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Polyborylation of azulenes

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ABSTRACT

In the presence of an active Ir-based catalyst, azulene underwent stepwise borylation with bis(pinacolato)diboron to produce polyborylated products. The reactivity of the ring atoms toward borylation was found to decrease in the following order: 2-position>1,3-positions>6-position>5,7-positions. Extension of the borylation to some azulenes substituted at the five-membered ring was also examined. Furthermore, the reaction of 2,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**3a**) with an equivalent of hydrogen peroxide revealed that the oxidation proceeds preferentially at the 6-position. This indicates that the reactivity of the boryl group is governed by the π-polarization of the azulenyl skeleton.

1. Introduction

Owing to the π-electron polarization, azulene undergoes electrophilic substitution at the 1- and 3-positions of the five-membered ring and nucleophilic addition at the 4-, 6- and 8-positions of the seven-membered ring. Introduction of substituents into the 2-, 5- or 7-positions that are inert toward these reactions have therefore required multi-step synthesis including the construction of the azulene skeleton.[1] In this regard, the establishment of efficient synthetic methods for 2-, 5- or 7-substituted azulenes is an important issue in organic chemistry. We have recently reported the Ir-catalyzed direct borylation of azulenes through C–H activation (Scheme 1).[2] An outstanding feature of this reaction is that the protons in the five-membered ring, in particular, the proton attached to the 2-position, is preferentially substituted by a 4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl group (Bpin), where the steric effect of the substituent in an azulenyl skeleton affects the reactivity. Thus, the parent azulene undergoes the borylation to give **1a** together with a small quantity of **1b**, while 4,6,8-trimethylazulene is borylated to afford **2** in low yield, and borylation is little observed in azulenes substituted at the five-membered ring. We have been interested in developing the methodology to borylate the seven-membered ring of azulenes through the C–H activation. Application of such methodology to **1** as well as the inert substituted azulenes, if successful, would permit easy access to the derivatives whose five- and seven-membered rings are both functionalized by the transformation of the boryl group, since this class of compounds are difficult or impossible for their syntheses by conventional methods. In this paper, we report the Ir-catalyzed borylation at the seven-membered ring of substituted azulenes and the transformation of their boryl groups.

2. Results and discussion

2.1. Polyborylation of azulene

Recently, Ishiyama and Miyaura have revealed that the catalytic activity of 1/2[IrCl(cod)]$_2$/dtbpy (dtbpy=4,4′-di-*tert*-butyl-2,2′-bipyridine) is superior to that of 1/2[IrCl(cod)]$_2$/bpy (bpy=2,2′-bipyridine) due to the higher solubility of the former complex in hydrocarbon solvents.[3,4] Thus, we examined the borylation of azulene by using the dtbpy complex. Unlike our previous borylation technique based on the bpy complex (Scheme 1), the formation of 2,6-diborylated azulene **3a** was observed, although the yield was poor (4%) (Scheme 2). This indicates that **1a** undergoes subsequent borylation in its seven-membered ring. Hence, we attempted to borylate **1a** under various conditions (Table 1). In the presence of 1/2[IrCl(cod)]$_2$/bpy under reflux (about 80 °C), the reaction of **1a** with pin_2B_2 (0.5 equiv) afforded **3a** only in 3% yield (entry 1). Increasing the temperature and the use of an excess amount of pin_2B_2, however, dramatically improved the yield of **3a** and, furthermore, produced its regioisomer **3b** together with its further borylated derivative **4a** (entry 2). The dtbpy and dmbpy (4,4′-dimethyl-2,2′-bipyridine) ligands,[4] which are expected to enhance the activity of the Ir-based catalyst, did not result in any marked changes (entry 2

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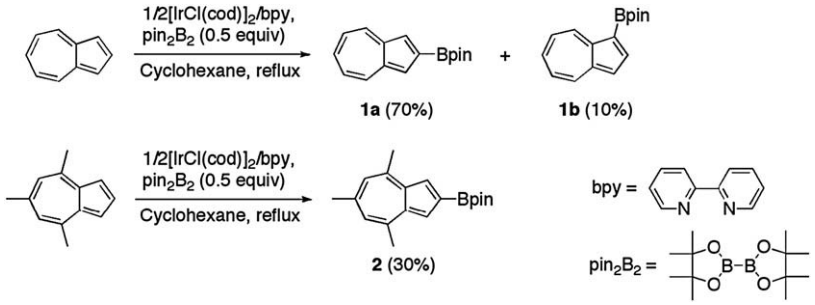
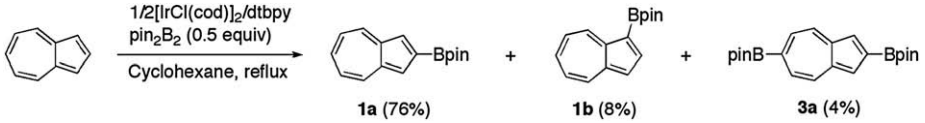
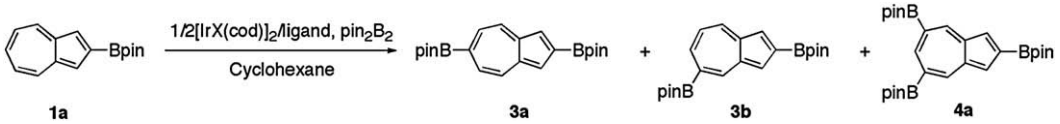


Scheme 1.



Scheme 2.

Table 1

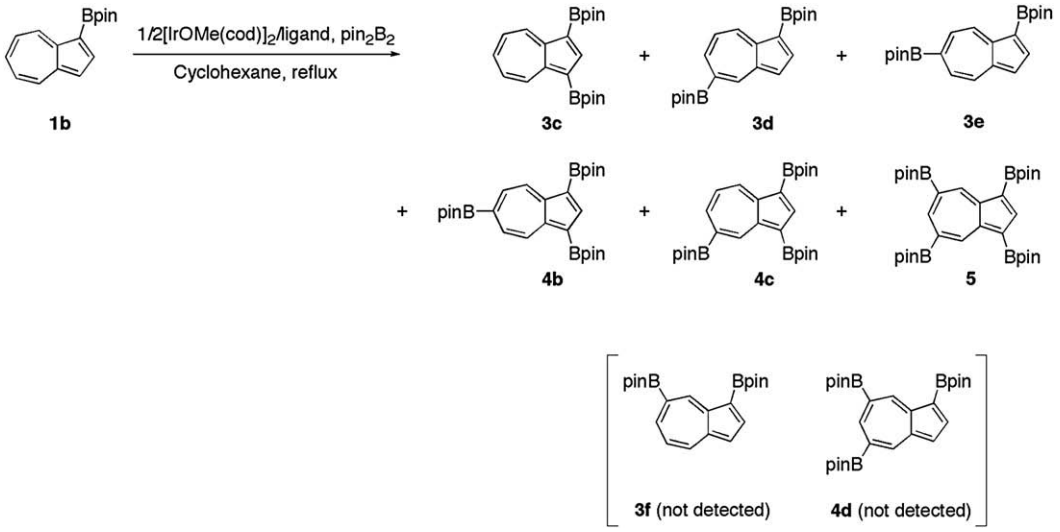


Entry	X/ligand	Temp (°C)	pin_2B_2 (equiv)	Yield (%)			Recovery (%)
				3a	**3b**	**4a**	**1a**
1	Cl/bpy	Reflux	0.5	3	0	0	86
2	Cl/bpy	100	0.7	35	25	2	25
3	Cl/dtbpy	100	0.7	40	30	2	21
4	Cl/dmbpy	100	0.7	34	30	2	20
5	OMe/dtbpy	Reflux	0.5	8	0	0	76
6	OMe/dtbpy	Reflux	0.7	32	24	2	29
7	OMe/dmbpy	Reflux	0.5	25	0	0	63
8	OMe/dmbpy	Reflux	0.7	46	41	2	5

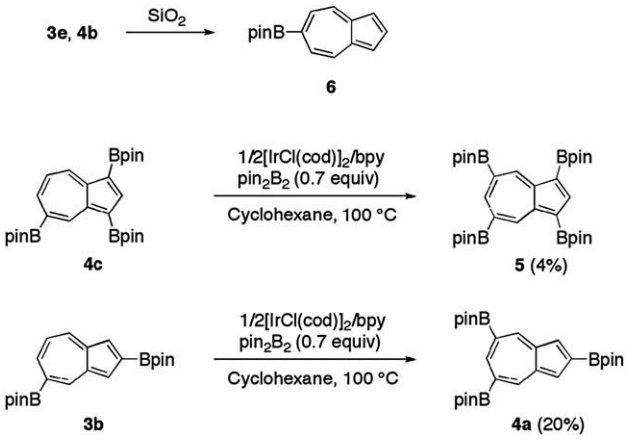
vs entries 3 and 4). Moreover, replacing of the 1/2[IrCl(cod)]$_2$ complex with a more active one (1/2[Ir(OMe)(cod)]$_2$)[4] made it possible to conduct the reaction at a lower temperature (entry 6). The most favorable results were obtained when a 1/2[Ir(OMe)(cod)]$_2$/dmbpy complex was employed in the presence of an excess amount of pin_2B_2 (entry 8). The site selectivity of the borylation process is higher with respect to the 6-position than the 5-position since the relative ratio (**3a**/**3b**) was higher than the statistical ratio (1:2). On the other hand, borylation at the 4-position was not observed. These findings suggest that **1a** is preferentially borylated at the electron-deficient 6-position, which is somewhat different from the tendencies in the borylation of benzene derivatives, where the electronic properties of the substituents do not exert significant influence on the regioselectivities while the steric effects sensitively participate in the process.[5a] Thus, the borylation of monosubstituted benzenes gives a mixture of *meta* and *para* products in statistical ratios (*m*/*p*=ca. 2:1)[5b] and does not take place at the hindered *ortho* position.[5c] Such differences in the reactivity of the azulene and benzene systems can be attributed to the unique conjugation of non-alternant azulene, which is influenced by the electronic effects of substituents due to its low aromatic resonance energy.

Taking into account the results of the borylation of **1a**, we subsequently examined the borylation of **1b** (Table 2). Initially, when we used 0.7 equiv of pin_2B_2 in the presence of a 1/2[Ir(OMe)(cod)]$_2$/dtbpy complex, five products were formed (confirmed by TLC), although most of **1b** remained unreacted. The two minor products, denoted by **4b** and **4c**, were separated by fractional recrystallization, while chromatographic separation of the filtrate revealed that the major products were **3c**–**e**. Compounds **3f** and **4d** were not detected. The use of an excess amount of pin_2B_2 (1.8 equiv) completely consumed **1b**. Thus, the TLC following the reaction showed that the initially formed **3c**–**e** gradually disappeared, with growing **4b** and **4c**, along with the subsequent formation of **5**. The outstanding feature of both **4c** and **5** in the ^{1}H NMR spectrum is the proton attached to the 4-position, whose signal appeared largely downfield (δ 9.7) due to the influence of the two adjacent boryl groups. On the basis of this finding, we excluded the possibility of formation of **3f** and assigned the structure of **3d**, whose proton signal due to the 4-position appeared more upfield (δ 8.93). The isolation of **3e** in a pure form failed since it gradually underwent deborylation under chromatographic separation on silica gel to give **6** (Scheme 3). In this regard, deborylation occurred easily in **4b**, giving **6** when dissolved in $CDCl_3$ or purified by chromatography on silica gel. These findings indicate that the introduction of the boryl group into the 6-position promotes the deborylation at the 1- and 3-positions, since such tendency was not observed in **1b**, **3a**, **3c** and **4c**. Throughout the borylation of **1b**, the 2-, 4- and 8-positions were inert. The relative ratio of **4b** and **4c**, like that of **3a** and **3b**, was higher than the statistical ratio (1:2). This

Table 2



Ligand	pin_2B_2 (equiv)	Yield (%)				
		3c	**3d**	**4b**	**4c**	**5**
dtbpy	1.8	7	5	33	30	5
dmbpy	1.8	0	9	31	28	7



Scheme 3.

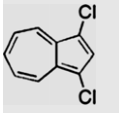
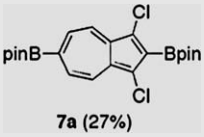
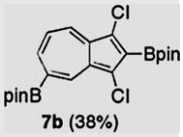
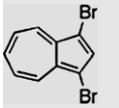
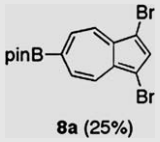
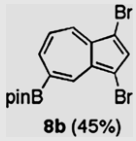
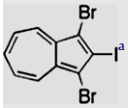
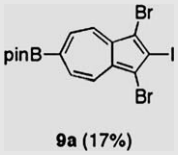
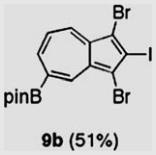
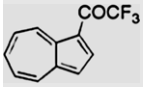
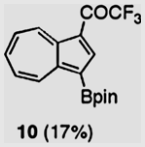
suggests that **1b** or **3c** is preferentially borylated at the 6-position compared to the 5-position. The reason of such site selectivity may be attributed to the steric effect of the bulky boryl group at the 1- or 3-position as well as the electron deficiency at the 6-position, since **3f** was not formed. This is supported by the fact that the yield of **5** from **4c** was lower than that of **4a** from **3b** (Scheme 3). In the present polyborylation of azulene, fluxional rearrangements of the boryl substituent(s) were not observed. Based on the borylation of **1**, therefore, it is summarized that the reactivity of the ring atoms in azulene toward polyborylation decreases in the following order: 2-position>1,3-positions>6-position>5,7-positions. The formation of π complex between the five-membered ring[6] and an iridium center in preference to the seven-membered ring seems to govern this site selectivity. Polycyclic aromatic hydrocarbons, such as naphthalene, pyrene and perylene, are known to undergo polyborylation by avoiding their ring junction.[7]

By using one of the active Ir-based catalysts, we attempted the borylation of azulenes substituted at the five-membered ring, which were inert in the previous study. Initially, the treatment of 1,3-dichloroazulene with 1.0 equiv of pin_2B_2 yielded a number of products. When an excess of pin_2B_2 was used, we obtained the two isomeric products **7a** and **7b**. Interestingly, both **7a** and **7b** possessed boryl groups in the hindered 2-position of the five-membered ring and at the seven-membered ring (Table 3). In contrast, a similar borylation process involving the use of 1,3-dibromoazulene took place only at the seven-membered ring to form the 5- and 6-borylated products **8a** and **8b**. Such differences in reactivity are indicative of differences in the atomic size of these halogen substituents. Furthermore, the borylation of 1,3-dibromo-2-iodoazulene gave **9a** and **9b**, while 1-trifluoroacetylazulene underwent borylation at the 3-position to afford **10**. Unlike the formation of **3a** and **3b**, the relative isomeric ratios in **7**, **8** and **9** were close to or over the statistical ratio (1:2). This suggests that the introduction of the less hindered and electronegative substituents into the 1- and 3-positions enhances the reactivity at the 5-position rather than the 6-position. Such effect of the substituent on the site selectivity of the borylation shows that non-alternant azulene is a unique conjugated system that is subject to electronic effect as well as steric effect.

Figure 1 displays the ^{13}C NMR data of azulene derivatives. It should be stressed that the introduction of the substituent into the 1- and 3-positions sensitively affected the chemical shifts due to the C5 and C7 signals (compared azulene with **1b** and **3c**). In this regard, we found that the site selectivity of the borylation at the 5,7-positions compared to the 6-position increases with downfield shift of the C5 and C7 signals of the substrate in the following order: **1a** (**3a**/**3b**=40:30; δ 122.7)<1,3-dichloroazulene (**7a**/**7b**=27:38; δ 123.3)<1,3-dibromoazulene (**8a**/**8b**=25:45; δ 124.0)<1,3-dibromo-2-iodoazulene (**9a**/**9b**=17:51; δ 125.3). The tendency of the deborylation in **3e** and **4b** may be understood by ^{13}C NMR study. With respect to the chemical shift due to the C1 signal, comparison of azulene (δ 118.1) with **6** (δ 117.5) revealed that introduction of the boryl substituent into the 6-position induces upfield shift of the signal. This suggests that the electron density on the C1 atom of **6** is slightly higher than that of azulene.[8] Such

Table 3

Substituted azulene $\xrightarrow[\text{Cyclohexane, 100 °C}]{1/2[IrCl(cod)]_2/dtbpy,\ pin_2B_2}$ Product

Substituted azulene	pin_2B_2 (equiv)	Product/yield (%)	
	2.1	 **7a (27%)**	 **7b (38%)**
	1.0	 **8a (25%)**	 **8b (45%)**
	1.0	 **9a (17%)**	 **9b (51%)**
	1.0	 **10 (17%)**	

[a] After 4 h, an additional amount of dtbpy (15 mol %) was added.

electronic effect seems to facilitate the protonation at the 1- and/or 3-positions of **3e** and **4b** since 3,6-di-*tert*-butyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene easily undergoes deborylation to give 1,6-di-*tert*-butylazulene.[9]

2.2. Oxidation of borylazulenes

In order to examine how the reactivity of the boryl group is affected by the positions to which it is attached, we carried out an oxidation reaction of **3a**, **4b** and **4c** (Scheme 4). Although the treatment of **3a** with an excess amount of hydrogen peroxide gave **11**, the use of one equivalent of hydrogen peroxide revealed that the oxidation takes place preferentially at the 6-position to give **12**. This result indicates that the reactivity of the boryl group is governed by the π-polarization of the azulenyl skeleton. Thus, the positively polarized seven-membered ring enhances the reactivity of the boryl substituent toward hydrogen peroxide in comparison with the negatively polarized five-membered ring. Compounds **4b** and **4c** also underwent oxidation preferentially at the seven-membered ring to give the corresponding products **13** and **14**, respectively (checked by TLC), but **13** easily underwent deborylation to form **15** when purified by chromatography on silica gel. Introduction of an electron-donating hydroxyl group as well as an electron-withdrawing boryl group into the 6-position appears to reduce the stability of the carbon–boron bond at the 1- and 3-positions. Compounds **11**,[10] **14** and **15**[11] gradually changed to an insoluble substance under ambient conditions. Addition of triethylamine to the solution of **11** accelerates its decomposition. The reason for such undesirable behaviors is attributed to the tautomeric effects of the less stable keto form. The ^1H NMR study of **11** showed that the enol form of this compound is present in DMSO, while the ratio of its keto form increases in $CHCl_3$.[10] In contrast to **15**, **12** was stable in air at room temperature. This may suggest the presence of the intermolecular interaction between the hydroxyl group and the boryl group. In order to isolate **13** and **14** as more stable forms, we attempted the acetylation of their hydroxyl groups. The choice of solvent was important in this reaction. Thus, the treatment of **13** with Ac_2O in DMSO afforded **16** along with **18** after purification by chromatography on silica gel, while a similar treatment of **14** yielded only **17**.

3. Summary

We have revealed that azulene undergoes stepwise borylation under the influence of active Ir-based catalysts. The order of reactivity of the ring atoms was estimated by the subsequent borylation of **1a** and **1b**. The seven-membered ring of azulene derivatives preferentially undergoes the borylation at the 6-position, which competes with the borylation at the 5-position depending on the steric or electronic effects of the substituents at the five-membered ring. The present reaction tolerates the introduction of the boryl group into the seven-membered ring, and the transformation of the resulting boron substituents ensures easy access to polysubstituted azulenes.

4. Experimental section

4.1. General

All reactions were carried out under argon, unless otherwise noted. ^1H and ^{13}C NMR spectra were recorded on a BRUKER AVANCE 400S spectrometer with tetramethylsilane as an internal standard. IR spectra were obtained as KBr pellets on a NICOLET AVATOR 370 DTGS spectrophotometer. $1/2[Ir(OMe)(cod)]_2$ was synthesized from $1/2[IrCl(cod)]_2$ in accordance with the reported procedure.[12]

4.2. Borylation of 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (1a)

Bis(pinacolato)diboron (pin_2B_2; 356 mg, 1.4 mmol), dmbpy (18 mg, 0.10 mmol), and $[Ir(OMe)(cod)]_2$ (33 mg, 0.05 mmol) were

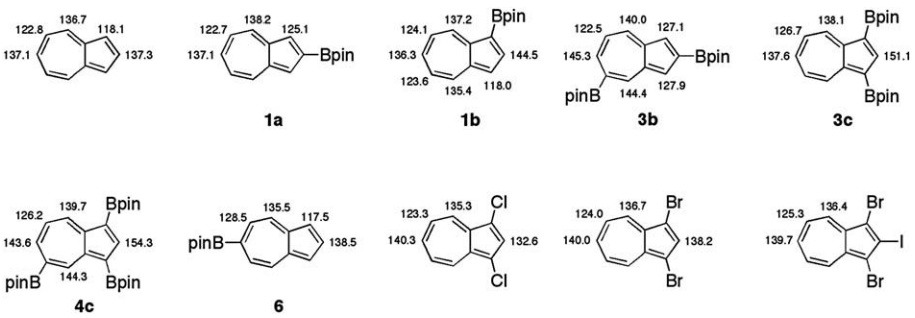
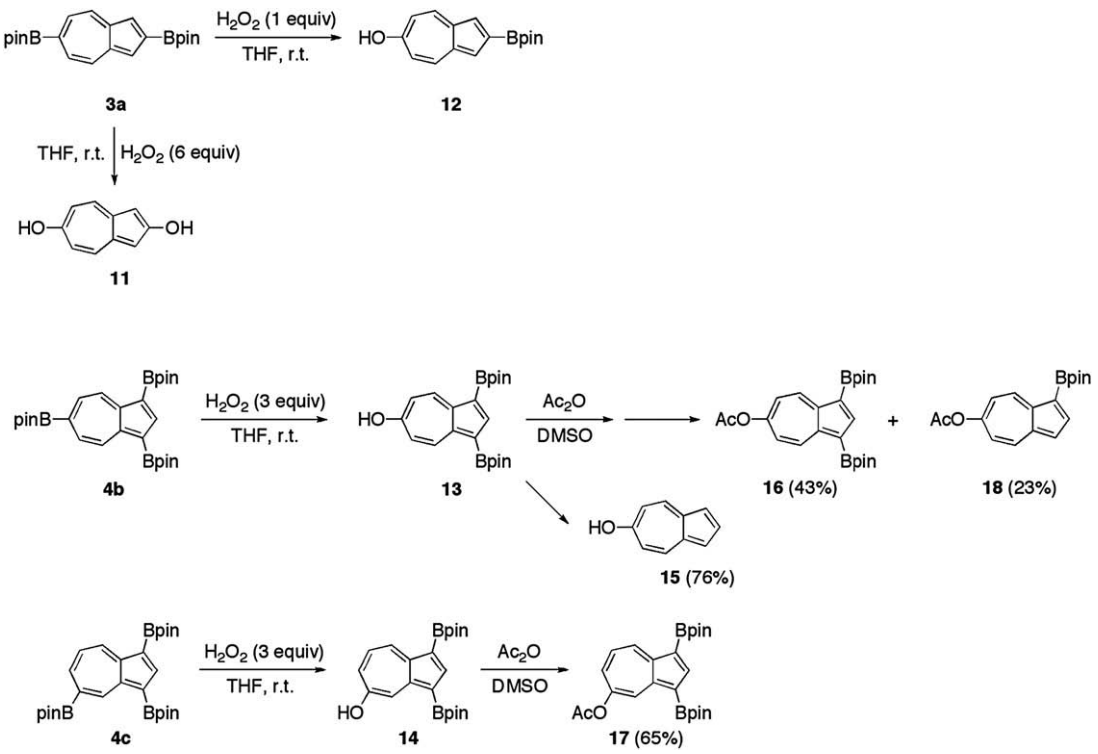


Figure 1. ^{13}C NMR spectral data in $CDCl_3$.



Scheme 4.

added to a solution of **1a** (508 mg, 2.0 mmol) in dry cyclohexane (12 mL), and the mixture was refluxed for 24 h. The reaction was quenched with water (5 mL) and the resulting mixture was extracted with hexane (30 mL×3). The organic layer was dried (Na_2SO_4) and concentrated to leave a residue, which was crystallized from THF–MeOH (1:10) to give **3a**. The filtrate was concentrated to give a residue, which was chromatographed on silica gel with hexane–AcOEt (10:1) to afford **3b** and **4a**.

*4.2.1. 2,6-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)-azulene (**3a**)*

Blue solid; yield 46% (351 mg); mp 260–274 °C (decomp.); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.39 (s, 12H), 1.40 (s, 12H), 7.66 (d, J=9.6 Hz, 2H), 7.73 (s, 2H), 8.34 (d, J=9.6 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.8, 24.9, 83.7, 84.5, 124.5, 128.4, 137.0, 141.7 ppm. Two azulene skeleton C signals were not observed. Anal. Calcd for $C_{22}H_{30}B_2O_4$: C, 69.52; H, 7.96. Found: C, 69.62; H, 8.06%.

*4.2.2. 2,5-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)-azulene (**3b**)*

Blue powder; yield 41% (312 mg); mp 187–189 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.39 (s, 12H), 1.40 (s, 12H), 7.10 (t, J=9.7 Hz, 1H), 7.79 (s, 1H), 7.83 (s, 1H), 8.10 (d, J=9.7 Hz, 1H), 8.33 (d, J=9.7 Hz, 1H), 8.82 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 25.0, 83.6, 84.2, 122.4, 127.1, 127.9, 139.9, 140.2 (×2), 144.3, 145.2 ppm. Two azulene skeleton C signals were not observed. Anal. Calcd for $C_{22}H_{30}B_2O_4$: C, 69.52; H, 7.96. Found: C, 69.45; H, 8.01%.

*4.2.3. 2,5,7-Tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)-azulene (**4a**)*

Blue powder; yield 2% (20 mg); mp 109–112 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.39 (s, 36H), 7.85 (s, 2H), 8.58 (s, 1H), 8.82 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9 (×2), 83.6, 84.2, 129.7, 139.9, 146.1, 151.6 ppm. Two azulene skeleton C signals were not observed. Anal. Calcd for $C_{28}H_{41}B_3O_6$: C, 66.46; H, 8.17. Found: C, 66.66; H, 8.32%.

4.3. Borylation of 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (1b)

Bis(pinacolato)diboron (pin_2B_2; 457 mg, 1.8 mmol), dtbpy (13 mg, 0.05 mmol), and $[Ir(OMe)(cod)]_2$ (17 mg, 0.025 mmol) were added to a solution of **1b** (254 mg, 1.0 mmol) in dry cyclohexane (10 mL) and the mixture was refluxed for 25 h. The reaction was quenched with water (5 mL) and the resulting mixture was extracted with hexane (50 mL×3). The organic layer was dried (Na_2SO_4) and concentrated to leave a residue, which was crystallized from THF–MeOH (1:10) to give **4b**. The filtrate was concentrated to give a residue, which was crystallized from THF–MeOH (1:10) to give **4c**. The filtrate was concentrated to give a residue, which was chromatographed on silica gel with hexane–AcOEt (10:1) to afford **3c**, **3d** and **5**. Compound **3e** was obtained as a mixture containing **3c** and **3d** when 0.7 equiv of pin_2B_2 was used. Isolation of **3e** was unsuccessful, since it was easily suffered from deborylation to form **6** when purified by column chromatography on silica gel.

*4.3.1. 1,3-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**3c**)*

Purple powder; yield 7% (27 mg); mp 168–170 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (s, 24H), 7.48 (t, J=9.9 Hz, 2H), 7.73 (t, J=9.9 Hz, 1H), 8.85 (s, 1H), 9.19 (d, J=9.9 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.0, 82.9, 126.7, 137.6, 138.1, 151.1, 155.4 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{22}H_{30}B_2O_4$: C, 69.52; H, 7.96. Found: C, 69.38; H, 8.12%.

*4.3.2. 1,5-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)-azulene (**3d**)*

Purple powder; yield 5% (19 mg); mp 193–194 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.41 (s, 12H), 1.42 (s, 12H), 7.40 (t, J=9.8 Hz, 1H), 7.52 (d, J=3.8 Hz, 1H), 8.20 (d, J=9.8 Hz, 1H), 8.32 (d, J=3.8 Hz, 1H), 8.93 (s, 1H), 9.18 (d, J=9.8 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 25.0, 82.9, 84.3, 121.5, 124.7, 140.0, 142.6, 143.6, 144.0, 145.0, 146.6 ppm. Two azulene skeleton C signals were not observed.

Anal. Calcd for $C_{22}H_{30}B_2O_4$: C, 69.52; H, 7.96. Found: C, 69.83; H, 7.93%.

*4.3.3. 1,6-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**3e**)*

^{1}H NMR (acetone-d_6, 400 MHz) δ 1.38 (s, 12H), 1.39 (s, 12H), 7.42 (d, J=3.7 Hz, 1H), 7.82 (d, J=9.6 Hz, 1H), 7.87 (d, J=9.6 Hz, 1H), 8.28 (d, J=3.7 Hz, 1H), 8.50 (d, J=9.6 Hz, 1H), 9.16 (d, J=9.8 Hz, 1H) ppm.

*4.3.4. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolanyl)azulene (**6**)*

Blue solid; mp 92–94 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (s, 12H), 7.39 (d, J=3.7 Hz, 2H), 7.73 (d, J=9.8 Hz, 2H), 7.97 (t, J=3.7 Hz, 1H), 8.37 (d, J=9.8 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 84.5, 117.5, 128.5, 135.5, 138.5, 141.3 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{16}H_{19}BO_2$: C, 75.62; H, 7.54. Found: C, 75.89; H, 7.75%.

*4.3.5. 1,3,6-Tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)-azulene (**4b**)*

Purple powder; yield 33% (167 mg); mp 202–204 °C; ^{1}H NMR (THF-d_8, 400 MHz) δ 1.39 (s, 36H), 7.98 (d, J=10.0 Hz, 2H), 8.70 (s, 1H), 9.17 (d, J=10.0 Hz, 2H) ppm; ^{13}C NMR (THF-d_8, 100 MHz) δ 25.3, 25.4, 83.5, 85.3, 133.0, 137.6, 153.3, 158.0 ppm. Two azulene skeleton C signals were not observed. Anal. Calcd for $C_{28}H_{41}B_3O_6$: C, 66.46; H, 8.17. Found: C, 66.49; H, 8.17%.

*4.3.6. 1,3,5-Tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)-azulene (**4c**)*

Purple powder; yield 30% (152 mg); mp 224–226 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.38 (s, 12H), 1.40 (s, 12H), 1.41 (s, 12H), 7.45 (t, J=9.8 Hz, 1H), 8.20 (d, J=9.8 Hz, 1H), 8.76 (s, 1H), 9.14 (d, J=9.8 Hz, 1H), 9.74 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 25.0 (×2), 82.9 (×2), 84.3, 126.2, 139.7, 143.6, 144.3, 150.4, 150.5, 154.3 ppm. Three azulene skeleton C signals were not observed. Anal. Calcd for $C_{28}H_{41}B_3O_6$: C, 66.46; H, 8.17. Found: C, 66.82; H, 8.26%.

*4.3.7. 1,3,5,7-Tetrakis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**5**)*

Red powder; yield 5% (32 mg); mp >300 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.41 (s, 48H), 8.62 (s, 1H), 8.70 (s, 1H), 9.73 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.0, 25.1, 82.9, 84.2, 146.0, 149.4, 149.8, 153.3 ppm. Two azulene skeleton C signals were not observed. Anal. Calcd for $C_{34}H_{52}B_4O_8$: C, 64.61; H, 8.29. Found: C, 65.00; H, 8.29%.

4.4. Borylation of azulenes substituted at the five-membered ring

A typical example is exemplified by the borylation of 1,3-dichloroazulene. Bis(pinacolato)diboron (pin_2B_2; 533 mg, 2.1 mmol), dtbpy (7 mg, 0.025 mmol), and $[IrCl(cod)]_2$ (8 mg, 0.0125 mmol) were added to a solution of 1,3-dichloroazulene (197 mg, 1.0 mmol) in dry cyclohexane (10 mL), and the mixture was heated at 100 °C for 24 h. The reaction was quenched with water (5 mL) and the resulting mixture was extracted with hexane (20 mL×3). The organic layer was dried (Na_2SO_4) and concentrated to leave a residue, which was purified by column chromatography on silica gel (hexane–AcOEt, 10:1) to give **7a** and **7b** as a mixture. Further purification using HPLC afforded the respective compounds.

*4.4.1. 1,3-Dichloro-2,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**7a**)*

Brown powder; yield 27% (121 mg); mp 295–300 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.38 (s, 12H), 1.44 (s, 12H), 7.63 (d, J=10.1 Hz, 2H), 8.27 (d, J=10.1 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.8, 24.9, 84.5, 84.8, 119.8, 129.0, 134.4, 134.9 ppm. Two azulene skeleton C signals were not observed. Anal. Calcd for $C_{22}H_{28}B_2Cl_2O_4$: C, 58.85; H, 6.29. Found: C, 58.78; H, 6.41%.

*4.4.2. 1,3-Dichloro-2,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**7b**)*

Green powder; yield 38% (171 mg); mp 184–186 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.38 (s, 12H), 1.45 (s, 12H), 7.09 (t, J=9.8 Hz, 1H), 8.11 (d, J=9.8 Hz, 1H), 8.30 (d, J=9.8 Hz, 1H), 8.76 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.8, 24.9, 84.4, 84.5, 122.3, 122.9, 123.0, 133.2, 133.3, 137.7, 142.1, 147.7 ppm. Two azulene skeleton C signals were not observed. Anal. Calcd for $C_{22}H_{28}B_2Cl_2O_4$: C, 58.85; H, 6.29. Found: C, 59.07; H, 6.29%.

*4.4.3. 1,3-Dibromo-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**8a**)*

Green solids; yield 25% (103 mg); mp 119–122 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (s, 12H), 7.80 (d, J=10.1 Hz, 2H), 7.82 (s, 1H), 8.26 (d, J=10.1 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 84.9, 102.2, 129.8, 135.6, 136.7, 139.3 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{16}H_{17}BBr_2O_2$: C, 46.65; H, 4.16. Found: C, 47.01; H, 4.02%.

*4.4.4. 1,3-Dibromo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**8b**)*

Blue solids; yield 45% (185 mg); mp 83–85 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.39 (s, 12H), 7.25 (t, J=9.8 Hz, 1H), 7.78 (s, 1H), 8.18 (d, J=9.8 Hz, 1H), 8.29 (d, J=9.8 Hz, 1H), 8.76 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 84.5, 104.6, 105.4, 123.6, 135.2, 135.4, 137.8, 138.1, 142.6, 146.4 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{16}H_{17}BBr_2O_2$: C, 46.65; H, 4.16. Found: C, 46.80; H, 4.08%.

*4.4.5. 1,3-Dibromo-2-iodo-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**9a**)*

Green powder; yield 17% (89 mg); mp 135–137 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (s, 12H), 7.82 (d, J=10.2 Hz, 2H), 8.25 (d, J=10.2 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 84.9, 109.6, 112.5, 131.1, 135.2, 136.3 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{16}H_{16}BBr_2IO_2$: C, 35.73; H, 3.00. Found: C, 36.13; H, 2.94%.

*4.4.6. 1,3-Dibromo-2-iodo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**9b**)*

Green powder; yield 51% (277 mg); mp 159–161 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (s, 12H), 7.27 (t, J=9.8 Hz, 1H), 8.22 (d, J=9.8 Hz, 1H), 8.29 (d, J=9.8 Hz, 1H), 8.78 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 84.7, 110.2, 111.9, 112.7, 124.8, 135.1, 135.2, 138.0, 142.5, 146.1 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{16}H_{16}BBr_2IO_2$: C, 35.73; H, 3.00. Found: C, 35.83; H, 2.87%.

*4.4.7. 1-Trifluoroacetyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (**10**)*

Orange powder; yield 17% (58 mg); mp 164–165 °C; ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.41 (s, 12H), 8.01 (t, J=9.7 Hz, 1H), 8.05 (t, J=9.7 Hz, 1H), 8.24 (t, J=9.7 Hz, 1H), 8.67 (q, J=2.6 Hz, 1H), 9.42 (d, J=9.7 Hz, 1H), 9.84 (d, J=9.7 Hz, 1H) ppm; ^{13}C NMR (acetone-d_6, 100 MHz) δ 25.2, 84.5, 118.1, 118.3 (q, J=292.0 Hz), 133.2, 134.2, 140.2, 142.0, 142.9, 147.8, 150.0 (q, J=3.6 Hz), 153.5, 176.0 (q, J=33.3 Hz) ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{18}H_{18}BF_3O_3$: C, 61.75; H, 5.18. Found: C, 62.12; H, 5.10%.

4.5. Oxidation of 3a with H_2O_2

To a solution of **3a** (380 mg, 1.0 mmol) in THF (10 mL) was added H_2O_2 (30% aqueous solution, 102 μL, 1.0 mmol) under ambient

conditions and the resulting solution was stirred for 5 h at room temperature. The reaction mixture was diluted with water and extracted with Et_2O (30 mL×3). The combined extracts were dried (Na_2SO_4) and concentrated to leave a residue, which was purified by column chromatography on silica gel (hexane–AcOEt, 3:1) to give **12**. A similar treatment of **3a** (380 mg, 1.0 mmol) in THF (10 mL) with H_2O_2 (30% aqueous solution, 0.61 mL, 6.0 mmol) for 24 h gave a reaction mixture containing **11**. The mixture was diluted with water and extracted with Et_2O (30 mL×3). The combined extracts were dried (Na_2SO_4) and concentrated to leave a residue, which was crystallized from hexane–AcOEt (10:1) to afford the pure compound.

4.5.1. 2,6-Dihydroxyazulene (*11*)

Orange powder; yield 50% (80 mg); mp 170–180 °C (decomp.) (lit.[10] 175–185 °C, decomp.); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 6.51 (s, 2H), 6.74 (d, J=10.9 Hz, 2H), 7.78 (d, J=10.9 Hz, 2H), 10.0 (s, 1H), 10.1 (br s, 1H) ppm.

4.5.2. 6-Hydroxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (*12*)

Purple solid; yield 74% (199 mg); mp 100–102 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.29 (s, 12H), 6.72 (d, J=10.8 Hz, 2H), 7.40 (s, 2H), 8.16 (d, J=10.8 Hz, 2H), 11.13 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ 25.0, 83.2, 112.1, 125.9, 135.4, 138.9, 168.8 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{16}H_{19}BO_3$: C, 71.14; H, 7.09. Found: C, 71.28; H, 7.21%.

4.6. Oxidation of 4b or 4c with H_2O_2. Trapping with acetic anhydride

To a solution of **4b** (102 mg, 0.2 mmol) in THF (2 mL) was added H_2O_2 (30% aqueous solution, 60 μL, 0.6 mmol) under ambient conditions and the resulting solution was stirred for 3 h at room temperature. The reaction mixture was diluted with water and extracted with Et_2O (10 mL×3). The combined extracts were dried (Na_2SO_4) and concentrated to leave a residue containing **13**. Purification of the residue by column chromatography on silica gel with hexane–AcOEt (10:1), however, resulted in the formation of **15**. Next, the residue was dissolved in DMSO (2 mL) and, after addition of Ac_2O (93 μL, 1.0 mmol), the resulting solution was stirred for 6 h at room temperature. The reaction mixture was neutralized with aqueous saturated Na_2CO_3 (5 mL) and extracted with hexane (10 mL×3). The combined extracts were dried (Na_2SO_4) and concentrated to leave a residue, which was purified by column chromatography on silica gel (hexane–AcOEt, 10:1) to give **16** and **18**. A similar treatment of **4c** with H_2O_2 followed by purification by column chromatography on silica gel with hexane–AcOEt (10:1) gave **14**, which was acetylated with Ac_2O in DMSO as described above to give **17**.

4.6.1. 6-Hydroxyazulene (*15*)

Pink solid; yield 76% (22 mg); mp 135–137 °C (lit.[11] 126–127 °C); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 6.75 (d, J=10.8 Hz, 2H), 7.15 (d, J=3.6 Hz, 2H), 7.41 (t, J=3.6 Hz, 1H), 8.15 (d, J=10.6 Hz, 2H), 10.84 (br s, 1H) ppm.

4.6.2. 6-Acetoxy-1,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (*16*)

Reddish purple solid; yield 43% (38 mg); mp 215–217 °C; ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.38 (s, 24H), 7.37 (d, J=11.0 Hz, 2H), 8.64 (s, 1H), 9.17 (d, J=11.0 Hz, 2H) ppm; ^{13}C NMR (acetone-d_6, 100 MHz) δ 21.1, 25.2, 83.7, 122.1, 137.2, 149.8, 155.0, 158.6, 169.8 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{24}H_{32}B_2O_6$: C, 65.79; H, 7.36. Found: C, 66.09; H, 7.32%.

4.6.3. 6-Acetoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (*18*)

Purple solid; yield 23% (14 mg); mp 135–137 °C; ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.38 (s, 12H), 2.33 (s, 3H), 7.18 (dd, J=2.4, 10.4 Hz, 1H), 7.22 (dd, J=2.4, 10.5 Hz, 1H), 7.45 (d, J=3.7 Hz, 1H), 8.19 (d, J=3.7 Hz, 1H), 8.47 (d, J=10.5 Hz, 1H), 9.11 (d, J=10.5 Hz, 1H) ppm; ^{13}C NMR (acetone-d_6, 100 MHz) δ 21.1, 25.3, 83.7, 120.3, 120.5, 121.1, 135.9, 137.1, 143.7, 145.5, 145.9, 158.5, 169.9 ppm. One azulene skeleton C signal was not observed. Anal. Calcd for $C_{18}H_{21}BO_4$: C, 69.26; H, 6.78. Found: C, 69.66; H, 6.58%.

4.6.4. 5-Acetoxy-1,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)azulene (*17*)

Purple solid; yield 65% (57 mg); mp 97–99 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.37 (s, 12H), 1.38 (s, 12H), 2.41 (s, 3H), 7.40 (t, J=10.2 Hz, 1H), 7.50 (dd, J=2.6, 10.6 Hz, 1H), 8.84 (s, 1H), 8.90 (d, J=2.7 Hz, 1H), 9.11 (d, J=9.6 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 25.0 (×2), 83.0, 83.1, 124.4, 131.5, 132.1, 136.7, 147.8, 147.9, 150.9, 156.6, 170.2 ppm. Two azulene skeleton C signals were not observed. Anal. Calcd for $C_{24}H_{32}B_2O_6$: C, 65.79; H, 7.36. Found: C, 65.73; H, 7.69%.

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