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

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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.

## Introduction

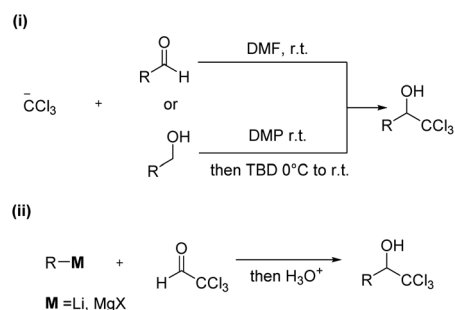
1-(Hetero)aryl-2,2,2-trichloroethanols are one of the most useful building blocks for the synthesis of bioactive compounds,<sup>1</sup> because the carbinol moiety is easily transformed to various  $\alpha$ -substituted carboxylic acid derivatives.<sup>2–6</sup> So far, 1-(hetero)aryl-2,2,2-trichloroethanols 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.

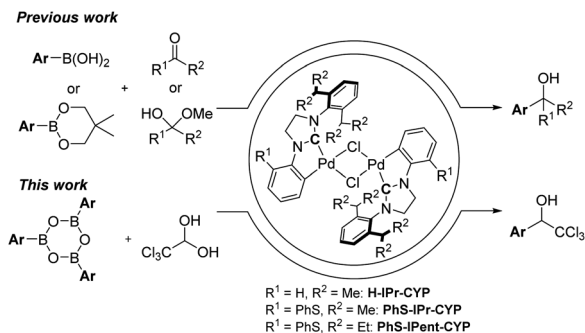
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Scheme 2 NHC-CYPs-catalyzed 1,2-addition of arylboron compounds and carbonyl compounds.

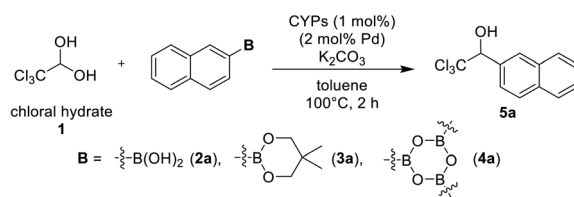
naphthaleneboronic acid **2a** and 4 equivalent of chloral hydrate afforded the desired product **5a** in 39% yield (entry 1). In this case, the yield of **5a** was improved by the use of an excess of **2a** relative to chloral hydrate (entry 2). Then, using 2-naphthaleneboronate **3a** instead of **2a** 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

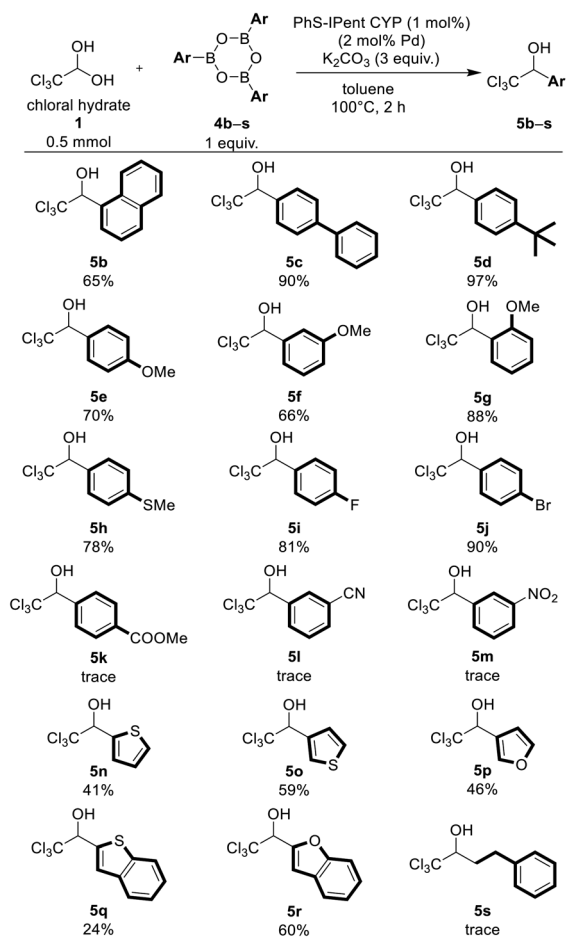


Entry	1 (mmol)	B (mmol)	K <sub>2</sub> CO <sub>3</sub> (mmol)	CYPs	Yield <sup>a</sup> (%)
1	2.0	0.5	0.5	PhS-IPr-CYP	39
2	0.5	1.5	1.5	PhS-IPr-CYP	66
3 <sup>b</sup>	0.5	1.5	1.5	PhS-IPr-CYP	70
4 <sup>c</sup>	0.5	0.5	1.5	PhS-IPr-CYP	82
5 <sup>c,d</sup>	0.5	0.5	1.5	PhS-IPr-CYP	81
6 <sup>c</sup>	0.5	0.5	1.5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

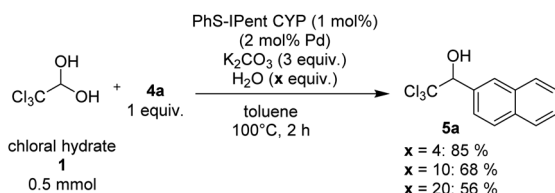
<sup>a</sup> Yields were determined by <sup>1</sup>H-NMR using triphenylmethane as an internal standard. <sup>b</sup> **3a** was used instead of **2a**. <sup>c</sup> **4a** was used instead of **2a**. <sup>d</sup> Dehydrated chloral was used instead of chloral hydrate. <sup>e</sup> Isolated yield.



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.

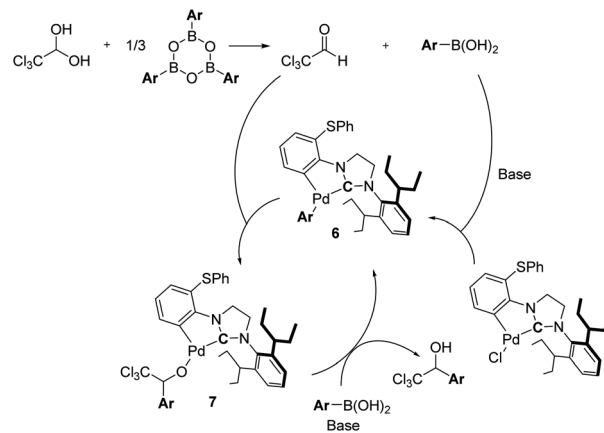


Scheme 3 The effect of the used amount of H<sub>2</sub>O on the catalytic addition reaction.

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.

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## 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. Lemaure, 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.

