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一类新型卤化偕二硼试剂的合成

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摘要 开发了一种新型偕二硼试剂-卤化偕二硼酸酯[X-CR(Bpin)$_2$], 该试剂性状稳定且易于大规模制备; 当使用烷基取代的偕二卤化物时, 可以高收率地制备四取代的卤代偕二硼酸酯, 为偕二硼试剂化学的开发提供了新的选择.
关键词 元素有机化学; 试剂化学; 有机硼; 偕二硼

A Novel Synthesis of Halogenated *gem*-Diboron Reagents

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Abstract A novel synthesis of halogenated *gem*-diboronates (X-CR(Bpin)$_2$) was developed. The reagents are stable and easy to prepare in a large scale. Tetra-substituted halogenated *gem*-diboronates can be prepared in high yields when using alkyl-substituted *gem*-dihalides, providing a new strategy for the synthesis of new *gem*-diboron compounds.
Keywords element-organic chemistry; reagent chemistry; organoboron; *gem*-diboron

1 Introduction

Organoboron compounds are fascinating synthetic building block in chemical society. Among various organoboron compounds, *gem*-diborons have attracted more and more attention due to the diverse transformation of C—B bonds.[1] Selective cross-couplings of C—B bonds with organohalides enable the synthesis of diverse alkyl boronates,[2] allene and fluorene derivatives.[3] The reactions of *gem*-diboronates with carboxylic acid and their derivatives produce structurally diverse enolates or enamines.[4] Similarly, the addition of *gem*-diboronates to imines/carbonyls efficiently synthesizes *β*-aminoboronates and *β*-oxylboronates.[1e,5] In addition, the Boron-Wittig reactions of *gem*-diboronates provide a nice route for synthesizing polysubstituted alkenyl boronic esters.[6]

The wide application of *gem*-diboronates has facilitated the development of strategies for their synthesis.[7] Currently, most of synthesized *gem*-diboronates were alkyl/aryl-substituted methylene *gem*-diboronates (Scheme 1a, **1a**) or (*gem*-diborylalkyl)lithiums (Scheme 1a, **1b**). In addition, boron and silicon-substituted methylene *gem*-diboronates were also used in organic synthesis.[8] (*gem*-Diborylalkyl)zinc species (Scheme 1a, **1c**) have also been synthesized from the reaction of (diborylmethyl)lithium with zinc(II) halides.[9] *α*-Halo monoboronates are versatile synthetic precursors in organic synthesis, which can derivate high value-added organoboron compounds, such as *α*-aminoboron, *α*-oxoboron, *α*-thioboron through selective carbon-halogen bond transformation.[10] We envisioned that practical synthesis of halogenated *gem*-diboronates (Scheme 1a, **2**) would be much appealing, as both C—B bonds and C—halide bond are highly transformable which leaves more room for molecule design. To our surprise, very rare synthesis of *α*-halo *gem*-diboronates has been reported. In 1974, Matteson and co-worker activated 1,1,1-triborylmethane *in situ* with MeLi to obtain diborylmethyl carbanion, which was subsequently reacted with Br_2, and the target product was obtained in a low yield of 23% (Scheme 1b).[11] The inherent difficulty of 1,1,1-triboromethane and the high toxicity and corrosiveness of Br_2 limit the wide application of this compound, and no other strategies have been developed since then.[12] 1,2-Metallate rearrangement is a typical transformation in organoboron chemistry. We and others have shown the well migration ability of Bpin group in the transformation of B_2pin_2 in

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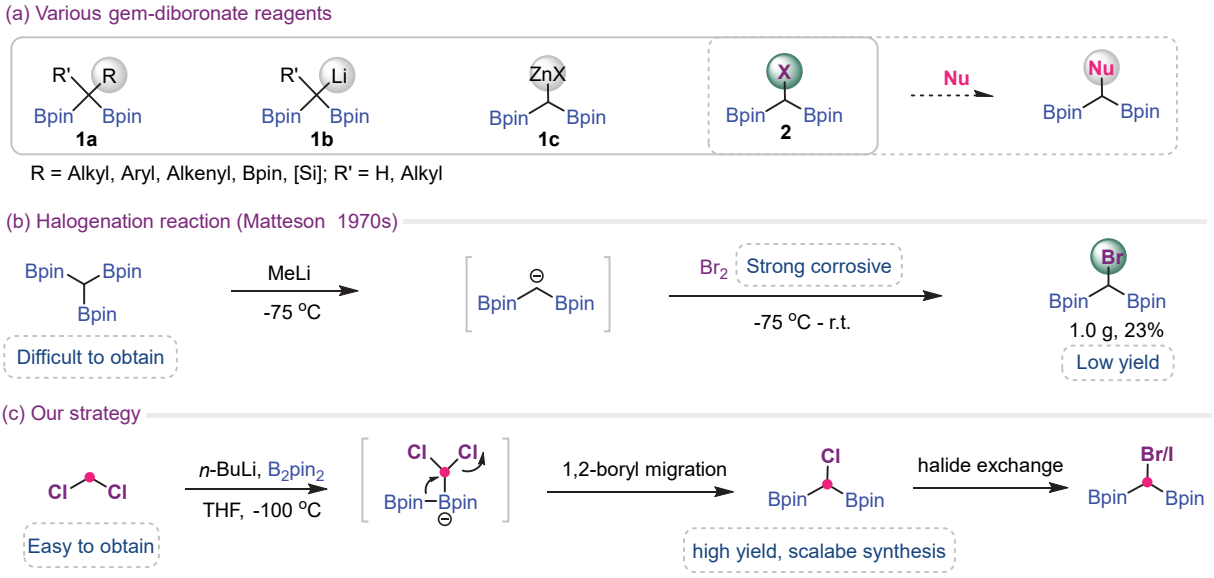
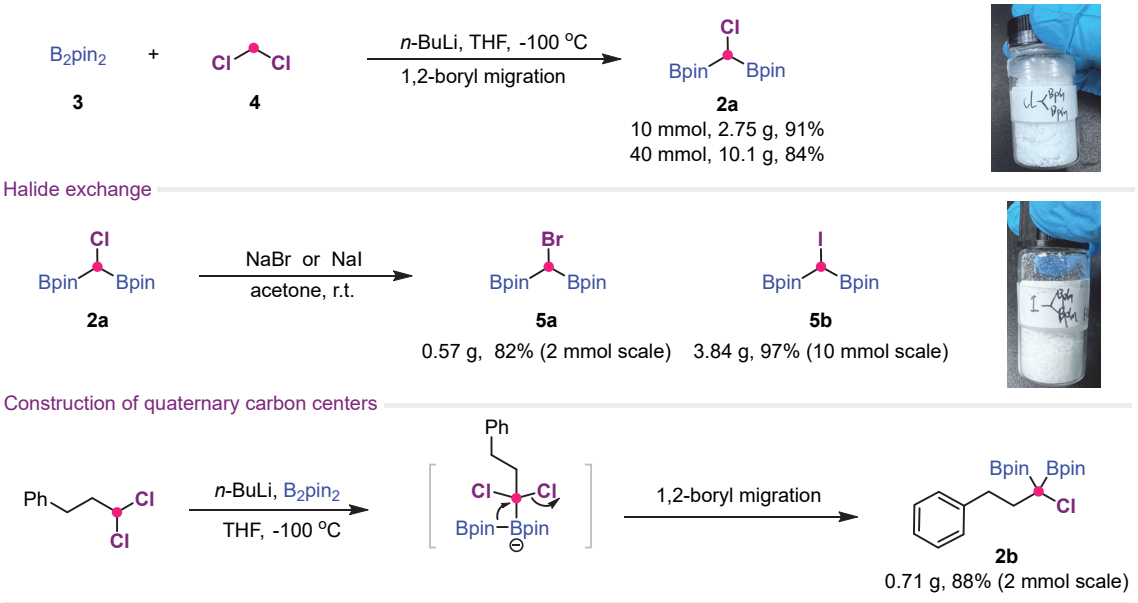


Scheme 1 Strategies for the synthesis of *gem*-diboronate reagents

1,2-metallate rearrangements.[7a,7c,7f,13] Inspired by the Matteson reaction for the synthesis of *α*-halomonoboronates,[14] we herein used B_2pin_2 to react with lithiated dichoromethane to provide a high yielding and scalable synthesis of *α*-halo *gem*-diboronates, in which Bpin is a proper migration group (Scheme 1c).

2 Result and discussion

At a low temperature, a strong base was used to deprotonate dichloromethane, and a 1,2-migration reaction with B_2pin_2 was carried out. A 10 mmol scale synthesis successfully afforded 2.75 g of chloro *gem*-diboronate **2a** in 91% yield (Scheme 2). The compound is a white solid which is insensitive to water and air. The reagents used in the reaction are inexpensive and readily available, and they are all commercially available without further purification. In order to further prove the synthetic value of this reagent, a 10 g-level reaction was carried out, and the target product **2a** was obtained in 84% yield. Subsequently, bromine/iodine substituted *gem*-diborylmethanes **5a** and **5b** were easily obtained by halide exchange with sodium bromide or sodium iodide. Importantly, when alkyl-substituted *gem*-dichloro compounds were used instead of dichloromethane, chloro *gem*-diboronate **2b** containing a quaternary carbon center was successfully obtained in 88% yield. In the case of phenyl-substituted *gem*-dichloride, a relatively complex mixture with trace amount of desired product was observed under the reaction conditions.



Scheme 2 Synthesis of X-CR(Bpin)$_2$

3 Conclusions

In summary, we have developed a new synthesis of halogenated *gem*-diboronates via 1,2-boryl migration strategy. The reagents were synthesized from cheap and readily available raw materials and were facile to prepare in a large scale. The existence of carbon-halogen bonds and carbon-boron bonds endows the multi-functional reagent with diverse possibilities for subsequent transformations. At present, we are further studying the controllable transformation of these reagents.

4 Experimental section

4.1 General information

All reactions were isolated from moisture and oxygen by a nitrogen atmosphere with a sealed tube. All glassware was oven dried at 110 °C for hours and cooled down under vacuum. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 100～200 mesh silica gel or through SepaBeamTM Machine SPB-3006012. Gas chromatographic analyses were performed on GC-2010 Plus gas chromatography instrument with an FID detector. GC-MS spectra were recorded on a GCMS-QP2010 SE. The High-Resolution MS analyses were performed on a Agilent 6530 Accurate-Mass Q-TOF LC/MS with ESI mode. NMR spectra were recorded on 400 MHz for ^{1}H NMR and 101 MHz for ^{13}C NMR, using tetramethylsilane as an internal reference and $CDCl_3$ as a solvent. Chemical shift values for protons were reported downfield from tetramethylsilane and were referenced to residual proton of TMS (δ 0.00). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 101 MHz. Chemical shifts for carbons were reported downfield from tetramethylsilane and were referenced to the carbon resonance of $CDCl_3$ (δ 77.0). The boron-bound carbon was not detected due to quadrupolar relaxation.

4.2 General procedure for the synthesis of chloro *gem*-diboronate **2a**

An oven-dried 100 mL screw-cap round-bottom Schlenk tube equipped with a Teflon stir bar was added with dichloromethane (0.96 mL, 1.5 equiv.) and anhydrous THF (20 mL) under N_2 atmosphere, then the tube was cooled to −100 °C followed by dropwise addition of *n*-BuLi (6.875 mL, 1.1 equiv., 1.6 mol/L in hexane) via a syringe. The reaction mixture was stirred at the same temperature for 45 min, a solution of B_2pin_2 (2.54 g, 10 mmol) in THF (5 mL) was added to the reaction at the same temperature. Then the resultant mixture was allowed to slowly warm to room temperature and stirred overnight. After the reaction was completed, large amount of DCM was added to precipitate LiCl and the solution was filtered and concentrated. A sufficiently pure target product can be obtained, which can also be further purified by recrystallization from *n*-hexane at low temperature.

4.3 General procedure for the synthesis of bromine *gem*-diboronate **5a**

An oven-dried 100 mL screw-cap round-bottom Schlenk tube equipped with a Teflon stir bar was added with chloro *gem*-diboronate (604 mg, 2 mmol) and sodium bromine (1.03 g, 5.0 equiv.) in acetone (10 mL), the reaction mixture was stirred at room temperature overnight, the suspension was filtrated and the filtrate evaporated under reduced pressure. The residue was diluted with water and extracted with hexane. The organic layer was dried over Na_2SO_4, filtrated and concentrated. The target product was recrystallized with *n*-hexane at low temperature.

4.4 General procedure for the synthesis of iodine *gem*-diboronate **5b**

An oven-dried 100 mL screw-cap round-bottom Schlenk tube equipped with a Teflon stir bar was added with chloro *gem*-diboronate (3.02 g, 10 mmol) and sodium iodine (7.5 g, 3.0 equiv.) in acetone (50 mL), the reaction mixture was stirred at room temperature overnight, the suspension was filtrated and the filtrate evaporated under reduced pressure. The residue was diluted with water and extracted with hexane. The organic layer was dried over Na_2SO_4, filtrated and concentrated. The target product was recrystallized with *n*-hexane at low temperature.

4.5 General procedure for the synthesis of **2b**

An oven-dried 100 mL screw-cap round-bottom Schlenk tube equipped with a Teflon stir bar was added with dichloropropylbenzene (4.5 mmol, 1.5 equiv.) and anhydrous THF (6 mL) under N_2 atmosphere, then the tube was cooled to −100 °C followed by dropwise addition of *n*-BuLi (2.06 mL, 1.1 equiv., 1.6 mol/L in hexane) via a syringe. The reaction mixture was stirred at the same temperature for 45 min, a solution of B_2pin_2 (762 mg, 3 mmol) in THF (2 mL) was added to the reaction at the same temperature. Then the resultant mixture was allowed to slowly warm to room temperature and stirred overnight. After the reaction was completed, large amount of DCM was added to precipitate LiCl and the solution was filtered and concentrated under vacuum to afford the crude product, which was purified by flash chromatography to give the target product **2b**.

2,2'-(Chloromethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**2a**): White solid, 2.75 g, 91% yield (in 10.0 mmol scale). m.p. 92～93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.93 (s, 1H), 1.28 (s, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 84.5, 24.6, 24.4; ^{11}B NMR (128 MHz, $CDCl_3$) δ: 31.75; HRMS (ESI) calcd for $C_{13}H_{25}B_2ClO_4$ $[M+Na]^+$: 325.1520, found 325.1526.

2,2'-(Bromomethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**5a**): White solid, 567.5 mg, 82% yield (in 2.0 mmol scale). m.p. 64～65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.54 (s, 1H), 1.27 (s, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 84.5, 24.6, 24.5; ^{11}B NMR (128 MHz, $CDCl_3$) δ: 31.75. HRMS (ESI) calcd for $C_{13}H_{25}B_2BrO_4$ $[M+H]^+$:

347.1195, found 347.1193.

2,2'-(Iodomethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**5b**): White solid, 3.84 g, 97% yield (in 10.0 mmol scale). m.p. 75～76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.07 (s, 1H), 1.26 (d, J=3.0 Hz, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 84.3, 24.4, 24.3; ^{11}B NMR (128 MHz, $CDCl_3$) δ: 32.50. HRMS (ESI) calcd for $C_{13}H_{25}B_2IO_4$ [M+Na]$^+$: 417.0876, found 417.0883.

2,2'-(1-Chloro-3-phenylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**2b**): White solid, 714.6 mg, 88% yield (in 2.0 mmol scale). m.p. 85～86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.28～7.19 (m, 4H), 7.18～7.12 (m, 1H), 2.84～2.76 (m, 2H), 2.25～2.17 (m, 2H), 1.28 (s, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.0, 128.4, 128.1, 125.6, 84.3, 37.9, 33.5, 24.4(2), 24.3(5); ^{11}B NMR (128 MHz, $CDCl_3$) δ: 32.17. HRMS (ESI) calcd for $C_{21}H_{33}B_2ClO_4$ [M+H]$^+$: 407.2326, found 407.2336.

Supporting Information NMR spectra of all products. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

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