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 $C_{54}H_{58}Al_2N_4$.

3: HC≡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. ^{1}H NMR (200 MHz, C_6D_6): δ = 0.13 (s, 18H; ≡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≡), 125.40 (br; Al-C≡), 141.80 (br; Al-C=), 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^+ − AlMe$_2$], 100); elemental analysis (C H N) is correct for $C_{26}H_{47}AlN_2Si_3$.

Received: May 4, 2000 [Z15078]

[1] a) G. Wilk, H. Müller, *Justus Liebigs Ann. Chem.* **1960**, *629*, 222; b) J. J. Eisch, W. C. Kaska, *J. Am. Chem. Soc.* **1963**, *85*, 2165; c) P. Binger, *Angew. Chem*. **1963**, *75*, 918; *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 686; d) R. Rienäcker, D. Schwengers, *Liebigs Ann. Chem*. **1970**, *737*, 182.

[2] a) D. Stucky, A. M. McPherson, W. E. Rhine, J. J. Eisch, J. L. Considine, *J. Am. Chem. Soc.* **1974**, *96*, 1941; b) M. J. Albright, W. M. Butler, T. J. Anderson, M. D. Glick, J. P. Oliver, *J. Am. Chem. Soc.* **1976**, *98*, 3995.

[3] a) G. Erker, M. Albrecht, C. Krüger, M. Nolte, S. Werner, *Organometallics* **1991**, *10*, 3791; b) G. Erker, M. Albrecht, C. Krüger, M. Nolte, S. Werner, *Organometallics* **1993**, *12*, 4979; c) M. Albrecht, G. Erker, M. Nolte, C. Krüger, *J. Organomet. Chem*. **1992**, *427*, C21.

[4] B. M. Trost, M. R. Ghadiri, *J. Am. Chem. Soc.* **1986**, *108*, 1098, and references therein.

[5] a) Recently, pyrazolato ligands have attracted interest in transition metal chemistry owing to their η^2- and η^5-coordination. See: J. R. Perera, M. J. Heeg, H. B. Schlegel, C. H. Winter, *J. Am. Chem. Soc.* **1999**, *121*, 4536, and references therein; N. C. Mösch-Zanetti, R. Krätzner, C. Lehmann, T. R. Schneider, I. Usón, *Eur. J. Inorg. Chem*. **2000**, 13; b) a homoleptic aluminum compound [Al(η^2-*t*Bu$_2$pz)$_3$] was prepared: G. B. Deacon, E. E. Dilbridge, C. M. Forsyth, P. C. Junk, B. W. Skelton, A. H. White, *Aust. J. Chem*. **1999**, *52*, 733; c) only a few crystallographically characterized μ-η^1-η^1-pyrazolate complexes of aluminum are known: C.-C. Chang, T.-Y. Her, F.-Y. Hsieh, C.-Y. Yang, M.-Y. Chiang, G.-H. Lee, Y. Wang, S.-M. Peng, *J. Chin. Chem. Soc*. **1994**, *41*, 783; M. H. Chisholm, N. W. Eilerts, J. C. Huffman, *Inorg. Chem*. **1996**, *35*, 445; D. J. Darensbourg, E. L. Maynard, M. W. Holtcamp, K. K. Klausmeyer, J. H. Reibenspies, *Inorg. Chem*. **1996**, *35*, 2682.

[6] C. Fernández-Castaño, C. Foces-Foces, N. Jagerovic, J. Elguero, *J. Mol. Struct. (THEOCHEM)* **1995**, *355*, 265.

[7] R. A. Kovar, J. O. Callaway, C. H. van Dyke, N. D. Miro, *Inorg. Synth.* **1975**, *17*, 36.

[8] H. W. Roesky, W. Zheng, unpublished results.

[9] X-ray structure determination: The data were collected on a Stoe–Siemens–Huber four-circle instrument (−140 °C) for **2** and **3**, with graphite-monochromated Mo$_{K\alpha}$ radiation (λ = 0.71073 Å). The structures were solved by direct methods and refined against F^2 on all data by full-matrix least-squares with SHELXS-97.[13] **2**: $C_{54}H_{58}Al_2N_4$, M_r = 817, monoclinic, space group $C2/c$, a = 22.079(4), b = 9.541(2), c = 23.734(5) Å, β = 96.60(3)°, V = 4966.20(17) Å^3, Z = 4, ρ_{calcd} = 1.093 Mg m^{-3}, crystal size: 0.6 × 0.4 × 0.2 mm^3, $F(000)$ = 1744, μ(Mo$_{K\alpha}$) = 0.096 mm^{-1}. The total number of reflections measured was 3145 in the range 4.66 ≤ 2θ ≤ 43.46°, of which 2924 were unique, 2309 with $F > 4\sigma(F)$, 277 parameters. Final R indices: R_1 = 0.0487 ($I > 2\sigma(I)$) and wR_2 = 0.1125 (all data). Residual electron density, max./min. 253/−238 e nm^{-3}. **3**: $C_{26}H_{47}AlN_2Si_3 \cdot C_4H_8O$, M_r = 571, monoclinic, space group $P2_1/n$, a = 12.261(3), b = 16.424(3), c = 20.151(4) Å, β = 103.02(3)°, V = 3954(1) Å^3, Z = 4, ρ_{calcd} = 0.959 Mg m^{-3}, crystal size: 0.5 × 0.5 × 0.15 mm^3, $F(000)$ = 1248, μ(Mo$_{K\alpha}$) = 0.163 mm^{-1}. The total number of reflections measured was 6909 in the range 4.34 ≤ 2θ ≤ 49.46°, of which 6650 were unique. 5289 with $F > 4\sigma(F)$, 277 parameters. Final R indices: R_1 = 0.0530 ($I > 2\sigma(I)$) and wR_2 = 0.1351 (all data). Residual electron density, max./min. 312/−326 e nm^{-3}. The THF molecule was modeled as threefold disordered. Owing to this disorder, the oxygen atom of THF could not be localized and was modeled as a CH_2 group. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-143738 (**2**) and CCDC-143739 (**3**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[10] a) N. L. Narvor, L. Toupet, C. Lapinte, *J. Am. Chem. Soc*. **1995**, *117*, 7129; b) T. Yamagata, H. Imoto, T. Saito, *Acta Crystallogr. Sect. C* **1997**, *53*, 859; c) R. Beckhaus, M. Wagner, V. V. Burlakov, W. Baumann, N. Peulecke, A. Spannenberg, R. Kempe, U. Rosenthal, *Z. Anorg. Allg. Chem*. **1998**, *624*, 129.

[11] a) H. Suzuki, T. Murafuji, N. Azuma, *J. Chem. Soc. Perkin Trans. 1* **1992**, 1593; b) L. Guo, J. D. Bradshaw, D. B. McConville, C. A. Tessier, W. J. Young, *Organometallics* **1997**, *16*, 1685.

[12] a) The idealized D_{2h} symmetry consists of a planar six-membered Al_2N_4 ring with linear Al−C≡C bonds making 90° dihedral angles with the ring; b) I. B. Bersuker, V. Z. Polinger, *Vibronic Interactions in Molecules and Crystals*, Springer, Berlin, **1989**; c) L. F. Chibotaru, F. Cimpoesu, *Int. J. Quant. Chem.* **1997**, *65*, 37. d) Calculations were carried out with the GAMESS package in the RHF limit, with STO-3G basis: M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis, J. A. Montgomery, *J. Comput. Chem.* **1993**, *14*, 1347. e) We computed the vibronic curvature $K_v(A_u)$ = −0.2942 mdyn Å^{-1}, while the nonvibronic curvature is $K_0(A_u)$ = +0.2846 mdyn Å^{-1}. Thus, the total curvature is K_0+K_v = −0.0096 mdyn Å^{-1}.f) The vibronically transformed orbitals were obtained by a particular method. Technically, this resembles localization procedures, but is related with the vibronic terms.

[13] G. M. Sheldrick, SHELXL-97, Program for Crystal Structure Refinement, University of Göttingen, Germany, **1997**.

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

Johanne Renaud,* Claus-Dieter Graf, and Lukas Oberer

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

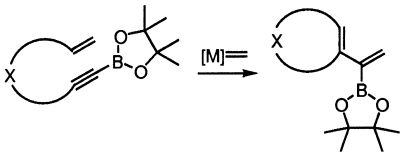
[*] Dr. J. Renaud, Dr. C.-D. Graf, L. Oberer[+]
Novartis Pharma AG
K-136.3.25
4002 Basle (Switzerland)
Fax: (+41) 61-696-6071
E-mail: johanne.renaud@pharma.novartis.com

[+] NMR analyses.

Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

  1433-7851/00/3917-3101 $ 17.50+.50/0

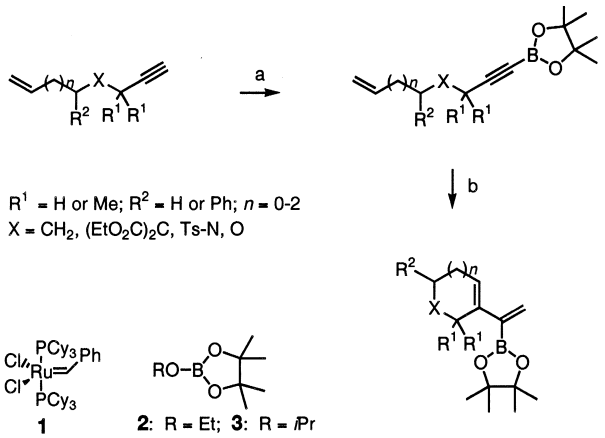
motif.[2, 3] We recently demonstrated that cyclic alkenylboronates can be obtained by RCM of dienylboronic esters.[4] In connection with these studies, we considered the enyne ring-closing metathesis reaction as a practical and concise strategy for the construction of cyclic 1,3-dienylboronates [Eq.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



(1)

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.

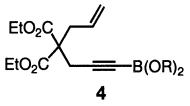
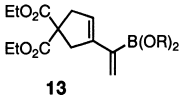
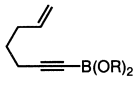
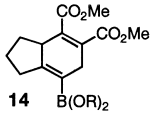
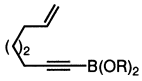
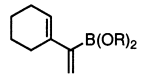
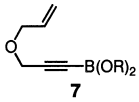
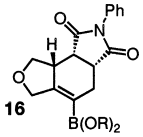
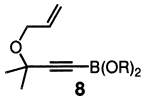
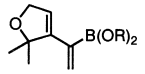
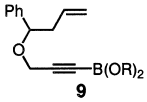
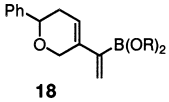
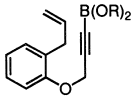
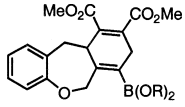
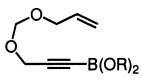
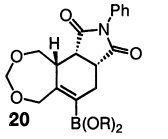
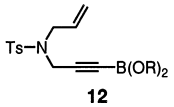
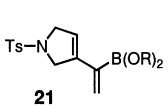
Our synthetic route towards the preparation of the metathesis substrates is summarized in Scheme 1. The critical alkyn-1-ylboronate moiety was introduced by trapping an alkynyllithium intermediate with a 2-alkoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2** or **3**) followed by treatment with anhydrous 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, Et_2O or THF, −78 °C, 5–15 min; **2** or **3**, 1–3 h; HCl in Et_2O, −78 °C to RT; Procedure B: LDA was replaced by *n*BuLi. b) $[(Cy_3P)_2Cl_2Ru{=}CHPh]$ (**1**, 5–10 mol %), benzene or CH_2Cl_2, 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 CH_2Cl_2 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).

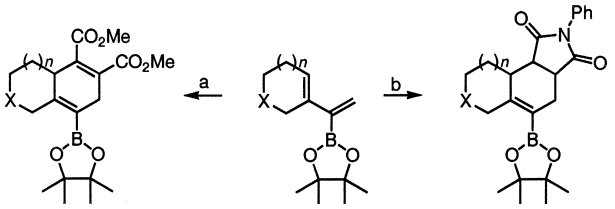
Table 1. Synthesis of 1,3-dialkenylboronates by enyne metathesis.[a]

Entry	Enyne	Product	Yield[b] [%]	Time [h]	Solvent[a]
1	 **4**	 **13**	87[c]	14	A
2	 **5**	 **14**	86[d, e]	1	A
3	 **6**	 **15**	93	5	A
4	 **7**	 **16**	94[d, f]	3	B
5	 **8**	 **17**	93	2	A
6	 **9**	 **18**	95	6	A
7	 **10**	 **19**	65[d, f]	12	B
8	 **11**	 **20**	81[d, f, g]	12	B
9	 **12**	 **21**	91	3	A

[a] Metathesis conditions: 5–10 mol % catalyst **1**, 0.06 M, RT. Solvent A: CH_2Cl_2; solvent B: benzene. [b] Yields refer to isolated products. [c] Ethylene atmosphere. [d] Overall yield from the alkynylboronate. [e] Diels–Alder conditions: $MeO_2CC{\equiv}CCO_2Me$, $EtAlCl_2$, CH_2Cl_2, −78 to 0 °C, 2 h. [f] Diels–Alder conditions: $MeO_2CC{\equiv}CCO_2Me$ or *N*-phenylmaleimide, benzene, 80 °C, 1 h. [g] Two diastereoisomers (*dr* = 7:1). $B(OR)_2 = B(OCMe_2)_2$; 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 dienylboronic 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-

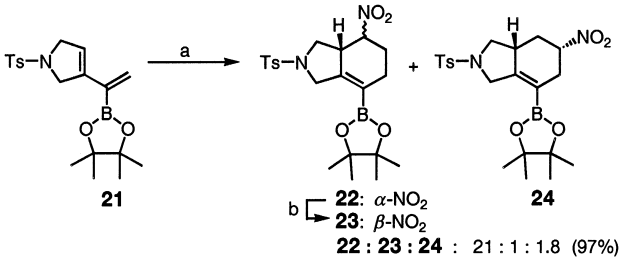
  1433-7851/00/3917-3102 $ 17.50+.50/0



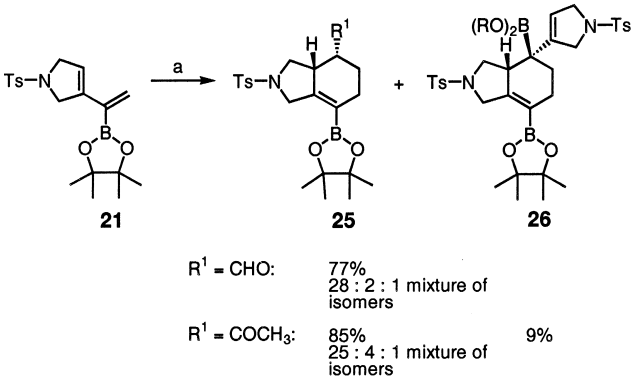
Scheme 2. Diels–Alder cycloaddition reaction of 1,3-dialkenylboronates. a) $MeO_2CC{\equiv}CCO_2Me$, $EtAlCl_2$, CH_2Cl_2, -78 to $0\,^\circ C$, 2 h or $MeO_2CC{\equiv}C\text{-}CO_2Me$, benzene, $80\,^\circ C$, 1 h. b) *N*-Phenylmaleimide, benzene, $80\,^\circ C$, 1 h.

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 $40\,^\circ C$ 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, $40\,^\circ C$, 2 h. b) NaOMe (1.2 equiv), THF:MeOH (3:1), RT, 2 h, 73%.

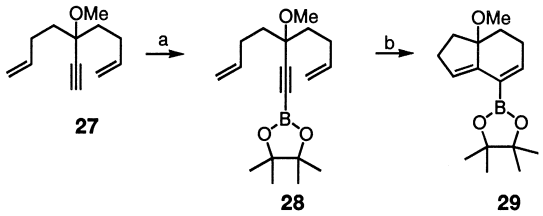


Scheme 4. Selectivity of the Diels–Alder cycloaddition reaction. a) For $R^1 = CHO$: CH_2CHCHO (10 equiv), benzene, $65\,^\circ C$, 3 h. For $R^1 = COCH_3$: $CH_2CHCOCH_3$ (10 equiv), benzene, $70\,^\circ C$, 4 h.

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]

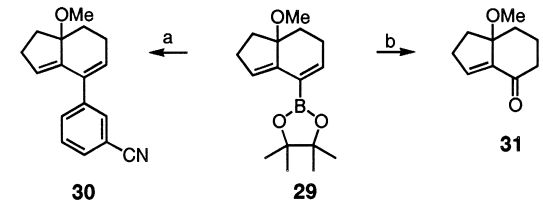
Likewise, the reaction of **21** with acrolein or methyl vinyl ketone was highly regio- and stereoselective and produced one predominant isomer (Scheme 4). A minor component of the mixture was shown to be the β-epimer of **25**.[14] By analogy with the results obtained in the cycloaddition reaction with 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 dienyne **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, $-78\,^\circ C$, 20 min; 2-ethoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2**), 2 h; HCl in Et_2O, $-78\,^\circ C$ to RT; removal of solvents and filtration. b) $[(Cy_3P)_2Cl_2Ru{=}CHPh]$ (**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 $[PdCl_2(dppf)]\cdot CH_2Cl_2$ in refluxing DME furnished the cross-coupling product **30**.



Scheme 6. Conversion of dienylboronate **29** to **30** and **31**. a) 3-Bromobenzonitrile, CsF, $[PdCl_2(dppf)]\cdot CH_2Cl_2$, DME, reflux, 14 h, 88%. b) Me_3NO (anhydrous), THF, $70\,^\circ C$, 1.5 h, 76%. 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-boronates are in progress.

Received: March 29, 2000 [Z14917]

[1] Recent reviews on metathesis: a) A. Fürstner, *Top. Organomet. Chem.* **1998**, *1*, 1 – 231; b) R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413 – 4450; c) S. K. Armstrong, *J. Chem. Soc. Perkin Trans. 1* **1998**, 371 – 388; d) M. Schuster, S. Blechert, *Angew. Chem.* **1997**, *109*, 2124 – 2145; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2036 – 2056.

[2] The two reported examples of enyne metathesis of acetylenes bearing silyl substituents provide the corresponding dienes in 20 and 7 % yield, respectively: a) J. S. Clark, G. P. Trevitt, D. Boyall, B. Stammen, *Chem. Commun.* **1998**, 2629 – 2630; b) reference [31].

[3] For recent studies on intramolecular enyne and dienyne metathesis, see: a) M. Mori, T. Kitamura, N. Sakakibara, Y. Sato, *Org. Lett.* **2000**, *2*, 543 – 545; b) T. R. Hoye, S. M. Donaldson, T. J. Vos, *Org. Lett.* **1999**, *1*, 277 – 279; c) M. A. Leeuwenburgh, C. Kulker, H. I. Duynstee, H. S. Overkleeft, G. A. van der Marel, J. H. van Boom, *Tetrahedron* **1999**, *55*, 8253 – 8262; d) A. G. M. Barrett, S. P. D. Baugh, D. C. Braddock, K. Flack, V. C. Gibson, M. R. Giles, E. L. Marshall, P. A. Procopiou, A. J. P. White, D. J. Williams, *J. Org. Chem.* **1998**, *63*, 7893 – 7907; e) M. Mori, N. Sakakibara, A. Kinoshita, *J. Org. Chem.* **1998**, *63*, 6082 – 6083; f) M. Picquet, C. Bruneau, P. H. Dixneuf, *Chem. Commun.* **1998**, 2249 – 2250; g) D. A. Heerding, D. T. Takata, C. Kwon, W. F. Huffman, J. Samanen, *Tetrahedron Lett.* **1998**, *39*, 6815 – 6818; h) S. Kotha, N. Sreenivasachary, E. Brahmachary, *Tetrahedron Lett.* **1998**, *39*, 2805 – 2808; i) K. Hammer, K. Undheim, *Tetrahedron* **1997**, *53*, 10603 – 10614; j) A. Kinoshita, M. Mori, *Heterocycles* **1997**, *46*, 287 – 299; k) S.-H. Kim, W. J. Zuercher, N. B. Bowden, R. H. Grubbs, *J. Org. Chem.* **1996**, *61*, 1073 – 1081; l) A. Kinoshita, M. Mori, *Synlett* **1994**, 1020 – 1022; m) N. Chatani, T. Morimoto, T. Muto, S. Murai, *J. Am. Chem. Soc.* **1994**, *116*, 6049 – 6050.

[4] J. Renaud, S. G. Ouellet, *J. Am. Chem. Soc.* **1998**, *120*, 7995 – 7996.

[5] a) Pd-catalyzed cross-coupling reactions: N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457 – 2483; b) addition to iminium ions: R. A. Batey, D. B. MacKay, V. Santhakumar, *J. Am. Chem. Soc.* **1999**, *121*, 5075 – 5076; c) oxidation to ketones: G. Desurmont, S. Dalton, D. M. Giolando, M. Srebnik, *J. Org. Chem.* **1996**, *61*, 7943 – 7946.

[6] H. C. Brown, N. G. Bhat, M. Srebnik, *Tetrahedron Lett.* **1988**, *29*, 2631 – 2634.

[7] The alkynylboronic esters are susceptible to hydrolysis and were therefore most conveniently isolated by distillation of the crude reaction mixture.

[8] $[(Cy_3P)_2Cl_2Ru{=}CHPh]$ (**1**): a) P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100 – 110; b) P. Schwab, M. B. France, J. W. Ziller, R. H. Grubbs, *Angew. Chem.* **1995**, *107*, 2179 – 2181; Angew. *Chem. Int. Ed. Engl.* **1995**, *34*, 2039 – 2041.

[9] Two independent experiments were generally performed, one of which was conducted in an NMR tube to monitor the reaction time.

[10] a) The facile dimerization reaction of a 1,3-butadien-2-ylboronic ester has been reported: A. Kamabuchi, N. Miyaura, A. Suzuki, *Tetrahedron Lett.* **1993**, *34*, 4827 – 4828; b) for the dimerization of other 1,3-dienes, see reference [3b], and references therein.

[11] P.-Y. Renard, Y. Six, J.-Y. Lallemand, *Tetrahedron Lett.* **1997**, *38*, 6589 – 6590.

[12] The structural assignments were based on the data obtained from ^{1}H NMR spectra (coupling constants) and in addition on COSY, HSQC, and ROESY experiments.

[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 iPr$_2$NH$_2$Cl 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**

Ana M. Caamaño, M. Eugenio Vázquez, José Martínez-Costas, Luis Castedo, and José L. Mascareñas*

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

[*] Prof. Dr. J. L. Mascareñas, A. M. Caamaño, M. E. Vázquez, Prof. Dr. L. Castedo
Departamento de Química Orgánica y Unidad Asociada al CSIC
Universidad de Santiago de Compostela
15706 Santiago de Compostela (Spain)
Fax: (+34) 981-595-012
E-mail: qojoselm@usc.es

Dr. J. Martínez-Costas
Departamento de Bioquímica y Biología Molecular
Universidad de Santiago de Compostela
15706 Santiago de Compostela (Spain)

[**] This work was supported by the Spanish M.E.C. (PB97 – 0524) and the Xunta de Galicia (XUGA 20906B96). A.M.C and E.V. thank the Xunta de Galicia and the University of Santiago for their predoctoral fellowships. We are grateful to Prof. M. Mosquera and Prof. J. Benavente for allowing us to use the spectrofluorimetry and radioactivity facilities, respectively, and to Dr. Chris Abell (Cambridge University, Iberdrola Visiting Professor at the University of Santiago) for critical reading of the manuscript.

  1433-7851/00/3917-3104 $ 17.50+.50/0