

127.78, 128.31, 132.04 (s, Ph); MS(EI): m/z (%): 816 ($[M^+]$ 100); IR: $\tilde{\nu}$ = 2143, 2129, 1596, 756, 691 cm^{-1} ; elemental analysis (C H N) is correct for $\text{C}_{34}\text{H}_{38}\text{Al}_2\text{N}_4$.

3: $\text{HC}\equiv\text{CSiMe}_3$ (2.0 mL, 14 mmol) was added in excess to a solution of **1** (0.83 g, 2.0 mmol) in toluene (50 mL). The mixture was stirred under reflux for 1.5 h and then for 2 h at room temperature. The solvent was removed and **3** was isolated in hexane as white crystals at -26°C (1.0 g, 51 %). Single crystals suitable for X-ray diffraction analysis were obtained from THF at -26°C . M.p. 133°C . ^1H NMR (200 MHz, C_6D_6): δ = 0.13 (s, 18H; $\equiv\text{CSiMe}_3$), 0.44 (s, 9H; SiMe_3), 0.81 (s, 9H; C3-*t*Bu), 1.56 (s, 9H; C1-*t*Bu), 5.79 (s, 1H; C2-H), 7.42 (s, 1H; C44-H); ^{13}C NMR (125 MHz, C_6D_6): δ = -0.08 (s; Si1- Me_3), 0.29 (s; Si2(3)- Me_3), 32.91 (s; C10), 31.34 (s; C30), 30.79 (s; C31(32,33)), 29.52 (s; C11(12,13)), 103.80 (s; C44), 116.35 (s; Si2-C $\equiv$), 125.40 (br; Al-C $\equiv$), 141.80 (br; Al-C $\equiv$), 134.62 (s; C2), 152.00 (s; C1), 163.08 (s; C3); ^{29}Si NMR (99 MHz, C_6D_6): δ = -21.51 (s; Si2(3)), -5.74 (s; Si1); IR: $\tilde{\nu}$ = 3041, 2075, 1941, 1079, 955, 857, 618 cm^{-1} ; MS(EI): m/z (%): 498 ($[M^+]$, 20), 441 ($[M^+ - \text{AlMe}_2]$, 100); elemental analysis (C H N) is correct for $\text{C}_{26}\text{H}_{47}\text{AlN}_2\text{Si}_3$.

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Ruthenium-Catalyzed Enyne Metathesis of Acetylenic Boronates: A Concise Route for the Construction of Cyclic 1,3-Dienylboronic Esters

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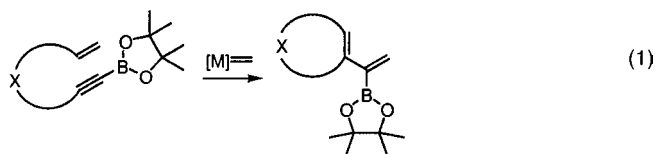
Since its inception in the late 1980s, the ring-closing metathesis (RCM) reaction of dienes has inspired a plethora of exciting studies.^[1] In comparison, the enyne ring-closing metathesis reaction is less well documented. Most reports on this topic are confined to the assembly of compounds containing an unsubstituted or an alkyl-substituted 1,3-dienyl

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[†] NMR analyses.

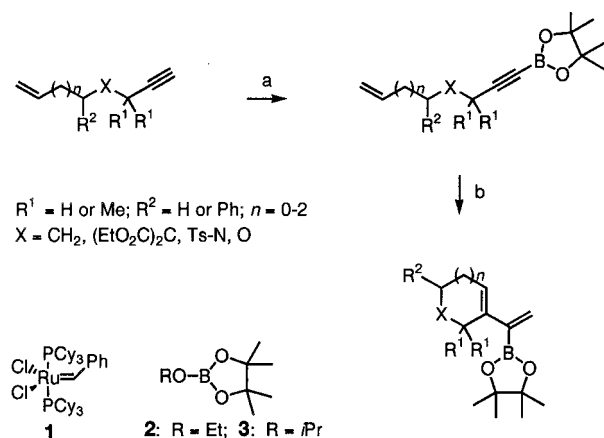
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motif.^[2, 3] We recently demonstrated that cyclic alkenylboronates can be obtained by RCM of dienyloboronic esters.^[4] In connection with these studies, we considered the enyne ring-closing metathesis reaction as a practical and concise strategy for the construction of cyclic 1,3-dienylboronates [Eq. (1)]. In



addition to being amenable to further functionalization by manipulation of the vinylboronate moiety,^[5] 1,3-dialkenylboronic esters are well poised to enter into Diels–Alder cycloaddition reactions and therefore constitute highly versatile synthetic intermediates. Here we disclose the first examples of conversion of en-1-ynylboronic esters into five- to seven-membered carbocyclic and heterocyclic 1,3-dialkenyl-2-boronates by enyne metathesis. Additionally, we report that these dienes readily undergo cycloaddition reactions with high regio- and stereoselectivity.

Our synthetic route towards the preparation of the metathesis substrates is summarized in Scheme 1. The critical alkynyl-1-ylboronate moiety was introduced by trapping an alkynyllithium intermediate with a 2-alkoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2** or **3**) followed by treatment with anhydrous ethereal HCl, according to a procedure described by Brown et al.^[6, 7]



Scheme 1. Synthesis and enyne metathesis of en-1-ynylboronates. a) Procedure A: LDA, Et₂O or THF, −78 °C, 5–15 min; **2** or **3**, 1–3 h; HCl in Et₂O, −78 °C to RT; Procedure B: LDA was replaced by *n*BuLi. b) [(C₃P)₂Cl₂Ru=CHPh] (**1**, 5–10 mol %), benzene or CH₂Cl₂, RT. Ts = *p*-toluenesulfonyl; LDA = lithium diisopropylamide.

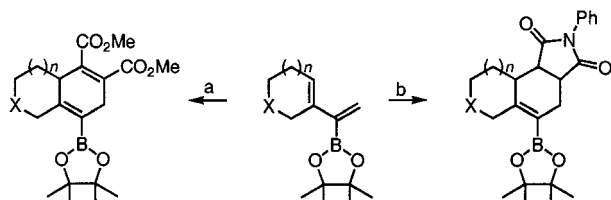
With the alkynylboronic esters in hand, we next established the experimental conditions for the ring-closing enyne metathesis (Scheme 1). The reactions were routinely carried out in the presence of 5–10 mol % of Grubbs' catalyst (**1**)^[8] in CH₂Cl₂ at room temperature.^[9] As shown in Table 1, the ruthenium-promoted enyne metathesis efficiently converts a range of substrates into five- and six-membered carbocyclic and heterocyclic 1,3-dienylboronates. The yields are excellent, ranging from 87 to 95%, and the reactions are generally complete within 1–14 h (Table 1, entries 1, 3, 5, 6, and 9).

Table 1. Synthesis of 1,3-dialkenylboronates by enyne metathesis.^[a]

Entry	Enyne	Product	Yield ^[b] [%]	Time [h]	Solvent ^[a]
1		13 	87 ^[c]	14	A
2		14 	86 ^[d, e]	1	A
3		15 	93	5	A
4		16 	94 ^[d, f]	3	B
5		17 	93	2	A
6		18 	95	6	A
7		19 	65 ^[d, f]	12	B
8		20 	81 ^[d, f, g]	12	B
9		21 	91	3	A

[a] Metathesis conditions: 5–10 mol % catalyst **1**, 0.06 M, RT. Solvent A: CH₂Cl₂; solvent B: benzene. [b] Yields refer to isolated products. [c] Ethylene atmosphere. [d] Overall yield from the alkynylboronate. [e] Diels–Alder conditions: MeO₂CC≡CCO₂Me, EtAlCl₂, CH₂Cl₂, −78 to 0 °C, 2 h. [f] Diels–Alder conditions: MeO₂CC≡CCO₂Me or *N*-phenylmaleimide, benzene, 80 °C, 1 h. [g] Two diastereoisomers (*dr* = 7:1). B(OR)₂ = B(OCMe₂)₂; Ts = *p*-toluenesulfonyl. Further details on the experimental procedure can be found in the Supporting Information.

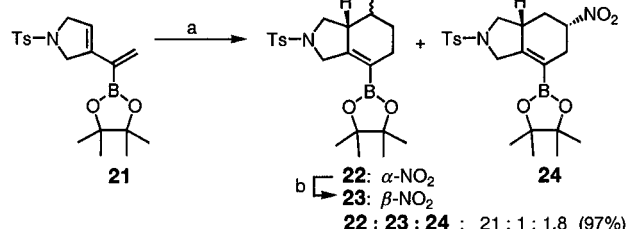
Whilst five of the 1,3-dialkenylboronic esters synthesized were isolated in good yield after chromatography (Table 1, **13**, **15**, **17**, **18**, and **21**), the four containing unsubstituted five- or seven-membered rings proved to be unstable upon concentration, most likely because of dimerization.^[10] To circumvent this problem, these dienyloboronic esters were directly transformed into Diels–Alder adducts (Scheme 2). Thus, reaction of the intermediate 1,3-dialkenylboronates with *N*-phenylmaleimide or with dimethyl acetylenedicarboxylate under thermal or Lewis acid catalyzed conditions^[11] led cleanly to the expected cycloaddition products (Table 1, entries 2, 4, 7, and 8). The tandem enyne metathesis/Diels–Alder cyclo-



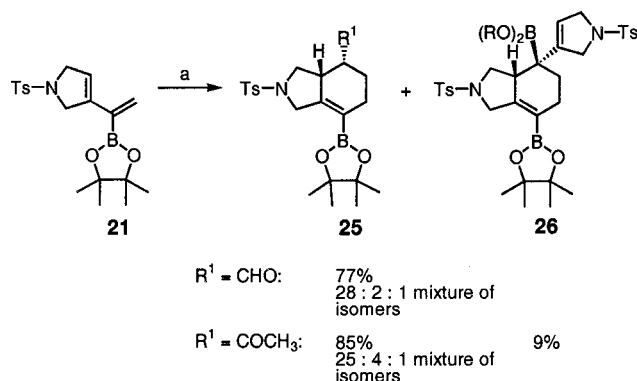
Scheme 2. Diels–Alder cycloaddition reaction of 1,3-dialkenylboronates. a) $\text{MeO}_2\text{CC}\equiv\text{CCO}_2\text{Me}$, EtAlCl_2 , CH_2Cl_2 , -78 to 0°C , 2 h or $\text{MeO}_2\text{CC}\equiv\text{CCO}_2\text{Me}$, benzene, 80°C , 1 h. b) *N*-Phenylmaleimide, benzene, 80°C , 1 h.

addition sequence was accomplished efficiently without removal of the ruthenium catalyst in yields of 65 to 94%. Although **16** resulted from the exclusive *endo* addition of the dienophile, adduct **20** was obtained as a 7:1 mixture of the *endo:exo* isomers.^[12]

The ability of cyclic 1,3-dialkenylboronic esters to undergo Diels–Alder reactions in a regio-^[13] and stereoselective fashion was substantiated by examining the cycloaddition reactions of dialkenylboronate **21** (Schemes 3 and 4). Treatment of **21** with an excess of nitroethylene at 40°C for 2 h furnished one major product (**22**) in 89% yield, along with a



Scheme 3. Selectivity of the Diels–Alder reaction with nitroethylene. a) CH_2CHNO_2 (10 equiv), benzene, 40°C , 2 h. b) NaOMe (1.2 equiv), $\text{THF}:\text{MeOH}$ (3:1), RT, 2 h, 73%.



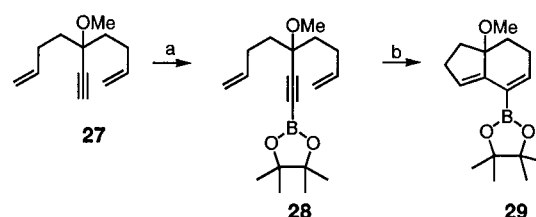
Scheme 4. Selectivity of the Diels–Alder cycloaddition reaction. a) For $\text{R}^1 = \text{CHO}$: CH_2CHCHO (10 equiv), benzene, 65°C , 3 h. For $\text{R}^1 = \text{COCH}_3$: $\text{CH}_2\text{CHCOCH}_3$ (10 equiv), benzene, 70°C , 4 h.

mixture of isomers **23** and **24** (1:1.8; 8% yield), which accounted for most of the remaining material (Scheme 3). The identity of the major compound **22** was ascertained by X-ray crystallography, and the structures of **23** and **24** were assigned on the basis of NMR experiments.^[12] The structure of **23** was also confirmed independently by epimerization of **22** under basic conditions.^[14]

Likewise, the reaction of **21** with acrolein or methyl vinyl ketone was highly regio- and stereoselective and produced

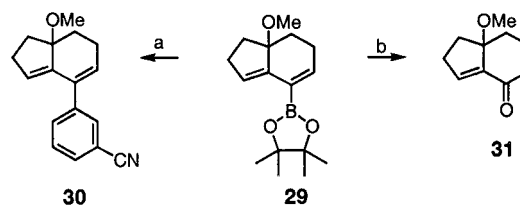
one predominant isomer (Scheme 4). A minor component of the mixture was shown to be the β -epimer of **25**.^[14] By analogy with the results obtained in the cycloaddition reaction with nitroethylene, the other minor product was assigned the structure corresponding to the *endo* regioisomer. In the reaction of **21** with methyl vinyl ketone, by-product **26** resulting from dimerization of **21** was isolated in 9% yield.^[12]

To broaden the utility of our synthetic route to cyclic 1,3-dienyl-2-boronic esters, we tackled the conversion of higher molecular weight alkynylboronic esters into their cyclic counterparts, with the aim of circumventing the purification step. We examined the transformation of diyne **27** into the bicyclic vinylboronate **29** (Scheme 5). We were gratified to find that the crude alkynylboronate **28** cleanly underwent



Scheme 5. Synthesis of bicyclic dienylboronate **29**. a) LDA , THF , -78°C , 20 min; 2-ethoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2**), 2 h; HCl in Et_2O , -78°C to RT; removal of solvents and filtration. b) $[(\text{Cy}_3\text{P})_2\text{-Cl}_2\text{Ru}=\text{CHPh}]$ (**1**, 5 mol %), CH_2Cl_2 , RT, 3 h, 70%.

ruthenium-promoted metathesis in 70% yield.^[15] The resultant bicyclic dialkenylboronic ester **29** was efficiently oxidized to the corresponding enone **31** by treatment with anhydrous Me_3NO in refluxing THF (Scheme 6). Alternatively, reaction of **29** with 3-bromobenzonitrile in the presence of CsF and a catalytic amount of $[\text{PdCl}_2(\text{dppf})] \cdot \text{CH}_2\text{Cl}_2$ in refluxing DME furnished the cross-coupling product **30**.



Scheme 6. Conversion of dienylboronate **29** to **30** and **31**. a) 3-Bromobenzonitrile, CsF , $[\text{PdCl}_2(\text{dppf})] \cdot \text{CH}_2\text{Cl}_2$, DME, reflux, 14 h, 88%. b) Me_3NO (anhydrous), THF , 70°C , 1.5 h, 76%. $\text{dppf} = 1,1'$ -bis(diphenylphosphanyl)-ferrocene.

In summary, we have developed an unprecedented enyne metathesis-based approach for the concise construction of cyclic 1,3-dialkenylboronates. We have further demonstrated that these 1,3-dialkenylboronic esters undergo Diels–Alder reactions with electron-deficient dienophiles with excellent regio- and stereoselectivity to give vinylboronates of higher molecular complexity in a short sequence of steps. Further investigations to broaden the scope of this enyne metathesis and to explore asymmetric Diels–Alder cycloadditions by using chiral, enantiomerically pure 1,3-dienyl-2-boronic esters are in progress.

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- [13] The cycloaddition reaction of 1,3-butadien-2-ylboronic ester with acrolein and methyl vinyl ketone was shown to yield regioselectively the 1,4-disubstituted products; see reference [10a].
- [14] Epimerization of the Diels–Alder adducts with NaOMe (1.2 equiv) in THF:MeOH (3:1) at room temperature afforded quantitatively the β epimers; this allowed identification of one of the minor isomers.
- [15] The LiCl or *i*Pr₂NH₂Cl resulting from the preparation of the intermediate alkynylboronate **28** was removed by filtration through Whatman glass fiber filters before the metathesis reaction.

A Light-Modulated Sequence-Specific DNA-Binding Peptide**

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In eukaryotes, gene expression is primarily regulated at the transcription level through the action of a host of sequence-specific DNA-binding proteins known as transcription factors.^[1] At any given time, most transcription factors are present in the cell in an inactive form and they become activated upon sensing and responding to specific external signals.^[2] In a number of cases, it has been shown that activation involves the transcription factor undergoing a stimulus-induced conformational change that converts it from a non DNA binding protein into a form capable of recognizing the appropriate binding site at the promotor.^[3] We reasoned that molecules mimicking this natural activation mechanism, which are capable of binding to specific DNA sequences with high affinity only after receiving an external stimulus, might offer a promising potential for applications in cell biology and molecular medicine^[4] and could provide new insights into the mechanisms underlying DNA recognition. As a first step towards this goal, we have designed a peptide whose sequence-specific DNA-binding affinity can be modulated by light.^[5]

Our design is inspired by the well-known ability of artificially dimerized basic regions (BRs) of bZIP proteins to recognize DNA sites.^[6,7] We envisaged that appropriate linking of these BRs through a rigid photoresponsive device such as an azobenzene moiety, capable of undergoing a substantial geometrical change upon irradiation,^[8] might allow modulation of the site-specific DNA affinity of the resulting dimer. In designing the system we sought to favor the DNA-binding ability of the *cis* over the *trans* isomer by taking advantage of the considerably shorter distance between the benzylic carbon atoms of the *cis*-azobenzene template and the favorable preorientation of its recognition arms to grip the major groove of the DNA (Scheme 1). Molecular modeling corroborated this idea for hybrid **3** (Scheme 2); each of the peptide segments of **3** consists of amino acids 226–248 from the BR of the yeast transcription

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