

Communication

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1,n-Bisborylalkanes via Radical Boron Migration

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Supporting Information Placeholder

ABSTRACT: A systematic study of radical boron migration in diboronate complexes to form synthetically valuable 1,nbisborylalkanes is reported. The boronate complexes are readily generated by reaction of commercial bis(pinacolato)diboron with alkyl Grignard compounds. C-radical generation at defined position with respect to the diboron moiety is either achieved via intermolecular H-abstraction with a CF₃-radical or via alkene perfluoroalkyl radical addition. It is shown that radical 1,2- and 1,4- boron migration to provide geminal and 1,3-bisborylalkanes are efficient transformations. The 1,5-boron migration in the homologous series leading to 1,4-bisborylalkanes is also occurring, albeit with lower efficiency. Experimental results are supported by DFT calculations which also reveal the corresponding 1,3-boron migration in such diboronate complexes to be feasible.

Bisborylalkanes are functionalized and versatile building blocks in organic synthesis. Such B-compounds can act as coupling partners in transition metal catalyzed cross-coupling reactions or as radical precursors and both boryl moieties can in principle be selectively converted to different functionalities.¹ Boronate complexes are reactive intermediates that are readily generated by the reaction of organoboronic esters with organometallic reagents. These B-ate complexes are reducing species that also undergo facile hydrolysis.² Recently, radical chemistry on boronate complexes has emerged.³ It was found that C-radicals of type I derived from boronate complexes are readily oxidized by single electron transfer (SET) to give zwitter ions of type II in a radical/polar cross over step (Scheme 1, A). Intermediates II in turn undergo a Mattesontype 1,2-alkyl/aryl shift to afford α -functionalized boronic esters III.⁴ Although such transformations on boronate complexes generated from alkyl and aryl boronic esters are meanwhile well investigated, the corresponding radical reactions on diboronate complexes derived from diborons (see IV) are underdeveloped. Along these lines, Shi recently reported the construction of 1,1bisborylalkanes enabled by radical addition/1,2-boron migration. As mechanism of the boron migration, it was proposed that diboronate complexes IV (m = 0) are SET-oxidized to intermediates of type II (R' = BPin) which rearrange to geminal bisborylalkanes via an ionic process.⁵ Herein, we disclose our results on the systematic study of radical boron migration in radical anions of type IV (m = 0.4) to give intermediates V where the two B-atoms can interact. SET-oxidation finally leads to 1,nbisborylalkanes VI (Scheme 1, B). Considering, the 1,2-boron shift, the radicals VIII are generated from ate complexes VII via intermolecular hydrogen atom transfer (HAT)^{4d} (Scheme 1, C). Further, we will provide mechanistic insights into the reported⁵ 1,2boron migration. In all other cases, site selective C-radical generation (see XI) is achieved via radical addition to B-ate complexes of type X (Scheme 1, D).

The 1,2-boron shift to access geminal bisborylalkanes was studied first. Notably, 1,1-bisborylalkanes are important building blocks to

access multifunctionalized compounds.^{6,7} The current methods to prepare these compounds use gem-dihalides,⁸ diazo compounds,⁹ alkynes,¹⁰ alkenes etc.,¹¹ as substrates and mostly require a transition metal to catalyze or mediate the transformation.¹² It is of interest to develop a convenient method to access 1,1bisborylalkanes from simple starting materials under transition metal free conditions.

Scheme 1. Synthesis of 1,n-bisborylalkanes via radical boron migration

A) 1,2-alkyl/aryl migration via radical/polar cross over (ref 4)



B) 1,n-boron radical migration strategy



C) 1,1-bisborylalkanes via 1,2-boron migration



D) 1,n-bisborylalkanes via remote boron migration



In 2019, our group achieved transition metal free cross coupling of organometallic reagents and organoboronic esters by intermolecular α -HAT on the corresponding boronate complexes with the trifluoromethyl radical followed by SET-oxidation and ionic 1,2-alkyl/aryl migration.^{4d} Encouraged by this study, we decided to apply this strategy to prepare 1,1-bisborylalkanes via diboronate complexes (see Scheme 1, C). The reaction of bis(pinacolato)diboron (B₂Pin₂) with cyclopentylmagnesium bromide (1.2 equiv) targeting gem-bisborylalkane **2a** was selected for optimization (Table 1).

The diboronate complex **1a** was generated in 1,2-dimethoxyethane (DME) at 0 °C. The solvent was exchanged by acetonitrile and CF₃I was chosen as the terminal oxidant with the CF₃-radical engaging in selective HAT-abstraction at the α -position to the B-atom in B-ate complexes.^{4a} Pleasingly, with tris[2-phenylpyridinato-C²,*N*]iridium(III) (Ir(ppy)₃, 1mol%) as a smart initiator¹³ at room temperature, **2a** was formed in 59% yield (Table 1, entry 1). Besides **2a**, we detected 8% cyclopentylboronic acid pinacol ester

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(Cp-BPin) and 14% B₂Pin₂. Other metal based and organic initiators gave similar results (entry 2-6). The complex derived from cyclopentylmagnesium chloride provided a slightly lower yield (52%, entry 7, compare with entry 3), but the yield significantly dropped to 18% with bis(neopentyl glycolato)diboron (B₂(neop)₂) in place of B₂Pin₂ (entry 8). Without redox initiator, the reaction also proceeded, albeit with lower efficiency (entry 9). Upon lowering the temperature, formation of cyclopentylboronic acid pinacol ester was suppressed and the yield of **2a** improved to 68% (entry 10). Initiation by simple UV (365 nm) irradiation at -20 °C led to a further improvement, providing **2a** in 76% yield (entry 11). The boronate complex derived from cyclopentyllithium gave a poor yield under the optimized conditions (16%, entry 12).

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 Table 1. Reaction optimization for the 1,1-diborylation of cyclopentylmagnesium bromide with B₂Pin₂ ^a



Entry	PC	2a	Cp-BPin	Conv
1	lr(ppy) ₃	59%	8%	86%
2	Ir(ppy) ₂ (dtbbpy)PF ₆	62%	7%	85%
3	Ru(bpy) ₃ (PF ₆) ₂	63%	9%	82%
4	Eosin Y	56%	8%	83%
5	Rose Bengal	35%	20%	82%
6	Rhodamine B base	49%	5%	74%
7 ^b	Ru(bpy) ₃ (PF ₆) ₂	52%	7%	82%
8 ^c	Ru(bpy) ₃ (PF ₆) ₂	18%	28%	100%
9	-	30%	20%	65%
10 ^d	$Ru(bpy)_3(PF_6)_2$	68%	<1%	82%
11 ^e	-	76% (74% ^f)	<1%	91%
12 ^g	-	16%	17%	61%

^a Reactions conducted on a 0.2 mmol scale in CH₃CN (2 mL), conversion determined based on the recovered bisboryl reagent, yields were determined by GC analysis with n-tetradecane as the crude internal standard on reaction mixture. Cyclopentylmagnesium chloride of used instead cyclopentylmagnesium с bromide. Bis(neopentyl glycolato)diboron $(B_2(neop)_2)$ used instead of bis(pinacolato)diboron (B2Pin2). d Reaction conducted at -20 °C. e 365 nm (3 W) at -20 °C. ^f Isolated yield. ^g Cyclopentyllithium used instead of cyclopentylmagnesium bromide.

With optimized conditions in hand, we prepared a series of 1,1bisborylalkanes from different alkyl Grignard reagents (Table 2). Both primary (**2c-d**) and secondary (**2a-b**, **2e-o**) alkylmagnesium bromides engaged in the transformation to afford 1,1bisborylalkanes in moderate to good yields (28-80%). Some functionalities such as phenyl, trifluoromethyl and alkoxy moieties were tolerated. The reaction was found to be sensitive to sterics. For example, ate complex **1b** derived from 3-phenyl cyclopentylmagnesium bromide delivered the 1,1-bisboron compound **2b** with a decreased yield (44%) as compared to its less bulky congener **1a** (74%). Considering diboronate complexes derived from primary alkylmagnesium bromides, the less bulky ethyl derivative (**2c**) gave a slightly better yield than the corresponding butyl-ate complex (**2d**). For complexes generated from secondary alkylmagnesium bromides, the least bulky isopropyl system provided the highest yield (80%, 2e). Due to the higher steric demand of an ethyl over a methyl group, the yield of 20 was lower than the yields obtained for 1,1-bisborylalkanes 2en. Of note, as Grignard reagents can be easily accessed from commercial alkylbromides, the introduced method offers a cheap and convenient approach to 1,1-bisborylalkanes.

Table 2. Geminal diborylation of alkylmagnesium bromides- scope a



^a Conducted at 0.2 mmol scale. Isolated yields provided in all cases.

 Table 3. Reaction optimization for 1,3,4-trifunctionalization

 of homoallyImagnesium bromide – 1,4-boron migration^a

B ₂ Pin ₂	MgBr (1.2 equiv) DME 0 °C, 1 h	MgBr ⁺ OBPin B →	Pi PC (1 mol%) C₄F₀l (1.5 equiv) solvent 465 nm (3W) rt, 12 h	BPin C ₄ F ₉	PinB +I C_4F9 4a-I
Entry	PC	solvent	4a	4a-l	Conv
1	lr(ppy) ₃	CH ₃ CN	79%	4%	87%
2	lr(ppy) ₃	DMSO	<1%	33%	85%
3	lr(ppy) ₃	DMF	5%	11%	91%
4	lr(ppy) ₃	DMA	2%	2%	93%
5	Eosin Y	CH₃CN	76%	3%	77%
6	Rose Bengal	CH ₃ CN	75%	4%	80%
7	Rhodamine B base	CH ₃ CN	79%	3%	80%
8	-	CH ₃ CN	44%	16%	94%
9 ^b	Rhodamine B base	CH₃CN	87% (83% ^c)	3%	90%
10 ^d	-	CH ₃ CN	87%	3%	95%
11 ^e	Rhodamine B base	CH ₃ CN	5%	-	57%

^a Reactions conducted on a 0.2 mmol scale in the specified solvent (2 mL), conversion (Conv) determined based on recovered bisboryl reagent, yields determined by crude GC analysis with n-tetradecane as internal standard. ^b Conducted at -20 °C. ^c Isolated yield. ^d 365 nm (3 W) at -20 °C. ^e But-3-enyllithium, in situ generated by

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lithium/iodine exchange reaction of *t*-BuLi and 4-iodo-1-butene, used instead of but-3-enylmagnesium bromide, THF instead of DME as solvent.

We noted that there is currently no general method available for the synthesis of 1,n-bisborylalkanes $(n > 1)^{8a,14}$ and assumed the unprecedented remote radical B-migration to offer an new approach to access such compounds. Along these lines, we first addressed the 1,4-boron migration and selected 3a, generated by reacting B₂Pin₂ with but-3-envlmagnesium bromide, as model substrate. To our delight, visible light irradiation (465 nm) of 3a in the presence of C_4F_9I (1.5 equiv) and $Ir(ppy)_3$ (1 mol%) as an initiator in CH₃CN provided the 1,3-bisborylalkane 4a in 79% yield besides the iodine atom transfer product 4a-I (4%) and recovered B₂Pin₂ (13%) (Table 3, entry 1). Solvent screening revealed that in CH₃CN better yields were obtained than in other polar solvents like DMSO, DMF and DMA (entry 1-4). Ir(ppy)₃ could be replaced by organic dyes such as Eosin Y, Rose Bengal, and Rhodamine B base without diminishing the yield (76-79%, entry 5-7). Without redox initiator, the reaction also worked, but with lower efficiency (44%, entry 8) and with the cheap organic Rhodamine B base as smart initiator, the yield further increased to 87% upon lowering the temperature to -20 °C (entry 9). Notably, simple UV irradiation (365 nm) at -20 °C in the absence of any initiator provided a similar vield (entry 10). The boronate complex derived from but-3enviliation environment of the optimized conditions (5%, entry 11).

Table 4. 1,4- and 1,5-boron migration reactions ^a



^a Conducted on a 0.2 mmol scale. ^b *n*-C₆F₁₃Br was used. ^c Reaction conducted at room temperature.

Scope study of the trifunctionalization of homoallyl Grignard reagents was conducted by applying the visible light/Rhodamine B base initiation protocol (Table 3, entry 9) that proved to be more general than the UV-initiation protocol. The perfluoroalkyl radical precursor was varied first keeping complex **3a** as the acceptor (Table 4). Linear n-perfluoroalkyl iodides provided the trifunctionalized 1,3-diboranes **4b-e** in excellent yields (82-93%). The less reactive n-perfluoroalkyl bromide also worked as Cradical precursor, but as compared to the iodides, yield slightly dropped (62%, **4f**). With perfluoroisopropyl iodide a 64% yield of **4g** was obtained. 1-Chloro-2-iodotetrafluoroethane reacted chemoselectively at the I-bearing C-atom to give **4h** (61%). Iodoacetonitrile and ethyl iodoacetate only gave trace amounts of the targeted products (not shown). Unfortunately, diastereoselectivity for the 1,4-boron shift in open chain systems was very low (see **4i**, **4j**). However, for the cyclic rigid diboronate complex **3k**, 1,4-syn-boron-migration selectivity was complete and also the initial CF₃-radical addition occurred with excellent stereocontrol (*trans*-addition) to provide product **4k** as a single diastereoisomer (64%).

With 4-pentenylmagnesium bromide as starting material, we next addressed the 1,5-boron migration and noted that with perfluoroalkyl iodides as C-radical precursors, the I-atom transfer compounds **5-I** (not shown) were formed as major products and targets **5** were obtained in low yields. Therefore, we had to switch to the less reactive bromides. A moderate 31% yield of **5a** was achieved with n-perfluorohexyl bromide under the conditions optimized for the 1,4-boron shift. Yield could be slightly improved to 44% (see **5b**) by installing a 3,3-dimethyl substitution pattern, benefitting from the Thorpe-Ingold effect.¹⁵

We also attempted the 1,6-boron migration on the homologous diboronate complex derived from 5-hexenylmagnesium bromide with CF_3I as the radical precursor. However, the targeted 1,5 bisborylalkane was not identified and the reaction provided the corresponding I-atom transfer product as the major product. Switching to n-perfluorohexyl bromide, the 1,6-boron migration product **6** could not be identified, indicating that this migration cannot compete with other processes.

Finally, to complete the series we tackled the 1,3-boron migration. The required diboronate complex was formed by the reaction of allylmagnesium bromide with B₂Pin₂. However, neither with perfluorobutyl iodide nor with its bromide any 1,2-bisborylalkane was identified and B₂Pin₂ was formed in large amount (85%) as major product. Hence, SET-oxidation of allyl-B₂Pin₂MgX under all tested conditions generating the stabilized allyl radical was too fast and therefore this alkene could not act as a radical acceptor under the applied conditions. Since we did not find any suitable system to experimentally investigate the 1,3-boron migration, we decided to approach that problem by using computational chemistry. DFT calculations¹⁶ were performed on a series of pent-(*m*+*1*)-yl substituted radical anions **7a-d** (m=0-3, Scheme 2) to get a full picture on the boron migration aptitude in these diboronate radical anions.

Scheme 2. DFT model calculations of diboronate radical anion rearrangements



PWPB95-D3//PBE0-D3/def2-TZVP + COSMO-RS(MeCN)

In the study of the reactions, we have found bisborane radical anion intermediates **8** with the spin localized in a B–B single electron bond, similar to those found in the 1,2-carboboration of alkenes with B_2Cat_2 .¹⁷ In case of the 1,2-boron migration (m=0),¹⁸ the initial radical **7a** exhibits this structure already, which means that

1,2-boron radical migration is a spontaneous and barrierless process. In the case of the distonic (m>0) radical anions 7b-7d, a cyclization occurs with low free energy barriers (7-12 kcal/mol) to form the analogous intermediates 8b-8d exergonically. These will readily transfer likely assisted by the MgBr counter cation^{17c} one electron to the iodo reagent and regenerate the trifluoromethyl radical, forming the 1,(m+1)-bisborylalkanes 9a-d. Compared to the 1,4-boron migration, the barrier for the radical 1,3-boron migration increases (from 7.1 kcal/mol to 11.8 kcal/mol). The 1,5boron migration (8.1 kcal/mol) showed a slightly higher barrier than the 1,4-shift. In case of radical anion 7b (1,3-boron migration), in the computation we did not find any indication for facile Bfragmentation leading to the B₂Pin₂-radical anion along with 1pentene. This supports our suggestion that the observed formation of B₂Pin₂ in the reaction with allyl-B₂Pin₂MgX is likely caused by initial SET-oxidation of allyl-B2Pin2MgX rather than βfragmentation of the corresponding distonic radical anion of type 7b.

In summary, radical 1,2- and 1,4-boron migration reactions in diboronate complexes derived from B_2Pin_2 are preparative useful processes to access synthetically valuable 1,1- and 1,3-bisborylalkanes. Considering the 1,3-functionalized compounds, high selectivity in the boron migration can be achieved in cyclic systems. The 1,5-boron migration leading to 1,4-bisborylalkanes is also occurring, albeit with lower efficiency. The experimental findings on the B-shift were supported by DFT calculations which further revealed that the currently experimentally inaccessible 1,3-boron migration to be feasible. Since B_2Pin_2 is commercially available and the Grignard reagents are readily prepared from the corresponding alkyl bromides, the introduced methods offers a straightforward approach to 1,n-bisborylalkanes.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: xxx.

Experimental details and characterization data (PDF) NMR spectrum of new compounds (PDF) DFT calculations (PDF)

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Notes

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generated by HAT or radical addition	1,1-bisborylalkanes (m = 0) 1,3-bisborylalkanes (m = 2) 1,4-bisborylalkanes (m = 3)	
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