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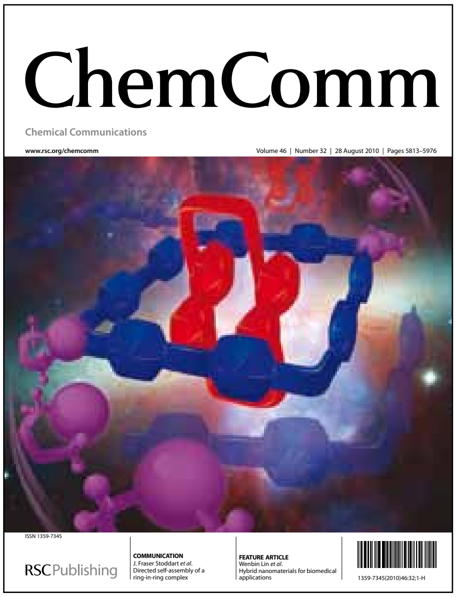

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ARTICLE TYPE

Preparation of allylboronates by Pd-catalysed borylative cyclisation of dienynes[‡]

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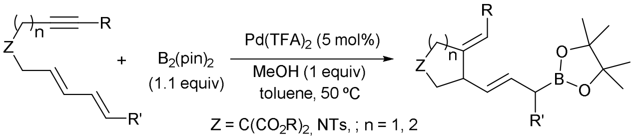
Reaction of a variety of dienynes with bis(pinacolato) diboron catalysed by Pd bis(trifluoroacetate) affords allylic boronates containing five or six member carbo- or heterocycles, by concomitant formation of one C-C and one C-B bonds. Resulting allylboronates can be employed for a variety of subsequent transformations

Enynes are versatile starting compounds for the metal-catalysed formation of carbocycles, allowing formation of a wide variety of structures. Reactions include cycloisomerization,[1] skeletal rearrangements,[2] and alkoxy-cyclization,[3] among other processes. Especially interesting are the cyclization reactions in which a boron atom is incorporated, since the resulting derivatives can be further functionalized. Thus, the boron functional group can be used as a reagent, or advantage of the stability and tolerance of boron compounds can be taken to develop further transformations without affecting this group. Initial works employed reagents containing B-Si and B-Sn bonds for the functionalization of 1,6-enynes.[4,5] Some years ago, we described a Pd-catalyzed borylative cyclisation of 1,6-enynes for the preparation of cyclopentane-derived homoallylic boronates in good yields, smooth conditions, and in the presence of functional groups, since there is no need to use highly nucleophilic and basic Li or Mg nucleophiles.[6] Cascade borylative polycyclisation of different enediynes,[7] 1,7-enynes,[8] and borylative cyclisation of enallenes and allenynes allow the preparation of alkyl and allylboronates as well.[9] These reactions have been recently used for synthetic purposes.[10] Especially efficient Pd-catalysed oxidative borylative cyclisation of enallenes,[11] and allenynes,[12] to afford homoallyl- or alkenylboronates has also been developed by Bäckvall.

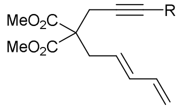
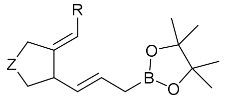
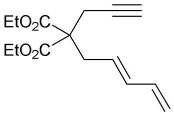
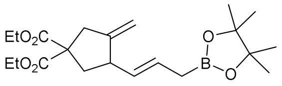
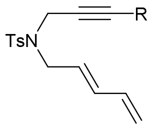
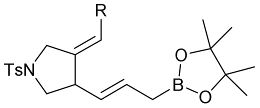
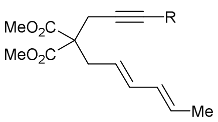
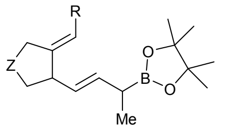
In this communication, we report the Pd-catalysed borylative cyclisation of 1,3-dien-8-ynes to give allylboronates in smooth conditions, avoiding the use of highly reactive precursors.



This reaction leads to the formation of five and six-member rings, and can be considered as a formal 1,9- or 1,10-hydroboration with concomitant cyclisation. Borylation is highly regioselective, and takes place at the terminal alkene carbon of the starting diene.

The presence of the allylboronate group confers this reaction a high potential from a synthetic point of view.[13]

Table 1. Pd-Catalyzed borylative cyclisation of dienynes. (Reaction conditions: $B_2(pin)_2$ (1.1 equiv), $Pd(TFA)_2$ 5 mol %, MeOH (1 equiv), toluene, [substrate] = 0.2 M. Unless otherwise stated, T =50ºC)

Entry	Substrate	t(h)	Product	Yield (%)[a]
				
1	**1a**	3	**2a:** R =H	64
2	**1b**	4.5	**2b:** R = Me	55
3	**1c**	5	**2c:** R = TMS	53[b]
4	**1d**	8.5	**2d:** R = Ph	49
5	**1e**	6.5	**2e:** R = *p*-MeOC$_6$H$_4$	50
6	**1f**	8	**2f:** R = 2-thiophenyl	55
				
7	**1g**	4.5	**2g**	57
				
8	**1h**	18	**2h :** R = Me	47[b]
9	**1i**	4.5	**2i :** R = H	38
				
10	**1j**	18	**2j :** R = H	68[b,c]
11	**1k**	4.5	**2k :** R = Me	74[c]

[a] Isolated yields. [b] To ensure complete conversion, extra $Pd(TFA)_2$ (2.5 mol%) was added after some hours, and the reaction was heated up to 70ºC (see ESI) . [c] Only one isomer observed by ^1H and ^{13}C NMR.

For this reason, we tried to find optimized conditions.. Interestingly, $Pd(O_2CCF_3)_2$ resulted to be much more convenient

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compared with $Pd(OAc)_2$, and provided products in moderate to high yields. In general, reactions take place at higher temperature compared to 1,6-enynes. Toluene was the solvent of choice, and MeOH (1 equiv) is added as a proton source. We explored the reaction scope under the optimised conditions shown in Table 1As it can be seen, reaction has been extended to a variety of dienynes. Both terminal (entries 1, 7, 9 and 10) and internal alkynes can be employed. All products show the same configuration on the C-C double bond derived from the starting alkyne group, being the reaction stereoselective. Although terminal dienes were used for almost all cases, substitution of the distal carbon of the diene also afforded good yields (entries 10 and 11) of single diastereoisomers (relative configuration was not determined). Different tethering groups can be used, yields being comparable except for the tosylamide derivatives, which afforded poorer results (entries 8 and 9). Nevertheless, the ability to construct N-heterocycles substituted with an allyboronate is important in itself.

A plausible reaction pathway is depicted in Figure 1. Reaction probably starts with the reduction of Pd(II) precatalyst to Pd(0), the actual catalyst, followed by formation of a Pd hydride by protonation with the alcohol. Insertion of the alkyne on the Pd-H bond to afford intermediate **B** accounts for the configuration observed for the resulting alkene in all cases.

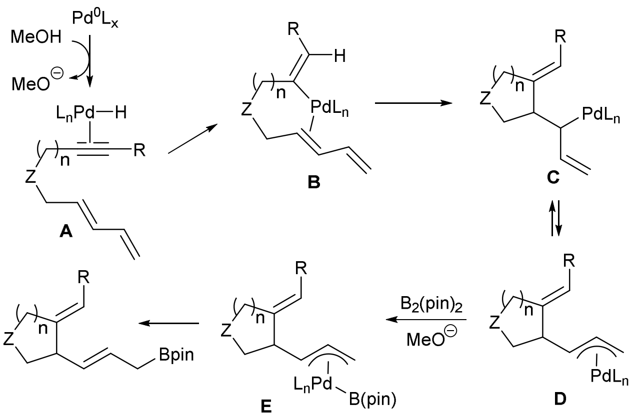

Figure 1

Alternatively, intermediate **B** could be formed by oxidative cyclometalation of the enyne, followed by protonolysis of the alkenyl-Pd bond. High activation barrier previously calculated for this process suggests it less likely to occur.[6,14] Carbometallation of the proximal C-C doble bond in the alkenyl-Pd intermediate **B** would give rise to allyl-Pd intermediate **C**. Both η^1 and η^3 types of allyl-Pd complexes could exist in solution. Since no additional ligand is used, η^3-allyl complex **D** is supposed to be readily formed. Transmetalation with $B_2(pin)_2$, probably assisted by methoxide, would afford intermediate **E**. B-C reductive elimination leads to the final product. In principle, two possible regioisomers could be formed from intermediate **E**, depending on the allyl terminal carbon that could be involved in this process. Interestingly, is fully regioselective, affording the less hindered isomer in all cases.[15] This result contrasts with our previous results concerning the borylative cyclization of allenynes. In that case, both possible regiosomers are formed depending on the relative steric hindrance of terminal allyl carbons.[9]

Reaction also worked for homologue enediyne **3**, although a lower yield of the desired allylboronate was obtained (36 %, Figure 2). The higher flexibility of the carbon chain may be responsible for this behaviour, since competing intermolecular reactions may operate. In contrast, we reported good yields for the formation of 6-member rings by borylative cyclization of 1,7-enynes.[8,16]

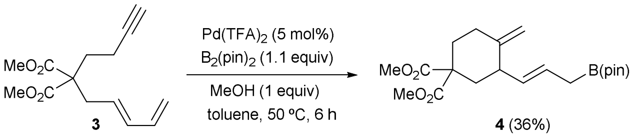

Figure 2

Oxidation of allylboronates can be performed under standard conditions to give the corresponding alcohols in excellent yields (Figure 3).[17] In this way, a formal 1,6-hydration of the starting dienenye involving a concomitant C-C bond formation can be achieved in two steps.

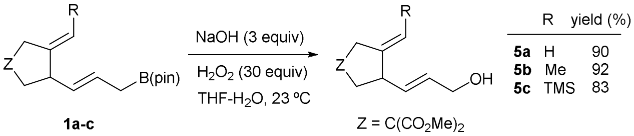

Figure 3

Moreover, oxidation of the borylative cyclization reaction crude obtained from **1c**, without isolation of the allyboronate, afforded the corresponding alcohol **5c** in better yield compared to the stepwise process (Figure 4).

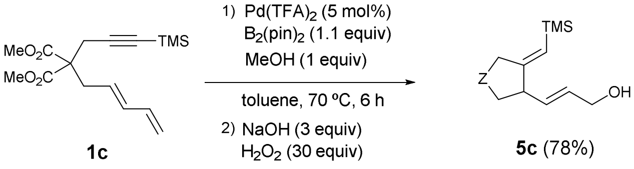

Figure 4

Some other transformations of the allylboronates illustrate the high synthetic potential of these derivatives. Thus, allyltrifluoroborate salts,[18] which are often used as convenient nucleophiles for Suzuki couplings, can be prepared as shown below (Figure 5).

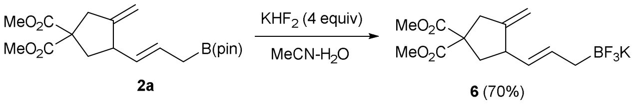

Figure 5

On the other hand, allylation of aldehydes takes place under smooth conditions. This reaction is usually employed for the formation of branched homoallyl alcohols by reaction of γ–carbon of the boronate with the aldehyde, through a cyclic transition state. Noticeably, when the reaction was performed in the presence of a $Sc(OTf)_3$, derivatives exerting from reaction at the α–carbon were obtained (Figure 6). Compounds **7a** and **7b**

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are obtained as mixtures of compounds, presumably diastereomers, which could not be separated. This unusual regioselectivity has been recently reported, and may be consequence of the presence of the Lewis acid.[19] One-pot reaction from **1a** afforded just 35 % of **7a**.[20]

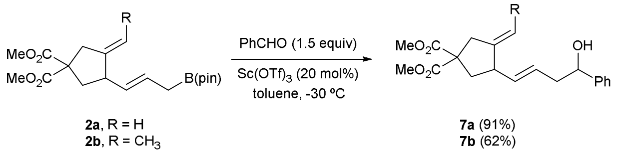

Figure 6

Finally, we employed the allylboronate **2a** as nucleophilic coupling partner in a Suzuki cross-coupling reaction with *p*-cyanoiodobenzene, under the conditions stated below (Figure 7). Reaction was not comp letely regioselective, affording a mixture of linear and branched products. Unexpectedly, the more hindered branched derivative **8** exerting from cross-coupling of the internal allyl carbon, was the major compound.[21]

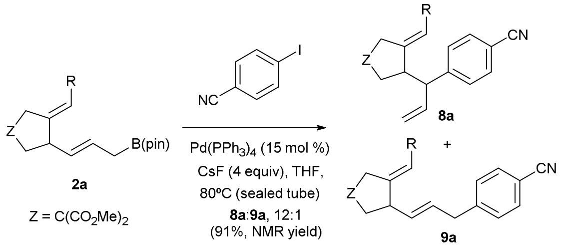

Figure 7

Formation of both regioisomers can be explained by two divergent reductive eliminations involving either terminal allyl carbons in a putative allyl(aryl)Pd(II). Alternatively, insertion of the C-C double bond of the allylboronate into an aryl-Pd bond, followed by deborylation of the resulting akyl-Pd intermediate is also feasible. This has been recently proposed for the Suzuki reaction of 3,3-disubstituted allylboronates.[22] According to the regioselectivity observed in the formation of allylboronates from allenynes in our previous work,[8] as well as the regioselectivity observed in Table 1, formation of a π-allyl complexes by transmetalation is less likely, since a linear derivative **9**, would have been the preferred isomer. Therefore, insertion of the C-C double bond of the allylboronate into an initially formed aryl-Pd complex, and subsequent deborylation seem to take place in this case. In conclusion, we have developed a general borylative cyclisation of dienynes containing an allylboronate. The reaction is general, tolerates substitution in both the diene and alkyne fragments, and takes place under smooth conditions giving rise to carbo- or heterocycles containing an allylboronate. These products constitute useful synthetic intermediates and can be further functionalised.

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Notes and references

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† Electronic Supplementary Information (ESI) available: experimental procedures, data and compuational details. See DOI: 10.1039/b000000x/

1 C. Aubert, O. Buisine, M. Malacria, *Chem. Rev.* 2002, **102**, 813; G. C. Lloyd-Jones, *Org. Biomol. Chem.*, 2003, **1**, 215; A. M. Echavarren, C. Nevado, *Chem. Soc. Rev.*, 2004, **33**, 431.
2 S. T. Diver, A. J. Giessert, *Chem. Rev.*, 2004, **104**, 1317; B. Schmidt, *Angew. Chem. Int. Ed,* 2003, **42**, 4996.
3 M. P. Muñoz, M. Méndez, C. Nevado, D. J. Cárdenas, A. M. Echavarren, Synthesis, 2003, 2898.
4 S. Onozawa, Y. Hatanaka, M. Tanaka, *Chem. Commun*., 1997, **13**, 1229.
5 Onozawa, S.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* 1997, **16***,* 5389.
6 J. Marco-Martínez, V. López-Carrillo, E. Buñuel, R. Simancas, D. J. Cárdenas, *J. Am. Chem. Soc.*, 2007, **129**, 1874.
7 J. Marco-Martínez, E. Buñuel, R. Muñoz-Rodríguez, D. J. Cárdenas, *Org. Lett.*, 2008, **10**, 3619; J. Marco-Martínez, E. Buñuel, R. López-Durán, D. J. Cárdenas, *Chem. Eur. J.*, 2011, **17**, 2734.
8 V. Pardo-Rodríguez, E. Buñuel, D. Collado-Sanz, D. J. Cárdenas, *Chem. Commun.* 2012, **48**, 10517.
9 V. Pardo-Rodríguez, J. Marco-Martínez, E. Buñuel, D. J. Cárdenas, *Org. Lett.*, 2009, **11**, 4548.
10 A. M. Camelio, T. Barton, F. Guo, T. Shaw, D. Siegel, *Org. Lett.*, 2011, **13**, 1517.
11 A. K. Å. Persson, T. Jiang, M. T. Johnson, J.-E. Bäckvall, *Angew. Chem. Int. Ed.*, 2011, **50**, 6155.
12 Y. Deng, T. Bartholomeyzik, A. K. Å. Persson, J. Sun, J.-E. Bäckvall, *Angew. Chem. Int. Ed*., 2012, **51**, 2703.
13 a) D. G. Hall, H. Lachance, *Allylboration of Carbonyl Compounds*; Wiley: Hoboken, New Jersey, 2012; b) D. G. Hall, *Boronic Acids*; Wiley-VCH: Weinheim, Germany, 2005.
14 B. Martín-Matute, E. Buñuel, M. Méndez, C. Nieto-Oberhuber, D. J. Cárdenas, A. M. Echavarren, *J. Organomet. Chem.* 2003, **687**, 410.
15 J. M. Larsson, K. J. Szabó, J. Am. Chem. Soc., 2013, 135, 443.
16 Reviews containing examples of cyclisation of 1,7-enynes: O. Geis, H. Schmalz, *Angew. Chem. Int. Ed*., 1998, **37**, 911; J. Blanco-Urgoiti, L. Añorbe, L. Pérez-Serrano, G. Domínguez, J. Pérez-Castells, *Chem. Soc. Rev*., 2004, **33**, 32; M. Rodríguez-Rivero, J. Adrio, J. C. Carretero, *Eur. J. Org. Chem*., 2002, **17**, 2881; S. T. Ingate, J. L. Marco-Contelles, J. *Org. Prep. Proced. Int.*, 1998, **30**, 123.
17 H. R. Snyder, J. A. Kuck, J. R. Johnson, *J. Am. Chem. Soc.*, 1938, **60**,105.
18 a) R. A. Batey, A. N. Thadani, D. V. Smil, *Tetrahedron Lett.*, 1999, **40**, 4289; b) R. A. Batey, A. N. Thadani, D. V. Smil, A. J. Lough, *Synthesis*, 2000, 990; c) F. Nowrouzi, A. N. Thadani, R. A. Batey, *Org. Lett.*, 2009, **11**, 2631; d) Y. Yamamoto, S.Takada, N. Miyaura, *Chem. Lett.*, 2006, **35**, 704; e) Y. Yamamoto, S.Takada, N. Miyaura, *Organometallics*, 2009, **28**, 152; f) N. Solin, O. A. Wallner, K. J. Szabó, *Org. Lett.*, 2005, **7**, 689; g) O. A. Wallner, K. J. Szabó, *Chem. Eur. J.*, 2006, **12**, 6976; h) J. Aydin, A. Rydén, K. J. Szabó, *Tetrahedron: Asymmetry*, 2008, **19**, 1867.
19 a) S. Kobayashi, T. Endo, M. Ueno, Angew. Chem. Int. Ed., 2011, 50, 12262; b) S. Kobayashi, T. Endo, U. Schneider, M. Ueno, Chem. Commun., 2010, 46, 1260. Isomerisation from γ–adduct has been also proposed: c) K.-T. Tan, S.-S. Chng, H.-S. Cheng, T.-P. Loh, *J. Am. Chem. Soc.*, 2003, **125**, 2958; d) N. Selander, K. J. Szabó, *J. Org. Chem.*, 2009, **74**, 5695.
20 a) N. Selander, A. Kipke, S. Sebelius, K. J. Szabó, *J. Am. Chem. Soc*., 2007, **129**, 13723; b) G. W. Kabalka, B. Venkataiah, G. Dong, *Tetrahedron Lett.*, 2005, **46**, 4209; c) H. Ito, T. Okura, K. Matsuura, M. Sawamura, *Angew. Chem. Int. Ed.*, 2010, **49**, 560.
21 Compounds **8** and **9** could not be isolated from each other by column chromatography. Nevertheless they could be separated by GC-MS. This analysis revealed that **8** is a mixture of diastereoisomers in roughly 1:1 ratio.
22 Y. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* , 2013, **135**, 10642. See also: S. Sebelius, V. J. Olsson, O. A. Wallner, K. J. Szabó, *J. Am. Chem. Soc*., 2006, **128**, 8150.