Journal of Organometallic Chemistry 819 (2016) 138–146

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Dendritic *bis*- and *tetrakis*-iminodiacetic acid-boronate complexes in one-pot cross-coupling reactions

Anindra Sharma, Prabhat Kumar, Rita Pal, Narayanaswamy Jayaraman*

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560012, India

ARTICLE INFO

Article history:
Received 9 March 2016
Received in revised form
20 May 2016
Accepted 24 June 2016
Available online 25 June 2016

Keywords:
Boronates
Cross-coupling reactions
Dendrimers
Hydrolysis
Iminodiacetic acid
Suzuki-Miyaura reaction

ABSTRACT

Iminodiacetic acids are versatile metal chelating ligands. We herein undertook a study of dendritic *bis*- and *tetrakis*-iminodiacetic acids functionalized at the peripheries of branched core moieties. The dendritic iminodiacetic acids are synthesized by *O*- and *N*-alkylations of chosen alcohol and amine reactive sites emanating from a branched core. In order to identify the reactivities of such dendritic iminodiacetic acids, chelation with arylboronates is conducted. An assessment of the hydrolysis under aq. basic condition shows that dendritic boronates hydrolyze to boronic acid significantly slower than monomeric boronates. Slower hydrolysis of dendritic boronates is taken advantage, in order to conduct competitive C–C bond-forming Suzuki-Miyaura cross-coupling reactions. Teraryl synthesis is performed using monomeric and dendritic boronates. The iterative, multiple aryl-aryl bond formation is conducted subsequently, so as to prepare tetraaryls, through consecutive reactions of chosen boronic acid, monomeric boronate, dendritic boronate and aryl bromide, in one-pot. The study shows that slower hydrolysis of dendritic boronate is valuable in order to conduct multiple consecutive aryl-aryl bond formation.

1. Introduction

Iminodiacetic acid is a versatile chelating ligand for metal ions, aided by additional coordination of the imine moiety of the ligand with the metal ions [1–4]. Ethylenediamine tetraacetic acid is a prime example of the versatility of this ligand to metal ion coordination [5]. Iminodiacetic acid is a valuable ligand for organometallic reactions, for example, the value of this ligand in boronate complex formation and subsequent slow release to boronic acid from the complex in Suzuki-Miyaura cross-coupling reactions has been exploited elegantly by Burke and co-workers [6], as a strategy to mitigate a major undesired homocoupling of boronic acids in the cross-coupling reactions. With innumerable occasions in which iminodiacetic acid ligands are involved, we undertook a study in which this ligand is installed multiply in a dendritic fashion. Dendritic structures are characterized by the presence of building blocks arranged symmetrically around a core atom or moiety. Seminal early reports on the synthesis of cascade molecules by Vögtle [7], poly(amidoamine) series by Tomalia [8], arborals by Newkome [9], poly(benzyl ether) series by Fréchet [10], poly(propylene imine) series by Meijer [11] and phosphorus dendrimer series by Caminade and Majoral [12] established a new direction to the synthesis and studies of highly branched molecules. Ever since these reports, interest in highly branched and monodispersed macromolecules is established thoroughly in multiple directions of studies [13–16], including stabilization of metal catalysts by dendritic ligands [17,18]. With the advancements in dendritic structures, we undertook an effort to study the iminodiacetic acid ligand when arranged in a branched fashion. Dendritic iminodiacetic acids were synthesized, following which, the benefits of the newly formed dendritic iminodiacetic acids were assessed through formation of boronate ester complexes. The dendritic boronates were utilized subsequently in Suzuki-Miyaura iterative cross-coupling reaction, so as to form ter- and tetraaryls in one-pot. Synthesis and studies of new dendritic iminodiacetic acids and their boronate complexes in the cross-coupling reactions are reported herein.

2. Results and discussion

2.1. Synthesis bis- and tetrakis-iminodiacetic acids

Molecular structures of the target *bis*- (**1**) and *tetrakis*-iminodiacetic acids (**2**) containing branched dendritic structures are

* Corresponding author.
E-mail address: jayaraman@orgchem.iisc.ernet.in (N. Jayaraman).

http://dx.doi.org/10.1016/j.jorganchem.2016.06.030
0022-328X/

shown in Fig. 1. These dendritic iminodiacetic acids were synthesized, from commercially available monomer building blocks, namely, bromoethyl acetate and bromoacetonitrile.

Synthesis of zero generation **1** and first generation **2** dendrimers was initiated using 2,2′-diaminoethyl ether (**3**) as the core, by as divergent assembly method. Thus, iterative reactions of *O*- and *N*-alkylations and functional group reductions, in a multistep synthetic sequence, were utilized to prepare **1** and **2** (Scheme 1). The diamine derivative **3**, in turn, was prepared by subjecting diethylene glycol to *bis*-*O*-tosylation, reaction of the resulting *bis*-*O*-tosylate with NaN_3 and reduction of the resulting *bis*-azide to *bis*-amine **3**. Reaction of **3** with ethyl bromoacetate afforded *tetrakis*-ester **4**, in 90% yield. *Tetrakis*-ester derivative **4** was subjected to reduction in the presence of $LiAlH_4$ in THF to the corresponding *tetrakis*-alcohol **5**, in a nearly quantitative yield (Scheme 1).

The progress of reduction of ester functionalities in **4** was monitored by the disappearance of stretching frequency at 1741 cm^{-1} in the IR spectrum. Upon completion of the reaction, *tetrakis*-alcohol **5** was isolated from inorganic salts through differential solubilisation in MeOH and in $CHCl_3$. *Tetrakis*-alcohol **5** was reacted subsequently with bromoacetonitrile in THF:DMF (1:1), in the presence of NaH, under reflux. The resulting reaction mixture was purified (SiO_2) to afford *tetrakis*-nitrile **6**, in 56% yield. *Tetrakis*-nitrile **6** was reduced to *tetrakis*-amine **7**, using Raney-Co catalyst and H_2 (50 atm), in a nearly quantitative yield. The progress of the nitrile reduction in **6** to amine was monitored by the disappearance stretching frequency at ~2209 cm^{-1} in the IR spectrum. The iterative reaction of *N*-alkylation of *tetrakis*-amine **7** with ethyl bromoacetate and purification of the reaction mixture (SiO_2, CH_2Cl_2/MeOH linear gradient) afforded *octakis*-ester **8**, in 48% yield (Scheme 1). The newly-formed *tetrakis*- (**4**) and *octakis*- (**8**) esters were hydrolysed under aq. alkaline conditions to afford the corresponding *tetrakis*- and *octakis*-acids **1** and **2**, respectively, in quantitative yields. The structural homogeneities of the *bis*- (**1**) and *tetrakis*- (**2**) iminodiacetic acids were verified by physical methods. Changes in the chemical shifts of the $-CH_2-$ group adjacent to the peripheral functionality were observed periodically. Thus, disappearance of the singlet at ~3.59 ppm of $-CH_2CO_2Et$ group and appearance of resonances at ~2.56 and ~3.64 ppm, corresponding to $-CH_2CH_2OH$, were observed, consistent with the presence of these functional groups. Similarly, disappearance of the signal at 4.29 ppm of $-CH_2CN$ and appearance of resonances at ~3.45 and ~2.74 ppm of $-CH_2CH_2NH_2$ were observed for the nitrile to amine reaction. Functional group changes at the peripheries were also confirmed by ^{13}C NMR spectroscopy. Disappearance of −CN resonance at ~116 ppm and the appearance of carbonyl group resonance of the ester functionality at ~171 ppm confirmed complete conversion of nitrile to amine. Similarly, reduction of ester to alcohol led to the appearance of a signal at ~62 ppm ($-CH_2OH$). The constitutions of the dendrimers were confirmed further by mass spectrometry in each case. Fig. 2 provides overlay spectra of the conversion of *tetrakis*-ester **4** to *octakis*-ester **8**, involving *tetrakis*-alcohol **5** and *tetrakis*-nitrile **6** intermediates.

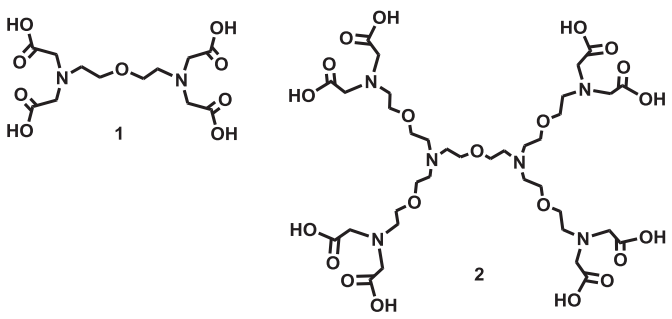


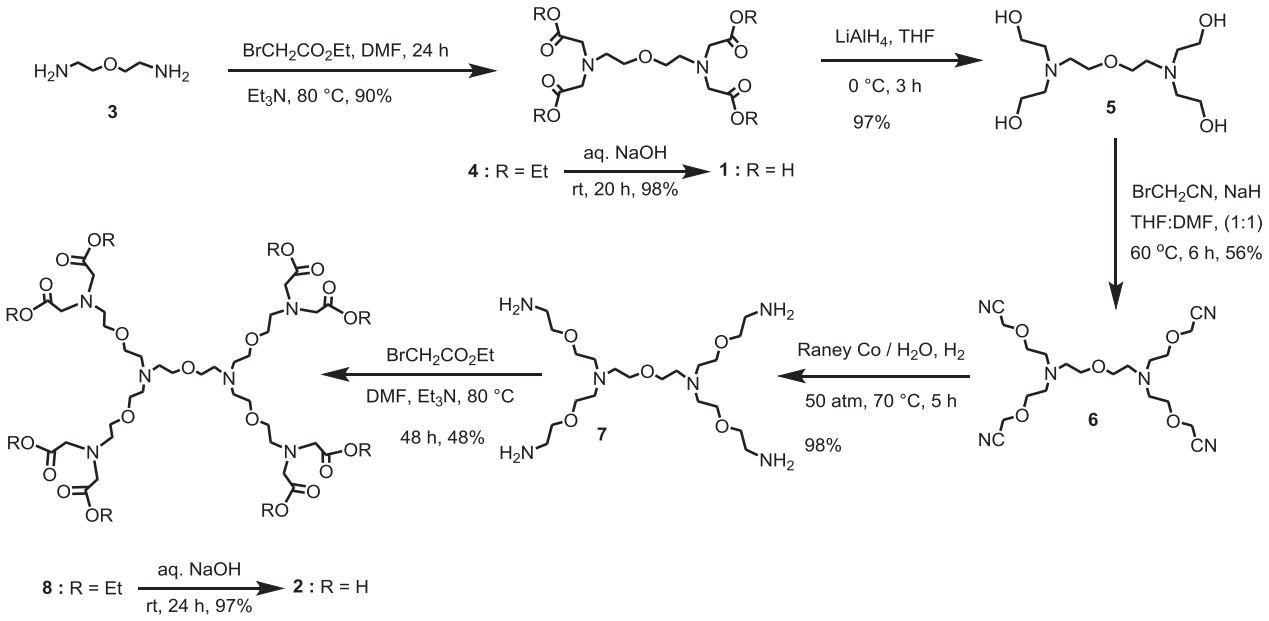
Fig. 1. Molecular structures of the dendritic iminodiacetic acids.

2.2. Studies of boronate complexes of *1* and *2*

Following synthesis of *bis*- (**1**) and *tetrakis*-iminodiacetic acids (**2**), their complexation with boronic acid and subsequent reactions of boronates were investigated. Iminodiacetic acid forms the corresponding boronate upon reaction with a boronic acid. Additional coordination of imine moiety to boron centre in the boronate complex provides stability to the complex, and thus, iminodiacetic acid boronate complexes are considered orthogonal to the reactivity of boronic acids. Facile hydrolysis of iminodiacetic acid-boronate complex releases the reactive boronic acid. Such a stability of a boronate and its lability under hydrolytic condition to form boronic acid is exploited elegantly in the particular class of boronic acid mediated reactions, namely, the Suzuki-Miyaura cross-coupling reactions [19–21]. The boronate mediated Suzuki-Miyaura cross-coupling reactions are developed immensely in order to overcome pertinent difficulties of protodeboronation, oxidation and homocoupling competing reactions [22], as demonstrated by Lloyd-Jones and co-workers. Important to sustained developments in Suzuki-Miyaura *C–C* bond forming reactions are: (i) the discovery of 'slow-release' methodology, in which the reactive boronic acid is generated *in situ* through controlled basic hydrolysis of a boronate ester, developed by Burke and co-workers [23–26]; (ii) the development of 1,8-diaminonaphthalene as the protecting group of boronic acids, the deprotection to the reactive boronic acid implemented through an acid treatment, reported by Suginome and co-workers [27,28] and (iii) the development of organotrifluoroborate as a robust surrogate of boronic acid, which hydrolyzes in protic media to generate the boronic acid [29–32]. We followed these developments in order to identify the reactivities of dendritic *bis*- and *tetrakis*-iminodiacetic acids.

Syntheses of *bis*- and *tetrakis*-boronates **9** and **10** were conducted upon reaction of arylboronic acids with dendritic iminodiacetic acids **1** and **2** in DMF or DMSO-PhMe (1:5) for ~24–48 h, with azeotropic removal of water from the reaction mixture (Scheme 2) [33].

The formation of the phenyl *bis*-boronate ester (**9a**) was ascertained from ^1H NMR spectrum, following the early report of iminodiacetic acid-boronate complexes studied by Wrackmeyer and co-workers [34]. The diastereotopic methylene protons of iminodiacetate portion in dendritic phenyl *bis*-boronates appeared as a well-resolved pair of doublets at δ 4.39 and 4.22, with a geminal coupling constant of 17.1 Hz. Aromatic protons appeared as a set of multiplets between δ 7.49 and 7.35 ppm. Internal methylene protons adjacent to ether and tertiary nitrogen moieties resonated as triplets at δ 3.89 and 3.07 ppm, respectively. In ^{13}C NMR spectrum, the diastereotopic methylene carbon resonated at δ 59.2 ppm, whereas carbons adjacent to tertiary nitrogen and ether moieties appeared at δ 57.8 and 66.3 ppm, respectively. Carbonyl carbon of the ester moiety appeared at δ 168.5 ppm. ^{11}B NMR spectrum of dendritic phenyl *bis*-boronate showed chemical shift at δ 11.9, as compared to phenyl boronic acid δ value 29.5. Composition of the phenyl *bis*-boronate (**9a**) was also confirmed by mass spectrometry, which showed molecular ion peak at *m/z* 531.1716, corresponding to the sodium adduct. *Tetrakis*-boronates (**10**) followed a similar trend as that of *bis*-boronates. In ^1H NMR spectrum of **10a**, the diastereotopic methylene protons appeared as a pair of doublets at δ 4.45 and 4.26, with geminal coupling constant of 17.2 Hz, whereas the aromatic protons resonated as two multiplets between δ 7.53 and 7.36 ppm. The methylene protons of ether moiety of the



Scheme 1. Synthesis of *bis*- (**1**) and *tetrakis*- (**2**) dendritic iminodiacetic acids.

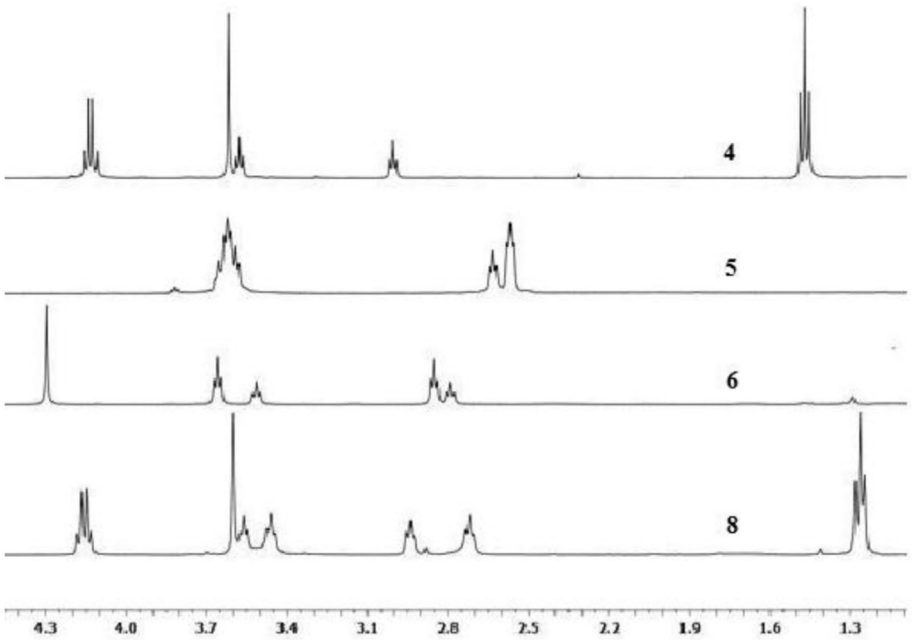
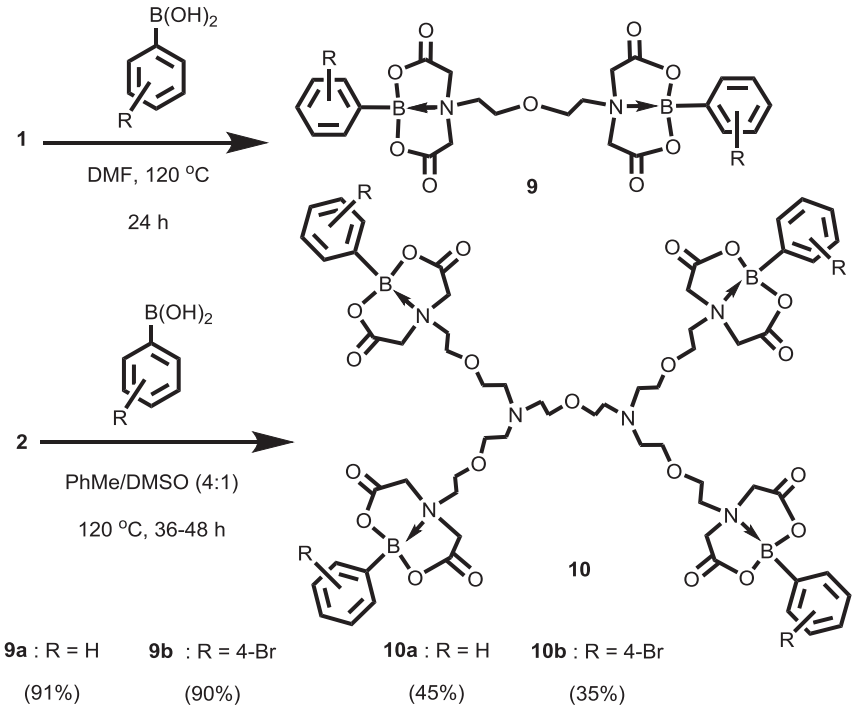


Fig. 2. Overlay of ^{1}H NMR spectra of the conversion of *tetrakis*-ester **4** to *octakis*-ester **8**.

dendrimer resonated as triplets at δ 3.82 and 3.63 ppm ($J = 4.3$ Hz), whereas tertiary nitrogen attached methylene protons of dendritic backbone appeared as triplets at 2.98 and 2.89 ppm. In ^{13}C NMR spectrum of **10a**, carbonyl carbon resonated at δ 168.8 ppm, whereas diastereotopic methylene carbon at δ 60.9 ppm. Carbons adjacent to tertiary nitrogen and ether moieties appeared at δ 59.3 and 78.2 ppm, respectively. ^{11}B NMR spectrum showed resonance at δ 11.8 ppm. The structure of **10a** (R = H) was confirmed by mass spectrometry, which showed a signal, corresponding to the $[M + Na]^{+}$ adduct. Aryl *bis*- (**9b**) and *tetrakis*- (**10b**) boronates were characterized similarly through ^{1}H, ^{13}C and ^{11}B NMR spectroscopies. Mass spectrometric analysis could not be secured for these aryl *tetrakis*-boronates.

Hydrolytic stabilities of *bis*- and *tetrakis*-boronoates **9a** and **10a** were assessed subsequently. In order to compare the rate of hydrolysis, monomeric boronate phenyl *N*-methyliminodiacetic acid boronate **I** was used. The hydrolysis of boronates (5 mM) was performed using aq. K_3PO_4 (50 mM, pH 7.8) in CD_3CN at 40 °C, and ^{1}H NMR spectra were recorded at periodic time intervals until the hydrolysis reached a plateau. The analysis was aided through integration of two sets of diasterotopic methylene protons, as compared to methoxy proton of *p*-bromoanisole, used as the internal standard. The progress of hydrolysis was plotted as a function of time and fitted to an exponential decay curve, from which the rate constants were calculated (Table 1).

As shown in Table 1, the *tetrakis*-boronate **10a** was ~20 times



Scheme 2. Synthesis of dendritic *bis*- and *tetrakis*-boronates.

Table 1
First order rate constants (k) of **I**, **9a** and **10a**, at 40 °C in CD_3CN.

Compound	k (10^{-4} s^{-1})	Compound	k (10^{-4} s^{-1})	Compound	k (10^{-4} s^{-1})
I	4.5	**9a**	3.8	**10a**	0.21

slower in hydrolysis, in comparison to monomeric boronate **I**. *Bis*-boronate also hydrolysed relatively slower than monomer boronates. Hydrolysis would be initiated by the attack of the base at the susceptible carbonyl carbon of the boronate, leading to a tetrahedral oxyanion adduct. We premise that either the formation or break-down of this adduct might account for the observed differences in the rates of hydrolysis. Presence of non-covalent interactions between hydroxyl group of the tetrahedral adduct and the dendritic scaffold might stabilize the intermediate and such a stability in the case of *tetrakis*-boronate would be absent for the monomeric or the *bis*-boronate complexes studied herein. From ^{11}B NMR monitoring, neither evolution of a new peak nor shifting of peak in the first few hours of the hydrolytic conditions occurred with *tetrakis*-system, suggesting that the N→B coordination was intact during this period. Thus, although we are unable to precisely account the significantly enhanced hydrolytic stability of the *tetrakis*-system, possible origin of the effect might be accounted as given above.

The slower hydrolysis of dendritic boronates was assessed subsequently in competitive Suzuki-Miyaura cross-coupling reactions involving aryl boronates and aryl bromides. Initial reactions were conducted using *bis*- and *tetrakis*-boronates with bromobenzene, and the reactivity profiles were compared with phenylboronic acid and **I**. The reactions were performed in the presence of base and catalyst (10 mol%) in aq. DMF, at 80 °C (Scheme 3). Formation of biphenyl was monitored through GC-MS analysis of the reaction mixture. Fig. 3 shows a plot of the biphenyl formation mediated by phenylboronic acid and various phenyl boronates.

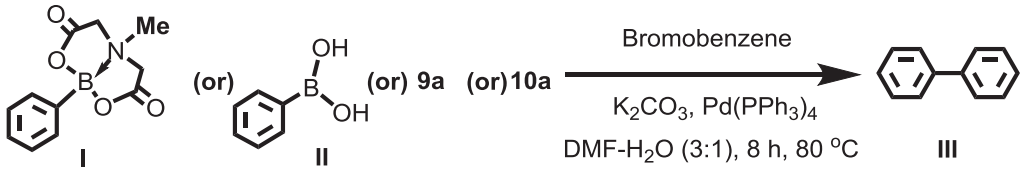
The above experiments show that whereas phenylboronic acid and boronate **I** afford >80% biphenyl within 1 h, dendritic *bis*- (**9a**) and *tetrakis*- (**10a**) boronates afford much reduced yields. After 1 h, *tetrakis*-boronate **10a** afforded only 49% of biphenyl product and completion of the reaction took several hours, as a result of significantly reduced hydrolysis to the corresponding reactive boronic acid. In these reactions, it is noted that the biphenyl formation may have occurred well as a result of a competitive homocoupling of boronates as a source reaction, which warranted us to conduct the reaction with differing aryl boronates. Further reactions were thus conducted using substituted aryl-boronates and boronic acids.

A monomeric boronate **IV/VII**, *bis*- or *tetrakis*-phenyl boronate and 1-bromonaphthalene were thus subjected to the cross-coupling reaction. The reactions were conducted in one pot in a mixture of **IV**/**VII**, **9b**/**10b** and aryl bromide, in DMF/water (3:1) at 40 °C, in the presence of K_2CO_3 (3 mol equivalents) and $Pd(PPh_3)_4$ catalyst (10 mol%) (Scheme 4).

The *bis*- and *tetrakis*-boronates were normalized and thus, for a molar equivalent of *bis*-boronate and *tetrakis*-boronate, 2 and 4 equivalents of monomeric boronate and 1-bromonathphthalene, respectively, were used. The progress of the reaction was followed through GC-MS analysis. After 8 h of reaction duration, the reaction mixture was analysed and formation of **V**, **VI** and **11** were identified. The products formed in this reaction are given in Table 2.

From the above reactions, we infer that terphenyl product forms in higher yields with dendritic boronates, as a result of slower hydrolysis of dendritic boronates and faster hydrolysis of monomeric boronate **IV**/**VII**. This observation prompted us to continue the one-pot cross-coupling reaction with bifunctional monomeric and dendritic boronates.

An effort was thus undertaken to access tetraphenyl, involving three different types of boronates and an aryl bromide. The cross-coupling reaction was initiated by the reaction of *m*-tolylboronic acid with bifunctional monomer boronate **IX** in DMF, in the presence of $Pd(PPh_3)_4$ (cat.) and K_2CO_3 at 80 °C, in DMF under anhydrous conditions. The design of the experiment is shown in Scheme



Scheme 3. Suzuki-Miyaura cross-coupling reaction mediated by boronic acid or boronates.

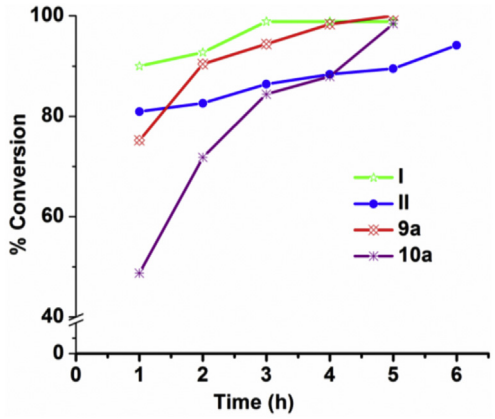
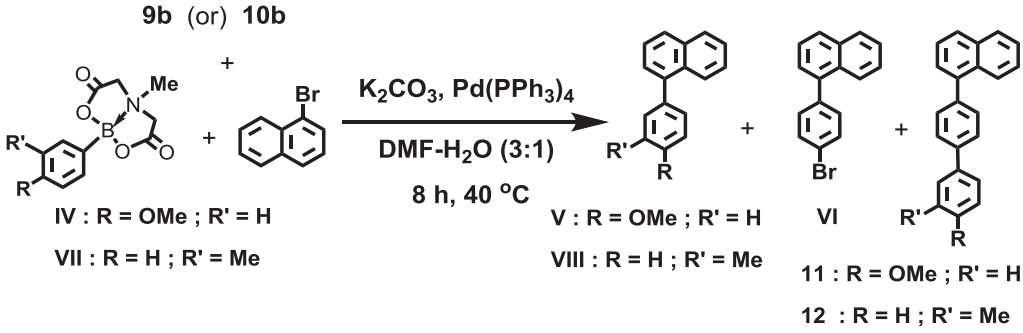


Fig. 3. A plot of the formation of biphenyl *vs* time involving different boron reagents **I**, **II**, **9a** and **10a**.

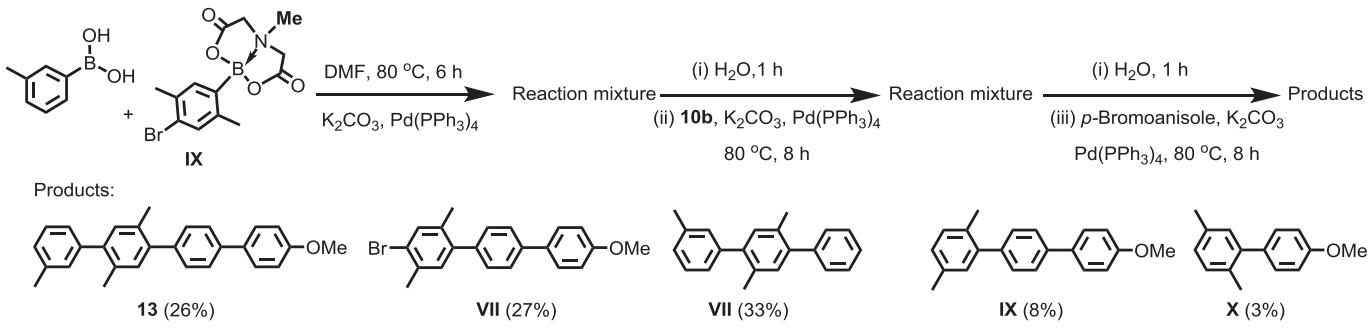
5. After 6 h of reaction, H_2O was added to the reaction mixture and stirred for 1 h, so as to hydrolyze the monomer boronate. The reaction was then continued by the addition of required molar equivalent of *tetrakis*-boronate to the reaction mixture. Further amounts of the catalyst and the base were added as that of the initial step. The reaction was continued for 8 h, followed by further addition of H_2O to the reaction mixture. In the subsequent step, the *p*-bromoanisole was added to the reaction mixture, along with addition of the catalyst and the base. After 8 h, the reaction mixture was worked up and the crude product was analysed by GC-MS technique. The analysis showed formation of tetraaryl derivative, in addition to teraryl and biaryl derivatives as shown in Scheme 5. Formation of the tetraaryl derivative **11** in 26% yield, resulting from three consecutive C–C bond formation reactions of boronates, was observed. Apart from this product, a considerable amount of teraryl derivatives **VII** – **IX** formed, along with a small amount of biaryl derivative **X**. These products put together accounted for ~97% of



Scheme 4. One-pot two step iterative Suzuki-Miyaura cross-coupling reactions.

Table 2
Percentage yields of products formed in one-step iterative Suzuki-Miyaura cross-coupling reaction, given in Scheme 4.

Monomer boronate	Dendritic boronate	V	VI	11	Monomer boronate	Dendritic boronate	VIII	VI	12
IV	**9b**	20	13	47	**VII**	**9b**	3	29	44
	10b	2	4	88		**10b**	10	20	70



Scheme 5. One-pot iterative Suzuki-Miyaura cross-coupling reactions.

products of the reaction. The product formation was varying, with terphenyls accounting for ~68% of the total yield. Formation of terphenyls and biphenyl products suggested a protodeboronation, during the catalytic cycle. Identity of the tetraphenyl derivative **11** was further confirmed by isolation through column chromatography (SiO_2) and characterization. Formation of tetraphenyl was conducted further with two more variations in the phenyl boronic acid and aryl bromide, following a similar sequence of the reaction as in Scheme 5. The sequence of iterative, one-pot reaction led to formation of tetraphenyl derivatives **XI** and **XII** (Fig. 4), in 29 and 13% yields, respectively.

Major products in the reactions involving above boronates and aryl bromides were terphenyl (35–55%) and biphenyl derivatives (~30%), that result from the competitive protodeboronation.

3. Conclusion

The work illustrates the facile formation of dendritic *bis*- and *tetrakis*-boronates from the corresponding dendritic iminodiacetic acids. The dendritic boronates are hydrolytically more stable than monomeric boronates and this hydrolytic stability was taken advantage to conduct Suzuki-Miyaura cross-coupling reactions, in conjunction with chosen monomeric boronates, boronic acids and aryl bromides. In a one-pot sequential reaction, formation of terphenyls and tetraphenyls are achieved, using bifunctional *bis*- and *tetrakis*-boronates as key reactants. Boronates that hydrolyze to boronic acid slower than monomeric boronate hydrolysis is hitherto unknown. The present work illustrates that dendritic boronates, especially *tetrakis*-boronate hydrolyzes ~20 times slower than monomeric boronates. Such hydrolytically more stable boronates are valuable to conduct one-pot, iterative, multiple C–C bond forming reactions to ter- and tetraaryls along with chosen boronic acids and aryl bromides.

4. Experimental

4.1. General methods

Chemicals were purchased from commercial sources and were used without further purification. Solvents were dried and distilled according to literature procedures. Monomer *N*-methyliminodiacetic acid boronates were obtained following the literature procedure. Analytical TLC was performed on commercial Merck plates coated with alumina GF254 (0.25 mm) or silica gel 60 F254. Neutral alumina or silica gel (100–200 mesh) was used for column chromatography. Compounds were visualized by exposure to UV light or iodine vapour. Microanalyses were performed on an automated C, H, and N analyser. IR spectra were recorded as thin films of neat sample. Mass spectral analysis was performed on an electrospray ionization mass spectrometer. ^{1}H, ^{13}C and ^{11}B NMR spectra were recorded on an instrument operating at 400, 100 and 128 MHz, respectively. Chemical shift values are reported in ppm relative to TMS and the following abbreviations are used to explain the multiplicities: s, singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; m, multiplet; br, broad. Coupling constants (*J*) are given in Hertz (Hz). GC-MS analyses were performed using the gas chromatograph fitted with a flame ionization detector (He carrier gas, 1.2 L min^{-1}, detector temperature 250 °C, detector voltage 0.1 kV) and a fused silica column (30 μ, 0.25 mm) and spectra were acquired in the EI mode. The retention times and peak integrations were obtained through chromatogram and mass spectral analysis.

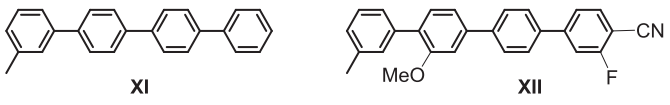


Fig. 4. Tetraphenyls **XI** and **XII** prepared through iterative, one-pot cross-coupling reactions involving the sequence of *m*-tolylboronic acid + 4-bromophenyl monomer boronate + **10b** + bromobenzene (in the case of **XI**) and *m*-tolylboronic acid + 4-bromo-3-anisyl monomer boronate + **9b** + 2-fluoro-4-bromobenzonitrile (in the case of **XII**), in the presence of the catalyst and base.

4.1.1. 4-Cascade:1-aza-4-oxahexylidine[2]:ethanoic acid ethyl ester (**4**) [35]

A mixture of *bis*-amine (**3**) (7.0 g, 67.2 mmol), Et_3N (82.8 mL, 591.6 mmol) and ethyl bromoacetate (16.4 mL, 148.3 mmol) in DMF (50 mL) was stirred at 80 °C for 24 h. The reaction mixture was then filtered and filtrate concentrated *in vacuo*. The crude reaction mixture was dissolved in $CHCl_3$, washed with water, dried over Na_2SO_4, solvent removed *in vacuo* and the resulting residue was purified by column chromatography to afford **4**, as a yellow liquid; yield: 27.1 g, (90%); FT-IR (neat) (cm^{-1}) *ν*: 2937, 2905, 1741, 1447, 1371, 1193, 1115, 1030; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.15 (q, J = 7.1 Hz, 8 H, OCH_2CH_3), 3.59 (s, 8 H, $COCH_2N$), 3.55 (t, J = 5.6 Hz, 4 H, CH_2OCH_2), 2.92 (t, J = 5.6 Hz, 4 H, NCH_2) 1.26 (t, J = 7.1 Hz, 12 H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.29, 70.10, 60.33, 55.81, 53.54, 14.14; HR-MS: m/z = 471.2318, calcd. for $C_{20}H_{36}N_2O_9Na$: 471.2319 $[M+Na]^+$. Elemental analysis: calcd. for $C_{20}H_{36}N_2O_9$: C, 53.56; H, 8.09; N, 6.25; found: C, 53.77; H, 7.78; N, 6.21.

4.1.2. 4-Cascade:1-aza-4-oxahexylidine[2]:ethanol (**5**)

A solution of the ester functionalized dendrimer in THF (27.0 g, 60.2 mmol) was added drop-wise to a suspension of $LiAlH_4$ (11.3 g, 289.7 mmol) in THF at 0 °C and stirred for 3 h at room temperature. The reaction mixture was cooled, quenched with ice, filtered and the filtrate concentrated *in vacuo*. The inorganic salt was precipitated using MeOH, filtered, and the filtrate concentrated. The resulting residue was re-dissolved in $CHCl_3$, filtered and filtrate concentrated *in vacuo* to afford **5**, as a viscous liquid; yield: 16.4 g; (97%). FT-IR (neat) (cm^{-1}) *ν*: 3357, 2877, 1654, 1438, 1114, 1075, 1041, 870; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.65–3.58 (m, 12 H, CH_2OCH_2), 2.62 (t, J = 4.8 Hz, 4 H, NCH_2), 2.56 (t, J = 4.6 Hz, 8 H, NCH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 67.2, 62.11, 58.24, 57.64, 52.79; HRMS: m/z = 303.1896, calcd. for $C_{12}H_{28}N_2O_5Na$ $[M+Na]^+$: 303.1896.

4.1.3. 4-Cascade:1-aza-4-oxahexylidine[2]:3-oxo-1-pentylidinenitrile (**6**)

NaH (0.26 g, 10.8 mmol) was added in portions to a solution of **5** (0.5 g, 1.78 mmol) in THF:DMF (1:1) and stirred at 60 °C for 2 h, followed by the addition of bromoacetonitrile (0.6 mL, 8.6 mmol) in THF. The reaction mixture stirred at 60 °C for 6 h cooled, filtered through celite and filtrate concentrated *in vacuo*. The crude reaction mixture was dissolved in $CHCl_3$, washed with water (3 × 15 mL), dried over Na_2SO_4, concentrated *in vacuo* and the resulting crude reaction mixture was purified (SiO_2), to afford **6**, as a viscous liquid; yield: 0.44 g (56%); FT-IR (neat) (cm^{-1}) *ν*: 3618, 2921, 2861, 2355, 2209, 1706, 1342, 1107; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.29 (s, 8 H, OCH_2CN), 3.64 (t, J = 5.4 Hz, 8 H, OCH_2), 3.50 (t, J = 5.7 Hz, 4 H, OCH_2), 2.82 (t, J = 5.4 Hz, 8 H, NCH_2), 2.76 (t, J = 5.7 Hz, 4 H, NCH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.1, 69.9, 69.5, 56.4, 54.4, 54.3; HRMS: m/z = 437.2516, calcd. for $C_{20}H_{32}N_6O_5H$ $[M+H]^+$: 437.2512. Elemental analysis: calcd. for $C_{20}H_{32}N_6O_5$: C, 55.03; H, 7.39; N, 19.25; found: C, 55.25; H, 7.32; N, 18.97.

4.1.4. 4-Cascade:1-aza-4-oxahexylidine[2]:3-oxo-1-pentylidineamine (**7**)

6 (1.0 g, 2.30 mmol) was transferred to a hydrogenation reactor vessel, mixed with Raney-Co in H_2O (1.0 g, 500 mL), hydrogenated (H_2, 50 atm.) at 70 °C for 5 h, cooled, filtered and the filtrate

concentrated *in vacuo* to afford **7**, as a viscous liquid; yield = 1.01 g; (98%); FT-IR (neat) (cm^{-1}) ν: 3397, 2973, 1627, 1489, 1123, 1028; ^1H NMR (400 MHz, D_2O) δ = 3.53 (m, 12 H, OCH_2), 3.45 (t, J = 5.0 Hz, 8 H, OCH_2), 2.74 (bs, 8 H, NCH_2), 2.69 (bs, 12 H, NCH_2); ^{13}C NMR (100 MHz, D_2O) δ = 70.8, 67.8, 53.0, 39.6.

4.1.5. 8-Cascade:4-oxabutylidine [2]:(1-aza-4-oxahexylidine):ethanoic acid ethyl ester (**8**)

Ethyl bromoacetate (1.1 mL, 9.9 mmol) was added drop wise to a solution of **7** (0.5 g, 1.1 mmol) and Et_3N (2.7 mL, 19.3 mmol) in DMF (5 mL), stirred at 80 °C for 48 h. The reaction mixture was then worked up as described in the general procedure to afford **8**, as a liquid; yield: 0.6 g (48%); FT-IR (neat) (cm^{-1}) ν: 2980, 2936, 1745, 1370, 1193, 1116, 1031, 970; ^1H NMR (400 MHz, $CDCl_3$) δ = 4.15 (q, J = 7.0 Hz, 16 H, OCH_2CH_3), 3.60 (s, 16 H, $COCH_2N$), 3.54 (t, J = 5.7 Hz, 8 H, OCH_2), 3.46 (t, J = 5.7 Hz, 12 H, OCH_2), 2.94 (t, J = 5.4 Hz, 8 H, NCH_2), 2.72 (t, J = 5.7 Hz, 12 H, NCH_2) 1.26 (t, J = 7.1 Hz, 24 H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.2, 70.1, 69.4, 60.29, 55.7, 54.4, 55.3, 14.1; HRMS: m/z = 1163.6527, calcd. for $C_{52}H_{96}N_6O_{21}Na$ $[M+Na]^+$: 1163.6526; Elemental analysis: calcd for $C_{52}H_{96}N_6O_{21}$: C, 54.72; H, 8.48; N, 7.36; found: C, 54.94; H, 8.32; N, 7.14.

4.1.6. 4-Cascade:1-aza-4-oxahexylidine[2]:ethanoic acid (**1**)

NaOH (0.54 g, 13.4 mmol) was added to a solution of **4** (1.0 g, 2.23 mmol) in THF:water (1:1) and stirred at rt for 20 h. The reaction mixture was neutralized by Amberlite IR-120H resin and filtered through sintered funnel. The resin was washed 2–3 times with MeOH (25 mL) and the filtrate concentrated *in vacuo* and the resulting residue was triturated with hexane, ethyl acetate and CH_2Cl_2 several times to afford *tetra*-acid **1**, as a white solid; yield: 0.72 g (98%); FT-IR (neat) (cm^{-1}) ν: 3448, 3016, 2518, 1731, 1635, 1398, 1248, 1129, 903, 699; ^1H NMR (400 MHz, D_2O) δ = 3.80 (s, 8 H, NCH_2CO), 3.71 (t, J = 3.8 Hz, 4 H, CH_2OCH_2), 3.43 (t, J = 3.8 Hz, 4 H, CH_2NCH_2); ^{13}C NMR (100 MHz, D_2O) δ = 169.2, 64.8, 56.8, 55.4; HRMS: m/z 359.1067, calcd. for $C_{12}H_{20}N_2O_9Na$ $[M+Na]^+$: 359.1067.

4.1.7. 8-Cascade:4-oxabutylidine [2]:(1-aza-4-oxahexylidine):ethanoic acid (**2**)

NaOH (0.21 g, 5.3 mmol) was added to a solution of **8** (0.5 g, 0.44 mmol) in THF:water (1:1) and stirred at rt for 24 h. The reaction mixture was worked up as described in the general procedure to afford **2**, as a white solid; yield: 0.38 g (94%); FT-IR (KBr) (cm $^{-1}$) ν: 3427, 1735, 1636, 1400, 1255, 1127, 905, 694; ^1H NMR (400 MHz, D_2O) δ = 4.31 (s, 16 H, NCH_2CO), 4.09 (bs, 12 H, CH_2OCH_2), 4.04 (bs, 8 H, CH_2OCH_2), 3.84 (bs, 8 H, CH_2NCH_2), 3.60 (bs, 12 H, CH_2NCH_2); ^{13}C NMR (100 MHz, D_2O) δ = 169.1, 64.9, 64.4, 56.6; 55.5, 53.4, 53.2; HRMS: m/z = 917.4204, calcd. for $C_{36}H_{64}N_6O_{21}H$: 917.4203.

4.1.8. Phenyl bis-boronate (**9a**)

Phenyl boronic acid (0.20 g, 1.64 mmol) was added to a solution of **1** (0.25 g, 0.74 mmol) in DMF (25 mL), stirred at 120 °C, under an inert atmosphere for 24 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The resulting residue was dissolved in EtOAc (100 mL), washed with aq. $NaHCO_3$ (2 × 10 mL), water (2 × 10 mL), dried (Na_2SO_4), concentrated and dried *in vacuo*. The crude product was purified (SiO_2) (hexane/acetone eluent) to afford **9a**, as a white solid; yield = 0.35 g (91%); FT-IR (neat) (cm^{-1}) ν: 3503, 1769, 1435, 1296, 1226, 1044, 854, 757, 706; ^1H NMR (400 MHz, acetone-d_6) δ = 7.49 (m, 4 H, ArH), 7.35 (m, 6 H, ArH), 4.39 (d, J = 17.1 Hz, 4 H, $NCHCO$), 4.22 (d, J = 17.1 Hz, 4 H, $NCHCO$), 3.89 (t, J = 4.7 Hz, 4 H, CH_2OCH_2), 3.07 (t, J = 4.7 Hz, 4 H, CH_2NCH_2); ^{13}C NMR (100 MHz, acetone-d_6) δ = 168.5, 132.4, 128.9, 127.7, 66.3, 59.2, 57.8; ^{11}B NMR (128 MHz, acetone-d_6) δ = 11.9; HRMS: m/z = 531.1716, calcd. for $C_{24}H_{26}B_2N_2O_9Na$ $[M+Na]^+$: 531.1717.

4.1.9. 4-Bromophenyl bis-boronate (**9b**)

4-Bromophenyl boronic acid (0.33 g, 1.64 mmol) was added to a solution of **1** (0.25 g, 0.74 mmol) in DMF (25 mL), stirred at 120 °C under an inert atmosphere for 24 h. The reaction mixture was then worked up as described in the case of preparation of **9a**, to afford **9b**, as a white solid; yield: 0.45 g (90%); FT-IR (neat) (cm^{-1}) ν: 3348, 3018, 2962, 1746, 1584, 1288, 1221, 1037, 983, 858, 807; ^1H NMR (400 MHz, CD_3CN) δ = 7.58 (d, J = 7.76 Hz, 4 H, ArH), 7.43 (d, J = 7.88 Hz, 4 H, ArH), 4.13 (d, J = 17.24 Hz, 4 H, $NCHCO$), 3.98 (d, J = 17.2 Hz, 4 H, $NCHCO$), 3.56 (t, J = 4.16 Hz, 4 H, CH_2OCH_2), 2.81 (t, J = 4.16 Hz, 4 H, CH_2NCH_2); ^{13}C NMR (100 MHz, CD_3CN) δ = 168.6, 135.8, 134.6, 130.9, 65.9, 59.2, 57.7; ^{11}B NMR (100 MHz, CD_3CN) δ = 11.7.

4.1.10. Phenyl tetrakis-boronate (**10a**)

Phenylboronic acid (0.058 g, 0.48 mmol) was added to a solution of **2** (0.100 g, 0.11 mmol) in DMSO-PhMe (1:4) (15 mL), stirred at 120 °C under an inert atmosphere for 36 h. The reaction mixture was then worked up as described in the case of preparation of **9a**, to afford phenyl *tetrakis*-boronate (**10a**), as a white solid; yield: 0.062 g; (45%); FT-IR (neat) (cm^{-1}) ν: 3423, 1766, 1436, 1295, 1226, 1021, 856, 758; ^1H NMR (400 MHz, CD_3CN) δ = 7.53 (m, 8H, ArH), 7.36 (m, 12H, ArH), 4.45 (d, J = 17.2 Hz, 8H, $NCHCO$), 4.26 (d, J = 17.2 Hz, 8H, $NCHCO$), 3.82 (t, J = 4.3 Hz, 8H, CH_2OCH_2), 3.63 (m, 12H, CH_2OCH_2), 2.98 (t, J = 4.3 Hz, 8H, CH_2NCH_2), 2.89 (m, 12H, CH_2NCH_2); ^{13}C NMR (100 MHz, acetone-d_6) δ = 168.8, 132.4, 128.9, 127.7, 78.2, 60.9, 59.3; ^{11}B NMR (128 MHz, acetone-d_6) δ = 11.8; HRMS: m/z = 1283.5359, calcd. for $C_{60}H_{76}$ $B_4N_6O_{21}Na$ $[M+Na]^+$: 1283.5328.

4.1.11. 4-Bromophenyl tetrakis-boronate (**10b**)

4-Bromophenylboronic acid (0.107 g, 0.53 mmol) was added to a solution of **2** (0.11 g, 0.12 mmol) in DMSO-PhMe (1:4) (15 mL), stirred at 120 °C under an inert atmosphere for 36 h and worked up as described in the case of preparation of **9a**, to afford 4-bromophenyl *tetrakis*-boronate (**10b**), as a white solid; yield: 0.067 g (35%); ^1H NMR (400 MHz, CD_3CN) δ = 7.54 (d, J = 7.2 Hz, 8 H, ArH), 7.48 (d, J = 8 Hz, 8 H, ArH), 4.49 (d, J = 17.2 Hz, 2 H, $NCHCO$), 4.24 (d, J = 17.6 Hz, 8 H, $NCHCO$), 3.84 (bs, 12 H, CH_2OCH_2), 3.57 (bs, 8 H, CH_2OCH_2), 3.10–2.84 (bs, 20 H, CH_2NCH_2); ^{13}C NMR (100 MHz, CD_3CN) δ = 168.9, 135.5, 133.8, 113.2, 112.7, 68.7, 68.5, 65.6, 65.4, 59.0, 57.5; ^{11}B NMR (128 MHz, CD_3CN) δ = 11.6.

4.1.12. Hydrolysis of boronates

Stock solutions of boronates in acetonitrile-d_3 were prepared as follows: **I** (1.9 mg, 0.008 mmol), **9a** (2.0 mg, 0.004 mmol) or **10a** (2.5 mg, 0.002 mmol) were dissolved in acetonitrile-d_3 (500 μL). Each boronate solution was admixed with 4-bromo anisole (1.5 mg). The solution was transferred to an NMR tube, a solution of K_3PO_4 in D_2O (50 mM, 40 μL) was added and ^1H NMR spectra were recorded at defined time intervals (0, 0.5 h, 1.0 h, 2.0 h, etc.) at 40 °C. The percentage of boronate remaining was calculated by comparing the ratio of the integrated OCH_3 singlet of 4-bromoanisole (3.78 ppm, internal std) to that of the NCH_2 doublets of the boronates.

4.1.13. Suzuki-Miyaura cross-coupling reaction

$Pd(PPh_3)_4$ (2.26 mg, 1.96 μmol for **9a**) (0.9 mg, 0.78 μmol for **10a**) (4.96 mg, 4.29 μmol for **I**) (9.48 mg, 8.2 μmol for **II**) and bromobenzene (3.08 mg, 19.6 μmol for **9a**, 1.24 mg, 7.92 μmol for **10a**, 6.74 mg, 42.9 μmol for **II**, 12.87 mg, 82.0 μmol for **I**)) were added to a solution of **9a** (5.0 mg, 9.8 μmol) or **10a** (2.5 mg, 1.98 μmol) or **I** (10.0 mg, 82.0 μmol) or **II** (10 mg, 42.9 μmol) in DMF/H_2O (1:1)

(4 mL), stirred at room temperature for ~5 min under nitrogen atmosphere, followed by addition of K_2CO_3 (16.23 mg, 117.6 μmol for **9a)** (6.6 mg, 47.5 μmol for **10a**) (35.5 mg, 257.4 μmol for **I**) (67.9 mg, 492.0 μmol for **II**). The reaction mixture was stirred at 80 °C under an inert atmosphere, aliquot of the reaction mixture was taken out at periodic time intervals and worked up in EtOAc and H_2O. The EtOAc portion was dried (Na_2SO_4) and concentrated *in vacuo*. An MeOH solution of the resulting product was analysed by GC-MS analysis, using fused silica column.

4.1.14. One-pot, two-step iterative cross-coupling reaction to the synthesis of teraryls

$Pd(PPh_3)_4$ (16.3 mg, 0.014 mmol for **9b**) (2.8 mg, 0.0024 mmol for **10b**) and 1-bromo naphthalene (27.9 mg, 0.134 mmol for **9b**) (4.0 mg, 0.0193 mmol for **10b**) were added to a solution of **9b** (23.5 mg, 0.035 mmol) or **10b** (7.6 mg, 0.0048 mmol) and **IV** (18.6 mg, 0.070 mmol for **9b**) (5.1 mg, 0.0193 mmol for **10b**) or **VII** (17.3 mg, 0.070 mmol for **9b**) (4.8 mg, 0.0193 mmol for **10b**) in DMF/H_2O (3:1) (4 mL), stirred at room temperature for 5 min under nitrogen atmosphere, followed by addition of K_2CO_3 (39.0 mg, 0.283 mmol for **9b**) (4.0 mg, 0.028 mmol for **10b**). The reaction mixture stirred at 40 °C under inert atmosphere for 6 h, 200 μL aliquot was taken and worked up in EtOAc (3 mL) and H_2O (10 mL). The EtOAc layer was dried (an. Na_2SO_4) and concentrated and dried *in vacuo*. The resulting product was diluted with 200 μL of MeOH and analysed by GC-MS analysis, using fused silica column.

4.1.15. Cross-coupling reaction to tetraaryl derivative **13**

Catalyst $Pd(PPh_3)_4$ (2.3 mg), K_2CO_3 (6.7 mg) were added to a solution of **IX** (5.5 mg) and *m*-tolylboronic acid (2.2 mg) in DMF (5 mL), stirred at 80 °C for 6 h, water (0.5 mL) was then added and stirred further for 1 h at same temperature. The reaction mixture was added with **10b** (6.4 mg), catalyst (2.3 mg) and K_2CO_3 (6.7 mg) and stirring continued for 8 h. Further amount of water (0.5 mL), followed by *p*-bromoanisole, catalyst (2.3 mg) and K_2CO_3 (6.7 mg) were added to the reaction mixture, and stirring continued for 8 h. The reaction mixture was worked up as given before and analysed by GC-MS analysis. The crude reaction mixture was also purified (SiO_2) (eluent: 2% EtOAc in hexane) to afford **13**, as a white solid; yield: 1.8 mg (26%). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.60–7.56 (t, J = 8.0 Hz, 4 H, ArH), 7.47–7.43 (t, J = 8.0 Hz, 3 H, ArH), 7.36–7.31 (m, 2 H, ArH), 7.20 (d, J = 7.2 Hz, 1 H, ArH), 7.12 (br, 2 H, ArH), 7.02 (d, J = 8.4 Hz, 2 H, ArH), 3.88 (s, 3 H, $ArOCH_3$), 2.43 (s, 3 H, $ArCH_3$), 2.42 (s, 3 H, ArCH_3), 2.24 (s, 3 H, ArCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.2, 140.8, 140.7, 137.7, 134.6, 133.7, 133.6, 131.9, 129.6, 128.6, 128.1, 127.9, 127.7, 126.7, 126.8, 126.0, 123.3, 114.1, 55.3, 22.2, 21.4, 19.6; GC-MS *m/z* calcd. for $C_{28}H_{26}O$: 378.5; found 378.0.

Acknowledgements

We are grateful to Department of Science and Technology, New Delhi, for a financial support. Council of Scientific and Industrial Research, New Delhi, is acknowledged for a fellowship to PK.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jorganchem.2016.06.030.

References

[1] C. Kremer, J. Torres, S. Dominguez, Lanthanide complexes with oda, ida, and nta: from discrete coordination compounds to supramolecular assemblies, J. Mol. Struct. 879 (2008) 130–149.
[2] G. Anderegg, F. Arnaud-Neu, R. Delgado, J. Felcman, K. Popov, Critical evaluation of stability constants of metal complexes of complexones for biomedical and environmental applications, Pure Appl. Chem. 77 (2005) 1445–1495.
[3] S.E. Castillo-Blum, N. Barba-Behrens, Coordination chemistry of some biologically active ligands, Coord. Chem. Rev. 196 (2000) 3–30.
[4] D. Parker, Excitement in f block: structure, dynamics and function of nine-coordinate chiral lanthanide complexes in aqueous media, Chem. Soc. Rev. 33 (2004) 156–165.
[5] Andris Molnar (Ed.), EDTA: Synthesis, Uses and Environmental Concerns, Nova Science Publishers, Inc., Hauppauge, N. Y, 2014.
[6] D.M. Knapp, E.P. Gillis, M.D. Burke, A general solution for unstable boronic acids: slow-release cross-coupling from air-stable MIDA boronates, J. Am. Chem. Soc. 131 (2009) 6961–6963.
[7] E. Buhleier, W. Wehner, F. Vögtle, "Cascade"- and "nonskid-chain-like" synthesis of molecular cavity topologies, Synthesis (1978) 155–158.
[8] D.A. Tomalia, H. Baker, J. Dewald, M. Hall, C. Kallos, S. Martin, J. Roeck, P. Smith, A new class of polymers: starburst-dendritic macromolecules, Polym. J. (Tokyo) 17 (1985) 117–132.
[9] G.R. Newkome, Z. Yao, G.R. Baker, V.K. Gupta, Cascade molecules: a new approach to micelles. A [27]-Arborol, J. Org. Chem. 50 (1985) 2003–2004.
[10] C.J. Hawker, J.M.J. Fréchet, Preparation of polymers with controlled molecular architecture. A new convergent approach to dendritic macromolecules, J. Am. Chem. Soc. 112 (1990) 7638–7647.
[11] E.M.M. de Brabander-van den Berg, E.W. Meijer, Poly(propy1ene imine) dendrimers: large scale synthesis by hetereogeneously catalyzed hydrogenations, Angew. Chem. Int. Ed. Engl. 32 (1993) 1308–1311.
[12] C. Galliot, D. Prevote, A.-M. Caminade, J.-P. Majoral, Polyaminophosphine containing dendrimers. Syntheses and characterization, J. Am. Chem. Soc. 117 (1995) 5470–5476.
[13] U. Boas, J.B. Christensen, P.M.H. Heegaard, Dendrimers: design, synthesis and chemical properties, J. Mater. Chem. 16 (2006) 3785–3798.
[14] D. Astruc, E. Boisselier, C. Ornelas, Dendrimers designed for functions: from physical, photophysical, and supramolecular properties to applications in sensing, catalysis, molecular electronics, photonics, and nanomedicine, Chem. Rev. 110 (2010) 1857–1959.
[15] G.R. Newkome, C. Shreiner, Dendrimers derived from 1→3 branching motifs, Chem. Rev. 110 (2010) 6338–6442.
[16] G.M. Soliman, A. Sharma, D. Maysinger, A. Kakkar, Dendrimers and miktoarm polymers based multivalent nanocarriers for efficient and targeted drug delivery, Chem. Commun. 47 (2011) 9572–9787.
[17] M. Keller, A. Hameau, G. Spataro, S. Ladeira, A.-M. Caminade, J.-P. Majoral, A. Quali, An efficient and recyclable dendritic catalyst able to dramatically decrease palladium leaching in Suzuki couplings, Green Chem. 14 (2012) 2807–2815.
[18] G. Jayamurugan, P. Umesh, N. Jayaraman, Preparation and catalytic studies of palladium nanoparticles stabilized by dendritic phosphine ligand-functionalized silica, J. Mol. Catal. A Chem. 307 (2009) 142–148.
[19] N. Miyaura, A. Suzuki, Palladium-catalyzed cross-coupling reactions of organoboron compounds, Chem. Rev. 95 (1995) 2457–2483.
[20] A. Suzuki, Recent advances in the cross-coupling reactions of organoboron derivatives with organic electrophiles, 1995-1998, J. Organomet. Chem. 576 (1999) 147–168.
[21] N.E. Leadbeater, Fast, easy, clean chemistry by using water as a solvent and microwave heating: the Suzuki coupling as an illustration, Chem. Commun. (2005) 2881–2902.
[22] A.J.J. Lennox, G.C. Lloyd-Jones, The slow-release strategy in Suzuki-Miyaura coupling, Isr. J. Chem. 50 (2010) 664–674;
(b) A.J.J. Lennox, G.C. Lloyd-Jones, Organotrifluoroborate hydrolysis: boronic acid release mechanism and an acid-base paradox in cross-coupling, J. Am. Chem. Soc. 134 (2012) 7431–7441;
(c) A.J.J. Lennox, G.C. Lloyd-Jones, Transmetalation in the Suzuki-Miyaura coupling: the fork in the trail, Angew. Chem. Int. Ed. 52 (2013) 7362–7370;
(f) A.J.J. Lennox, G.C. Lloyd-Jones, Selection of boron reagents for Suzuki–Miyaura coupling, Chem. Soc. Rev. 43 (2014) 412–443.
[23] S.J. Lee, K.C. Gray, J.S. Paek, M.D. Burke, Simple, efficient, and modular syntheses of polyene natural products via iterative cross-coupling, J. Am. Chem. Soc. 130 (2008) 466–468.
[24] J.R. Struble, S.J. Lee, M.D. Burke, Ethynyl MIDA boronate: a readily accessible and highly versatile building block for small molecule synthesis, Tetrahedron 66 (2010) 4710–4718.
[25] E.M. Woerly, J.R. Struble, N. Palyam, S.P. O'Hara, M.D. Burke, (Z)-(2-Bromovinyl)-MIDA boronate: a readily accessible and highly versatile building block for small molecule synthesis, Tetrahedron 67 (2011) 4333–4343.
[26] J. Li, S.G. Ballmer, E.P. Gillis, S. Fujii, M.J. Schmidt, A.M.E. Palazzolo, J.W. Lehmann, G.F. Morehouse, M.D. Burke, Synthesis of many different types of organic small molecules using one automated process, Science 347 (2015) 1221–1226.
[27] H. Noguchi, K. Hojo, M. Suginome, Boron-masking strategy for the selective synthesis of oligoarenes via iterative Suzuki-Miyaura coupling, J. Am. Chem. Soc. 129 (2007) 758–759.
[28] N. Iwadate, M. Suginome, Differentially protected biboron for regioselective diboration of alkynes: internal-selective cross-coupling of 1-alkene-1,2-diboronic acid derivative, J. Am. Chem. Soc. 132 (2010) 2548–2549 (and references therein).
[29] G.A. Molander, N. Ellis, Organotrifluoroborates: protected boronic acids that expand the versatility of the Suzuki coupling reaction, Acc. Chem. Res. 40 (2007) 275–286.

[30] S. Darses, J.-P. Genet, Potassium organotrifluoroborates: New perspectives in organic synthesis, Chem. Rev. 108 (2008) 288–325.
[31] G.A. Molander, B. Canturk, Organotrifluoroborates and monocoordinated palladium complexes as catalysts-A perfect combination for Suzuki–Miyaura coupling, Angew. Chem. Int. Ed. 48 (2009) 9240–9261.
[32] J. Raushel, D.L. Sandrok, K.V. Josyula, D. Pakyz, G.A. Molander, Reinvestigation of aminomethyltrifluoroborates and their application in Suzuki-Miyaura cross-coupling reactions, J. Org. Chem. 76 (2011) 2762–2769.
[33] S.G. Ballmer, E.P. Gillis, M.D. Burke, B-Protected haloboronic acids for iterative cross-coupling, Org. Synth. 86 (2009) 344–359.
[34] T. Mancilla, B. Contreras, B. Wrackmeyer, New bicyclic organylboronic esters derived from iminodiacetic acids, J. Organomet. Chem. 307 (1986) 1–6.
[35] Nomenclature follows the guidelines proposed by Newkome and co-workers, G.R. Newkome, G.R. Baker, J.K. Young, J.G. Traynham, A systematic nomenclature for cascade polymers, Polymer 31 (1993) 641–651.