dienes (Scheme 3).

Scheme 3. Synthesis of cyclic dienes *via* a RCEM-CM sequence.



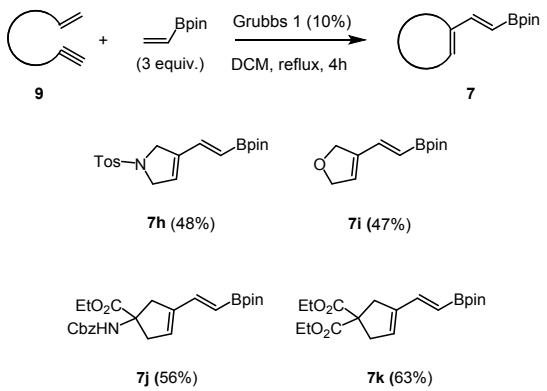
Hence, our investigations started with enyne **9h** as a model substrate. Conducting the RCEM reaction in DCM at RT for 18h in the presence of the 1st-generation Grubbs catalyst afforded a mixture of dienes **10** and **7h** (55/45 with no residual starting material) (Eq 1). In the absence of vinyl-Bpin, the ring closure was complete under the same experimental conditions (Eq 2). Conversely, a 15% conversion was observed with enyne **11** where the boronic ester function was already present on the alkene moiety (Eq 3).[29] In parallel, cross metathesis of the isolated diene **10** with vinyl-Bpin was carried out, to deliver only moderate amounts of **7h** (Eq 4). These results suggest that the cyclization step takes place first in the tandem RCEM/CM sequence. Finally, the best results were obtained by conducting this process at reflux in DCM with three equivalents of vinyl-Bpin over 4h to give boronate-substituted diene **7h** in 48% isolated yield (Eq 5).[30]



The scope of this approach was then evaluated under these optimized conditions with various other enynes

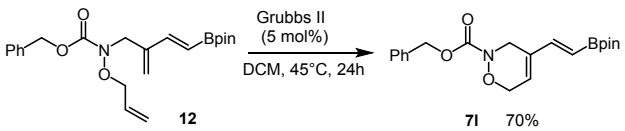
(Scheme 4). As previously observed for **7h**, besides variable amounts of pinBCH=CHBpin resulting from the self-coupling of pinacol vinylboronate, dienes **7h**-**7k** were obtained as (*E*)-isomers ($^3J_{H-H}$ = 18.2 to 18.5 Hz) in moderate isolated yields mainly due to the low stability of these compounds during the purification step, in particular in the case of the dihydrofuran derivative **7i**.

Scheme 4. Synthesis of cyclic dienyl boronic esters 7h-7k *via* a RCEM/CM sequence.



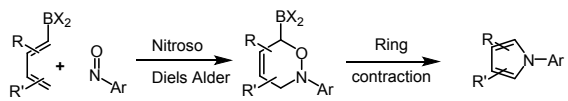
Having at our disposal the triene **12**,[31] we also envisaged whether this compound could constitute a valuable precursor of a different cyclic dienyl boronic ester **7l**, provided that the metathesis reaction was regioselective. This was indeed found to be the case and, after heating in DCM for 24h at 45°C in the presence of the Grubbs 2nd generation catalyst, the expected boronate **7l** was obtained in 70% yield, without any traces of the 7-membered ring (Scheme 5). Its structure was confirmed by single crystal X-ray diffraction analysis.[32]

Scheme 5. Synthesis of diene 7l from 12 *via* a RCM reaction.



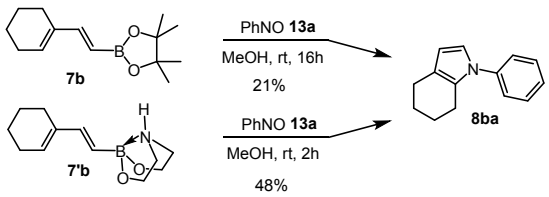
Having developed access to a series of different cyclic boryl dienes **7a-l**, we then undertook to evaluate their reactivity in the presence of aryl nitroso compounds in order to obtain the corresponding fused pyrroles. Mechanistic aspects of this reaction have been already investigated and we rationalized the observed formation of pyrroles by a [4+2]-Diels−Alder cycloaddition, followed by a ring contraction of the resulting oxazine (Scheme 6).[21]

Scheme 6. Proposed mechanism for the formation of pyrroles from the corresponding boronodienes and arylnitroso compounds.



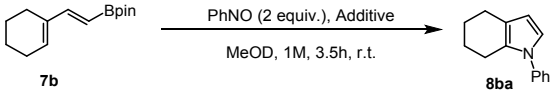
To our knowledge, the only example of cyclic reactants described to date was reported by us, giving a low yield of pyrrole **8ba** from **7b** and nitrosobenzene **13a**. Replacement of pinacol by diethanolamine (which causes quaternization of boron, making the diene more electron-rich, and thus increases the reactivity towards ArNO) had a beneficial effect as exemplified in Scheme 7.[21]

Scheme 7. Synthesis of pyrrole 8ba from 7b or its diethanolamine derivative 7'b.[21]



However, although tetracoordinated diethanolamine esters, such as **7'b**, appear *a priori* to be more suitable in these cycloaddition reactions through higher reactivity towards nitroso species, their synthesis is sometimes challenging, often involving only modest yields due to the products not always being crystalline or readily isolated in a pure form.[33] Pinacol boronate esters remain the most readily accessible, stable derivatives and are by far the most used in organic synthesis. Therefore, we decided to study the influence of an additional, external base/nucleophile, that could be added *in situ* to achieve quaternization of the boron atom as in the case of **7'b** and, thus, significantly potentially increase the yield in the nitroso additions reactions. Indeed, this strategy was viable and improved reactivity was observed with different basic/nucleophilic additives compared to those involving the pinacol ester alone, as exemplified in Table 1.

Table 1. Optimization of the Diels-Alder cycloaddition/cycle contraction cascade for 7b and PhNO.



entry	additive	equiv.	yield (%)[a]
1	-	-	21
2	PPh_3	1.0	20
3	TMP	1.0	27
4	DMAP	1.0	30
5	Diethanolamine	1.0	33
6	Bu_4NOH	1.0	36
7	DBN	1.0	44
8	DBU	1.0	49
9	DBU	0.8	51 (41)[b]
10	DBU	0.5	26
11	DBU [c]	0.8	44
12	DBU, mol. sieves [d]	0.8	49

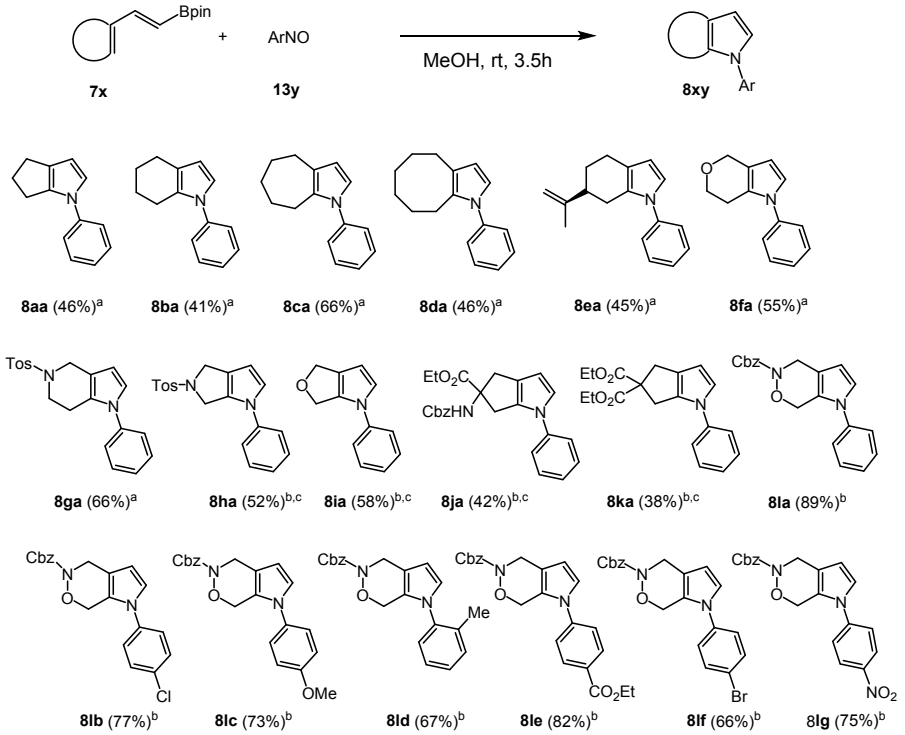
[a] Yield determined by ^{1}H NMR on the reaction crude with 1,3,5-trimethoxybenzene as internal standard. [b] Yield in isolated product after

purification by silica gel chromatography. [c] Dropwise addition of a diene solution to a mixture DBU and PhNO.[d] Under argon with anhydrous DBU and molecular sieves previously activated under 1 mbar at 150 °C for 16 h.

Examining Table 1, it can be seen that the addition of triphenylphosphine was only poorly effective (20%, entry 2) compared with no additive (entry 1). However, the use of an amine, in general terms, enhanced product yields, perhaps surprisingly so considering that even the use of a highly hindered secondary amine, i.e. 2,2,6,6,6-tetramethylpiperidine (TMP, entry 3), increased the yield of pyrrole **8ba** to 27%. The use of the more nucleophilic DMAP did not show any marked enhancement over the more hindered TMP (entry 4). Diethanolamine and tetra-*n*-butylammonium hydroxide both gave slightly better results (entries 5 and 6). However, it was the bicyclic and stronger amidine bases, DBN and DBU, that were the most efficient at assisting the conversion of diene **7b** to the pyrrole **8ba** (entries 7 and 8). Focussing more on the use of DBU, it was found that its amount could be advantageously reduced to 0.8 equivalents (see entry 9 and 10). Further optimization by slow addition of the diene to the nitrosobenzene/DBU mixture or the presence of molecular sieves gave no positive significant improvement (see entries 11-12). Hence, using the best conditions developed herein, the yields, although still moderate, were significantly improved up to 41% (entry 9), therefore providing a useful entry to the desired pyrrole systems considering that two successive reactions were involved in this process.

We then examined the wider application of this reaction to establish the scope of the Diels Alder cycloaddition/cycle contraction cascade to access fused pyrroles from a variety of cyclic dienes **7**.

Scheme 8. Synthesis of fused pyrroles 8 from cyclic dienyl boronic esters 7.



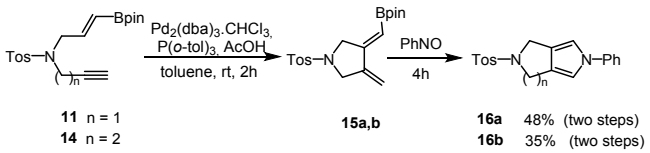
[a] With addition of 0.8 equiv. of DBU.[b] Without DBU.[c] Overall yield starting from enynes **9h-k** (three steps sequence).

As can be seen in Scheme 8, the borodiene additions proceeded in moderate to good yields using nitrosobenzene, i.e. yields varying from 41-89%. There does not appear to be any particular trend with respect to yields and ring size or electronics. Running the reactions of dienes **7b**, **7c** and **7g** with nitrosobenzene and without the addition of DBU caused a considerable drop in the yields of cycloadduct in both cases, i.e. from 41% to 21% (for **7b**), 66% to 31% (for **7c**) and 66% to 42% (for **7g**). This reinforces the positive role that DBU plays in this reaction, but it is not clear precisely what that is. In view of the production of azo and azo-oxide side products in competition with the main cycloaddition reaction,[21] DBU may act to slow the disproportion reaction relative to the cycloaddition-rearrangement to the pyrrole, hence improving overall conversion. Nevertheless, Scheme 8 also shows that the DBU approach is not absolutely necessary if the diene is reactive enough. Hence, the reactions of substituted nitrosobenzenes to diene **7l** successfully produced a range of 6,5-fused cycloadducts in 66-89% yields. The diene **7l** seems to be the most reactive system examined in this reaction to date, whether reacting with either electron rich or electron deficient nitrosobenzenes (see adducts **8la-8lg**, Scheme 8). All the NMR data were in agreement with the

proposed structures and, in the case of **8ga**, it was confirmed by single crystal X-ray diffraction analysis.[32]

The successful application of the aryl nitroso-cycloaddition to the cyclic boronate-substituted diene, rearrangement and pyrrole formation was also extended to outer-ring diene systems of type **15** (Scheme 9), thus giving access to 3,4-connected compounds **16**, another family of annulated pyrroles. To exemplify this type of approach, the precursors **15a** and **15b** were synthesized by a palladium-catalyzed cycloisomerization of the corresponding enynes **11** and **14** according our previously reported procedure.[34] Due to a low stability observed during purification by chromatography on silica gel, these dienes were not isolated and we carried out the following step in the same pot without removing the palladium catalyst. Products **16a-b** were thus obtained in moderate yields, mainly due to a partial deborylation of **15** during the cycloisomerisation process as previously observed for similar processes (Scheme 9).[34]

Scheme 9. Synthesis of fused pyrroles 16a-b from enynes 11 and 14.



CONCLUSION

In summary, we have realized the synthesis of a series of fused pyrroles from the corresponding 1,3-dienyl boronate esters, which adds to the chemist's armory of classical synthetic methods for accessing pyrrole-containing products and especially the more unusual fused bicyclic systems. For this particular application, a new route involving a ring closing enyne metathesis / cross-metathesis sequence was also developed to access novel boryl dienes that, subsequently, give access to a supplementary range of products with diversified structures.

EXPERIMENTAL SECTION

Solvents were freshly distilled from sodium/benzophenone (THF, toluene) or phosphorus pentoxide (DCM). Methanol and other commercially available chemicals were used without further purification. Column chromatography purifications were performed over silica gel (Merck Geduran 60, 0.063–0.200 mm). Flash chromatography purifications were performed on a Grace Reveleris™ with Puriflash™ 15µm flash cartridges (Interchim). NMR spectra were recorded at 300 or 400 MHz for ^{1}H, 75 or 101 MHz for ^{13}C and 96 or 128 MHz for ^{11}B. ^{1}H and ^{13}C NMR chemical shifts were referenced to Me_4Si as internal reference, and ^{11}B NMR chemical shifts to external $BF_3{\cdot}OEt_2$. All ^{13}C and ^{11}B NMR were proton-decoupled. High-resolution mass spectra (HMRS) were obtained on a Q-TOF instrument and measured using either electrospray ionization (ESI) or atmospheric solids analysis probe (ASAP). X-ray crystallographic data were collected on an APEXII crystal diffractometer. Specific rotation (in deg cm^3 g^{-1}) was measured on a Perkin Elmer-341 polarimeter. Melting points were measured on a melting point apparatus. Stuart SMP10.

1-Ethynylcyclopent-1-ene,[35] 1-ethynylcyclohex-1-ene,[36] 1-ethynylcyclohept-1-ene,[37] 1-ethynylcyclooct-1-ene,[37] 5,6-dihydro-*2H*-pyran-3-carbaldehyde,[38] 1-tosyl-1,2,3,6-tetrahydropyridine-4-carbaldehyde,[39] **9h**,[40] **10**,[41] **11**,[34] **9j**,[42] **9k** [43] were prepared as previously described. Perillaldehyde and 3-(allyloxy)-1-propyne **9i** are commercially available.

General procedure for the synthesis of boronates 7a-7d by catalytic hydroboration. To a mixture of 1-ethynylcycloalk-1-ene (1.86 mmol) and Schwartz catalyst (104 mg, 0.37 mmol) at 0 °C under argon atmosphere, was added dropwise H-Bpin (216 µL, 1.49 mmol). The reaction mixture was stirred at room temperature for 64 h, then diluted with Et_2O (10 mL). H_2O (5 mL) was cautiously added. The aqueous layer was extracted with Et_2O (3×15 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous $MgSO_4$ and evaporated. The crude product was purified by filtration on silica gel pad, eluted with a 95/5 pentane/Et_2O mixture or by distillation.

*(E)-2-(2-(Cyclopent-1-en-1-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7a**)*. 158 mg (72%). Colorless oil, bp = 70-80°C/0.1 mbar. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, *J* = 18.0 Hz, 1H), 5.94-5.86 (m, 1H), 5.41 (d, *J* = 18.0 Hz, 1H), 2.44 (t, *J* = 7.6 Hz, 4H), 1.91 (quint, *J* = 7.6 Hz, 2H), 1.28 (s, 12H). The spectroscopic data match with those reported in the literature.[44]

*(E)-2-(2-(Cyclohex-1-en-1-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7b**)*. 197 mg (84%). Colorless oil, bp = 90-110°C/0.1 mbar. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J* = 18.2 Hz, 1H), 6.01-5.92 (m, 1H), 5.42 (d, *J* = 18.2 Hz, 1H), 2.19-2.10 (m, 4H), 1.70-1.54 (m, 4H), 1.27 (s, 12H). The spectroscopic data match with those reported in the literature.[44]

*(E)-2-(2-(Cyclohept-1-en-1-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7c**)*. 325 mg (70%). Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (d, *J* = 18.2 Hz, 1H), 6.09 (t, *J* = 6.8 Hz, 1H), 5.45 (d, *J* = 18.2 Hz, 1H), 2.37-2.29 (m, 2H), 2.29-2.19 (m, 2H), 1.80-1.70 (m, 2H), 1.54-1.42 (m, 4H), 1.26 (s, 12H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 153.9, 144.4, 139.1, 83.1, 32.3, 29.0, 26.7, 26.4, 26.2, 24.9. The carbon α to boron was not observed. ^{11}B{^{1}H} NMR (96 MHz, $CDCl_3$) δ 29.8. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{15}H_{25}O_2{}^{11}BNa$ 271.1840, found 271.1843.

*(E)-2-(2-(Cyclooct-1-en-1-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7d**)*. 421 mg (86%). Colorless oil, bp = 100-120°C/0.1 mbar. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (d, *J* = 18.2 Hz, 1H), 5.92 (t, *J* = 8.3 Hz, 1H), 5.48 (d, *J* = 18.2 Hz, 1H), 2.44-2.35 (m, 2H), 2.27-2.15 (m, 2H), 1.58-1.36 (m, 8H), 1.28 (s, 12H). ^{13}C{^{1}H} NMR (75 MHz,

$CDCl_3$) δ 153.0, 140.9, 137.3, 83.2, 30.3, 28.6, 27.6, 27.0, 26.2, 25.0, 23.9. The carbon α to boron was not observed. $^{11}B\{^1H\}$ NMR (96 MHz, $CDCl_3$) δ 29.6. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{16}H_{27}O_2{}^{11}BNa$ 285.1996, found 285.1997.

General procedure for the synthesis of boronates 7e-7g via a Boron-Wittig reaction. An oven-dried Schlenk charged with bis(4,4,5,5-tetramethyl- 1,3,2-dioxaborolan-2-yl)methane (429 mg, 1.6 mmol) and dry THF (2.1 mL) was sealed under argon with a septum cap. The reaction vial was cooled to 0°C, and a solution of LiTMP (235 mg, 1.6 mmol) in dry THF (1.6 mL) was added dropwise. The reaction was allowed to stir for 5 min. at 0°C and then cooled to -78°C. After addition of a solution of the aldehyde (1.3 mmol) in dry THF (2.8 mL), the reaction mixture was stirred at -78°C for additional 5 h. Upon completion, the solvent was removed under reduced pressure. The product was isolated by silica gel chromatography (cyclohexane/EtOAc: 100/0 to 90/10).

*(S,E)-4,4,5,5-Tetramethyl-2-(2-(4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)vinyl)-1,3,2-dioxaborolane (**7e**)*. 76 mg (59%). Colorless oil, R_f= 0.52 (cyclohexane/EtOAc: 95/5). ^1H NMR (300 MHz, $CDCl_3$) δ 7.03 (d, *J* = 18.2 Hz, 1H), 6.00-5.92 (m, 1H), 5.42 (d, *J* = 18.2 Hz, 1H), 4.76-4.64 (m, 2H), 2.37-2.22 (m, 2H), 2.21-2.01 (m, 3H), 1.94-1.82 (m, 1H), 1.72 (d, *J* = 1.0 Hz, 3H), 1.55-1.38 (m, 1H), 1.26 (s, 12H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 152.7, 149.5, 136.9, 133.5, 112.7 (br), 108.9, 83.1, 41.2, 31.7, 27.4, 24.9, 24.3, 20.9. $^{11}B\{^1H\}$ NMR (96 MHz, $CDCl_3$) δ 31.0. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{17}H_{27}O_2{}^{11}BNa$ 297.1996, found 297.1996.

*(E)-2-(2-(3,6-Dihydro-2H-pyran-4-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7f**)*. 174 mg (56%). Colorless oil, R_f= 0.24 (Cyclohexane/EtOAc: 9/1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.91 (d, *J* = 18.7 Hz, 1H), 6.03 (s, 1H), 5.26 (d, *J* = 18.7 Hz, 1H), 4.35-4.27 (m, 2H), 3.74 (t, *J* = 5.5 Hz, 2H), 2.30-2.23 (m, 2H), 1.26 (s, 12H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 148.8, 136.2, 129.9, 83.4, 65.3, 64.2, 26.1, 24.9. The carbon α to boron was not observed. $^{11}B\{^1H\}$ NMR (128 MHz, $CDCl_3$) δ 30.4. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{13}H_{21}O_3{}^{11}BNa$ 259.1476, found, 259.1479.

*(E)-5-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-1-tosyl-1,2,3,6-tetrahydropyridine (**7g**)*. 318 mg (62%). White solid, mp = 130-132 °C. R_f= 0.18 (cyclohexane/EtOAc: 9/1). ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 6.90 (d, *J* = 18.6 Hz, 1H), 5.97-5.92 (m, 1H), 5.36 (d, *J* = 18.6 Hz, 1H), 3.74-3.66 (m, 2H), 3.17 (t, *J* = 5.7 Hz, 2H), 2.42 (s, 3H), 2.38-2.29 (m, 2H), 1.26 (s, 12H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.7, 143.7, 133.43, 133.41, 130.3, 129.8, 127.8, 83.5, 44.4, 42.7, 26.1, 24.9, 21.6. The carbon α to boron was not observed. $^{11}B\{^1H\}$ NMR (96 MHz, $CDCl_3$) δ 30.1. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{20}H_{28}NO_4{}^{11}BNaS$ 412.1724, found 412.1724.

General procedure for the synthesis of boronates 7h-7k *via* a RCEM-CM sequence. In a dry 2-neck round-bottom flask, under an argon atmosphere, was dissolved enyne (1.0 mmol) in anhydrous DCM (35 mL). To this solution was added vinylboronic acid pinacol ester (509 µL, 3.0 mmol). The resulting mixture was degassed by slow bubbling of argon for 10 minutes before the introduction of Grubbs 1 catalyst (81 mg, 0.1 mmol). The reaction mixture was stirred at reflux for 4 hours. DCM was evaporated and the product was purified by flash chromatography (cyclohexane/EtOAc: 100/0 to 95/5). The reaction was also carried out on a 2.5 mmol scale for **7h**.

*(E)-3-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-1-tosyl-2,5-dihydro-1H-pyrrole (**7h**)*. 180 mg (48%). 650 mg (69%) on a 2.5 mmol scale. Colorless oil, R_f= 0.59 (cyclohexane/EtOAc: 95/5). ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 6.98 (d, *J* = 18.4 Hz, 1H), 5.72 (brs, 1H), 5.34 (d, *J* = 18.4 Hz, 1H), 4.21 (s, 4H), 2.42 (s, 3H), 1.26 (s, 12H). The spectroscopic data match with those reported in the literature.[34]

*(E)-2-(2-(2,5-Dihydrofuran-3-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7i**)*. 103 mg (47%). Colorless oil, R_f= 0.69 (cyclohexane/EtOAc: 8/2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.16 (d, *J* = 18.5 Hz, 1H), 5.97 (brs, 1H), 5.31 (d, *J* = 18.3 Hz, 1H), 4.79-4.67 (m, 4H), 1.27 (s, 12H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 141.4, 139.7, 128.3, 83.6, 76.3, 74.2, 24.9. The carbon α to boron was not observed. $^{11}B\{^1H\}$ NMR (128 MHz, $CDCl_3$) δ 29.3. HRMS (ESI+) $(M+H)^+$ calculated for $C_{12}H_{20}{}^{11}BO_3$ 223.1505, found 223.1495.

*Ethyl (E)-1-((benzyloxycarbonyl)amino)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)cyclopent-3-ene-1-carboxylate (**7j**)*. 247 mg (56%). Colorless oil, R_f= 0.37 (cyclohexane/EtOAc: 8/2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.37-7.31 (m, 5H), 7.16 (d, *J* = 18.2 Hz, 1H), 5.80 (s, 1H), 5.40 (brs, 1H), 5.39 (d, *J* = 18.2 Hz, 1H), 5.09 (s, 2H), 4.27-4.11 (m, 2H), 3.26-3.07 (m, 2H), 2.87-2.70 (m, 2H), 1.27 (s, 12H), 1.21 (t, *J* = 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.8, 155.4, 144.8, 141.1, 136.4, 130.7, 128.6, 128.2, 128.2, 118.2 (br), 83.4, 66.8, 64.4, 61.9, 45.0, 43.1, 24.9, 14.2. $^{11}B\{^1H\}$ NMR (128 MHz, $CDCl_3$) δ 31.0. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{24}H_{32}NO_6{}^{11}BNa$ 464.2215, found 464.2218.

*Diethyl (E)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)cyclopent-3-ene-1,1-dicarboxylate (**7k**)*. Colorless oil, 229 mg (63%). R_f= 0.42 (cyclohexane/EtOAc: 8/2).^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 18.3 Hz, 1H), 5.73-5.77 (m, 1H), 5.45 (d, *J* = 18.4 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 4H), 3.10-3.15 (m, 4H), 1.27 (s, 12H), 1.25 (t, *J* = 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 172.0, 144.8, 141.3, 130.7, 118.2 (br), 83.4, 61.7, 58.9, 41.2, 39.1, 24.9, 14.1. $^{11}B\{^1H\}$ NMR (128 MHz, $CDCl_3$) δ 31.2. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{19}H_{29}NO_6{}^{11}BNa$ 387.1955, found 387.1952.

Synthesis of benzyl (*E*)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-3,6-dihydro-2H-1,2-oxazine-2-carboxylate (*7l*). In a flame dried Schlenk flask under an argon flow, boronated triene **12** (170 mg, 0.43 mmol) [31] was dissolved in anhydrous degassed dry DCM (13 mL) and Grubbs catalyst 2nd generation (18 mg, 0.021 mmol) was

added. The reaction mixture was stirred at 45 °C for 24 h. After evaporation of the solvent, the residue was purified by silica gel chromatography (cyclohexane/EtOAc: 100/0 to 80/20) to afford **7l** as a white solid (98 mg, 70%), mp = 124-5 °C. R_f= 0.05 (cyclohexane/EtOAc: 8/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.29 (m, 5H), 6.97 (d, *J* = 18.5 Hz, 1H), 5.98 (brs, 1H), 5.48 (d, *J* = 18.5 Hz, 1H), 5.21 (s, 2H), 4.53 (d, *J* = 2.7 Hz, 2H), 4.31 (d, *J* = 2.1 Hz, 2H), 1.27 (s, 12H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.5, 147.0, 136.0, 133.0, 128.7, 128.4, 128.3, 127.2, 115.8 (br), 83.6, 68.7, 67.9, 44.8, 24.9.^{11}B{^{1}H} NMR (96 MHz, $CDCl_3$) δ 30.0. HRMS (ESI+) $(M+H)^+$ calculated for $C_{20}H_{27}NO_5{}^{10}B$ 371.2019, found 371.2015.

General procedure for the synthesis of fused pyrroles 8aa to 8ga. In a flame dried round-bottom flask under an argon atmosphere, was dissolved boronated diene **7** (0.30 mmol) in MeOH (0.3 mL) and DBU (38 mg, 37µL, 0.25 mmol). The resulting mixture was stirred at room temperature for 5 minutes and PhNO (64 mg, 0.60 mmol was added. The reaction was stirred for 3.5 hours at room temperature. MeOH was evaporated and the residue was purified by silica gel chromatography (cyclohexane/EtOAc: 100/0 to 95/5).

1-Phenyl-1,4,5,6-tetrahydrocyclopenta[b]pyrrole (8aa).[45] 25 mg (46%). Yellow oil, R_f= 0.68 (pentane/Et_2O: 94/6). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.34 (m, 4H), 7.25-7.18 (m, 1H), 6.94 (d, *J* = 2.8 Hz, 1H), 6.13 (d, *J* = 2.9 Hz, 1H), 2.89 (t, *J* = 7.0 Hz, 2H), 2.70 (t, *J* = 7.0 Hz, 2H), 2.47 (p, *J* = 7.1 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 140.9, 137.2, 129.5, 129.2, 125.2, 122.4, 121.0, 105.4, 29.4, 26.9, 25.5.

*1-Phenyl-4,5,6,7-tetrahydro-1H-indole (**8ba**)*. 24 mg (41%). Colorless oil, R_f = 0.43 (cyclohexane/EtOAc: 95/5). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.38 (m, 2H), 7.33-7.27 (m, 3H), 6.77 (d, *J* = 2.6 Hz, 1H), 6.10 (d, *J* = 2.6 Hz, 1H), 2.60 (m, 4H), 1.85-1.73 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ ppm 140.4, 129.2, 128.2, 126.2, 124.6, 120.0, 119.1, 108.2, 23.8, 23.6, 23.5, 23.3. The spectroscopic data match with those reported in the literature.[21]

1-Phenyl-1,4,5,6,7,8-hexahydrocyclohepta[b]pyrrole (8ca). [45] 41 mg (66%). Yellow oil, R_f= 0.59 (cyclohexane /EtOAc: 95/5). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.39 (m, 2H), 7.36-7.30 (m, 1H), 7.29-7.23 (m, 2H), 6.60 (d, *J* = 2.7 Hz, 1H), 6.06 (d, *J* = 2.7 Hz, 1H), 2.71-2.59 (m, 4H), 1.89-1.79 (m, 2H), 1.79-1.69 (m, 2H), 1.68-1.58 (m, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 140.7, 131.9, 129.0, 126.7, 126.3, 123.9, 119.0, 109.7, 32.4, 29.0, 28.7, 27.9, 27.1.

*1-Phenyl-4,5,6,7,8,9-hexahydro-1H-cycloocta[b]pyrrole (**8da**)*. 31 mg (46%). Yellow oil, R_f= 0.63 (cyclohexane/EtOAc: 95/5). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.39 (m, 2H), 7.37-7.27 (m, 3H), 6.68 (d, *J* = 2.8 Hz, 1H), 6.06 (d, *J* = 2.8 Hz, 1H), 2.70-2.58 (m, 4H), 1.72-1.61 (m, 2H), 1.59-1.39 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 140.9, 130.1, 129.1, 126.9, 126.4, 121.7, 120.1, 108.8, 31.3, 30.2, 26.1, 26.0, 25.8, 23.3. HRMS (ESI+) $(M+H)^+$ calculated for $C_{16}H_{20}N$ 226.1590, found 226.1590.

*(R)-1-Phenyl-6-(prop-1-en-2-yl)-4,5,6,7-tetrahydro-1H-indole (**8ea**)*. 32 mg (45%). Yellow oil, R_f= 0.27 (cyclohexane). $[\alpha]^{20}_D$ = -48.2 (c= 0.01, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, *J* = 7.7 Hz, 2H), 7.33-7.28 (m, 3H), 6.80 (d, *J* = 2.9 Hz, 1H), 6.13 (d, *J* = 2.9 Hz, 1H), 4.78 (s, 2H), 2.78-2.53 (m, 4H), 2.42-2.32 (m, 1H), 2.04-1.94 (m, 1H), 1.78 (s, 3H), 1.76-1.66 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.8, 140.3, 129.3, 127.9, 126.3, 124.7, 120.4, 118.8, 109.3, 108.0, 42.9, 29.0, 28.9, 23.5, 21.0. HRMS (ASAP+) $(M+H)^+$ calculated for $C_{17}H_{20}N$ 238.1596, found 238.1591.

*1-Phenyl-1,4,5,7-tetrahydropyrano[3,4-b]pyrrole (**8fa**)*. 33 mg (55%). White solid, mp = 55-57°C, R_f= 0.19 (pentane/Et_2O : 95/5). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-7.40 (m, 2H), 7.31 (dt, *J* = 7.0, 3.0 Hz, 3H), 6.82 (d, *J* = 2.9 Hz, 1H), 6.07 (d, *J* = 2.9 Hz, 1H), 4.76 (t, *J* = 1.6 Hz, 2H), 3.93 (t, *J* = 5.5 Hz, 2H), 2.72 (t, *J* = 5.5 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 139.7, 129.4, 126.5, 124.9, 124.2, 120.5, 117.8, 105.1, 65.6, 65.1, 24.7. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{13}H_{13}NONa$ 222.0889, found 222.0889.

*1-Phenyl-5-tosyl-4,5,6,7-tetrahydro-1H-pyrrolo[3,2-c]pyridine (**8ga**)*. 70 mg (66%). Yellow solid, mp = 138-139°C, R_f= 0.27 (cyclohexane/EtOAc: 9/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.34-7.28 (m, 3H), 7.19 (d, *J* = 7.8 Hz, 2H), 6.77 (d, *J* = 2.9 Hz, 1H), 6.05 (d, *J* = 2.9 Hz, 1H), 4.23 (s, 2H), 3.39 (t, *J* = 5.7 Hz, 2H), 2.70 (t, *J* = 5.7 Hz, 2H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.5, 139.5, 134.4, 129.7, 129.5, 127.8, 126.8, 125.0, 124.3, 121.2, 115.1, 106.0, 44.6, 44.0, 23.9, 21.6. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{20}H_{20}N_2O_2NaS$ 375.1138, found 375.1140.

General procedure for the synthesis of fused pyrroles 8ha to 8ka.

In a flame dried round-bottom flask under an argon atmosphere, was dissolved in MeOH (0.3 mL) the crude boronated diene **7** (0.30 mmol) resulting from the RCEM-CM sequence after evaporation of the methylene chloride. To this mixture was added PhNO at room temperature (64 mg, 0.60 mmol). The reaction was stirred for 3.5 hours. MeOH was evaporated and the residue was purified by silica gel chromatography (cyclohexane/EtOAc: 100/0 to 95/5). The reaction was also carried out on a 1.7 mmol scale for **8ha**.

*1-Phenyl-5-tosyl-1,4,5,6-tetrahydropyrrolo[3,4-b]pyrrole (**8ha**)*. 53 mg (52%). 270 mg (47%) on a 1.7 mmol scale. Yellow oil, R_f= 0.20 (cyclohexane/EtOAc: 9/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.46-7.38 (m, 2H), 7.34-7.19 (m, 5H), 6.93 (d, *J* = 2.9 Hz, 1H), 6.07 (d, *J* = 2.9 Hz, 1H),4.67-4.59 (m, 2H), 4.51-4.44 (m, 2H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 143.6, 139.6, 134.8, 130.0, 130.0, 129.1, 127.6, 126.2, 123.5, 122.7, 120.6, 104.1, 49.6, 49.0, 21.6. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{19}H_{18}N_2O_2NaS$ 361.0981, found 361.0979.

*1-Phenyl-4,6-dihydro-1H-furo[3,4-b]pyrrole (**8ia**)*. 32 mg (58%). Colorless oil, R_f= 0.75 (cyclohexane/EtOAc: 8/2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.37 (m, 2H), 7.26-7.18 (m, 3H), 7.05 (d, *J* = 2.8 Hz, 1H), 6.15 (d, *J* = 2.8 Hz, 1H), 5.10-5.03 (m, 2H), 5.00-4.93 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 139.8, 133.5, 129.8, 126.6, 125.5, 123.2, 119.7,

103.2, 69.4, 67.6. HRMS (ASAP+) $(M+H)^+$ calculated for $C_{12}H_{12}NO$ 186.0919, found 186.0912.

*Ethyl 5-(((benzyloxy)carbonyl)amino)-1-phenyl-1,4,5,6-tetrahydrocyclopenta[b]pyrrole-5-carboxylate (**8ja**)*. 51 mg (42%). Yellow oil, R_f= 0.19 (cyclohexane/EtOAc: 9/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.28 (m, 9H), 7.23 (t, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 2.9 Hz, 1H), 6.08 (d, *J* = 2.9 Hz, 1H), 5.53 (brs, 1H), 5.15-5.01 (m, 2H), 4.29-4.11 (m, 2H), 3.82 (d, *J* = 15.7 Hz, 1H), 3.33-3.16 (m, 2H), 2.88 (d, *J* = 15.3 Hz, 1H), 1.23 (t, *J* = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 173.2, 155.5, 140.3, 136.4, 133.3, 129.6, 128.6, 128.3, 128.2, 125.6, 123.7, 123.2, 121.0, 105.2, 70.6, 67.0, 61.9, 39.4, 38.7, 14.2. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{24}H_{24}N_2O_4Na$ 427.1628, found 427.1634.

*Diethyl 1-phenyl-4,6-dihydrocyclopenta[b]pyrrole-5,5(1H)-dicarboxylate (**8ka**).* 37 mg (38%). Colorless oil, R_f= 0.61 (cyclohexane/EtOAc: 8/2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.38 (m, 2H), 7.40-7.33 (m, 2H), 7.27-7.22 (m, 1H), 6.94 (d, *J* = 2.9 Hz, 1H), 6.08 (d, *J* = 2.9 Hz, 1H), 4.24 (qd, *J* = 7.1, 1.3 Hz, 4H), 3.59 (s, 2H), 3.39 (s, 2H), 1.29 (t, *J* = 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 171.8, 140.4, 132.5, 129.6, 125.5, 125.4, 123.4, 121.1, 105.2, 65.2, 61.9, 35.1, 34.3, 14.2. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{19}H_{21}NO_4Na$ 350.1368, found 350.1360.

General procedure for the synthesis of fused pyrroles 8la to 8lg. In a flame dried round-bottom flask under an argon atmosphere, was dissolved boronated diene **7l** (0.20 mmol) and ArNO (0.40 mmol) in DCM/MeOH (6/1) (2 mL). The resulting mixture was stirred at room temperature for 24h. The solvent was evaporated and the residue was purified by silica gel chromatography (cyclohexane/EtOAc: 100/0 to 95/5).

*Benzyl 1-phenyl-4,7-dihydropyrrolo[3,2-d][1,2]oxazine-5(1H)-carboxylate (**8la**)*. 59 mg (89%). Orange oil, R_f = 0.30 (cyclohexane/EtOAc: 6/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.29 (m, 8H), 7.22-7.17 (m, 2H), 6.87 (d, *J* = 2.9 Hz, 1H), 6.19 (d, *J* = 2.9 Hz, 1H), 5.26 (s, 2H), 5.00 (s, 2H), 4.76 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 155.6, 139.1, 136.1, 129.8, 128.7, 128.4, 128.3, 126.9, 123.4, 123.1, 121.0, 114.7, 106.3, 68.0, 67.9, 45.1. HRMS (ESI+) $(M+H)^+$ calculated for $C_{20}H_{19}N_2O_3$ 335.1396, found 335.1391.

*Benzyl 1-(4-chlorophenyl)-4,7-dihydropyrrolo[3,2-d][1,2]oxazine-5(1H)-carboxylate (**8lb**)*. 57 mg (77%). Yellow oil, R_f= 0.35 (cyclohexane/EtOAc: 6/1).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.31 (m, 7H), 7.14-7.09 (m, 2H), 6.82 (d, *J* = 2.9 Hz, 1H), 6.19 (d, *J* = 2.9 Hz, 1H), 5.26 (s, 2H), 4.96 (s, 2H), 4.74 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 155.6, 137.7, 136.1, 132.6, 130.0, 128.7, 128.4, 128.3, 124.3, 123.4, 121.0, 115.1, 106.7, 68.0, 67.7, 45.1. HRMS (ESI+) $(M+H)^+$ calculated for $C_{20}H_{18}ClN_2O_3$ 369.1006, found 369.1013.

*Benzyl 1-(4-methoxyphenyl)-4,7-dihydropyrrolo[3,2-d][1,2]oxazine-5(1H)-carboxylate (**8lc**)*. 53 mg (73%). Orange oil, R_f = 0.15 **(**cyclohexane/EtOAc: 6/1) (^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.31 (m, 5H), 7.15-7.09 (m, 2H), 6.97-6.91 (m, 2H), 6.78 (d, *J* = 2.9 Hz, 1H), 6.15 (d, *J* = 2.9 Hz, 1H), 5.25 (s, 2H), 4.94 (s, 2H), 4.75 (s, 2H), 3.84 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.6, 155.6, 136.1, 132.2, 128.7, 128.4, 128.3, 124.8, 123.6, 121.3, 114.9, 114.0, 105.7, 67.9, 67.8, 55.7, 45.1. HRMS (ESI+) $(M+H)^+$ calculated for $C_{21}H_{21}N_2O_4$365.1501, found 365.1500.

*Benzyl 1-(2-methylphenyl)-4,7-dihydropyrrolo[3,2-d][1,2]oxazine-5(1H)-carboxylate (**8ld**)*. 46 mg (67%). Yellow oil. R_f = 0.25 (cyclohexane/EtOAc: 6/1).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.29 (m, 7H), 7.24 (m, 1H), 7.14 (m, 1H), 6.63 (d, *J* = 2.8 Hz, 1H), 6.16 (d, *J* = 2.8 Hz, 1H), 5.24 (s, 2H), 4.76 (s, 2H), 4.70 (s, 2H), 2.08 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 155.7, 137.9, 136.2, 135.3, 131.3, 128.7, 128.6, 128.3, 128.2, 127.4, 126.8, 124.3, 122.0, 113.0, 105.2, 67.8, 67.5, 45.0, 17.4. HRMS (ESI+) $(M+H)^+$ calculated for $C_{21}H_{21}N_2O_3$ 349.1552, found 349.1548.

*Benzyl 1-(4-(ethoxycarbonyl)phenyl)-4,7-dihydropyrrolo[3,2-d][1,2]oxazine-5(1H)-carboxylate (**8le**)*. 66 mg, (82%). Orange oil. R_f = 0.25 (cyclohexane/EtOAc: 6/1).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13-8.10 (m, 2H), 7.43-7.32 (m, 5H), 7.23-7.19 (m, 2H), 6.91 (d, *J*= 3.0 Hz, 1H), 6.22 (d, *J*= 3.0 Hz, 1H), 5.26 (s, 2H), 5.02 (s, 2H), 4.74 (s, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.8, 155.7, 142.7, 136.1, 131.4, 128.7, 128.6, 128.4, 128.3, 123.5, 122.1, 120.8, 115.9, 107.3, 68.0, 67.9, 61.4, 45.1, 14.5. HRMS (ESI+) $(M+H)^+$ calculated for $C_{23}H_{23}N_2O_5$ 407.1607, found 407.1603.

*Benzyl 1-(4-bromophenyl)-4,7-dihydropyrrolo[3,2-d][1,2]oxazine-5(1H)-carboxylate (**8lf**)*. 58 mg (66%). Yellow solid, mp = 92-95 °C. R_f = 0.35 (cyclohexane/EtOAc: 6/1,). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.52 (m, 2H), 7.44-7.31 (m, 5H), 7.08-7.02 (m, 2H), 6.82 (d, *J*= 2.9 Hz, 1H), 6.19 (d, *J* = 2.9 Hz, 1H), 5.25 (s, 2H), 4.97 (s, 2H), 4.74 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 155.6, 138.2, 136.1, 132.9, 128.7, 128.4, 128.3, 124.6, 123.4, 120.9, 120.4, 115.2, 106.8, 68.0, 67.7, 45.1. HRMS (ESI+) $(M+H)^+$ calculated for $C_{20}H_{18}{}^{79}BrN_2O_3$ 413.0501, found 413.0507.

*Benzyl 1-(4-nitrophenyl)-4,7-dihydropyrrolo[3,2-d][1,2]oxazine-5(1H)-carboxylate (**8lg**)*. 56 mg (75%). Yellow solid, mp = 143-144 °C, R_f= 0.30 (cyclohexane/EtOAc: 6/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 9.0 Hz, 2H), 7.46-7.28 (m, 7H), 6.97 (d, *J* = 3.0 Hz, 1H), 6.29 (d, *J* = 3.0 Hz, 1H), 5.29 (s, 2H), 5.06 (s, 2H), 4.76 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 155.5, 145.5, 144.1, 135.8, 128.6, 128.4, 128.3, 125.6, 123.5, 122.2, 120.8, 116.9, 108.3, 68.0, 67.7, 45.0. HRMS (ESI+) $(M+H)^+$ calculated for $C_{20}H_{18}N_3O_5$ 380.1246, found 380.1261.

Synthesis of (*E*)-*N*-(But-3-yn-1-yl)-4-methyl-*N*-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)benzenesulfonamide 14. To a Schlenk flame dried under an argon atmosphere were sequentially added *N*-(but-3-yn-1-yl)-4-methylbenzenesulfonamide (214 mg, 0.96 mmol), (*E*)-2-(3-chloroprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (289 mg, 1.43 mmol), potassium carbonate (264 mg, 1.91 mmol), Bu_4NI (177 mg, 0.48 mmol) and anhydrous DMF (8 mL). The Schlenk was closed with a

glass stopper and the reaction mixture was heated to 50°C in an oil bath for 65 hours. After cooling to room temperature, water (30 mL) and EtOAc (35 mL) were added. Layers were separated and the organic phase was washed with water (2×30 mL), dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by silica gel chromatography (cyclohexane/ EtOAc: 100/0 to 80/20) to afford **14** as a colorless oil (228 mg, 61%). R_f= 0.30 (cyclohexane/EtOAc: 80/20).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 6.39 (dt, *J* = 18.0, 5.7 Hz, 1H), 5.53 (dt, *J* = 18.0, 1.6 Hz, 1H), 3.91 (dd, *J* = 5.7, 1.6 Hz, 2H), 3.31-3.27 (m, 2H), 2.46-2.39 (m, 5H), 1.95 (t, *J* = 2.7 Hz, 1H), 1.24 (s, 12H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.0, 143.5, 137.0, 129.8, 127.3, 122.6, 83.5, 81.1, 70.3, 52.5, 46.6, 24.9, 21.6, 19.3. $^{11}B\{^1H\}$ NMR (128 MHz, $CDCl_3$) δ 29.4. HRMS (ESI+) $(M+H)^+$ calculated for $C_{20}H_{29}{}^{10}BNO_4S$ 389.1924, found 389.1947.

General procedure for the palladium-catalyzed isomerisation/ring contraction sequence of boronated enynes 11 and 14.

A flame dried Schlenk was charged with $Pd_2dba_3.CHCl_3$ (5.2 mg, 0.05 mmol), tri-*o*-tolylphosphine (3.0 mg, 0.01 mmol), acetic acid (0.6 µL, 0.001 mmol) and toluene (1 mL). After stirring 15 min at room temperature, enyne **14** (0.2 mmol) was added and the mixture was kept 2 hours at room temperature under an argon atmosphere. To this crude mixture was then added PhNO (64 mg, 0.6 mmol). After stirring for 4h at room temperature, the volatiles were removed and the residue was purified by silica gel chromatography (cyclohexane/EtOAc: 100/0 to 85/15).

*5-Phenyl-2-tosyl-1,2,3,5-tetrahydropyrrolo[3,4-c]pyrrole **(16a)***. 32 mg (48%). Colorless oil. R_f= 0.44 (cyclohexane/EtOAc: 8/2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.43-7.35 (m, 2H), 7.33-7.26 (m, 5H), 6.74 (s, 2H), 4.47 (s, 4H), 2.41 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 143.5, 140.85, 134.45, 129.9, 129.8, 127.7, 126.1, 124.9, 120.8, 110.7, 48.2, 21.7. HRMS (ESI+) $(M+Na)^+$calculated for $C_{19}H_{18}N_2O_2SNa$ 361.0987, found 361.0981.

*2-Phenyl-5-tosyl-4,5,6,7-tetrahydro-2H-pyrrolo[3,4-c]pyridine **(16b)***. 24 mg (35%). Colorless oil. R_f= 0.14 (cyclohexane/EtOAc: 9/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.68 (m, 2H), 7.42-7.37 (m, 2H), 7.34-7.28 (m, 4H), 7.24 (tt, *J* = 7.1, 1.2 Hz, 1H), 6.78 (s, 2H), 4.25 (s, 2H), 3.39 (t, *J* = 5.9 Hz, 2H), 2.82 (t, *J* = 5.9 Hz, 2H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 143.5, 140.7, 134.2, 129.7, 129.7, 127.8, 125.7, 120.3, 118.3, 117.3, 115.1, 113.6, 44.8, 43.7, 22.5, 21.7. HRMS (ESI+) $(M+Na)^+$ calculated for $C_{20}H_{20}N_2O_2SNa$ 375.1143, found 375.1141.

ASSOCIATED CONTENT

Supporting Information

^{1}H, ^{13}C and ^{11}B spectra of compounds **7**, **8, 14** and **16a-b**; X-ray diffraction data of **7l**. This material is available free of charge on the ACS Publications website at DOI:

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Notes

The authors declare no competing financial interest.

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(31) The triene **12** was obtained *via* the allylation with allyl bromide of the ene product resulting from the reaction of *in situ* generated benzyl nitrosoformate with pinacol (*E*) (3-methyl-1,3-butadien-1-yl)boronate (manuscript in preparation).

(32) For the X-ray structure of **7l** and **8ga**, see supporting information. CCDC 1950726 and 1983371 respectively contain the supplementary crystallographic data. These data can be obtained free of charge from Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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