


 Cite this: *RSC Adv.*, 2021, **11**, 17734

# Pd-catalyzed synthesis of 1-(hetero)aryl-2,2,2-trichloroethanols using chloral hydrate and (hetero)arylborexines†

 Minori Shimizu,<sup>a</sup> Yuta Okuda,<sup>b</sup> Koki Toyoda,<sup>c</sup> Ryo Akiyama,<sup>b</sup> Hiraku Shinozaki<sup>c</sup> and Tetsuya Yamamoto \*<sup>abc</sup>

1-(Hetero)aryl-2,2,2-trichloroethanols are useful key intermediates for the synthesis of various bioactive compounds. Herein, we describe N-heterocyclic carbene (NHC)-coordinated cyclometallated palladium complex (CYP)-catalyzed (hetero)aryl addition of chloral hydrate using (hetero)arylborexines, providing a new approach to 1-(hetero)aryl-2,2,2-trichloroethanols. Notably, PhS-IPent-CYP which coordinated the bulky yet flexible 2,6-di(pentan-3-yl)aniline (IPent)-based NHC showed good catalytic activities and promoted the transformation in 24–97% yields.

 Received 26th March 2021  
 Accepted 11th May 2021

DOI: 10.1039/d1ra02403e

[rsc.li/rsc-advances](http://rsc.li/rsc-advances)

## Introduction

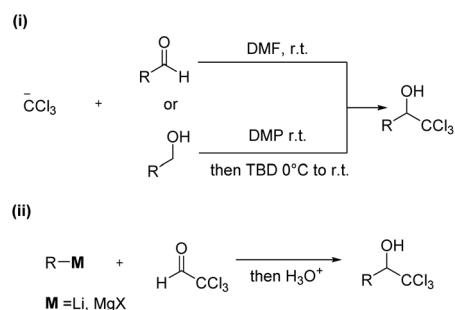
1-(Hetero)aryl-2,2,2-trichloroethanols are one of the most useful building blocks for the synthesis of bioactive compounds,<sup>1</sup> because the carbinol moiety is easily transformed to various  $\alpha$ -substituted carboxylic acid derivatives.<sup>2–6</sup> So far, 1-(hetero)aryl-2,2,2-trichloroethanols have two kinds of possible synthetic routes as depicted in Scheme 1. One is an addition of the trichloromethyl anion to carbonyl compounds such as aldehydes or ketones (i).<sup>7</sup> This way has generally needed the use of toxic trichloromethyl anion sources such as chloroform and trichloroacetic acid. The other is an addition of moisture-sensitive organometallic reagents such as organomagnesium compounds to dehydrated chloral (ii).<sup>8</sup>

The transition metal-catalyzed 1,2-addition of organoboronic acids and their derivatives to carbonyl compounds is a convenient method compared to the Grignard reaction, because this could be conducted in the presence of water.<sup>9</sup> Although several research groups have reported the Rh-catalyzed 1,2-addition of arylboronic acids to trifluoromethyl ketones,<sup>10</sup> the transition metal-catalyzed addition of arylboron compounds to trichloromethyl carbonyl compounds such as chloral have not been examined yet. It is well known that N-heterocyclic carbenes (NHC) coordinated palladium complexes are useful for various applications such as

anticancer drugs, OLEDs and catalysts.<sup>11</sup> Recently, we have developed the NHC coordinated cyclometallated palladium complexes (CYPs) that catalyzed the 1,2-addition of organoboron compounds to a wide range of carbonyl compounds including hemiacetals such as aqueous formaldehyde and glyoxylate hemiacetals (Scheme 2).<sup>12</sup> Therefore, we envisaged that the NHC-CYPs exhibit a good catalytic activity of the addition of arylboron compounds to chloral hydrate without a dehydration process. Here, we report the direct aryl addition to chloral hydrate with triarylborexines using NHC-CYPs as a catalyst.

## Results and discussion

At first, we examined CYPs-catalyzed 1,2-addition of chloral hydrate **1** and 2-naphthylboron compounds (Table 1). PhS-IPr-CYP have catalyzed the addition of arylboronic acids to an excess amount of aqueous formaldehyde to provide the corresponding benzylic alcohols in satisfactory yields,<sup>12a,d</sup> although PhS-IPr-CYP catalyzed reaction of 2-



Scheme 1 Previous synthesis of trichloromethylcarbinols.

<sup>a</sup>Department of Materials and Life Sciences, Tokyo Denki University, 5 Senju-Asahicho, Adachi Tokyo 120-8551, Japan. E-mail: t-yamamoto@mail.dendai.ac.jp

<sup>b</sup>Department of Materials Science and Engineering, Tokyo Denki University, 5 Senju-Asahicho, Adachi-ku, Tokyo 120-8551, Japan

<sup>c</sup>Department of Applied Chemistry, Tokyo Denki University, 5 Senju-Asahicho, Adachi-ku, Tokyo 120-8551, Japan

† Electronic supplementary information (ESI) available. See DOI: 10.1039/d1ra02403e





Scheme 2 NHC-CYPs-catalyzed 1,2-addition of arylboron compounds and carbonyl compounds.

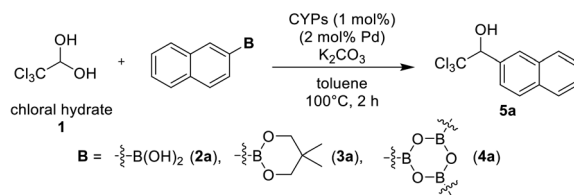
naphthaleneboronic acid **2a** and 4 equivalent of chloral hydrate afforded the desired product **5a** in 39% yield (entry 1). In this case, the yield of **5a** was improved by the use of an excess of **2a** relative to chloral hydrate (entry 2). Then, using 2-naphthaleneboronate **3a** instead of **2a** increased slightly the yield of **3a** to 70% (entry 3). We have confirmed the efficacy of arylboroxines in the arylation of trifluoroacetaldehyde hemiacetal from a preliminary investigation.<sup>12c</sup> When this reaction was performed using tri(naphthalene-2-yl)boroxine **4a**, the yield of **5a** was improved considerably to 82% (entry 4). Dehydrated chloral was usable as well as chloral hydrate for this addition reaction (entry 5). H-IPr-CYP has shown more catalytic activity than PhS-IPr-CYP in the CYPs-catalyzed arylation of glyoxylate hemiacetals,<sup>12b</sup> but it was not suitable for this reaction (entry 6). PhS-IPent-CYP having sterically bulky alkyl group had more active towards the addition than PhS-IPr-CYP (entry 7).

Under the optimized conditions, we synthesized various functionalized trichloromethyl carbinols using PhS-IPent-CYP catalyzed reaction (Table 2). Substrates bearing sterically hindered 1-naphthyl group was also converted to the

corresponding alcohol **5b** in moderate yield of 65%. Arylboroxines bearing electron-donating groups like *tert*-butyl, phenyl, methoxy and methylthio groups furnished the corresponding products **5c–5h** in satisfactory yields of 66–97%. Interestingly, sterically bulky 2-methoxyphenylboroxine reacted more smoothly than 3-methoxyphenyl and 4-methoxyphenylboroxines. 4-Fluorophenyl and 4-bromophenylboroxines provided the corresponding products **5i** and **5j** in excellent yields, but the reaction using arylboroxines having strong electron-withdrawing groups such as nitrile, nitro or methoxycarbonyl group have not afforded the products **5k–5m**. Remarkably, the bromo group on the aromatic ring remained intact, and the Suzuki–Miyaura cross-coupling product did not observe under this reaction condition. This catalytic reaction was also applicable to heteroarylboroxines containing oxygen or sulfur atom and provided the products **5n–5r** in low to moderate yields, but was not applicable to an aliphatic boroxine such as 2-phenylethylboroxine **4s**.

Since arylboroxines are more suitable for this reaction than arylboronic acids, we examined an experiment under the reaction conditions with H<sub>2</sub>O (Scheme 3). Because arylboroxines is known to rapidly absorb H<sub>2</sub>O and transform to boronic acids, and adding water is expected to reduce the dehydration performance of boroxine. Practically, the yield declined as the amount of H<sub>2</sub>O added increased, indicating that arylboroxines may be involved in the dehydration step of chloral hydrate. So, we proposed a plausible catalytic cycle which is described in Scheme 4. Initially, dehydrated chloral and arylboronic acids are generated from the hydrolysis of arylboroxines by chloral hydrate. Then arylpalladium intermediate **6** is formed from a base-promoted transmetalation between an arylboronic acid and PhS-IPent-CYP, alkoxypalladium **7** is generated from an insertion of the aryl group on **6** to chloral. Finally, a transmetalation of complex **7** between an arylboronic acid

Table 1 Optimization of reaction conditions of CYPs-catalyzed 1,2-addition of chloral hydrate **1** and 2-naphthalenelboron compounds



| Entry            | 1 (mmol) | B (mmol) | K <sub>2</sub> CO <sub>3</sub> (mmol) | CYPs          | Yield <sup>a</sup> (%) |
|------------------|----------|----------|---------------------------------------|---------------|------------------------|
| 1                | 2.0      | 0.5      | 0.5                                   | PhS-IPr-CYP   | 39                     |
| 2                | 0.5      | 1.5      | 1.5                                   | PhS-IPr-CYP   | 66                     |
| 3 <sup>b</sup>   | 0.5      | 1.5      | 1.5                                   | PhS-IPr-CYP   | 70                     |
| 4 <sup>c</sup>   | 0.5      | 0.5      | 1.5                                   | PhS-IPr-CYP   | 82                     |
| 5 <sup>c,d</sup> | 0.5      | 0.5      | 1.5                                   | PhS-IPr-CYP   | 81                     |
| 6 <sup>c</sup>   | 0.5      | 0.5      | 1.5                                   | H-IPr-CYP     | 73                     |
| 7 <sup>c</sup>   | 0.5      | 0.5      | 1.5                                   | PhS-IPent-CYP | 95 (95) <sup>e</sup>   |

<sup>a</sup> Yields were determined by <sup>1</sup>H-NMR using triphenylmethane as an internal standard. <sup>b</sup> **3a** was used instead of **2a**. <sup>c</sup> **4a** was used instead of **2a**. <sup>d</sup> Dehydrated chloral was used instead of chloral hydrate. <sup>e</sup> Isolated yield.



Table 2 PhS-IPent-CYP-catalyzed 1,2-addition of arylboroxines 4 to chloral hydrate 1<sup>a</sup>



<sup>a</sup> Reaction conditions: 1 (1 equiv., 0.5 mmol), 4 (1.0 equiv., 0.5 mmol), K<sub>2</sub>CO<sub>3</sub> (3.0 equiv., 1.5 mmol), PhS-IPent-CYP (0.005 mmol, 1 mol%) and toluene (1 mL) at 100 °C for 2 h in a sealed tube. Isolated yield.

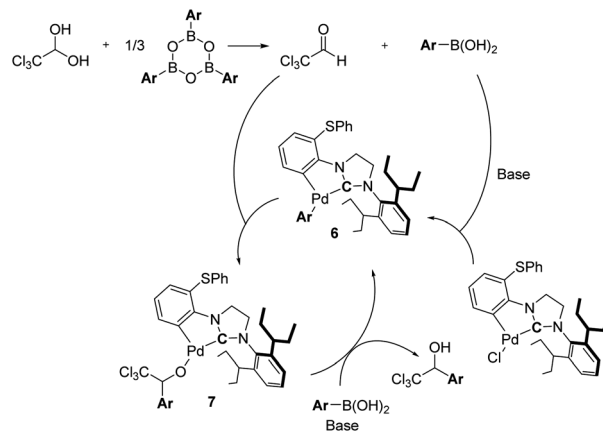


Scheme 3 The effect of the used amount of H<sub>2</sub>O on the catalytic addition reaction.

results in the formation of 1-(hetero)aryl-2,2,2-trichloroethanol and the regeneration of complex 6.

## Conclusions

We have achieved a nucleophilic arylation to chloral hydrate using PhS-IPent-CYP as a catalyst. The use of arylboroxine is critical for this reaction, and arylboroxines have acted not only



Scheme 4 Proposed reaction mechanism.

as an arylcarbanion source but also as a dehydrating agent for chloral hydrate.

## Experimental

### General

All reactions were carried out under an argon atmosphere. <sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F NMR spectra were recorded on an AVANCE III 400 spectrometer (400.15 MHz) at ambient temperature. Melting points were recorded on Yanako MP-S3. HRMS were recorded on a Thermo Fisher Scientific Exactive (Orbitrap) using ESI or APCI. Commercially available organic and inorganic compounds were used without purification. PhS-IPr-CYP,<sup>12a</sup> H-IPr-CYP,<sup>12a</sup> PhS-IPent-CYP<sup>12d</sup> and arylboroxines 4<sup>13</sup> were prepared according to the literature procedures.

### Preparation and characterizations of compounds

**2,2,2-Trichloro-1-(naphthalen-2-yl)ethan-1-ol<sup>7b</sup> 5a.** Chloral hydrate (83 mg, 0.50 mmol), 2-naphthyl boroxine (231 mg, 0.500 mmol), PhS-IPent-CYP (6.1 mg, 0.0050 mmol) and potassium carbonate (207 mg, 1.50 mmol) were charged in 10 mL test tube sealed with a rubber septum. The test tube was evacuated and backfilled with argon. This sequence was repeated three times. Then dehydrated toluene (1 mL) was added *via* the rubber septum with syringe. In an argon flow, the rubber septum was replaced with a Teflon liner screw cap. The sealed test tube was placed into an oil bath preheated 100 °C. After the reaction was stirred for 2 h and cooled to room temperature, the obtained crude was purified by passing it through a silica gel column with a hexane/ethyl acetate to give 131 mg (0.475 mmol, 95%) of product 5a as a pale yellow solid, mp 93–94 °C (lit.<sup>7b</sup> 93–94 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 8.09 (s, 1H, ArH), 7.85–7.90 (m, 3H, ArH), 7.88 (dd, *J*<sub>1</sub> = 7.3 Hz, *J*<sub>2</sub> = 9.8 Hz, 1H, ArH), 7.52 (t, *J* = 4.1 Hz, 2H, ArH), 5.40 (d, *J* = 3.4 Hz, 1H, CH(OH)CCl<sub>3</sub>), 3.39 (d, *J* = 3.4 Hz, 1H, OH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 133.8 (Ar), 132.5 (Ar), 132.3 (Ar), 129.3 (Ar), 128.4 (Ar), 127.7 (Ar), 127.4 (Ar), 126.9 (Ar), 126.4 (Ar), 126.2 (Ar), 103.3 (CCl<sub>3</sub>), 84.7 (CH(OH)CCl<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>-</sup> calcd for C<sub>12</sub>H<sub>9</sub>OCl<sub>4</sub>: 308.9413. Found: 308.9424.



**2,2,2-Trichloro-1-(naphthalen-1-yl)ethan-1-ol<sup>3d</sup> 5b.** Product **5b** was prepared by utilizing the general procedure using 1-naphthyl boroxine (231 mg, 0.500 mmol) and was isolated as a pale yellow liquid (91 mg, 0.33 mmol, 66%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 8.28 (d, *J* = 8.5 Hz, 1H, ArH), 8.09 (d, *J* = 8.5 Hz, 1H, ArH), 7.91–7.97 (m, 2H, ArH), 7.51–7.62 (m, 3H, ArH), 6.23 (d, *J* = 4.2 Hz, 1H, CH(OH)CCl<sub>3</sub>), 3.45 (d, *J* = 4.2 Hz, 1H, OH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 133.5 (Ar), 132.0 (Ar), 131.4 (Ar), 130.3 (Ar), 129.0 (Ar), 127.2 (Ar), 126.4 (Ar), 125.6 (Ar), 124.9 (Ar), 123.7 (Ar), 103.5 (CCl<sub>3</sub>), 79.0 (CH(OH)CCl<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>12</sub>H<sub>9</sub>OCl<sub>4</sub>: 308.9413. Found: 308.9422.

**1-([1,1'-Biphenyl]-4-yl)-2,2,2-trichloroethan-ol 5c.** Product **5c** was prepared by utilizing the general procedure using 4-biphenyl boroxine (270 mg, 0.500 mmol) and was isolated as a pale yellow solid (136 mg, 0.451 mmol, 90%), mp 119–120 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.70 (s, 1H, Ar), 7.67 (s, 1H, Ar), 7.59–7.62 (m, 4H, Ar), 7.45 (t, *J* = 7.5 Hz, 2H, Ar), 7.36 (t, *J* = 7.5 Hz, 1H, Ar), 5.26 (s, 1H, CH(OH)CCl<sub>3</sub>), 3.32 (s, 1H, OH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 142.4 (Ar), 140.4 (Ar), 133.8 (Ar), 129.7 (Ar), 128.9 (Ar), 127.7 (Ar), 127.2 (Ar), 126.6 (Ar), 103.2 (CCl<sub>3</sub>), 84.4 (CH(OH)CCl<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>14</sub>H<sub>11</sub>OCl<sub>4</sub>: 334.9569. Found: 334.9583.

**1-(4-(tert-Buthyl)phenyl)-2,2,2-trichloroethan-ol<sup>7a</sup> 5d.** Product **5d** was prepared by utilizing the general procedure using 4-tert-buthylphenyl boroxine (240 mg, 0.500 mmol) and was isolated as a pale yellow solid (95 mg, 0.34 mmol, 67%), mp 77–78 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.52 (d, *J* = 8.4 Hz, 2H, ArH), 7.39 (d, *J* = 8.4 Hz, 2H, ArH), 5.16 (d, *J* = 4.1 Hz, 1H, CH(OH)CCl<sub>3</sub>), 3.33 (d, *J* = 4.1 Hz, 1H, OH) 1.32 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 152.6 (Ar), 132.0 (Ar), 128.9 (Ar), 124.8 (Ar), 103.3 (CCl<sub>3</sub>), 84.4 (CH(OH)CCl<sub>3</sub>), 34.7 (C(CH<sub>3</sub>)<sub>3</sub>), 31.3 (C(CH<sub>3</sub>)<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>12</sub>H<sub>15</sub>OCl<sub>4</sub>: 314.9882. Found: 314.9894.

**2,2,2-Trichloro-1-(4-methoxyphenyl)ethan-1-ol<sup>7b</sup> 5e.** Product **5e** was prepared by utilizing the general procedure using 4-methoxyphenyl boroxine (201 mg, 0.500 mmol) and was isolated as a pale yellow liquid (90 mg, 0.35 mmol, 70%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.52 (d, *J* = 8.7 Hz, 2H, ArH), 6.90 (d, *J* = 8.7 Hz, 2H, ArH), 5.15 (d, *J* = 2.3 Hz, 1H, CH(OH)CCl<sub>3</sub>), 3.81 (s, 3H, OCH<sub>3</sub>), 3.35 (d, *J* = 2.3 Hz, 1H, OH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 160.4 (Ar), 130.4 (Ar), 127.0 (Ar), 113.2 (Ar), 103.5 (CCl<sub>3</sub>), 84.2 (CH(OH)CCl<sub>3</sub>), 55.3 (OCH<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>9</sub>H<sub>9</sub>O<sub>2</sub>Cl<sub>4</sub>: 288.9362. Found: 288.9374.

**2,2,2-Trichloro-1-(3-methoxyphenyl)ethan-1-ol 5f.** Product **5f** was prepared by utilizing the general procedure using 3-methoxyphenyl boroxine (201 mg, 0.500 mmol) and was isolated as a colourless liquid (85 mg, 0.33 mmol, 66%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.28 (dd, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>2</sub> = 8.0 Hz, 1H, ArH), 7.16–7.17 (m, 2H, ArH), 6.94 (d, *J* = 8.0 Hz, 1H, ArH), 5.16 (d, *J* = 4 Hz, 1H, CH(OH)CCl<sub>3</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 3.43 (d, *J* = 12 Hz, 1H, OH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 159.0 (Ar), 136.4 (Ar), 128.8 (Ar), 121.8 (Ar), 115.0 (Ar), 114.9 (Ar), 103.0 (CCl<sub>3</sub>), 84.4 (CH(OH)CCl<sub>3</sub>), 55.3 (OCH<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>9</sub>H<sub>9</sub>O<sub>2</sub>Cl<sub>4</sub>: 288.9362. Found: 288.9372.

**2,2,2-Trichloro-1-(2-methoxyphenyl)ethan-1-ol 5g.** Product **5g** was prepared by utilizing the general procedure using 2-methoxyphenyl boroxine (201 mg, 0.500 mmol) and was isolated as a colourless liquid (113 mg, 0.44 mmol, 88%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.60 (dd, *J*<sub>1</sub> = 1.7 Hz, *J*<sub>2</sub> = 7.7 Hz, 1H, ArH), 7.35 (m, 1H, ArH), 6.91–7.01 (m, 1H, ArH), 5.59 (d, *J* = 6.9 Hz, 1H, CH(OH)CCl<sub>3</sub>), 4.25 (d, *J* = 6.9 Hz, 1H, OH), 3.84 (s, 3H, OCH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 157.7 (Ar), 130.6 (Ar), 130.4 (Ar), 123.5 (Ar), 120.5 (Ar), 111.2 (Ar), 103.5 (CCl<sub>3</sub>), 80.3 (CH(OH)CCl<sub>3</sub>), 55.6 (OCH<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>9</sub>H<sub>9</sub>O<sub>2</sub>Cl<sub>4</sub>: 288.9362. Found: 288.9371.

**2,2,2-Trichloro-1-(4-(methylthio)phenyl)ethan-1-ol 5h.** Product **5h** was prepared by utilizing the general procedure using 4-(methylthio)phenyl boroxine (225 mg, 0.500 mmol) and was isolated as a pale yellow solid (107 mg, 0.394 mmol, 78%), mp 89.5–90.0 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.50 (d, *J* = 8.4 Hz, 2H, ArH), 7.23 (d, *J* = 8.4 Hz, 2H, ArH), 5.14 (d, *J* = 3.0 Hz, 1H, CH(OH)CCl<sub>3</sub>), 3.46 (d, *J* = 3.0 Hz, 1H, OH), 2.48 (s, 3H, SCH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 140.4 (Ar), 131.4 (Ar), 129.6 (Ar), 125.3 (Ar), 103.1 (CCl<sub>3</sub>), 84.2 (CH(OH)CCl<sub>3</sub>), 15.2 (SCH<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>9</sub>H<sub>9</sub>OCl<sub>4</sub>S: 304.9134. Found: 304.9146.

**2,2,2-Trichloro-1-(4-fluorophenyl)ethan-1-ol<sup>1c</sup> 5i.** Product **5i** was prepared by utilizing the general procedure using 4-fluorophenyl boroxine (183 mg, 0.500 mmol) and was isolated as a pale yellow liquid (99 mg, 0.41 mmol, 81%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.58–7.61 (m, 2H, ArH), 7.07 (t, *J* = 8.7 Hz, 2H, ArH), 5.20 (d, *J* = 3.1 Hz, 1H, CH(OH)CCl<sub>3</sub>), 3.40 (d, *J* = 3.1 Hz, 1H, OH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 163.4 (d, <sup>1</sup>*J*<sub>C-F</sub> = 247 Hz, Ar), 131.1 (d, <sup>2</sup>*J*<sub>C-F</sub> = 8.6 Hz, Ar), 130.6 (d, <sup>3</sup>*J*<sub>C-F</sub> = 3.0 Hz, Ar), 114.9 (d, <sup>4</sup>*J*<sub>C-F</sub> = 21.4 Hz, Ar), 103.1 (d, <sup>5</sup>*J*<sub>C-F</sub> = 2.4 Hz, CCl<sub>3</sub>), 83.8 (CH(OH)CCl<sub>3</sub>); <sup>19</sup>F (377 MHz, CDCl<sub>3</sub>, ppm): δ −117.8 (s, 1F, ArF); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>8</sub>H<sub>6</sub>OCl<sub>4</sub>F: 276.9162. Found: 276.9170.

**1-(4-Bromophenyl)-2,2,2-trichloroethan-1-ol<sup>7c</sup> 5j.** Product **5j** was prepared by utilizing the general procedure using 4-bromophenyl boroxine (274 mg, 0.500 mmol) and was isolated as a pale yellow liquid (138 mg, 0.45 mmol, 90%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.49–7.56 (m, 4H, ArH), 5.18 (s, 1H, CH(OH)CCl<sub>3</sub>), 3.59 (s, 1H, OH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 133.8 (Ar), 131.1 (Ar), 130.9 (Ar), 123.9 (Ar), 102.7 (CCl<sub>3</sub>), 83.9 (CH(OH)CCl<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>8</sub>H<sub>6</sub>OBrCl<sub>4</sub>: 336.8362. Found: 336.8374.

**2,2,2-Trichloro-1-(thiophen-2-yl)ethan-1-ol<sup>7b</sup> 5n.** Product **5n** was prepared by utilizing the general procedure using 2-thiophene boroxine (165 mg, 0.500 mmol) and was isolated as a pale yellow liquid (47 mg, 0.20 mmol, 41%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 7.40 (dd, *J*<sub>1</sub> = 1.2 Hz, *J*<sub>2</sub> = 5.1 Hz, 1H, ArH), 7.31 (m, 1H, ArH), 7.04 (dd, *J*<sub>1</sub> = 3.6 Hz, *J*<sub>2</sub> = 5.1 Hz, 1H, ArH), 5.48 (d, *J* = 4.4 Hz, 1H, CH(OH)CCl<sub>3</sub>), 3.40 (d, *J* = 4.4 Hz, 1H, OH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, ppm): δ 137.3 (Ar), 129.2 (Ar), 127.1 (Ar), 126.3 (Ar), 102.5 (CCl<sub>3</sub>), 81.6 (CH(OH)CCl<sub>3</sub>); HRMS (EI) *m/z*: [M + Cl]<sup>−</sup> calcd for C<sub>6</sub>H<sub>5</sub>OCl<sub>4</sub>S: 264.8821. Found: 264.8833.

**2,2,2-Trichloro-1-(thiophen-3-yl)ethan-1-ol<sup>14</sup> 5o.** Product **5o** was prepared by utilizing the general procedure using 3-thiophene boroxine (165 mg, 0.500 mmol) and was isolated as a pale yellow





liquid (68 mg, 0.29 mmol, 59%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , ppm):  $\delta$  7.55 (t,  $J = 2.4$  Hz, 1H, ArH), 7.32 (m, 2H, ArH), 5.32 (d,  $J = 4.4$  Hz, 1H,  $\text{CH}(\text{OH})\text{CCl}_3$ ), 3.29 (d,  $J = 4.4$  Hz, 1H,  $\text{CCl}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , ppm):  $\delta$  136.0 (Ar), 127.6 (Ar), 126.2 (Ar), 125.2 (Ar), 102.8 ( $\text{CCl}_3$ ), 81.3 ( $\text{CH}(\text{OH})\text{CCl}_3$ ); HRMS (EI)  $m/z$ :  $[\text{M} + \text{Cl}]^-$  calcd for  $\text{C}_6\text{H}_5\text{OCl}_4\text{S}$ : 264.8821. Found: 264.8831.

**2,2,2-Trichloro-1-(furan-3-yl)ethan-1-ol 5p.** Product **5p** was prepared by utilizing the general procedure using 3-furan boroxine (141 mg, 0.500 mmol) and was isolated as a pale yellow liquid (50 mg, 0.23 mmol, 46%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , ppm):  $\delta$  7.66 (t,  $J = 0.7$  Hz, 1H, ArH), 7.45 (t,  $J = 1.7$  Hz, 1H, ArH), 6.66 (dd,  $J_1 = 0.7$  Hz,  $J_2 = 1.7$  Hz, 1H, ArH), 5.21 (d,  $J = 4.7$  Hz, 1H,  $\text{CH}(\text{OH})\text{CCl}_3$ ), 3.28 (d,  $J = 4.7$  Hz, 1H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , ppm):  $\delta$  142.8 (Ar), 142.6 (Ar), 120.8 (Ar), 110.0 (Ar), 102.8 ( $\text{CCl}_3$ ), 79.0 ( $\text{CH}(\text{OH})\text{CCl}_3$ ); HRMS (EI)  $m/z$ :  $[\text{M} + \text{Cl}]^-$  calcd for  $\text{C}_6\text{H}_5\text{O}_2\text{Cl}_4$ : 248.9049. Found: 248.9056.

**1-(Benzo[b]thiophene-2-yl)-2,2,2-trichloroethan-1-ol<sup>8a</sup> 5q.** Product **5q** was prepared by utilizing the general procedure using 2-benzo[b]thiophene boroxine (240 mg, 0.500 mmol) and was isolated as a pale yellow solid (34 mg, 0.12 mmol, 24%), mp 109–110 °C (lit.<sup>8a</sup> 109–110 °C).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , ppm):  $\delta$  7.82–7.89 (m, 2H, ArH), 7.59 (s, 1H, ArH), 7.39–7.41 (m, 2H, ArH), 5.57 (d,  $J = 4.4$  Hz, 1H,  $\text{CH}(\text{OH})\text{CCl}_3$ ), 3.48 (d,  $J = 4.4$  Hz, 1H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , ppm):  $\delta$  140.1 (Ar), 138.4 (Ar), 138.0 (Ar), 126.2 (Ar), 125.2 (Ar), 124.5 (Ar), 124.1 (Ar), 122.3 (Ar), 102.1 ( $\text{CCl}_3$ ), 82.0 ( $\text{CH}(\text{OH})\text{CCl}_3$ ); HRMS (EI)  $m/z$ :  $[\text{M} + \text{Cl}]^-$  calcd for  $\text{C}_{10}\text{H}_7\text{OCl}_4\text{S}$ : 314.8977. Found: 314.8992.

**1-(Benzofuran-2-yl)-2,2,2-trichloroethan-1-ol 5r.** Product **5r** was prepared by utilizing the general procedure using 2-benzofuran boroxine (207 mg, 0.500 mmol) and was isolated as a pale yellow solid (80 mg, 0.30 mmol, 60%), mp 71–72 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , ppm):  $\delta$  7.60 (m, 1H, ArH), 7.51 (m, 1H, ArH), 7.24–7.36 (m, 2H, ArH), 6.98 (s, 1H, ArH), 5.35 (d,  $J = 7.2$  Hz, 1H,  $\text{CH}(\text{OH})\text{CCl}_3$ ), 3.59 (d,  $J = 7.2$  Hz, 1H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , ppm):  $\delta$  154.7 (Ar), 150.7 (Ar), 127.4 (Ar), 125.3 (Ar), 123.3 (Ar), 121.6 (Ar), 111.6 (Ar), 107.9 (Ar), 100.9 ( $\text{CCl}_3$ ), 79.7 ( $\text{CH}(\text{OH})\text{CCl}_3$ ); HRMS (EI)  $m/z$ :  $[\text{M} + \text{Cl}]^-$  calcd. for  $\text{C}_{10}\text{H}_7\text{O}_2\text{Cl}_4$ : 298.9206. Found: 298.9216.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

We thank Prof. Mino, Chiba University, for the HRMS measurements. This work was supported in part by the Research Institute for Science and Technology, Tokyo Denki University Grant Number Q19E-06 and Q18E-04.

## Notes and references

- (a) I. Hwang, J. Kim, H. Kim and S. Kyung, *Bull. Korean Chem. Soc.*, 2009, **30**, 1475; (b) A. Schäfer, A. Wellner, M. Strauss, A. Schäfer, G. Wolber and R. Gust, *J. Med. Chem.*, 2012, **55**, 9607; (c) X. Zhu, C. T. Hu, J. Yang, L. A. Joyce, M. Qiu, M. D. Ward and B. Kahr, *J. Am. Chem. Soc.*, 2019, **141**, 16858.

- (a) E. J. Corey and J. O. Link, *J. Am. Chem. Soc.*, 1992, **114**, 1906; (b) R. O. Duthaler, *Tetrahedron*, 1994, **50**, 1539; (c) C. Mellin-Morlière, D. J. Aitken, S. D. Bull, S. G. Davis and H. Husson, *Tetrahedron: Asymmetry*, 2001, **12**, 149; (d) R. L. Tennyson, G. S. Cortez, H. J. Galicia, C. R. Kreiman, C. M. Thompson and D. Romo, *Org. Lett.*, 2002, **4**, 533; (e) A. Scaffidi, B. W. Skelton, R. V. Stick and A. H. White, *Aust. J. Chem.*, 2004, **57**, 723; (f) M. S. Perryman, M. E. Harris, J. L. Foster, A. Joshi, G. J. Clarkson and D. J. Fox, *Chem. Commun.*, 2013, **49**, 10022; (g) C. Hobson, M. S. Perryman, G. Kirby, G. J. Clarkson and D. J. Fox, *Tetrahedron Lett.*, 2018, **59**, 3965.
- (a) E. J. Corey and J. O. Link, *Tetrahedron Lett.*, 1992, **33**, 3431; (b) K. Funabiki, N. Honma, W. Hashimoto and M. Matsui, *Org. Lett.*, 2003, **5**, 2059; (c) H. Yu, Y. Fang, Y. Xia and J. Wu, *Synth. Commun.*, 2006, **36**, 2421; (d) S. Federico, T. Khan, N. Relitti, G. Chemi, M. Brindisi, S. Brogi, E. Novellino, D. M. Zisterer, G. Campiani, S. Gemma and S. Butini, *Tetrahedron Lett.*, 2018, **59**, 4466.
- (a) D. A. Dudley, A. M. Bunker, L. Chi, W. L. Cody, D. R. Holland, D. P. Ignasiak, N. Janiczek-Dolphin, T. B. McClanahan, T. E. Mertz, L. S. Narasimhan, S. T. Rapundalo, J. A. Trautschold, C. A. V. Huis and J. J. Edmunds, *J. Med. Chem.*, 2000, **43**, 4063; (b) J. Blanchet and J. Zhu, *Tetrahedron Lett.*, 2004, **45**, 4449; (c) M. S. Perryman, M. W. M. Earl, S. Greatorex, G. J. Clarkson and D. J. Fox, *Org. Biomol. Chem.*, 2015, **13**, 2360.
- (a) J. L. Shamshina and T. S. Snowden, *Org. Lett.*, 2006, **8**, 5881; (b) A. Scaffidi, B. W. Skelton, R. V. Stick and A. H. White, *Aust. J. Chem.*, 2006, **59**, 426.
- T. S. Snowden, *ARKIVOC*, 2012, 24, (ii), .
- (a) E. Y. Ko, C. H. Lim and K. Chung, *Bull. Korean Chem. Soc.*, 2006, **27**, 432; (b) M. K. Gupta, Z. Li and T. S. Snowden, *J. Org. Chem.*, 2012, **77**, 4854; (c) A. B. Jensen and A. T. Lindhardt, *J. Org. Chem.*, 2014, **79**, 1174; (d) M. K. Gupta, Z. Li and T. S. Snowden, *Org. Lett.*, 2014, **16**, 1602; (e) R. N. Ram and V. K. Soni, *J. Org. Chem.*, 2015, **80**, 8922.
- (a) R. P. Gajewski, J. L. Jackson, N. D. Jones, J. K. Swartzendruber and J. B. Deeter, *J. Org. Chem.*, 1989, **54**, 3311; (b) S. Dohi, K. Moriyama and H. Togo, *Eur. J. Org. Chem.*, 2013, **34**, 7815.
- (a) D. V. Partyka, *Chem. Rev.*, 2011, **111**, 1529; (b) C. S. Marques and A. J. Burke, *Catalytic Arylation Methods*, Wiley-VCH, 2014, p. 329.
- (a) S. L. X. Martina, B. C. J. Richard, J. G. de Vries, F. L. Feringa and A. J. Minnard, *Chem. Commun.*, 2006, **39**, 4093; (b) J. R. White, G. J. Price, P. K. Plucinsky and C. G. Frost, *Tetrahedron Lett.*, 2009, **50**, 7365; (c) V. R. Jumde, S. Facchetti and A. Iuliano, *Tetrahedron: Asymmetry*, 2010, **21**, 2775; (d) R. Luo, K. Li, Y. Hu and W. Tang, *Adv. Synth. Catal.*, 2013, **355**, 1297; (e) V. Valdivia, I. Fernández and N. Khiar, *Org. Biomol. Chem.*, 2014, **12**, 1211; (f) L. S. Dobson and G. Pattison, *Chem. Commun.*, 2016, **52**, 11116; (g) L. G. Borrego, R. Recio, M. Alcarranza, N. Khiar and I. Fernández, *Adv. Synth. Catal.*, 2018, **360**, 1273.



- 11 For selected recent examples: (a) M. Sreenivasulu, K. S. Kumar, P. R. Kumar, K. B. Chandrasekhar and M. Pal, *Org. Biomol. Chem.*, 2012, **10**, 1670; (b) A. F. Henwood, M. Lesieur, A. K. Bansal, V. Lemaire, D. Beljonne, D. G. Thompson, D. Graham, A. M. Z. Slawin, I. D. W. Samuel, C. S. J. Cazin and E. Zysman-Colman, *Chem. Sci.*, 2015, **6**, 3248; (c) T. T. H. Fong, C. N. Lok, C. Y. S. Chung, Y. M. E. Fung, P. K. Chow, P. K. Wan and C. M. Che, *Angew. Chem., Int. Ed.*, 2016, **55**, 11935; (d) F. Schroeter, J. Soellner and T. Strassner, *Organometallics*, 2018, **37**, 4267; (e) S. Y. Hussaini, R. A. Haque, T. Fatima, M. T. Agha, A. M. S. A. Majid and M. R. Razali, *J. Coord. Chem.*, 2018, **71**, 2787; (f) Q. Deng, Q. Zheng, B. Zuo and T. Tu, *Green Synth. Catal.*, 2020, **1**, 75.
- 12 (a) T. Yamamoto, A. Zhumagazin, T. Furusawa, R. Tanaka, T. Yamakawa, Y. Oe and T. Ohta, *Adv. Synth. Catal.*, 2014, **356**, 3525; (b) M. Sugaya, T. Yamamoto and H. Shinozaki, *Tetrahedron Lett.*, 2017, **58**, 2495; (c) M. S. T. Yagihashi, T. Yamamoto and H. Shinozaki, *The 8th Tokyo Conference on Advanced Catalytic Science and Technology*, Japan, August 6, 2018, p. P1200; (d) R. Akiyama, M. Sugaya, H. Shinozaki and T. Yamamoto, *Synth. Commun.*, 2019, **49**, 1193; (e) Y. Okuda, M. Nagaoka and T. Yamamoto, *ChemCatChem*, 2020, **12**, 6291.
- 13 Q. Xiao, L. Tian, R. Tan, Y. Xia, D. Qiu, Y. Zhang and J. Wang, *Org. Lett.*, 2012, **14**, 4230.
- 14 A. I. Ayi, R. Condom, T. N. Wade and R. Guedj, *J. Fluorine Chem.*, 1979, **14**, 437.

