Stereoselective Diels−Alder Reactions of gem-Diborylalkenes: Toward the Synthesis of gem-Diboron-Based Polymers

Nadim Eghbarieh, Nicole Hanania, Alon Zamir, Molhm Nassir, Tamar Stein,* and Ahmad Masarwa*

ABSTRACT: Although gem-diborylalkenes are known to be among the most valuable reagents in modern organic synthesis, providing a rapid access to a wide array of transformations, including the construction of C−C and C-heteroatom bonds, their use as dienophile-reactive groups has been rare. Herein we report the Diels−Alder (DA) reaction of (unsymmetrical) gem-diborylalkenes. These reactions provide a general and efficient method for the stereoselective conversion of gem-diborylalkenes to rapidly access 1,1-bisborylcyclohexenes. Using the same DA reaction manifold with borylated-dienes and gem-diborylalkenes, we also developed a concise, highly regioselective synthesis of 1,1,2-tris- and 1,1,3,4-tetrakis(boronates)-cyclohexenes, a family of compounds that currently lack efficient synthetic access. Furthermore, DFT calculations provided insight into the underlying factors that control the chemo-, regio-, and stereoselectivity of these DA reactions. This method also provides stereodivergent syntheses of gem-diborylnorbornenes. The utility of the gem-diborylnorbornene building blocks was demonstrated by ring-opening metathesis polymerization (ROMP), providing a highly modular approach to the first synthesis of the gem-diboron-based polymers. Additionally, these polymers have been successfully submitted to postpolymerization modification reactions. Given its simplicity and versatility, we believe that this novel DA and ROMP approach holds great promise for organoboron synthesis as well as organoboron-based polymers and that it will result in more novel transformations in both academic and industrial research.

INTRODUCTION

Organoboron reagents have had an enormous impact on the development of new chemical reactions1 and have extended the scope of accessible complex molecular scaffolds.3−4 Organoboronate compounds are particularly attractive owing to their wide availability and air stability,5 making them versatile reagents in organic synthesis.6−7

Although many synthetic methods utilize transformations of C−B bonds,8 the development of polyborolated reagents would enable greater structural diversity, an important objective.9 Therefore, over the past decade, much effort has been expended to synthesize new functionalized classes of polyboronates, which have been shown to be excellent building blocks for the modular construction of new compounds.9−12 Among polyboron-containing structural motifs, (unsymmetrical) gem-diboron derivatives (2, 3′) are a well-known emerging class with good potential for novel synthetic applications (Figure 1A).14−17 The special properties and structures of bisnucleophile gem-diboryl compounds 2 and 3′ (termed geminated organodimetallics)16,19 have attracted increasing attention from synthetic chemists, particularly in constructing C−C/C−heteroatom bonds. In recent years, gem-diboryl compounds 2 and 3′ have been widely adopted as coupling partners in synthetic chemistry.11,20 For example, gem-diborylalkenes 2 have served as building blocks for Suzuki−Miyaura cross-coupling, nucleophilic partners, reduc-

Figure 1. General scheme of the work. (A) Classifying of organoboron compounds. (B) The well-known boron-based polymer I. (C) The unprecedented gem-diboron based polymer II. (D) General scheme of the Diels−Alder reaction of polyboronated compounds 3 with 2 and the application of their cycloaddition product 4 in the ROMP reaction to generate the gem-diborylterpolymer II′. B = boron group.
tion approaches, Michael additions,\textsuperscript{21} radical chemistry,\textsuperscript{22} and other reactions.\textsuperscript{13,23}

Despite the fact that organoborons and \textsuperscript{1} and \textsuperscript{1′} (Figure 1A) have been applied in many fields including materials,\textsuperscript{24−29} polymer\textsuperscript{−29} I (Figure 1B), drugs,\textsuperscript{30} and, in industry, gem-diboryl units \textsuperscript{2} and \textsuperscript{3′} have seldom been employed in these fields, e.g., polymer II (Figure 1C).\textsuperscript{30} To this end, we contend that a new paradigm of research is needed to complementarily propel this gem-diboryl class of compounds to reach the same application level as their monoboron analogues.

As a part of a general program to investigate the reactivity and selectivity of gem-diboryl compounds in new synthetic applications, we sought to prepare variants bearing the gem-diboryl-norbornene group (4) because these strained compounds (∼27 kcal/mol of inherent strain) might offer new opportunities toward the ring-opening metathesis polymerization (ROMP) reaction\textsuperscript{31} and lead to unprecedented gem-diboryl-based polymer II' (Figure 1D).

\section*{RESULTS AND DISCUSSION}

We posited that an efficient way to prepare gem-diboryl-norbornene structural motifs 4 would be through a [4 + 2] cycloaddition reaction of gem-diborylalkenes 2 with cyclopentadiene (CP) 3. Although the [4 + 2] cycloaddition reactions of vinylboronates,\textsuperscript{32} e.g., 1, are well documented in the literature (Figure 2A),\textsuperscript{33−38} to the best of our knowledge, the use of gem-diborylkenes 2 in these types of reactions is rare,\textsuperscript{23} despite the potential to provide new and efficient strategies to efficiently construct complex molecules (Figure 2B).\textsuperscript{39,40}

Recently, we reported a photoredox-mediated reaction of gem-diborylalkenes\textsuperscript{22} and showed that gem-diborylalkenes 2 have similar electron deficiency as vinylboron 1;\textsuperscript{22} hence, 2 should serve as a suitable dienophile for this type of cycloaddition reaction. However, key challenges include (1) the steric repulsion introduced by the two groups of the bulky Bpin units in the TS of the cycloaddition reaction;\textsuperscript{37} (2) whether the regio- and stereoselectivity of the cycloaddition can be controlled when two unsymmetrical boron groups are placed on the geminated carbon of dienophile \textsuperscript{2′}; and (3) whether the reaction can proceed in a regioselective manner when borylated dienes react with 2 (Figure 2B).\textsuperscript{34}

To answer these questions, we first conducted computational studies on the Diels−Alder (DA) reaction to predict whether gem-diborylalkenes 2 could be used as dienophile reactive partners for the DA reaction.\textsuperscript{35,38} According to our computational studies of the energy profiles of the cycloaddition reactions of diene-Cp 3e with dienophiles 1 and 2 at room temperature (rt), the transition state of gemBpinBpin-TS is likely to be more energetically stabilized compared to vinylboronate TS Bpin-exo-TS by 1.4 kcal/mol (Figure 2C,D).

Moreover, the CHelpG population analysis\textsuperscript{40} on the carbons of the reactive double bond of the dienophiles (1 and 2) shows that the double bond of 2 has less electron concentration than the double bond in 1 (full details are given in the SI (pp S65, S66)).

Figure 2. Initial study and work plan. (A) The well-known DA reaction using the vinylboronates 1 with diene 3. (B) Description of our DA reaction of polyboronated compounds. (C) DFT calculations indicate that gem-diborylalkene 2 can undergo the DA reaction with diene 3e. (D) CYLview structures of the TSs of Bpin-exo-TS, Bpin-endo-TS, and gemBpinBpin-TS; the calculations were performed with Gaussian 16 software using the M06-2X.\textsuperscript{41} TS structures were visualized with CYLview.1.0b.\textsuperscript{42} B = boron group, Bpin = pinacolato-boron, Bdan = B-1,8-diaminonaphthalene.
These observations support the fact that 2 is slightly more "dienophilic" toward the DA reaction than 1, albeit more bulky (Figure 2C,D).

To investigate our proposed reaction, gem-diborylalkene 2, along with 3e, was subjected to DA reaction conditions (Figures 2C-2, 3A,B). We obtained the desired gem-diborylated cycloaddition product 4e in good yield at rt with toluene as solvent. Next, we investigated the scope of the DA reaction using readily available gem-diborylalkene 2 and various diene substrates (3) bearing aliphatic, aromatic, and heteroatom substituents (Figure 3B). Generally, the products (4a–g) were isolated in good yields under the established optimal conditions. The reaction also proceeded in very good yield on a gram scale, e.g., 4e. The reaction works well with anthracene derivative 3c, affording the gem-diborylcycloadduct 4c, which was confirmed by X-ray crystallographic analysis (see the CYLview structure of 4c, Figure 3B). In addition, the reaction works smoothly with hexachlorocyclopentadiene 3e-6Cl, forging the hexachloro cycloaddition product 4e-Cl.

Using bulky dienes (i.e., pentamethylcyclopentadiene 3f), along with adjusting the reaction temperature, played a critical role in achieving high yield and regioselectivity.
role in controlling diastereoselectivity (i.e., the syn vs anti outcomes on 4f; Figure 3B). Whereas at a high temperature (185 °C) the reaction proceeds with moderate diastereoselectivity (dr = 83:17), at room temperature the reaction afforded the bis-borylated compound 4f as the exclusive diastereoisomer (dr > 99:01). Interestingly, the product gem-diboryl-bicyclo[2.2.2]octane 4g-Si was obtained in a high regioselective mode, i.e., rr > 99:01 (Figure 3B).

The reaction also exhibits moderate regioselectivity when unsymmetrical dienes are used, giving the para adducts (4h−j). The relative structure 4O-d has been confirmed by 2D NMR NOESY. rr = regioisomeric ratio, dr = diastereomeric ratio, yields are isolated. Bpin = pinacolato-boron.

Figure 4. Oxidation reaction of 4. Examples of the utility of gem-diborylcyclohexenes 4 in the oxidation reaction that yields the ketone products 4O. The relative structure 4O-d has been confirmed by 2D NMR NOESY. rr = regioisomeric ratio, dr = diastereomeric ratio, yields are isolated. Bpin = pinacolato-boron.

Figure 5. Diels−Alder reaction with 2′. (A) General reaction conditions of the DA with unsymmetrical gem-diborylalkene 2′. (B) Examples of the DA products as a result of reaction of 2 with different dienes. (C) DFT calculations of the TSs of exo-BpinBdan-TS and endo-BpinBdan-TS; the calculations were performed with Gaussian 16 software using M06-2X.41 (D) DA reaction of 2′ with diene 3l leads to 1-Bdan-1,3,4-triBpin-cyclohexene 5l. (E) Stereoselective DA reaction of 2′ with diene E-3K leads regioselectively to diastereomers 5k and 5k′; the two 1,1,2-triboryl products were easily separated by column chromatography. The 1,2-regioselectivity manner has been determined by the X-ray structure of 5k′. The relative configuration of 5k has been confirmed by 2D NMR NOESY. X-ray and TS structures were visualized with CYLview 1.0b.42 rr = regioisomeric ratio, dr = diastereomeric ratio, yields are isolated. Bpin = pinacolato-boron, Bdan = B-1,8-diaminonaphthalene.

Figure 3C). Notably, the constitutional isomers in 4 (h, h′) and 4 (i, i′) can be easily separated by column chromatography (Figure 3C; see the SI).

Remarkably, the reaction of 2 with 3,4-diboryl diene 3l can create the exceptional 1,1,3,4-tetraborylcyclohexene skeleton 4l (Figure 3D). Moreover, we examined the DA reaction of 1-boron-diene 24,43 E-3k with gem-diborylalkene 2, and surprisingly, the reaction generated the rare 1,1,2-triboryl cyclic adduct 4k as the exclusive isomer with complete stereoselectivity (Figure 3E).12,43,44
support for the structures of 4k using X-ray crystallographic analysis (see CYLvies in Figure 3E). DFT calculations indicate that the TS of the 1,1,2-triboryl constitutional isomer is favored by 3 kcal/mol over the TS of the 1,1,3-triboryl isomer (1,1,2-triBpin-TS vs 1,1,3-triBpin-TS; Figure 3F).

Next, the polyborylated cycloadducts 4 were subjected to oxidation reactions using H₂O₂ (Figure 4). Oxygenated compounds 4O were obtained in a chemoselective manner (Figure 4). Thus, we have demonstrated that gem-diborylalkenes serve as ketene equivalents in [4 + 2] cycloadditions. Of note, 4d has been subjected to two oxidation reactions that lead chemoselectively to two different products, 4O-d and 4O-d'. In 4O-d, first the double bond was stereoselectively epoxidized and then the gem-di-Bpin unit underwent oxidation. However, in 4O-d' the geminal-Bpin position first underwent oxidation and then the double bond isomerizes due to the deprotonation of the acidic benzylic and allylic proton that is located α to the generated carbonyl (Figure 4; see proposed pathways in the SI). When triboryl compound 4k was subjected to the oxidation conditions, ketone 4O-k was selectively obtained, most likely resulting from oxidation of the gem-diboryl moiety to give a boron-enolate, which hydrolyzed in situ to finally give 4O-k (Figure 4; see proposed pathways in the SI).

Furthermore, we investigated the DA reaction using unsymmetrical 1,1-bisdi(boryl)alkenes (2' and 2-F). It was anticipated that the cycloaddition might proceed with good stereoselectivity (Figure 5).13 We were happy to discover that the reaction of 1,1-BpinBdan-ethene (2') with dienes 3a–d afforded the unsymmetrical gem-diborylalkene 5a–d (confirmed by X-ray crystallographic analyses of 5a and 5c) in good yield (Figure 5A,B). High diastereoselectivity was observed in the reaction of 1,1-BpinBdan-ethene (2') with CP, affording cycloaddition product 5c (endo:exo = 92:8). Our calculations indicate that the reaction favors the endo product 5c with the TS energy of endo-BpinBdan-TS, which is 2 kcal/mol less than that of exo-BpinBdan-TS (Figure 5C).24,35,36 This is in good agreement with the fact that the aromatic-planar Bdan group is less bulky than the Bpin group.3,33,37,48 Furthermore, it would appear that the diastereoselectivity in this case is driven primarily by steric (additional considerations for the relative stabilities of the different transition states are discussed in the SI (pp S65, S66)).

Moreover, the reaction of 2' with 3,4-diboryl diene 3l yielded 1,1,3,4-tetraborylcyclohexene adduct 5l (Figure 5D). Additionally, the DA reaction of 1-boron-diene4,33 (E-3k) with gem-diborylalkene 2' generated regioselectively the separable diastereomers of the 1,1,2-triboryl cyclic adduct with complete stereospecificity (5k, 5k'; Figure 5E).43 We have obtained unambiguous support for the structures of 5k' using X-ray crystallographic analysis (see CYLvies in Figure 5E). These two different boron groups can provide the basis for selective C–B sequential functionalization, which in turn reacts differently.13,49

Unlike boron esters, for example, the Bpin and Bdan groups, monoalkyl-trifluoroborate salts are known to be easily activated and to undergo rapid transmetalation with transition-metal complexes. In general, owing to their air, moisture, shelf, and thermal stability, as well as their occurrence as free-flowing crystalline solids, monotrifluoroborate salts have now become extremely popular reagents in synthesis. Thus, we attempted to use the gem-BpinBF₃Cs alkene 2-F as a dienophile for the DA reaction (Figure 6A). Unfortunately, the reaction did not afford the desired product (gem-diborylcyclohexene BF₃Cs containing 6) and instead led to decomposition (Figure 6A).

Alternatively, we sought to obtain product 6 using our recently reported conditions for late-stage trifluoroboration of gem-diborylalkanes 4 as an alternative method for the unsuccessful direct DA of 2-F with diene 3. (C) Examples of the trifluoroboration products as a result of reaction of 2 with different dienes. The relative configurations of 6b and 6d have been confirmed by 2D NMR NOESY. dr = diastereomeric ratio, yields are isolated. Bpin = pinacolato-boron.

![Figure 6](https://doi.org/10.1021/jacs.1c01471)
Organoboron polymers have attracted widespread attention, since they provide unique properties for catalysis, sensory materials, luminescent materials, and biomedical applications. Among them, polymers with pendant boronic acids/esters account for the majority, since boronic acids/esters could serve as responsive sites of sensitive materials or dynamic cross-linking points of self-assembled polymers and acids/esters can provide a new array of polymer properties to forge a wider diversity of gem-diboron-based polymers. Thus, gem-diborylnorbornenes hold great promise to serve as a monomer for ROMP reactions that form polymers containing gem-diboryl units. It is noteworthy that the ROMP reactions for the mono-boron-containing monomers are rarely reported, and there are only a few examples of very special side-chain boron groups.

In this regard, we chose the [Ru] Grubbs second-generation catalyst as a catalyst in the ROMP reactions, because its known to tolerate broad functional groups, air, and moisture, and this includes the fact that the Bpin group is expected to be intact to be colorless, the dark color of the organoboron polymers might be a result of the conjugated nature of the aromatic Bdan group. We subjected norbornenes 4e and 5c to ROMP polymerization reaction conditions using 1 mol % of the [Ru] Grubbs second-generation catalyst and tetrahydrofuran (THF) as a solvent.

The resulting polymer, poly-7-BpinBpin and poly-7-BpinBdan, respectively, in high conversions (Figure 8B). This transformation was followed by 1H NMR spectroscopy of both monomers 4e and 5c and their corresponding polymers poly-7-BpinBpin and poly-7-BpinBdan, respectively, as depicted in the SI (pp S51–S55). The resulting polymer, poly-7-BpinBpin, was observed to have a light yellowish color; it has a high molecular weight (MW = 4.85 × 10^4) and polydispersity indexes (PDI) of M_w/M_n = 1.29, based on gel permeation chromatography (GPC) (Figure 8B,C). Furthermore, the polymer poly-7-BpinBdan was dark green and has a lower molecular weight (MW = 9.19 × 10^3) and a higher PDI of M_w/M_n = 1.61 (Figure 8B,C). Although these pristine polymers are expected to be colorless, the dark color of the poly-7-BpinBdan might be a result of the conjugated nature of the aromatic Bdan group. While both polymers have different MW values, the diversity of organoboron polymers has been widely used, their gem-diboryl analogues have not been investigated; thus, they can provide a new array of polymer properties to forge a wider diversity of gem-diboron-based polymers. The relative configuration of 5f-end, the exo product of cyclopentadiene 3f with the unsymmetrical gem-diborylnorbornene 2'. The relative configuration of 5f-end was determined using X-ray crystallography (see the CYLview structure of 5f-end). The structure of the catalyzed Ru ROMP of norbornenes with gem-diborolalkene 2, which leads to norbornene 4f. Step 2: stereoselective trifluorination of norbornene 4f from the less hindered si-face, leading to the exo product 6f. Step 3: the gem-diborylnorbornene-BF_3/CsF 6f was directly converted to unsymmetrical gem-Bpin Bdan-norbornene 5f-exo in a stereospecific manner. X-ray structures were visualized with CYLview 1.0b.42 Dr = diastereomeric ratio, yields are isolated. Bpin = pinacolato-boron, Bdan = B-1,8-diaminonaphthalene.
poly-7-BpinBpin is closer to the one expected at a 1 mol % catalyst compared with literature.\textsuperscript{51}

Subsequently, we examined the potential of postpolymerization modifications of these gem-diboron-based polymers by the functionalization of the double bond and the replacements of gem-diboryl units (Figure 9A). These modifications include the hydrogenation of the ethylene moieties using p-toluenesulfonyl hydrazide 13 as a source for hydrogen (Figure 9B).\textsuperscript{54,55} The hydrogenation reactions proceed very efficiently for both gem-diboron-based polymers poly-7-BpinBpin and poly-7-BpinBdan to obtain the new hydrogenated polymers poly-8-BpinBpin and poly-8-BpinBdan, respectively, in a complete

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**Figure 9.** Postpolymerization modifications of gem-diboron-based polymers. (A) General scheme of the postpolymerization modifications of poly-7. (B) Hydrogenation of polymers poly-7-BpinBpin and poly-7-BpinBdan. (C) Trifluorination, protodeborylation, and deuterodeborylation reactions of poly-7-BpinBpin. (D) Examples of postpolymerization modifications of poly-8-BpinBpin and poly-11-Bpin-H which include trifluorination, protodeborylation, deuterodeborylation, and arylation. Bpin = pinacolato-boron, Bdan = B-1,8-diaminonaphthalene.
conversion (Figure 9B). The hydrogenated polymers poly-8-BpinBpin and poly-8-BpinBdan were distinctly confirmed by 1H and 13C NMR spectroscopy (for full details see the SI).55

Our efforts were also directed to the postpolymerization transformation of the boron groups through the selective replacement of one of the boron groups by trifluorination,50 protodeborylation,56 and deuterodeborylation56 as described in Figure 9C. Remarkably, the trifluorination50 reaction of polymer poly-7-BpinBpin represents an alternative method to the unsuccessful direct ROMP reaction of monomer Bpin-BF, Cs-norborenone 6b. Of note, these new polymers were confirmed by 1H, D, 19F, and 13C NMR spectroscopy (for full details see the SI).

Moreover, the hydrogenated polymer poly-8-BpinBpin underwent selective protodeborylation,56 and deuterodeborylation,56 which were then followed by a trifluorination reaction of poly-11-Bpin-H (Figure 9D). Overall, poly-7-BpinBpin underwent three chemoselective sequential postpolymerization modifications, i.e., hydrogenation, protodeborylation, and trifluorination, which eventually gave poly-7-BF,K-H (Figure 9B and D). Finally, poly-11-Bpin-H was subjected to the Pd-catalyzed Suzuki–Miyaura cross-coupling reaction, to replace the C–B bond with the new C–C bond, which forms the arylated polymer poly-14-Ar-H (Figure 9D).

These preliminary postpolymerization transformations have demonstrated the utility of a replaceable-main-chain-based strategy using boron and the double bond as the key elements for opening new opportunities for the synthesis of a variety of new polymers.

## SUMMARY

In conclusion, we have developed a method that addresses the long-standing challenge of regio- and stereoselective Diels–Alder cycloadditions with poly-alkenylboranes. This was achieved by introducing a new method that enables the use of (unsymmetrical) gem-diborylalkenes as a reasonable reactive dienophile for the DA reaction. The products of these reactions enable the formation of polyborated cycloadducts, particularly the 1,1,2-tri- and 1,1,3,4-tetaborylcyclic adduct, which would be difficult to accomplish with the existing strategies. In addition, the reaction offers the stereoindirect synthesis of norbornenes by using a diastereoselective trifluorination reaction. We demonstrate the use of the gem-diborylalkenes as ketene equivalents in [4 + 2] cycloadditions. Moreover, we utilized gem-diborylnorborenone in the synthesis, for the first time, of gem-diboryl-based polymers through ROMP. These polymers underwent successful postpolymerization modifications to access new polymers, which also demonstrates the potential diversity of the main chain replacement. Studies to achieve an enantioselective DA transformation using chiral gem-diborylalkenes53 as well as new postpolymerization transformations of gem-diborylcycloalkene-based polymers are currently under investigation and will be reported in due course.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.1c01471.

Supporting information and chemical compound information (PDF)

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CCDC 2058307–2058312 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

## AUTHOR INFORMATION

### Corresponding Authors

Tamar Stein — Institute of Chemistry and Fritz Haber Center for Molecular Dynamics Research, Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem 9190401, Israel; Email: tamar.stein@mail.huji.ac.il

Ahmad Masarwa — Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem 9190401, Israel; orcid.org/0000-0001-6992-5595; Email: Ahmad.Masarwa1@mail.huji.ac.il

### Authors

Nadim Eghbarieh — Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem 9190401, Israel

Nicole Hanania — Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem 9190401, Israel

Alon Zamir — Institute of Chemistry and Fritz Haber Center for Molecular Dynamics Research, Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem 9190401, Israel

Molhim Nassir — Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem 9190401, Israel

Complete contact information is available at: https://pubs.acs.org/10.1021/jacs.1c01471

### Author Contributions

N.E. and N.H. contributed equally to the work.

### Notes

The authors declare no competing financial interest.

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