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Azidosubstituted arylboronic acids: synthesis and Suzuki–Miyaura cross-coupling reactions

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Abstract—Arylboronic acids having a remote azido group were prepared from the corresponding azidosubstituted aryl bromides via lithiation and treatment with trialkyl borates. Preparative yields were achieved when the starting aryl bromides possessed *ortho*-alkoxy groups, which would stabilize the intermediate aryllithium species. Conventional Suzuki cross-coupling of the arylboronic acids proceeded generally well with retention of azido group; however, sometimes azidomethyl fragment underwent oxidative transformation into a nitrile.

1. Introduction

During the last decade the Suzuki–Miyaura cross-coupling leading to biaryls[1] has become a widely used technology in target synthesis, and in particular, medicinal chemistry.[2] In the synthesis of complex molecules, the organoboron component is usually less structurally complex than the more complicated aryl halide, which is due to the difficulties in preparing arylboronic acids bearing certain functional groups.[3] On the other hand, the employment of sophisticated arylboronic acids will be useful for combinatorial chemistry, that is, they may serve as multifunctional templates for the preparation of a broad variety of related compounds. The application of such arylboronic acids in medicinal chemistry is not unprecedented.[3]

The preparation of structurally diverse arylboronic acids bearing functional groups of electrophilic type from the corresponding aryl halides using organolithium protocol remained limited until Li and Nelson proposed an improved 'in situ quench' procedure when *n*-butyllithium was added to a mixture of aryl halide and triisopropyl borate.[4] Using this technique, arylboronic acids with nitrile, ester and nitro groups, as well as certain hetarylboronic acids, were prepared directly from the aryl/hetaryl halide precursors in reasonable yields.

To the best of our knowledge, organoboronic acids bearing an azido group are not documented in the literature.[5] The azido group is a well known precursor to various nitrogen containing compounds.[6] On the other hand, it is very convenient from the point of view of multistep synthesis: it may tolerate a variety of reagents and conditions, and its low polarity does not bring complications to isolation and purification.

2. Results and discussion

In our investigations we targeted compounds possessing a 2,3-dihydrobenzo[*b*]furan core, which is of interest in medicinal chemistry.[7] Aryl-substituted 2,3-dihydrobenzo-[*b*]furans are rare within the literature.[8] We proposed that the compounds of interest could be readily prepared from commercially available bromophenols **1**. Claisen rearrangement of their allyl ethers **2**, followed by oxidative cyclization of *o*-allylphenols **3** (Scheme 1), gave rise to 2-hydroxymethyldihydrobenzofurans **4**. The latter compounds were readily converted via mesylation into the key bromo azides **5**.

The conversion of aryl bromides **5** into the corresponding boronic acids by sequential *n*-BuLi–$B(OMe)_3$ treatment was found to be substrate dependent. Two 7-bromo derivatives **5a**,**b** gave boronic acids **6a**,**b** in good yields (Scheme 2), while 5-bromosubstituted compound furnished the target product in poor yield (Scheme 3).

Keywords: Azides; Boronic acids; Cross-coupling; 2,3-Dihydrobenzo[*b*]-furans; Nitriles.
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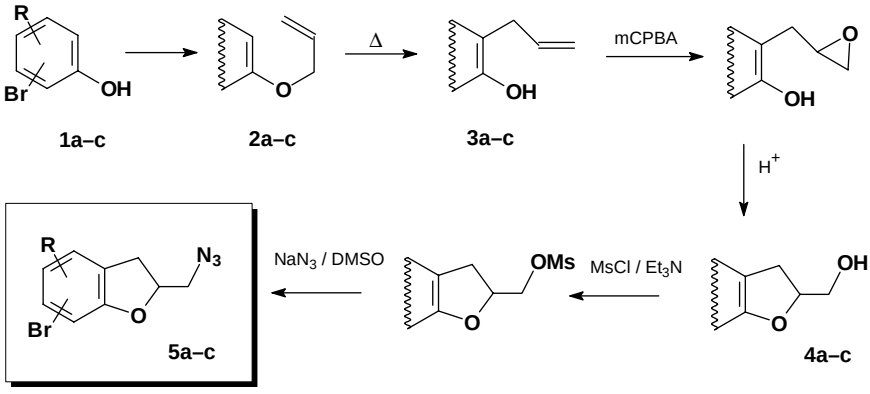
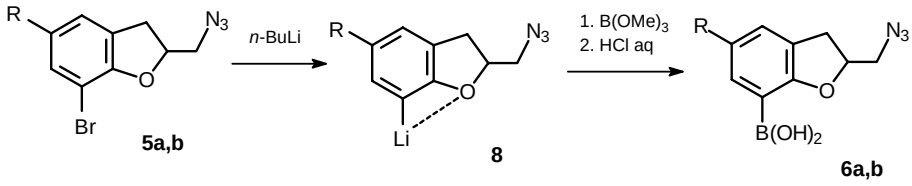
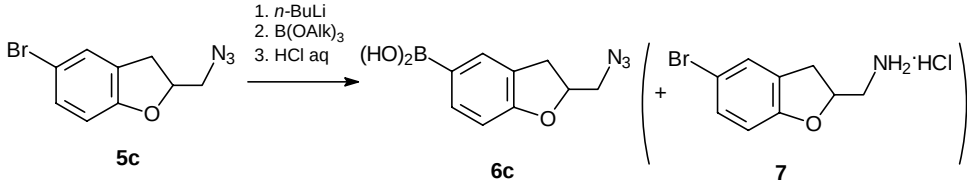


Scheme 1.

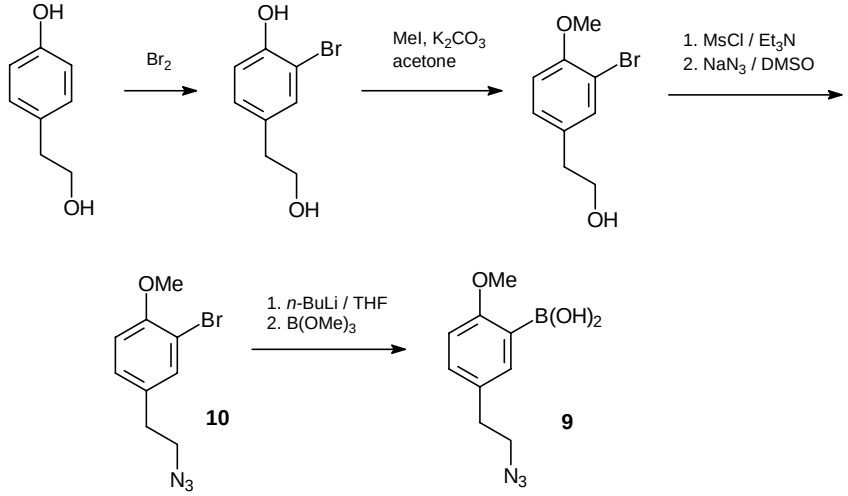


Scheme 2. R = H (**5a**,**6a**), Cl (**5b**,**6b**).



Scheme 3.

For the preparation of compound **6c**, two synthetic protocols were attempted, this is, sequential addition of *n*-BuLi and $B(OMe)_3$ to a THF solution of bromide **5c** and addition of *n*-BuLi to a THF/toluene solution of bromide **5c** and $B(O\text{-}i\text{-}Pr)_3$. Both procedures gave the target material **6c** in low yield ($\sim$10%),[9] while some differences were observed. In the first case, during the addition of *n*-BuLi prior to quenching with the electrophile, precipitation of a polymeric material took place and this material brought serious complications during the work up of the reaction mixture. Probably, the aryllithium, formed initially, may attack the azido function of another molecule (organoazides are known to react with organolithium compounds to form triazenes[6]). In the second case, the polymeric material was not formed in a large amount, while the major product was bromoamine **7** (isolated as the hydrochloride). Here, *n*-BuLi may preferentially add to the azido group rather than undergo the bromine–lithium exchange reaction.



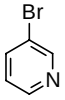
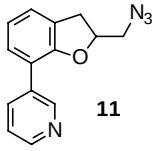
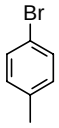
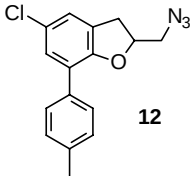
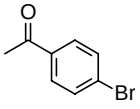
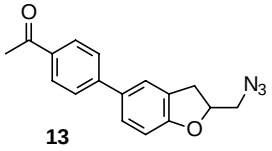
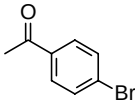
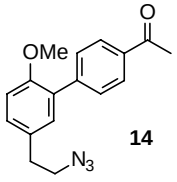
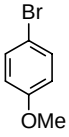
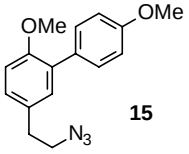
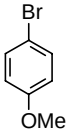
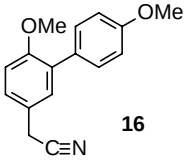
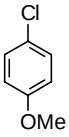
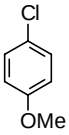
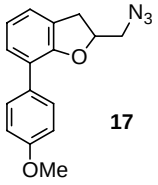
Scheme 4.

Butyltriazene, which may form, decomposes during the work-up of the reaction mixture and provides the amine **7** (cf. Ref. 10).

It is of particular note that bromides **5a**,**b** possessing alkoxy substitutents *ortho* to bromine atom give the organoboronic acids in good yields. This ether function presumably coordinates to the organolithium species, and after bromine–lithium exchange, it forms a stabilized chelate complex **8** (Scheme 2). Similarly, boronic acid **9** was prepared in good yield from *o*-bromoanisol derivative **10**, bearing a remote azido group (Scheme 4).

Organoboronic acids **6a–c** and **9** were screened using standard Suzuki cross-coupling reactions ($Pd(PPh_3)_4$, DME, Na_2CO_3 aq, 90 °C)[11] with several of aryl halides. It was important to let the aryl halide react with and $Pd(PPh_3)_4$ in DME for ca. 40 min prior to addition of other reaction components; during this period oxidative addition of aryl halide to palladium should take place. Most commonly, with

Table 1. Cross-coupling of azidosubstituted arylboronic acids with aryl halides

Entry	Boronic acid	Aryl halide	Catalyst[a]	Product	Isolated yield (%)
1	**5a**		$Pd(PPh_3)_4$	 **11**	71
2	**5b**		$Pd(PPh_3)_4$	 **12**	86
3	**5c**		$Pd(PPh_3)_4$	 **13**	77
4	**9**		$Pd(PPh_3)_4$	 **14**	68
5	**9**		$Pd(PPh_3)_4$	 **15**	78
6	**9**		$Pd(PPh_3)_4$	 **16**	32
7	**9**		$Pd(OAc)_2 \cdot 2L$	**16**	26
8	**5a**		$Pd(OAc)_2 \cdot 2L$	 **17**	34

[a] $Pd(PPh_3)_4$ with Na_2CO_3 (aq) in DME; $Pd(OAc)_2 \cdot 2L$ (L=2-dicyclohexylphosphino-2′-dimethylaminobiphenyl) with K_3PO_4 in toluene.

typical aryl bromides the reaction proceeded smoothly and the biaryl compounds **11**–**15** were obtained in good yields (Table 1, entries 1–5), with the azido group remaining intact. However, in some cases the analogous nitriles were obtained instead of azides. For example, nitrile **16** was obtained in a yield of 32% in a parallel experiment involving boronic acid **9** and 4-bromoanisol, when all the reagents were loaded simultaneously into the reaction vessel (entry 6). In some other experiments, this phenomenon could occur when the reaction mixture was accidently exposed to air, or when less active and sterically hindered hetaryl chlorides were used, that is, when the catalyst system has been somewhat different. Palladium-catalysed conversion of azidomethyl group into nitrile is not unprecedented (Pd/C or Pd black), although rare,[12,13] the yields being generally modest. Detailed investigations revealed that this reaction is balanced to 2/3 of nitrile and 1/3 of amine that may suggest red-ox disproportionation of the azidomethyl moiety; the use of an oxidant, however, did not allow raising the yield of the nitrile product.[12]

New possibilities of palladium chemistry over the past 5 years facilitate the employment of a broad variety of inactivated aryl chlorides in Suzuki reaction using bulky phosphines[14] or *N*-heterocyclic carbene[15] ligands (derived from imidazolium salts). Therefore, we attempted to couple azido-containing boronic acids **9** and **6a** with essentially inactive 4-chloroanisol (Table 1, entries 7 and 8 correspondingly) using efficient Buchwald catalytic system $Pd(OAc)_2$–2-dicyclohexylphosphino-2′-dimethylaminobiphenyl.[14a] The yields of biaryls appeared to be quite modest. Acid **9** was converted into nitrile **16** (yield 26%), while acid **6a** turned into azido-containing biaryl **17** (yield 34%, trace amounts of corresponding nitrile were also detected in the lower fractions during column chromatography). Probably, azido-group possessing certain oxidative properties would destroy this catalytic system based on Pd(II) and electron-rich phosphine while the rate of cross-coupling is slow.

3. Conclusion

To conclude, we have demonstrated that arylboronic acids bearing a remote azido group can be prepared in reasonable yields from the corresponding aryl bromides containing an *ortho*-positioned functional group, which can stabilize the intermediate organolithium species by intramolecular chelation. The azido-substituted arylboronic acids are useful substrates for Suzuki–Miyaura reactions, which could promote their use as perspective templates in combinatorial chemistry and some related fields. However, their application is limited to active aryl halides.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 at 400.13 MHz (^1H) or 100.62 MHz (^{13}C) using a DRX 400 Avance (Bruker) instrument. ^{11}B NMR spectra were recorded using an AMX 400 (Bruker) spectrometer at 128.3 MHz, the chemical shifts were referred to $Et_2O\cdot BF_3$ ($\delta_B=0.0$ ppm). Elemental analyses were performed at the Analytical Laboratory of the Nesmeyanov Institute of Organoelement Compounds, Moscow. The starting bromophenols and 4-(2-hydroxyethyl)phenol were commercially available and used as purchased. Trimethyl and triisopropyl borates were freshly distilled. All solvents used in reactions and as eluents for column chromatography were freshly distilled, THF was distilled from $LiAlH_4$ under argon.

4.1.1. *o*-Allylphenols 3a–c. A mixture of bromophenol **1** (50 mmol), allyl bromide (4.8 mL, 55 mmol), freshly powdered K_2CO_3 (15.2 g, 110 mmol) and acetone (100 mL) was stirred at reflux for 2.5 h (TLC monitoring) up to the complete consumption of the starting phenol **1**. The mixture was cooled, filtered and the filter cake was washed with acetone. Concentrating of the filtrate in vacuo gave the essentially pure aryl allyl ether **2**. The material obtained was heated under argon in a flask connected to a Vigreux column on an oil bath at 200–220 °C for 2–4 h (TLC monitoring). The product was then distilled from the same flask under reduced pressure.

4.1.1.1. 2-Allyl-6-bromophenol (3a). Bp 85–90 °C (1 Torr). Yield: 7.6 g (71%). Physicochemical properties were in agreement with the literature.[16]

4.1.1.2. 2-Allyl-6-bromo-4-chlorophenol (3b). Bp 101–105 °C (1 Torr). Yield: 8.9 g (83%). Physicochemical properties were in agreement with the literature.[16a]

4.1.1.3. 2-Allyl-4-bromophenol (3c). Bp 120 °C (1 Torr). Yield: 9.3 g (75%). Physicochemical properties were in agreement with the literature.[17]

4.1.2. 7-Bromo-2-hydroxymethyl-2,3-dihydrobenzo[*b*]-furan (4a). To a warm (35 °C) solution of 2-allyl-6-bromophenol (**3a**) (7.6 g, 35.7 mmol) in CH_2Cl_2 (60 mL), *m*-chloroperoxybenzoic acid (10 g of 75% material, 43 mmol) was added in portions, and the mixture was refluxed for 4 h and then cooled to ambient temperature. Methanesulfonic acid (1 mL) in CH_2Cl_2 (5 mL) was carefully added, and the mixture was vigorously stirred for 2 h (TLC control). The mixture was then treated with 5% NaOH (aq). The organic layer was separated and washed successively with solutions of $Na_2S_2O_3$, $NaHCO_3$, NaCl and dried with Na_2SO_4. The solution was concentrated in vacuo and the residue was subjected to column chromatography (gradient 0→100% CH_2Cl_2 in CCl_4 and then 0→2% MeOH in CH_2Cl_2) to afford 4.8 g (58%) of the title compound as a colourless oil. ^1H NMR δ 2.33 (br s, 1H), 3.16 (dd, 1H, $J=15.5$, 7.8 Hz), 3.31 (dd, 1H, $J=15.5$, 9.5 Hz), 3.75 (dd, 1H, $J=12.2$, 5.6 Hz), 3.90 (dd, 1H, $J=12.2$, 3.2 Hz), 4.97 (m, 1H), 6.72 (t, 1H, $J=7.8$ Hz), 7.08 (d, 1H, $J=7.1$ Hz), 7.25 (d, 1H, $J=8.1$ Hz). ^{13}C NMR δ 32.0t, 64.4t, 83.6d, 102.5s, 121.9d, 123.9d, 128.1d, 128.1s, 131.1s, 156.6s.

4.1.3. 7-Bromo-5-chloro-2-hydroxymethyl-2,3-dihydro-benzo[*b*]furan (4b). The title compound was prepared similarly to compound **4a** in a 61% yield, mp 69–70 °C. ^1H NMR δ 2.18 (br s, 1H), 3.17 (dd, 1H, $J=16.0$, 8.0 Hz), 3.30 (dd, 1H, $J=16.0$, 9.4 Hz), 3.74 (dd, 1H, $J=12.4$, 5.3 Hz), 3.91 (dd, 1H, $J=12.4$, 3.3 Hz), 4.99 (m, 1H), 7.05 (s, 1H), 7.25 (s, 1H). ^{13}C NMR δ 32.0t, 64.2t, 84.2d, 102.5s, 124.2d, 125.8s, 129.4s, 130.5d, 155.6s. Anal. Calcd for

$C_9H_8BrClO_2$: C, 41.02; H, 3.06; Cl+Br, 43.77. Found: C, 40.83; H, 3.02; Br+Cl, 43.86.

4.1.4. 5-Bromo-2-hydroxymethyl-2,3-dihydrobenzo[*b*]-furan (4c). The title compound was prepared similarly to compound **4a** in a 74% yield. ^{1}H NMR data were in good agreement with the literature.[18]

4.1.5. 2-Azidomethyl-7-bromo-2,3-dihydrobenzo[*b*]-furan (5a). To a stirred solution of alcohol **4a** (4.8 g, 21 mmol) and triethylamine (4 mL) in CH_2Cl_2 (20 mL), methanesulfonyl chloride (1.9 mL, 23 mmol) was slowly added at 0–5 °C. The reaction was accompanied by precipitation of solid triethylammonium chloride. After the mesylate formation was complete (ca. 1 h, TLC control), the mixture was treated with $NaHCO_3$ (aq), and the organic layer was separated and washed successively with solutions of HCl, NaCl, $NaHCO_3$ and dried with Na_2SO_4. Evaporating the solvent furnished the crude mesylate. This material was dissolved in a mixture of MeCN (23 mL) and DMSO (7 mL), 18-crown-6 ether (0.15 g) was added, and then sodium azide (2.8 g, 43 mmol) was added with stirring in one portion. The mixture was heated to a gentle reflux for 7–8 h (TLC monitoring). After the reaction was complete, the most of acetonitrile was distilled off, water (50 mL) was added to the residue, and the organic components were extracted with CH_2Cl_2. The combined extracts were washed with brine, dried with $CaCl_2$ and concentrated in vacuo. The remainder was subjected to column chromatography (gradient 0→25% CH_2Cl_2 in CCl_4) to afford 3.88 g (72%) of the title azide as a colourless oil. ^{1}H NMR δ 3.15 (dd, 1H, J=16.0, 6.6 Hz), 3.41 (dd, 1H, J=16.0, 9.5 Hz), 3.50 (dd, 1H, J=13.1, 5.4 Hz), 3.56 (dd, 1H, J=13.1, 4.2 Hz), 5.04 (m, 1H), 6.75 (t, 1H, J=7.8 Hz), 7.10 (dd, 1H, J=7.3, 1.0 Hz), 7.28 (br d, 1H, J=7.8 Hz). ^{13}C NMR δ 33.5t, 54.1t, 81.4d, 102.8s, 122.2d, 123.9d, 127.2s, 131.4d, 156.3s. Anal. Calcd for $C_9H_8BrN_3O$: C, 42.54; H, 3.17; Br, 31.45; N, 16.54. Found: C, 42.54; H, 3.05; Br, 31.42; N, 16.55.

4.1.6. 2-Azidomethyl-7-bromo-5-chloro-2,3-dihydrobenzo[*b*]furan (5b). The title compound was synthesized similarly to compound **5a** in a 66% yield, white solid, mp 66 °C. ^{1}H NMR δ 3.14 (dd, 1H, J=16.6, 6.9 Hz), 3.39 (dd, 1H, J=16.1, 9.8 Hz), 3.48 (dd, 1H, J=13.1, 5.4 Hz), 3.58 (dd, 1H, J=13.1, 4.2 Hz), 5.06 (m, 1H), 7.03 (br s, 1H), 7.28 (br s, 1H). ^{13}C NMR δ 33.4t, 54.0t, 82.0d, 102.7s, 124.1d, 126.1s, 128.5s, 130.7d, 155.3s. Anal. Calcd for $C_9H_7BrClN_3O$: C, 37.47; H, 2.45; Br, 27.69; Cl, 12.29; N, 14.56. Found: C, 37.58; H, 2.39; Br, 27.76; Cl, 12.41; N, 14.51.

4.1.7. 2-Azidomethyl-5-bromo-2,3-dihydrobenzo[*b*]-furan (5c). The title compound was synthesized similarly to compound **5a** in a 69% yield, oil. ^{1}H NMR δ 3.02 (dd, 1H, J=16.1, 6.6 Hz), 3.31 (dd, 1H, J=16.1, 9.5 Hz), 3.46 (dd, 1H, J=13.0, 6.1 Hz), 3.52 (dd, 1H, J=13.0, 4.2 Hz), 4.96 (m, 1H), 6.69 (d, 1H, J=8.5 Hz), 7.23 (br d, 1H, J=8.5 Hz), 7.28 (br s, 1H). ^{13}C NMR δ 32.6t, 54.3t, 81.6d, 111.1d, 112.6s, 127.9d, 128.3s, 131.1d, 158.2s. Anal. Calcd for $C_9H_8BrN_3O$: C, 42.54; H, 3.17; Br, 31.45; N, 16.54. Found: C, 42.52; H, 3.13; Br, 31.64; N, 16.62.

4.1.8. Synthesis of 5-(2-azidoethyl)-1-bromo-2-methoxybenzene (10). a. *2-Bromo-4-(2-hydroxyethyl)phenol*. To a stirred mixture of 4-(2-hydroxyethyl)phenol (4.14 g, 30 mmol), finely powdered $NaHCO_3$ (3.5 g, 42 mmol), CH_2Cl_2 (15 mL), MeOH (6 mL) a solution of bromine (1.53 mL, 30 mmol) in CH_2Cl_2 (6 mL) was added dropwise at 0–5 °C. According to TLC data, some unreacted starting material was left, along with the formation of another component with a higher R_f, presumably 2,6-dibromo derivative. Water was added to the reaction mixture, and the organic components were extracted with EtOAc. The extract was dried ($MgSO_4$), concentrated in vacuo and the residue was subjected to column chromatography using CH_2Cl_2 as an eluent to afford 2.9 g (44%) of the title monobromo derivative as a white solid, mp 91–93 °C. ^{1}H NMR (DMSO-d_6) δ 2.60 (t, 2H, J=6.9 Hz), 3.54 (t, 2H, J=6.9 Hz), 4.56 (br s, 1H), 6.85 (d, 1H, J=8.2 Hz), 7.0 (dd, 1H, J=8.2, 1.7 Hz), 7.31 (d, 1H, J=1.7 Hz), 9.89 (s, 1H). ^{13}C NMR (DMSO-d_6) δ 37.6t, 62.2t, 108.9s, 116.1d, 129.1d, 131.9s, 132.9d, 152.1s. Anal. Calcd for $C_8H_9BrO_2$: C, 44.27; H, 4.18; Br, 36.81. Found: C, 44.24; H, 4.20; Br, 36.85.

b. *1-Bromo-5-(2-hydroxyethyl)-2-methoxybenzene*. A mixture of 2-bromo-4-(2-hydroxyethyl)phenol (2.9 g, 13.4 mmol) from the previous step, methyl iodide (1.1 mL, 17.5 mmol), freshly powdered K_2CO_3 (2.42 g, 17.5 mmol) and acetone (20 mL) was stirred at 40 °C for 5 h until the full conversion of starting phenol (TLC monitiring). Acetone was then removed by distillation, water was added to the residue, and the organic components were extracted with ether. The extracts were dried ($MgSO_4$), concentrated in vacuo and the remainder was subjected to column chromatography using CH_2Cl_2 as an eluent to afford 2.9 g (93%) of the title methyl ether as a viscous oil, which would solidify on standing. ^{1}H NMR ($CDCl_3$) δ 1.63 (br s, 1H), 2.77 (t, 2H, J=6.6 Hz), 3.80 (t, 2H, J=6.6 Hz), 3.86 (s, 3H), 6.84 (d, 1H, J=8.3 Hz), 7.12 (dd, 1H, J=8.3, 2.1 Hz), 7.41 (d, 1H, J=2.1 Hz). ^{13}C NMR ($CDCl_3$) δ 37.8t, 56.2q, 63.4t, 111.6s, 112.0d, 128.9d, 132.2s, 133.6d, 154.5s. Anal. Calcd for $C_9H_{11}BrO_2$: C, 46.78; H, 4.80, Br, 34.58. Found: C, 46.82; H, 5.16; Br, 34.71.

c. *5-(2-Azidoethyl)-1-bromo-2-methoxybenzene* (**10**). Colourless viscous oil was obtained in a 75% yield from the preceding alcohol via its mesylation and azide substitution for mesylate group (see synthesis of compound **5a**). ^{1}H NMR ($CDCl_3$) δ 2.81 (t, 2H, J=7.1 Hz), 3.47 (t, 2H, J=7.1 Hz), 3.88 (s, 3H), 6.85 (d, 1H, J=8.3 Hz), 7.12 (dd, 1H, J=8.3, 2.2 Hz), 7.40 (d, 1H, J=2.2 Hz). ^{13}C NMR ($CDCl_3$) δ 34.1t, 52.3t, 56.3q, 111.7s, 112.1d, 128.7d, 131.6s, 133.5d, 154.8s. Anal. Calcd for $C_9H_{10}BrN_3O$: C, 42.21; H, 3.94; Br, 31.20; N, 16.43. Found: C, 42.28; H, 3.81; Br, 31.46; N, 16.37.

4.2. Boronic acids 6a–c and 9

A solution of bromoarene **5a–c** or **10** (14 mmol) in THF (47 mL) was placed under argon into a one-neck flask equipped with a magnetic stirring bar and adapter with a rubber septum and a gas inlet, which was connected to a manifold. The solution was cooled to ca. −80 °C and the traces of oxygen were removed by three-fold pumping—filling with argon. *n*-Butyllithium (8.4 mL of 1.7 M solution

in hexane, 14.3 mmol) was added dropwise during 10 min at the same temperature, and the mixture was stirred for additional 20 min. Trimethyl borate (6.3 mL, 55 mmol) was quickly added in one potion, and the mixture was allowed to reach ambient temperature. The flask was then put on a rotary evaporator and the most of volatile components were distilled off, the excess of trimethyl borate being removed by subsequent co-evaporation with toluene. The yellow viscous residue was shaken with water and ether and the layers were separated. The ethereal layer was treated with 5% NaOH (aq), and the alkaline solution was combined with the previous aqueous layer. The rest of neutral organic components were extracted from this aqueous phase with ether. The aqueous layer was cooled to 0–5 °C and acidified with 10% HCl (pH∼1), which caused precipitation of a solid material (sometimes the product emerged as oil, which would solidify on trituration). The product was collected by filtration, washed with water and dried in air. Usually, the material thus obtained was essentially pure. If a product required purification by column chromatography (2% MeOH in CH_2Cl_2 as eluent), one should note that during this operation boronic acids would form liquid methyl esters. To recover the acids, the material was triturated with water (solid was formed quickly) and then dried.

4.2.1. (2-Azidomethyl-2,3-dihydrobenzo[*b*]furan-7-yl)-boronic acid (6a). Yield 72%, mp 105–6 °C. ^{1}H NMR (DMSO-d_6) δ 2.94 (dd, 1H, J=16.0, 6.9 Hz), 3.29 (dd, 1H, J=16.0, 9.5 Hz), 3.54 (dd, 1H, J=13.5, 5.9 Hz), 3.68 (dd, 1H, J=13.5, 3.7 Hz), 5.03 (m, 1H), 6.84 (t, 1H, J=7.3 Hz), 7.27 (dd, 1H, J=7.3, 1.0 Hz), 7.41 (br d, 1H, J=7.3 Hz), 7.46 (s, 2H). ^{13}C NMR (DMSO-d_6) δ 31.6t, 53.8t, 81.3d, 120.3d, 125.5s, 127.3d, 133.6d, 163.5s. ^{11}B NMR (DMSO-d_6) δ 29.7. Anal. Calcd for $C_9H_{10}BN_3O_3$: C, 49.36; H, 4.60; B, 4.94; N, 19.19. Found: C, 49.30; H, 4.50; B, 5.03; N, 19.00.

4.2.2. (2-Azidomethyl-5-chloro-2,3-dihydrobenzo[*b*]-furan-7-yl)boronic acid (6b). Yield 69%, mp 159–60 °C. ^{1}H NMR (DMSO-d_6) δ 2.95 (dd, 1H, J=16.4, 6.6 Hz), 3.30 (dd, 1H, J=16.4, 9.8 Hz), 3.53 (dd, 1H, J=13.5, 5.9 Hz), 3.70 (dd, 1H, J=13.5, 3.4 Hz), 5.05 (m, 1H), 7.30 (s, 1H), 7.33 (s, 1H), 7.68 (s, 2H). ^{13}C NMR (DMSO-d_6) δ 31.5t, 53.7t, 82.0d, 124.1s, 126.8d, 128.6s, 132.5d, 162.2s. ^{11}B NMR (DMSO-d_6) δ 28.5. Anal. Calcd for $C_9H_9BClN_3O_3$: C, 42.65; H, 3.58. Found: C, 42.80; H, 3.60.

4.2.3. (2-Azidomethyl-2,3-dihydrobenzo[*b*]furan-5-yl)-boronic acid (6c). Yield 11%, mp 101–2 °C. ^{1}H NMR (DMSO-d_6) δ 2.93 (dd, 1H, J=15.9, 6.8 Hz), 3.29 (dd, 1H, J=15.9, 9.5 Hz), 3.50 (dd, 1H, J=13.2, 6.4 Hz), 3.64 (dd, 1H, J=13.2, 3.4 Hz), 4.99 (m, 1H), 6.74 (d, 1H, J=8.1 Hz), 7.59 (br d, 1H, J=8.1 Hz), 7.65 (br s, 1H), 7.76 (br s, 2H). ^{13}C NMR (DMSO-d_6) δ 31.8t, 54.0t, 81.4d, 108.3d, 125.7s, 131.1d, 134.8d, 160.7s. ^{11}B NMR (DMSO-d_6) δ 29.0. Anal. Calcd for $C_9H_{10}BN_3O_3$: C, 49.36; H, 4.60; B, 4.94; N, 19.19. Found: C, 49.60; H, 4.65; B, 4.78; N, 19.00.

4.2.4. 5-(2-Azidoethyl)-2-methoxyphenylboronic acid (9). Yield 64%, mp 54–5 °C. ^{1}H NMR (DMSO-d_6) δ 2.77 (t, 2H, J=7.1 Hz), 3.50 (t, 2H, J=7.1 Hz), 3.79 (s, 3H), 6.92 (d, 1H, J=8.3 Hz), 7.28 (dd, 1H, J=8.3, 2.1 Hz), 7.46 (d, 1H, J=2.1 Hz), 7.66 (br s, 2H). ^{13}C NMR (DMSO-d_6) δ 33.7t, 51.9t, 55.4q, 110.4d, 129.8s, 131.9d, 135.9d, 162.4s. ^{11}B NMR (DMSO-d_6) δ 30.1. Anal. Calcd for $C_9H_{12}BN_3O_3$: C, 48.91; H, 5.47; B, 4.89; N, 19.01. Found: C, 48.92; H, 5.70; B, 4.74; N, 18.85.

4.2.5. 2-Aminomethyl-5-bromo-2,3-dihydrobenzo[*b*]-furan hydrochloride (7). *n*-Butyllithium (14 mL of 1.7 M solution in hexane, 24 mmol) was added during 40 min at −80 °C to a stirred deaerated mixture of 2-azidomethyl-5-bromo-2,3-dihydrobenzo[*b*]furan (**5c**) (5.08 g, 20 mmol), triisopropyl borate (5.6 g, 30 mmol), toluene (32 mL) and THF (8 mL). The thick reaction mixture was allowed to reach the ambient temperature. The flask was put on a rotary evaporator and the most of volatile components were distilled off. The residue was treated with 5% NaOH to give three layers. The aqueous layer was separated and treated as described above in the syntheses of boronic acids **6**; the yield of (2-azidomethyl-2,3-dihydrobenzo[*b*]furan-5-yl)boronic acid (**6c**) was 208 mg (5%). The other two organic layers were vigorously shaken with 10% HCl, which finally led to the formation of two layers. The aqueous layer was separated, and the rest of neutral components were extracted with ether. Solid KOH pellets were added to reach alkaline pH, and the oil thus liberated was taken into ether. The extract was concentrated in vacuo, and then treated with minimum concd HCl. The slurry thus formed was mixed with *n*-butanol and evaporated to ca. 5 mL volume. The residue was triturated with ether and the precipitate was filtered off, washed with ether and dried in air to afford 1.83 g (34%) of the title compound as a white solid, mp 230 °C (dec). ^{1}H NMR (DMSO-d_6) δ 2.90–3.10 (several peaks, 2H), 3.31–3.42 (several peaks, 2H), 5.10 (m, 1H), 6.75 (d, 1H, J=8.4 Hz), 7.27 (dd, 1H, J=8.4, 2.2 Hz), 7.41 (d, 1H, J=2.2 Hz), 8.50 (br s, 3H). ^{13}C NMR (DMSO-d_6) δ 32.4t, 42.2t, 79.8d, 111.3d, 111.8s, 128.1d, 129.6s, 130.6d, 157.8s. Anal. Calcd for $C_9H_{11}BrClNO$: C, 40.86; H, 4.19; N, 5.29. Found: C, 40.78; H, 4.14; N, 5.17.

4.3. Cross-coupling reactions (general procedure)

All reactions were performed in a two-necked flask equipped with a rubber septum and a reflux condenser connected to a manifold, which was connected to suction and argon lines. To a degassed solution of aryl bromide (2 mmol) in 1,2-dimethoxyethane (2–3 mL), $Pd(PPh_3)_4$ (70 mg, ca. 3 mol%) was added, and the mixture was stirred for ca. 40 min. Boronic acid (1.5 mmol) was added, and the mixture was degassed by pumping—argon filling. Then a freshly prepared deaerated solution of sodium carbonate (0.848 g) in water (3.2 mL) was injected through the septum, and the mixture was refluxed for 6 h. The mixture was diluted with water, the organic products were extracted with ether, and the extracts were dried ($CaCl_2$ or Na_2SO_4) and concentrated in vacuo. The residue was subjected to column chromatography using hexane–ethyl acetate mixtures as eluents.

4.3.1. 2-Azidomethyl-7-(pyrid-3-yl)-2,3-dihydrobenzo[*b*]-furan (11). The title compound was prepared in a 71% yield from 3-bromopyridine and boronic acid **6a**, oil. ^{1}H NMR ($CDCl_3$) δ 3.12 (dd, 1H, J=15.7, 7.3 Hz), 3.38 (dd, 1H, J=15.7, 9.3 Hz), 3.53 (several peaks, 2H), 5.01 (m, 1H), 6.99 (t, 1H, J=7.6 Hz), 7.20 (dd, 1H, J=7.3, 1.0 Hz), 7.29–7.36

(several peaks, 2H), 8.03 (dt, 1H, J=7.8, 1.9 Hz), 8.54 (dd, 1H, J=4.7, 1.8 Hz), 8.92 (d, 1H, J=1.8 Hz). ^{13}C NMR ($CDCl_3$) δ 32.7t, 54.3t, 81.3d, 120.2s, 121.7d, 123.1d, 124.9d, 127.0s, 127.7d, 132.7s, 135.6d, 148.1d, 149.2d, 156.3s. Anal. Calcd for $C_{14}H_{12}N_4O$: C, 66.65; H, 4.79; N, 22.21. Found: C, 66.43; H, 4.73; N, 21.98.

4.3.2. 2-Azidomethyl-5-chloro-7-(4-methylphenyl)-2,3-dihydrobenzo[*b*]furan (12). The title compound was prepared in a 86% yield from 3-bromopyridine and boronic acid **6b**, mp 44–46 °C. ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H), 3.10 (dd, 1H, J=15.9, 7.3 Hz), 3.33 (dd, 1H, J=15.9, 9.3 Hz), 3.52 (several peaks, 2H), 5.00 (m, 1H), 7.10 (br s, 1H), 7.24 (d, J=8.3 Hz), 7.28 (br s, 1H), 7.56 (d, 2H, J=8.3 Hz). ^{13}C NMR ($CDCl_3$) δ 21.2q, 32.7t, 54.3t, 81.4d, 123.5d, 124.9s, 126.0s, 127.6d, 128.1d, 128.4s, 129.2d, 132.8s, 137.6s, 154.8s. Anal. Calcd for $C_{16}H_{14}ClN_3O$: C, 64.11; H, 4.71; Cl, 11.83; N, 14.02. Found: C, 64.14; H, 4.66; Cl, 12.00; N, 14.07.

4.3.3. 5-(4-Acetylphenyl)-2-azidomethyl-2,3-dihydrobenzo[*b*]furan (13). The title compound was prepared in a 77% yield from 4-bromoacetophenone and boronic acid **6c**, mp 75–75 °C. ^{1}H NMR ($CDCl_3$) δ 2.62 (s, 3H), 2.90 (dd, 1H, J=15.9, 6.9 Hz), 3.39 (dd, 1H, J=15.9, 9.5 Hz), 3.51 (dd, 1H, J=13.0, 5.9 Hz), 3.56 (dd, 1H, J=13.0, 3.9 Hz), 5.02 (m, 1H), 6.90 (d, 1H, J=8.3 Hz), 7.42 (d, 1H, J=8.3 Hz), 7.45 (s, 1H), 7.61 (d, 2H, J=8.3 Hz), 7.99 (d, 2H, J=8.3 Hz). ^{13}C NMR ($CDCl_3$) δ 26.5q, 32.6t, 54.5t, 81.7d, 109.9d, 123.9d, 126.6s, 127.7d, 128.9d, 133.0s, 135.3s, 145.6s, 159.4s, 197.6s. Anal. Calcd for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.49; H, 5.18; N, 14.33.

4.3.4. 4-Acetyl-5′-(2-azidoethyl)-2′-methoxybiphenyl (14). The title compound was prepared in a 68% yield from 4-bromoacetophenone and boronic acid **9**, oil. ^{1}H NMR ($CDCl_3$) δ 2.63 (s, 3H), 2.89 (t, 2H, J=7.3 Hz), 3.52 (t, 2H, J=7.3 Hz), 3.81 (s, 3H), 6.96 (d, 1H, J=8.3 Hz), 7.18–7.24 (several peaks, 2H), 7.63 (d, 2H, J=8.3 Hz), 8.00 (d, 2H, J=8.3 Hz). ^{13}C NMR ($CDCl_3$) δ 26.6q, 34.4t, 52.6t, 55.7q, 111.6d, 128.0d, 129.5d, 129.7d, 130.4s, 131.0d, 135.6s, 143.3s, 155.4s, 197.7s; one quaternary C is missing. Anal. Calcd for $C_{17}H_{17}N_3O_2$: C, 69.14; H, 5.80; N, 14.23. Found: C, 68.69; H, 5.75; N, 14.11.

4.3.5. 5-(2-Azidoethyl)-2,4′-dimethoxybiphenyl (15). The title compound was prepared in a 78% yield from 4-bromoanisol and boronic acid **9**, oil. ^{1}H NMR ($CDCl_3$) δ 2.89 (t, 2H, J=7.3 Hz), 3.52 (t, 2H, J=7.3 Hz), 3.81 (s, 3H), 3.86 (s, 3H), 6.92–6.99 (several peaks, 3H), 7.13–7.18 (several peaks, 2H), 7.45–7.50 (several peaks, 2H). ^{13}C NMR ($CDCl_3$) δ 34.5t, 52.7t, 55.3q, 55.7q, 111.5d, 113.5d, 128.2d, 130.2s, 130.5d, 130.6s, 130.7s, 131.0d, 155.4s, 158.7s. Anal. Calcd for $C_{16}H_{17}N_3O_2$: C, 67.83; H, 6.05; N, 14.83. Found: C, 67.91; H, 6.07; N, 14.68.

4.3.6. 4-Methoxy-3-(4-methoxyphenyl)phenylacetonitrile (16). To a degassed solution of 4-bromoanisol (249 mg, 1.33 mmol) and boronic acid **9** (221 mg, 1 mmol) in 1,2-dimethoxyethane (2.5 mL), $Pd(PPh_3)_4$ (35 mg, ca. 3 mol%) was added, and the mixture was degassed again by pumping—argon refilling. Then a freshly prepared deaerated solution of sodium carbonate (0.8 g) in water (3 mL) was injected through the septum, and the mixture was refluxed for 8 h (palladium black precipitated when the mixture reached an elevated temperature). The mixture was diluted with water, the organic products were extracted with ether, and the extracts were dried ($CaCl_2$) and concentrated in vacuo. The residue was subjected to column chromatography (gradient 2→20% EtOAc in hexane) to afford 82 mg (32%) of the title compound as a white solid, mp 65–67 °C. ^{1}H NMR ($CDCl_3$) δ 3.72 (s, 2H), 3.82 (s, 3H), 3.85 (s, 3H), 6.94–6.98 (several peaks, 3H), 7.22–7.25 (several peaks, 2H), 7.43–7.48 (several peaks, 2H). ^{13}C NMR ($CDCl_3$) δ 22.8t, 55.3q, 55.7q, 111.7d, 113.6d, 118.1s, 122.0s, 127.5d, 130.0s, 130.2d, 130.5d, 131.1s, 156.2s, 158.9s. Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.91; H, 5.87; N, 5.43.

The same compound **16** was obtained in 26% yield using boronic acid **9** and 4-chloroanisol essentially as described for compound **17** (see below).

4.3.7. 2-Azidomethyl-7-(4-methoxyphenyl)-2,3-dihydrobenzo[*b*]furan (17). A mixture of boronic acid **6a** (164 mg, 0.75 mmol), 4-chloroanisol (214 mg, 1.5 mmol), toluene (2 mL), $Pd(OAc)_2$ (11 mg, 0.045 mmol), 2-dicyclohexylphosphino-2′-dimethylaminobiphenyl (35 mg, 0.09 mmol) and K_3PO_4 (508 mg) was stirred under argon at 95 °C for 5 h. The reaction mixture was cooled, suspended in toluene (10 mL), silica gel (ca. 3 mL) was added, and the volatile components were removed under reduced pressure. The material thus obtained was loaded on a top of chromatography column packed with silica gel, and the products were eluted with gradient 0→10% EtOAc in hexane to give 72 mg (34%) of the title compound as a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 3.10 (dd, 1H, J=15.5, 7.1 Hz), 3.35 (dd, 1H, J=15.5, 9.5 Hz), 3.48–3.57 (several peaks, 2H), 3.85 (s, 3H), 4.98 (m, 1H), 6.93–6.99 (several peaks, 3H), 7.12 (br d, 1H, J=7.3 Hz), 7.28 (br d, 1H, J=7.8 Hz), 7.65 (d, 2H, J=8.8 Hz). ^{13}C NMR ($CDCl_3$) δ 32.9t, 54.5t, 55.3q, 80.9d, 113.8d, 121.4d, 123.4d, 123.6s, 126.5s, 127.7d, 129.4s, 129.5d, 155.9s, 158.9s. Anal. Calcd for $C_{16}H_{15}N_3O_2$: C, 68.31; H, 5.37; N, 14.94. Found: C, 68.18; H, 5.37; N, 14.72.

References and notes

1. For the reviews see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; pp 49–98.
2. For the recent cases, see e.g.: (a) Noeteberg, D.; Hamelink, E.; Hulten, J.; Wahlgren, M.; Vrang, L.; Samuelsson, B.; Hallberg, A. *J. Med. Chem.* **2003**, *46*, 734. (b) Zhou, J.; Zhang, A.; Klaess, T.; Johnson, K. M.; Wang, C. Z.; Ye, Y. P.; Kozikowski, A. P. *J. Med. Chem.* **2003**, *46*, 1997. (c) Mitsumori, S.; Tsuri, T.; Honma, T.; Hiramatsu, Y.; Okada, T.; Hashizume, H.; Inagaki, M.; Arimura, A.; Yasui, K.; Asanuma, F.; Kishino, J.; Ohtani, M. *J. Med. Chem.* **2003**, *46*, 2436. (d) Diguarher, T. L.; Chollet, A.-M.; Bertrand, M.; Hennig, P.; Raimbaud, E.; Sabatini, M.;

Guilbaud, N.; Pierre, A.; Tucker, G. C.; Casara, P. *J. Med. Chem.* **2003**, *46*, 3840. (e) Wang, L.; Wang, G. T.; Wang, X.; Tong, Y.; Sullivan, G.; Park, D.; Leonard, N. M.; Li, Q.; Cohen, J.; Gu, W.-Z.; Zhang, H.; Banch, J. L.; Jakob, C. G.; Hutchins, C. W.; Stoll, V. S.; Marsh, K.; Rosenberg, S. H.; Sham, H. L.; Lin, N.-H. *J. Med. Chem.* **2004**, *47*, 612. (f) Faucher, A.-M.; White, P. W.; Brochu, C.; Grand-Maitre, C.; Rancourt, J.; Fazal, G. *J. Med. Chem.* **2004**, *47*, 18. (g) Adamski-Werner, S.; Palaninathan, S. K.; Sacchettini, J. C.; Kelly, J. W. *J. Med. Chem.* **2004**, *47*, 355.

3. (a) Chang, L. L.; Ashton, W. T.; Flanagan, K. L.; Chen, T.-B.; O'Malley, S. S.; Zingaro, G. J.; Kivlighn, S. D.; Siegl, P. K. S.; Lotti, V. J.; Chang, R. S. L.; Greenlee, W. J. *J. Med. Chem.* **1995**, *38*, 3741. (b) Li, J. J.; Norton, M. B.; Reinhard, E. J.; Anderson, G. D.; Gregory, S. A.; Isakson, P. C.; Koboldt, C. M.; Masferrer, J. L.; Perkins, W. E.; Seibert, K.; Zhang, Y.; Zweifel, B. S.; Reitz, D. B. *J. Med. Chem.* **1996**, *39*, 1846. (c) Murugesan, N.; Gu, Z.; Stein, P. D.; Bisaha, S.; Spergel, S.; Girotra, R.; Lee, V. G.; Lloyd, J.; Misra, R. N.; Schmidt, J.; Mathur, A.; Stratton, L.; Kelly, Y. F.; Bird, E.; Waldron, T.; Liu, E. C.-K.; Zhang, R.; Lee, H.; Serafino, R.; Abboa-Offei, B.; Mathers, P.; Giancarli, M.; Seymour, A. A.; Webb, M. L.; Moreland, S.; Barrish, J. C.; Hunt, J. T. *J. Med. Chem.* **1998**, *41*, 5198. (d) Liao, Y.; Böttcher, H.; Harting, J.; Greiner, H.; Amsterdam, C. van; Cremers, T.; Sundell, S.; März, J.; Rautenberg, W.; Wikström, H. *J. Med. Chem.* **2000**, *43*, 517–525. (e) Murugesan, N.; Gu, Z.; Stein, P. D.; Spergel, S.; Mathur, A.; Leith, L.; Liu, E. C.-K.; Zhang, R.; Bird, E.; Waldron, T.; Marino, A.; Morrison, R. A.; Webb, M. L.; Moreland, S.; Barrish, J. C. *J. Med. Chem.* **2000**, *43*, 3111. (f) Murugesan, N.; Tellew, J. E.; Gu, Z.; Kunst, B. L.; Fadnis, L.; Cornelius, L. A.; Baska, R. A. F.; Yang, Y.; Beyer, S. M.; Monshizadegan, H.; Dickinson, K. E.; Panchal, B.; Valentine, M. T.; Chong, S.; Morrison, R. A.; Carlson, K. E.; Powell, J. R.; Moreland, S.; Barrish, J. C.; Kowala, M. C.; Macor, J. E. *J. Med. Chem.* **2002**, *45*, 3829. (g) Murugesan, N.; Gu, Z.; Spergel, S.; Young, M.; Chen, P.; Mathur, A.; Leith, L.; Hermsmeier, M.; Liu, E. C.-K.; Zhang, R.; Bird, E.; Waldron, T.; Marino, A.; Koplowitz, B.; Humphreys, W. G.; Chong, S.; Morrison, R. A.; Webb, M. L.; Moreland, S.; Trippodo, N.; Barrish, J. C. *J. Med. Chem.* **2003**, *46*, 125. (h) Michellys, P.-Y.; Ardecky, R. J.; Chen, J.-H.; D'Arrigo, J.; Grese, T. A.; Karanewsky, D. S.; Leibowitz, M. D.; Liu, S.; Mais, D. A.; Mapes, C. M.; Montrose-Rafizadeh, C.; Ogilvie, K. M.; Reifel-Miller, A.; Rungta, D.; Thompson, A. W.; Tyhonas, J. S.; Boehm, M. F. *J. Med. Chem.* **2003**, *46*, 4087.
4. Li, W.; Nelson, D. P.; Jensen, M. S.; Hoerrner, R. S.; Cai, D.; Larsen, R. D.; Reider, P. J. *J. Org. Chem.* **2002**, *67*, 5394.
5. In the very recent precedent, 2-(azidomethyl)phenylboronic acid was prepared by treatment 2-(bromomethyl)phenylboronic acid with NaN_3 in THF/H_2O mixture: Ganina, O. G.; Zamotaeva, S. G.; Nosarev, M. A.; Kosenkova, O. V.; Naumov, M. I.; Shavirin, A. S.; Finet, J.-P.; Fedorov, A. Y. *Izv. AN, ser. khim.* **2005**, 1560 [*Russ. Chem. Bull.*, (Engl. Transl.)].
6. Brown, B. R. *The Organic Chemistry of Aliphatic Nitrogen Compounds*; Clarendon: Oxford, 1994; pp 644–667.
7. Selected examples: (a) Matharu, S. S.; Rowlands, D. A.; Taylor, J. B.; Westwood, R. *J. Med. Chem.* **1977**, *20*, 197. (b) Clayson, J.; Jales, A.; Tyacke, R. J.; Hudson, A. L.; Nutt, D. J.; Lewis, J. W.; Husbands, S. M. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 939. (c) Klein, P.; Nelson, W. L. *J. Med. Chem.* **1992**, *35*, 4589. (d) Portoghese, P. S.; Nagase, H.; MaloneyHuss, K. E.; Lin, C.-E.; Takemori, A. E. *J. Med. Chem.* **1991**, *34*, 1715. (e) Hoffman, W. F.; Woltersdorf, O. W.; Novello, F. C.; Cragoe, E. J.; Spinger, J. P.; Watson, L. S.; Fanelli, G. M. *J. Med. Chem.* **1981**, *24*, 865. (f) Lee, C.-M.; Parks, J. A.; Bunnell, P. R.; Plattner, J. J.; Field, M. J.; Giebisch, G. H. *J. Med. Chem.* **1985**, *28*, 589. (g) Davis, L.; Agnew, M. N.; Effland, R. C.; Klein, J. T.; Kitzen, J. M.; Schwenkler, M. A. *J. Med. Chem.* **1983**, *26*, 1505. (h) Ohkawa, S.; Fukatsu, K.; Miki, S.; Hashimoto, T.; Sakamoto, J.; Doi, T.; Nagai, Y.; Aono, T. *J. Med. Chem.* **1997**, *40*, 559.
8. (a) Coleman, G. H.; Rigterink, R. H. Patent US 2548704, 1951; *Chem. Abstr.* **1951**, *45*, 8561. (b) Bradsher, C. K.; Reames, D. C. *J. Org. Chem.* **1978**, *43*, 3800. (c) Jimenez, M. C.; Leal, P.; Miranda, M. A.; Tormos, R. *J. Org. Chem.* **1995**, *60*, 3243. (d) Uozumi, Y.; Kato, K.; Hayashi, T. *J. Am. Chem. Soc.* **1997**, *119*, 5063. (e) Jimenez, M. C.; Miranda, M. A.; Tormos, R. *J. Org. Chem.* **1998**, *63*, 1323.
9. Boronic acid having a CH_2NHBoc fragment, which is synthetically equivalent to **6c**, was prepared in a good yield from bromoazide **5c** via reduction to primary amine, Boc protection and then treatment with 2 equiv of *n*-BuLi followed by quenching with $B(OMe)_3$.
10. For the acidic cleavage of triazenes to amines see: (a) Dimroth, O. *Ber. Dtsch. Chem. Ges.* **1906**, *39*, 3906. (b) Smith, R. H.; Denlinger, C. L.; Kupper, R.; Mehl, A.; Michejda, C. J. *J. Am. Chem. Soc.* **1986**, *108*, 3726.
11. (a) Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513. (b) Gronowitz, S.; Bobosik, V.; Lawitz, K. *Chem. Scr.* **1984**, *23*, 120. (c) Alo, B. I.; Kandil, A.; Patil, P. A.; Sharp, M. J.; Siddiqui, M. A.; Snieckus, V. *J. Org. Chem.* **1991**, *56*, 3763.
12. Hayashi, H.; Ohno, A.; Oka, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 506.
13. (a) Kappe, O. C. *Liebigs Ann. Chem.* **1990**, 505. (b) Mohanakrishnan, A. K.; Srinivasan, P. C. *Synth. Commun.* **1995**, *25*, 2415. (c) Genin, M. J.; Allwine, D. A.; Anderson, D. J.; Barbachyn, M. R.; Emmert, D. E.; Garmon, S. A.; Graber, D. R.; Grega, K. C.; Hester, J. B.; Hutchinson, D. K.; Morris, J.; Reischer, R. J.; Ford, C. W.; Zurenko, G. E.; Hamel, J. C.; Schaadt, R. D.; Stapert, D.; Yagi, B. H. *J. Med. Chem.* **2000**, *43*, 953.
14. (a) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550. (b) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020. (c) Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553. (d) Zapf, A.; Jackstell, R.; Rataboul, F.; Riermeier, T.; Monsees, A.; Fuhrmann, C.; Shaikh, N.; Dingerdissen, U.; Beller, M. *Chem. Commun.* **2004**, 38. (e) Barder, T. E.; Buchwald, S. L. *Org. Lett.* **2004**, *6*, 2649. (f) Colacot, T. J.; Shea, H. A. *Org. Lett.* **2004**, *6*, 3731. (g) Liu, B.; Moffett, K. K.; Joseph, R. W.; Dorsey, B. D. *Tetrahedron Lett.* **2005**, *46*, 1779. (h) Tewari, A.; Hein, M.; Zapf, A.; Beller, M. *Tetrahedron* **2005**, *61*, 9705.
15. (a) Gstöttmayr, C. W. K.; Böhm, V. P. W.; Herdtweck, E.; Grosche, M.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1363. (b) Navarro, O.; Kaur, H.; Mahjoor, P.; Nolan, S. P. *J. Org. Chem.* **2004**, *69*, 3173. (c) Lebel, H.; Janes, M. K.; Charette, A. B.; Nolan, S. P. *J. Am. Chem. Soc.* **2004**, *126*, 5046. (d) Arentsen, K.; Caddick, S.; Clocke, F. G. N.; Herring, A. P.; Hitchcock, P. B. *Tetrahedron Lett.* **2004**, *45*, 3511. (e) Wang, A.-E.; Zhong, J.; Xie, J.-H.; Li, K.; Zhou, Q.-L. *Adv. Synth. Catal.* **2004**, *346*, 595. (f) Song, C.; Ma, Y.; Chai, Q.; Ma, C.; Jiang, W.; Andrus, M. B. *Tetrahedron* **2005**, *61*, 7438. (g) Arensten, K.; Caddick, S.; Cloke, F. G. N.

Tetrahedron **2005**, *61*, 9710. (h) Navarro, O.; Marion, N.; Scott, N. M.; Gonzalez, J.; Amoroso, D.; Bell, A.; Nolan, S. P. *Tetrahedron* **2005**, *61*, 9716. (i) Huang, W.; Guo, J.; Xiao, Y.; Zhu, M.; Zou, G.; Tang, J. *Tetrahedron* **2005**, *61*, 9783.

16. (a) Piers, E.; Brown, R. K. *Can. J. Chem.* **1963**, *41*, 2917. (b) Hurd, W. *J. Am. Chem. Soc.* **1936**, *58*, 941.
17. (a) Goering, J. *J. Am. Chem. Soc.* **1958**, *80*, 3277. (b) White, W. N.; Gwynn, D.; Schlitt, R.; Girard, C.; Fife, W. J. *J. Am. Chem. Soc.* **1958**, *80*, 3271. (c) Lasek, W.; Makosza, M. *Synthesis* **1993**, 780. (d) Russell, M. G. N.; Baker, R.; Ball, R. G.; Thomas, S. R.; Tsou, N. N.; Castro, J. L. *J. Chem. Soc., Perkin Trans. 1* **2000**, 893.
18. Chapleo, C. B.; Myers, P. L.; Butler, R. C. M.; Davis, J. A.; Doxey, J. C.; Higgins, S. D.; Myers, M.; Roach, A. G.; Smith, C. F. C.; Stillings, M. R.; Welbourn, A. P. *J. Med. Chem.* **1984**, *27*, 570.