organic synthesis.<sup>[1]</sup> The synthesis of vinylic boron compounds by thermal Diels–Alder reactions is rare, since the low reactivity of alkynylboronic esters<sup>[2]</sup> and the instability of 2boron-functionalized 1,3-dienes<sup>[3]</sup> prohibit the efficient use of these materials in these reactions.

In contrast to the thermal Diels–Alder reactions with alkynylboronic esters, the cobalt(i)-catalyzed cycloaddition<sup>[4]</sup> of alkynylboron compounds **1** with the acyclic 1,3-dienes **2** proceeds under very mild conditions to generate the corresponding dihydroaromatic vinylboron compounds **3** in good yield (Scheme 1).<sup>[5]</sup> A catalyst system consisting of  $[CoBr_2(dppe)]$  (dppe = bis(diphenylphosphanyl)ethane), ZnI<sub>2</sub>, and Zn powder has proven to be very effective for the reaction of the alkynylboron compounds.



**Scheme 1.** Regioselective cobalt(1)-catalyzed Diels-Alder reaction of alkynylboronic esters with 1,3-dienes.

Alkynyl pinacol boronic esters, alkynyl diisopropylboronic esters, and alkynyl-9-BBN boranes can all be used as the dienophilic alkyne component. The latter cycloadducts are much more difficult to isolate than the pinacol derivatives, which can be purified by regular column chromatography on silica gel.

The reaction of the alkynylboron compounds with isoprene generates predominantly the regioisomer in which the methyl group of the diene and the boronic ester functionality have a *meta* relationship. Both the regioselectivity and the stability of the adducts increased on going from the 9-BBN derivatives to the isopropyl boronic esters to the pinacol boronic esters (Table 1). For the latter adducts the regioselectivity is generally very good (>95: < 5).<sup>[6]</sup> In most cases the other regioisomer could only be detected in traces.<sup>[7]</sup>

Based on the effective control of the regiochemistry, the mild reaction conditions, and the good yields of the sensitive dihydroaromatic products, we investigated the subsequent reactions of the cycloadducts as a platform for the efficient synthesis of more complex products. The complexity of the products could be increased significantly by palladium-catalyzed Suzuki coupling reactions (Scheme 2). The reaction sequence consisting of the cobalt-catalyzed Diels–Alder reaction, Suzuki coupling giving **4**, and mild oxidation with DDQ to yield **5** can be performed as a one-pot operation without isolation of the intermediates. The dihydroaromatic vinylic boron compounds **3** can be used in sp<sup>2</sup>/sp<sup>2</sup> and sp<sup>2</sup>/sp coupling reactions with the corresponding halides to generate intermediates **4**. Thus building blocks can be connected to give more complex polyfunctionalized structures (Table 2).

Catalytic Diels–Alder Reactions

## Alkynylboronic Esters as Efficient Dienophiles in Cobalt-Catalyzed Diels-Alder Reactions

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In memory of Konstantin Smolko

The palladium-catalyzed Suzuki coupling of boron-functionalized aromatic and vinylic building blocks has been established as a useful tool for carbon–carbon bond formation in

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Angew. Chem. Int. Ed. 2003, 42, 2795-2797

DOI: 10.1002/anie.200351404



R <sup>1</sup>	Diene	Product	Yield [%]
Ph	7	(Pin)B Ph	85
Ph	$\mathbf{x}$	(Pin)B	76
Ph		(Pin)B Ph	71
Ph		(Pin)B	68
Ph	OSiMe <sub>3</sub>	(Pin)B Ph	61
SiMe <sub>3</sub>		(Pin)B Me <sub>3</sub> Si	85
<u>}</u>		(Pin)B	91
Ph		(Pin)B Ph <sup>oor</sup>	63
MeO		(Pin)B MeO	76
	$R^{1}$ $Ph$ $Ph$ $Ph$ $Ph$ $SiMe_{3}$ $Ph$ $Ph$ $MeO \rightarrow m$	R1DienePh $\downarrow$ Ph $\downarrow$ Ph $\downarrow$ Ph $\downarrow$ Ph $\downarrow$ Ph $\downarrow$ SiMe <sub>3</sub> $\downarrow$ $\downarrow$ $\downarrow$ Ph $\downarrow$	R1DieneProductPh $\downarrow$ $\stackrel{(Pin)B}{}$ Ph $\downarrow$ $\stackrel{(Pin)B}{}$



**Table 2:** Results of the reaction sequence consisting of Diels-Alder reaction, Suzuki coupling, and DDQ oxidation.





**Scheme 2.** Suzuki coupling of the dihydroaromatic boron derivatives and subsequent oxidation. dppf=bis(diphenylphosphanyl)ferrocene, DDQ = dichlorodicyanobenzoquinone.



Tricyclic compounds can be prepared efficiently when the Suzuki coupling of the isopropenyl substituents building block **6** with alkoxy-functionalized aromatic halides is followed by oxidation with DDQ and cleavage of the ether with trimethylsilyl iodide (Scheme 3). Spontaneous cyclization<sup>[8]</sup> gives the framework of the family of cannabinoid natural products **7**. Structural variations are easily accessible by this



Scheme 3. Synthesis of heterocyclic compounds from polyfunctionalized dihydroaromatic boron compounds. TMSI = trimethylsilyl iodide.

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modular approach. For example, the Suzuki coupling of 2iodobenzylic alcohol and the following acid-catalyzed cyclization generates the structurally related product **8** in good yield. These and other reactions of dihydroaromatic boron compounds give an indication of the synthetic potential of this new class of compounds, which we are currently investigating.

## **Experimental Section**

Synthesis of 2-(5-methyl-2-thiophen-2-yl-phenyl)pyridine (Table 2, entry 9): A 10-mL Schlenk flask was charged with [CoBr<sub>2</sub>(dppe)] (31 mg, 0.05 mmol, 5 mol%), ZnI<sub>2</sub> (100 mg, 0.31 mmol, 31 mol%), and zinc dust (22 mg, 0.3 mmol, 30 mol%) in dry dichloromethane under a nitrogen atmosphere. After addition of 4,4,5,5-tetramethyl-(2-thiophen-2-yl-ethynyl)-1,3,2-dioxaborolane (234 mg, 1.0 mmol) and isoprene (82 mg, 1.2 mmol) the mixture was stirred for 16 h at ambient temperature (GC, GCMS monitoring). The solvents were removed, and the residue was dissolved in THF (5 mL) and aqueous NaOH solution (10%, 2 mL). Then 2-bromopyridine (170 mg, 1.1 mmol) and  $[PdCl_2(dppf)]$  (70 mg, 0.1 mmol, 10 mol%) were added. The solution was stirred over night at ambient temperature then diluted with water (20 mL) and diethyl ether (30 mL). The aqueous phase was extracted with diethyl ether  $(2 \times 20 \text{ mL})$ , washed with brine, and dried over Na2SO4. After the solvent was removed, the residue was dissolved in benzene (10 mL) and DDQ (300 mg, 1.32 mmol) was added in one portion. After 10 min basic Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (10% Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and 10% NaOH, 20 mL) was added and the mixture was stirred for another 5 min. The aqueous phase was extracted with diethyl ether (2 × 20 mL), washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. The crude product was purified by column chromatography on silica gel, eluting with pentane/diethyl ether (10:1), and the product was obtained as an oily mass (158 mg, 0.63 mmol, 63%). <sup>1</sup>H NMR ( $C_6D_6$ , 300 MHz):  $\delta = 2.33$  (s, 3 H), 6.57 (dd, 1 H, J = 3.5 Hz, 1.2 Hz), 6.77 (dd, 1 H, J = 3.6 Hz, 5.2 Hz), 6.97-7.20 (m, 4 H), 7.33-7.47 (m, 2H), 7.41 ppm (dd, J = 1.9 Hz, 7.7 Hz); <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>, 75 MHz):  $\delta = 21.0, 121.6, 124.9, 125.3, 126.7, 127.0, 129.2, 130.2, 130.6,$ 131.1, 135.4, 137.9, 139.6, 142.9, 149.3, 159.3 ppm; IR (KBr): *ν* = 3066 (m), 2919 (m), 1587 (s), 1562 (s), 1464 (s), 1429 (s), 818 (s), 789(s), 747 (s), 698 cm<sup>-1</sup> (s); MS (EI): *m/z* (%): 250 (*M*+-1, 100), 235 (7), 218 (13), 194 (22), 180 (4), 118 (5), 108 (5), 95 (3); HRMS: calcd for C<sub>16</sub>H<sub>12</sub>NS (*M*<sup>+</sup>-H): 250.0690, found: 250.0669.

Received: March 14, 2003 [Z51404]

**Keywords:** alkynes · boron compounds · Diels–Alder reactions · dihydroaromatic compounds · Suzuki reaction

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- [5] When Bu<sub>4</sub>NBH<sub>4</sub> was used as reducing agent for the generation of the active cobalt(t) catalyst, side reactions such as the reduction of the triple bond were observed.
- [6] The regioselectivity can be explained by steric effects as well as by an insertion of the alkynylboron derivative into the intermediate cobaltacycle in terms of a Michael addition.
- [7] Traces of a side product could be detected by GC and GCMS, which could be either a regioisomer or a double-bond isomer (1,3cyclohexadiene derivative).
- [8] Traces of water should be present so the reaction can reach completion within 5 minutes.