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Facile Synthesis of New Areneboronates as Terminal Ethyne Monomers

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Summary. *N*-Methyliminodiethyl 2-ethynylbenzeneboronate was obtained by lithiation of phenylacetylene, addition of trimethyl borate, hydrolysis, and azeotropic condensation with *N*-methyl diethanolamine. 4-(Cyano-(4-ethynylphenylamino)methyl)benzeneboronate was prepared by a facile and efficient procedure from 4-ethynylaniline and *N*-methyliminodiethyl 4-formylbenzeneboronate, followed by scandium-catalyzed cyanation. These terminal ethyne monomers were shown to undergo β-insertion with a *Schrock* metathesis catalyst to yield boronic acid-functionalized oligomers.

Keywords. Alkynes; Boronates; Homogeneous catalysis; Oligomers; Polymerizations.

Introduction

The ease with which boronic acids react with diols to give cyclic esters has led to their application in the carbohydrate field [1–3]. Immobilized boronate ligands have relevance as high affinity stationary phases in HPLC of sugars and related compounds [4]. Designed artificial receptors containing boronic acids provide general potential in life sciences [5] and host-guest chemistry [6]. Therefore, efficient and reproducible methods for the preparation of boronic acid-functionalized solid supports are highly demanded. As a rare example, polymerization of 4-vinylbenzeneboronic acid and the corresponding cyclic boroxine using free-radical and cationic initiation has been described previously [7]. Only a few other monomers with terminal ethynyl groups suitable for polymerizations were reported, namely 4-ethynylbenzeneboronic acid [8], the 2,2-dimethylpropane-1,3-diol boronate thereof [9], and the rather exotic 4-ethynyl-2-fluoropyridineboronic acid [10]. It was our intention to develop a simple access to ethynyl-substituted areneboronates which are attractive to potential applications.

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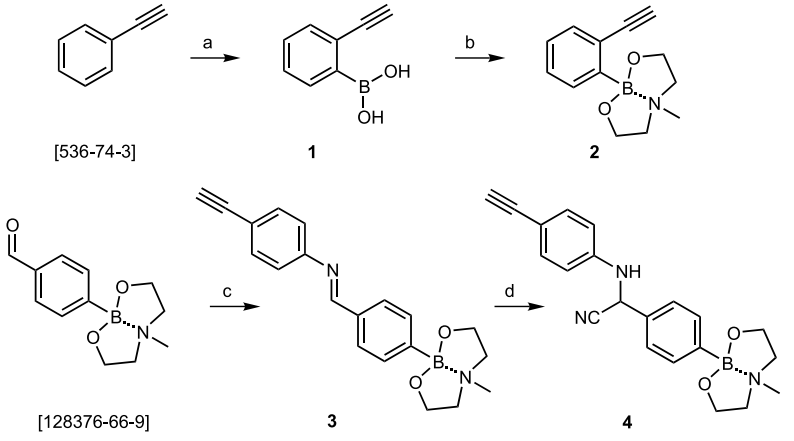
Results and Discussions

In this work, straightforward syntheses of new terminal ethyne monomers based on areneboronates for the final heterogenization by 1-alkyne polymerization are reported. To avoid interference due to the reactivity of the boronic acid moieties [11], suitable protection is needed for the combination of the required functionalities. A very convenient procedure with inexpensive starting materials afforded 2-ethynylbenzeneboronic acid (**1**) in acceptable yield. Thus, phenylacetylene was metalated by *Schlosser*'s base system [12], quenched with trimethyl borate [13], and hydrolyzed to the boronic acid **1**, which was converted to *N*-methyliminodiethyl 2-ethynylbenzeneboronate (**2**). Another approach was made from 4-formylbenzeneboronic acid [87199-17-5] [14]. Condensation of the corresponding *N*-methyliminodiethyl boronate [128376-66-9] and 4-ethynylaniline [14235-81-5] [15] yielded *N*-methyliminodiethyl 4-(4-ethynylphenyliminomethyl)benzeneboronate (**3**), which was converted to the more stable *N*-methyliminodiethyl 4-(cyano-(4-ethynylphenylamino)methyl)benzeneboronate (**4**) by $Sc(OTf)_3$-catalyzed cyanation [16] (Scheme 1). This procedure was superior to direct hydrogen cyanide addition which was found not to reach completion. All products crystallized readily on cooling, and the target compounds could be isolated in high yields and analytical purity.

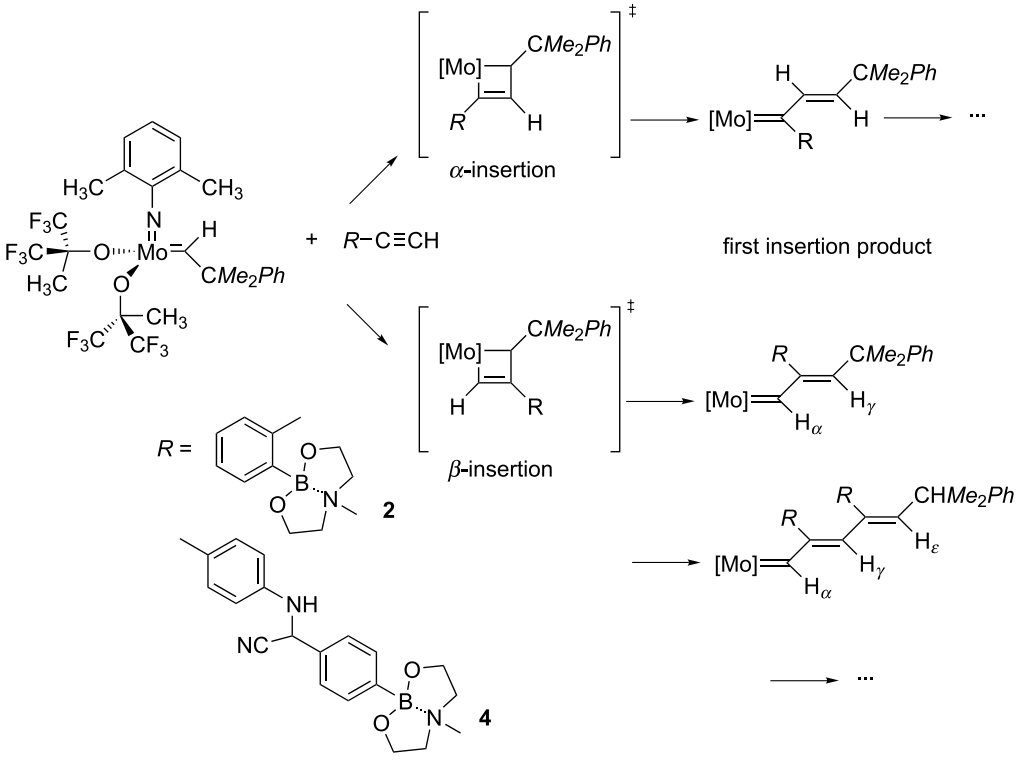
In preliminary experiments, the polymerization was investigated using one of the most reactive Mo-based *Schrock* catalysts, to demonstrate the viability of the intended target process. An illustration of the reaction and possible pathways is given in Scheme 2.

Thus, monomers **2** and **4** underwent β-insertion with the well-defined metathesis initiator Mo(N-2,6-Me_2–C_6H_3)(CHCMe_2Ph)(OC$Me$$(CF_3)_2)_2$ [17]. This selective mode of insertion was evidenced by in situ ^{1}H NMR spectroscopy. Thus, upon treatment of **2** with the initiator, a new alkylidene signal at $\delta = 11.77$ ppm and 2 new signals at $\delta = 6.24$ and 6.21 ppm, corresponding to the olefinic protons, were



a) 1) *Bu*^{t}OK/*Bu*^{n}Li, *THF*/hexane, -70°C, 2) B(O*Me*)$_3$, 3) H_2O/HCl; b) *N*-methyliminodiethanol, toluene; c) 4-ethynylaniline, toluene, 0.1 mol% pyridinium 4-toluenesulfonate; d) 1) Me_3SiCN, CH_2Cl_2, 1 mol% Sc(O*Tf*)$_3$, 0°C, 2) H_2O

Scheme 1



Scheme 2

observed. Similarly, when treating **4** with the initiator, a new alkylidene signal at $\delta = 12.18$ ppm and a new signal for H_γ at $\delta = 6.40$ ppm were observed. The fact that **4** undergoes β-insertion is not surprising at all, since this may be expected from the steric situation of the monomer. Thus, when approaching the CNO-face of the catalyst [18], only an orientation that results in β-addition is possible. In fact, this mode of insertion has been observed for all 4-substituted phenylalkynes [19–21]. However, reactivity of **2** is somewhat surprising since 2-substituted phenylacetylenes have a high tendency to undergo α-addition with *Schrock*-type initiators, particularly with the one used here [20–22]. However, since the *anti*-isomer is known to be the reactive species in *Schrock*-type catalysts [23], the mode of insertion switches from α- to β-addition in case the steric repulsion of the 2-substitutent of the phenylacetylene with the methyl group of the arylimino-ligand becomes the governing factor (Fig. 1), then again resulting in β-addition. Solubility of both poly-**2** and poly-**4** was low. In fact, only oligomers of both monomers with degrees of polymerization (DP) up to 15 were soluble in either *THF* or methylene chloride.

In summary, these preliminary experiments demonstrated that monomers **2** and **4** underwent β-insertion with the *Schrock* metathesis catalyst Mo(N-2,6-Me_2–C_6H_3)(CHCMe_2Ph)((OCMe(CF_3)$_2$)$_2$ in agreement with the elaborated model [19, 20, 24], as indicated by ^{1}H NMR, and are therefore compatible with the intended polymerization protocol. In addition, X-ray structures of the new boronate monomers **2**, **3**, and **4** are shown in Figs. 2–4, and crystallographic data and refinement details

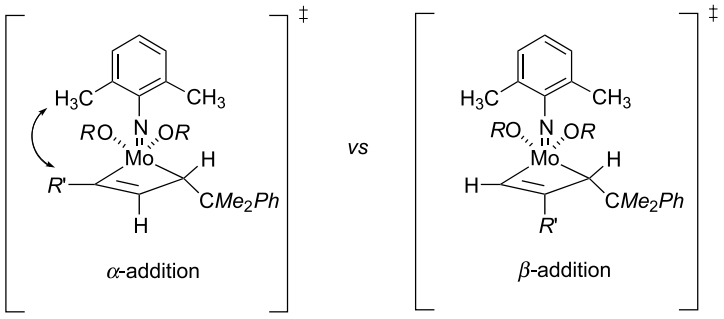


Fig. 1. Steric interaction of the R'-group of a terminal alkyne with the CH_3 substituent of the arylimino ligand in the transition state

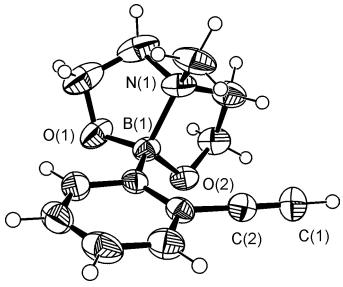


Fig. 2. Molecular structure of **2** (50% displacement ellipsoids)

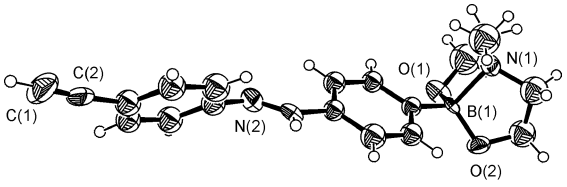


Fig. 3. Molecular structure of **3** (50% displacement ellipsoids); the solvent molecule was omitted for clarity

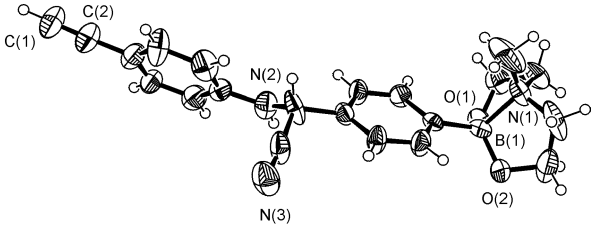


Fig. 4. Molecular structure of **4** (50% displacement ellipsoids); the solvent molecule was omitted for clarity

are given in Table 1. It is noteworthy that these crystals were not specially grown, they rather represent the quality of the bulk material as obtained.

Finally, the *N*-methyldiethanolamine adducts can be hydrolyzed back to boronic acids with mild aqueous acids [25] to yield the desired functionalized poly-

Table 1. Crystal data and structure refinement for compounds **2**, **3**, and **4**

	2	**3 · 0.5 CH_2Cl_2**	**4 · $CHCl_3$**
Molecular formula	$C_{13}H_{16}BNO_2$	$C_{20.50}H_{22}BClN_2O_2$	$C_{22}H_{23}BCl_3N_3O_2$
M_r	229.08	374.66	478.59
Crystal system	orthorhombic	orthorhombic	monoclinic
Space group	*Pbca*	*Pca*2(1)	*P*2(1)/*n*
a/Å	11.4173(3)	12.931(3)	11.689(4)
b/Å	11.1594(3)	28.209(6)	12.240(3)
c/Å	19.4802(6)	10.949(2)	17.499(4)
α/°	90	90	90
β/°	90	90	96.35(2)
γ/°	90	90	90
V/Å^3	2481.98(12)	3993.9(15)	2488.3(12)
Z	8	8	4
T/K	223(2)	213(2)	218(2)
D_{calc}/g cm^{-3}	1.226	1.246	1.278
Absorption coefficient/mm^{-1}	0.081	0.208	0.391
F (000)	976	1576	992
Color, habit	colorless prism	light yellow prism	light yellow plate
Crystal size/mm^3	0.35×0.35×0.4	0.4×0.25×0.15	0.35×0.18×0.10
θ Range for data collection/°	2.76–23.99	2.54–20.99	2.77–20.00
Index ranges	$-13\leq h\leq 0$, $-12\leq k\leq 0$, $-22\leq l\leq 22$	$-8\leq h\leq 13$, $0\leq k\leq 28$, $0\leq l\leq 10$	$0\leq h\leq 11$, $0\leq k\leq 11$, $-16\leq l\leq 16$
Reflections collected	3594	2782	2460
Independent reflections	1943 ($R_{int}=0.0135$)	2343 ($R_{int}=0.0374$)	2314 ($R_{int}=0.0337$)
Reflections with $I>2\sigma(I)$	1650	1511	1316
Data/restraints/parameters	1943/0/155	2343/1/308	2314/1/284
Goodness-of-fit on F^2	1.067	1.024	1.058
Final R indices [$I>2\sigma(I)$]	$R_1=0.0424$, $wR_2=0.1165$	$R_1=0.0696$, $wR_2=0.1551$	$R_1=0.0745$, $wR_2=0.1749$
R indices (all data)	$R_1=0.0505$, $wR_2=0.1223$	$R_1=0.1275$, $wR_2=0.1805$	$R_1=0.1398$, $wR_2=0.1995$

mers. Other potential uses of ethynyl boronic acids include *Suzuki*- and *Sonogashira*-type couplings [11].

Experimental

All chemicals were standard reagent grade (Aldrich) and used without further purification. The solvents were purified according to standard procedures. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AC 300 spectrometer (300 MHz) and were referenced to Si*Me*$_4$. Infrared spectra were recorded on a Nicolet 510 FT-IR instrument. Mass spectra were obtained on a Varian CH-7 spectrometer (EI, 70 eV). Melting points were taken on a *Kofler* hot-plate apparatus and are uncorrected. GPC data were determined in *THF* using a Waters 484 UV-VIS detector, a 717 Autosampler, a column thermostat (35°C), a 510 HPLC pump, a 490E UV-detector, a 410 RI detector, and a Millenium software package. Calibration plots were recorded using *PS*-standards. Elemental analyses were found to agree favorably with the calculated values. Diffraction intensity data were collected using graphite-monochromated Mo-K$_\alpha$-radiation ($\lambda=0.71073$ Å) on a Nonius Kappa CCD *via* ϕ- and ω-scans

(compound **2**) or a Bruker P4 diffractometer *via* ω-scans (**3** and **4**). The structures were solved by direct methods (SHELXS-97) and refined by full matrix least-squares against F^2 (SHELXL-97). All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were located by difference *Fourier* methods but, in the refinement, they were generated geometrically and refined with isotropic displacement parameters. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as CCDC-260722 (**2**), CCDC-260723 (**3**), and CCDC-260724 (**4**). 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).

2-Ethynylbenzeneboronic acid (**1**, $C_8H_7BO_2$)
To a cooled (−75°C) solution of 14.03 g (0.125 mol) *Bu*^{t}OK in 80 cm^3 *THF* and 80 cm^3 hexane was added 62.5 cm^3 2 *M*. (0.125 mol) *Bu*Li in pentane, and the mixture was stirred for 20 min. Then 5.48 cm^3 (0.05 mol) ethynylbenzene were added with a syringe. After 1 h, 8.52 cm^3 (0.075 mol) trimethylborate were added, and the mixture was allowed to attain room temperature. The reaction was quenched by the addition of 100 cm^3 H_2O. After the removal of the volatiles, 300 cm^3 H_2O and 20 cm^3 concentrated HCl were added. The solution was extracted with 150 cm^3 *Et*$_2$O, and the extracts were dried with anhydrous Na_2SO_4 and evaporated. The residue was dissolved in 20 cm^3 *THF* and allowed to stand in the refrigerator for several days to afford 2.2 g (30%) crystalline **1**. Mp 93–95°C (*THF*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.49$ (s, 1H), 6.41 (s, 2H), 7.41–7.44 (m, 2H), 7.54–7.56 (m, 1H), 8.00–8.03 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 81.4$, 85.0, 125.2, 128.9, 130.8, 1331.1, 135.7 ppm; IR (KBr): $\bar{\nu} = 3502$, 3365, 3268, 1592, 1559, 1343, 1073, 762 cm^{-1}.

N-Methyliminodiethyl 2-ethynylbenzeneboronate (**2**, $C_{13}H_{16}BNO_2$)
A solution of 750 mg (5.14 mmol) **1** and 612 mg (5.14 mmol) *N*-methyldiethanolamine in 120 cm^3 toluene was refluxed for 2 h. Water was removed azeotropically using a *Dean-Stark* trap. The solution was concentrated under reduced pressure and cooled to −30°C. The off-white precipitate was collected by filtration, washed with *Et*$_2$O, and dried to give 974 mg (83%) **2**. Mp 170–173°C (toluene); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.49$ (s, 3H), 3.14–3.18 (m, 4H), 3.20 (s, 1H), 4.06–4.18 (m, 4H), 7.20 (td, $J = 7.3$ Hz, $J = 1.7$ Hz, 1H), 7.27 (td, $J = 7.3$ Hz, $J = 1.3$ Hz, 1H), 7.49 (dd, $J = 7.3$ Hz, $J = 1.3$ Hz, 1H), 7.74 (dd, $J = 7.3$ Hz, $J = 1.3$ Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 46.4$, 61.1, 62.2, 78.1, 86.8, 125.9, 127.2, 127.7, 134.0, 134.1 ppm; IR (KBr): $\bar{\nu} = 3184$, 2849, 1468, 1080, 772, 722 cm^{-1}.

N-Methyliminodiethyl 4-(4-ethynylphenyliminomethyl)benzeneboronate (**3**, $C_{20}H_{21}BN_2O_2$)
A solution of 0.800 g (6.83 mmol) 4-ethynylaniline, 1.592 g (6.83 mmol) *N*-methyliminodiethyl 4-formylbenzeneboronate, and 2 mg (0.008 mmol) pyridinium 4-toluenesulfonate was refluxed for 16 h using a *Dean-Stark* trap. The product crystallized on cooling and was collected by filtration, washed with *Et*$_2$O, and dried to give 1.87 g (83%) **3**. Mp 185°C (CH_2Cl_2/*Et*$_2$O); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.29$ (s, 3H), 2.93–3.02 (m, 2H), 3.10 (s, 1H), 3.14–3.21 (m, 2H), 7.14 (d, $J = 8.4$ Hz, 2H), 7.51 (d, $J = 8.4$ Hz, 2H), 7.74 (d, $J = 8.1$ Hz, 2H), 7.82 (d, $J = 8.1$ Hz, 2H), 8.42 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 47.6$, 60.5, 62.3, 77.2, 83.6, 119.1, 120.9, 127.9, 132.9, 133.6, 135.1, 152.7, 161.8 ppm; IR (KBr): $\bar{\nu} = 3190$, 2871, 1627, 1594, 1206, 1085 cm^{-1}; MS (70 eV): m/z (%) = 333 (22), 332 (100), 127 (79).

N-Methyliminodiethyl 4-(cyano-(4-ethynylphenylamino)methyl)benzeneboronate
(**4**, $C_{21}H_{22}BN_3O_2$)
To a cooled (0°C) solution of 0.495 g (1.49 mmol) **3** in 50 cm^3 CH_2Cl_2 was added 7 mg (0.014 mmol) scandium triflate and 0.27 cm^3 (2.0 mmol) trimethylsilylcyanide. The mixture was stirred at room temperature for 16 h. Then, the solution was shaken with 2×50 cm^3 saturated aqueous $NaHCO_3$ and 2×50 cm^3 brine. The organic layer was dried with anhydrous Na_2SO_4, and the solvent was removed. The residue was recrystallized from $CHCl_3$/*Et*$_2$O to afford 0.464 g (87%) **4**. Mp 87°C ($CHCl_3$/*Et*$_2$O);

^{1}H NMR (300 MHz, *DMSO*-d_6): $\delta = 2.32$ (s, 3H), 2.97–3.06 (m, 2H), 3.19–3.26 (m, 2H), 3.35 (s, 1H), 4.10–4.25 (m, 4H), 5.75 (d, $J = 8.6$ Hz, 1H), 6.07 (d, $J = 8.6$ Hz, 1H), 6.86 (d, $J = 8.7$ Hz, 2H), 7.31 (d, $J = 8.7$ Hz, 2H), 7.45 (d, $J = 7.9$ Hz, 2H), 7.66 (d, $J = 7.9$ Hz, 2H) ppm; ^{13}C NMR (75 MHz, *DMSO*-d_6): $\delta = 47.9$, 49.7, 61.1, 62.9, 76.7, 84.7, 112.6, 114.3, 119.4, 126.6, 133.7, 134.8, 147.2 ppm; IR (KBr): $\bar{\nu} = 2100$, 1612 cm^{-1}; MS (70 eV): m/z (%) = 147 (68), 116 (75), 104 (100).

Investigation of the Type of Insertion

The *Schrock* catalyst Mo(N-2,6-Me_2–C_6H_3)(CHCMe_2Ph)((OCMe(CF_3)$_2$)$_2$ (20 mg, 28 μmol) was added to a solution of 13 mg (57 μmol) **2** or 10 mg (28 μmol) **4**, respectively, in 0.5 cm^3 C_6D_6 in an NMR tube. The reaction products were characterized by ^{1}H NMR (see text).

Polymerization of **2** *and* **4**

The *Schrock* initiator Mo(N-2,6-Me_2–C_6H_3)(CHCMe_2Ph)((OCMe(CF_3)$_2$)$_2$ (20 mg, 28 μmol) was added to a solution of 260 mg (570 μmol) **2** or 200 mg (570 μmol) **4**, respectively, in 10 cm^3 *THF*. The mixture was stirred at 20°C for 2 h and poured on pentane. The precipitate was collected, redissolved in *THF*, and analyzed by GPC.

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