$Et_2MeN{\cdot}HI$-Catalyzed Reaction of Arylboronic Acids with 2-Acyl-2,3-dihydro-4*H*-pyrans Leading to 2-Aryltetrahydrocyclopenta[1,3,2]dioxaboroles

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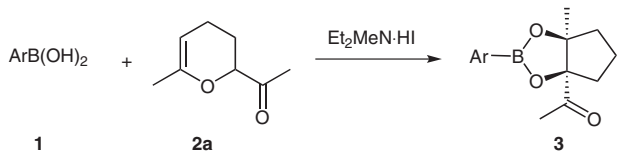
Abstract: The reaction of arylboronic acids with 2-acyl-2,3-dihydro-4*H*-pyrans proceeded smoothly in the presence of a catalytic amount of $Et_2MeN{\cdot}HI$ to give acyl-substituted 2-aryltetrahydrocyclopenta[1,3,2]dioxaboroles in good yields. The reaction is likely to involve the acid-catalyzed ring-opening reaction of pyrans, an intramolecular aldol reaction, and condensation with boronic acids.

Key words: ring contraction, dihydropyran, boronic acid, cyclopentanediol, boronic ester

The ring contraction reactions of easily available carbo- and heterocyclic compounds are useful methods in organic synthesis.[1] A variety of ring-contraction reactions have been developed thus far, which include Wolff rearrangement,[2] Favorskii rearrangement,[3] and Wagner–Meerwein rearrangement,[4] to name only a few. Many of these reactions are widely employed in the total synthesis of natural products.[1,5] During the course of our study on the development of novel catalytic transformations using enones as a substrate,[6] we found that the 2-acetyl-6-methyl-2,3-dihydropyran (**2a**; methyl vinyl ketone dimer) underwent ring contraction in the presence of boronic acids **1** and a catalytic amount of $Et_2MeN{\cdot}HI$ to give boronic acid *cis*-cyclopentanediol esters **3** in high yield and stereoselectivity (Scheme 1). Herein, we have generalized the reaction and report a novel $Et_2MeN{\cdot}HI$-catalyzed ring contraction of acyl-substituted dihydropyrans leading to 2-aryltetrahydrocyclopenta[1,3,2]dioxaboroles.

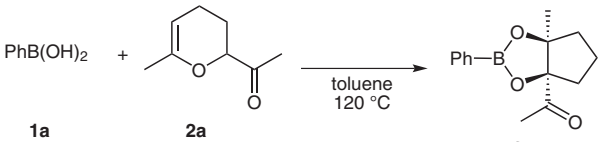


1 2a 3

Scheme 1 Formation of boronic acid *cis*-cyclopentanediol esters

The reaction of phenylboronic acid (**1a**) with acyl-substituted dihydropyran **2a** in toluene at reflux gave a 38% yield of the phenylboronic ester of 1-acetyl-1,2-cylopentanediol **3a** (Table 1, entry 1). In this reaction, the *cis*-isomer was formed selectively. The boronic ester formation was accelerated in the presence of one equivalent of water, which gave **3a** in 63% yield (entry 2). The addition of a catalytic amount of the amine salt, $Et_2MeN{\cdot}HI$, further accelerated boronic acid formation (entries 3–5), and improved the yields of boronic ester **3a** by up to 97% (entry 5). The reactions using *p*-toluenesulfonic acid and trifluoroacetic acid instead of $Et_2MeN{\cdot}HI$ gave **3a** in 41% and 43% yield, respectively.

Table 1 Ring Contraction Reaction of Dihydropyran **2a** in the Presence of Phenylboronic Acid **1a**[a]



1a 2a 3a

Entry	Additive	Time (h)	Yield (%)[b]
1	–	8	38
2	H_2O (1 equiv)	8	63
3	H_2O (1 equiv), $Et_2MeN{\cdot}HI$ (5 mol%)	4	70
4	H_2O (1 equiv), $Et_2MeN{\cdot}HI$ (5 mol%)	6	95
5	H_2O (1 equiv), $Et_2MeN{\cdot}HI$ (5 mol%)	8	97

[a] Conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), toluene (2 mL), 120 °C.
[b] Isolated yield after flash chromatography on SiO_2.

Having identified optimal conditions, we then investigated the generality of the present ring contraction reaction, and the results are shown in Table 2. *p*-Tolylboronic acid (**1b**) and *p*-methoxyphenylboronic acid (**1c**) also reacted with **2a** to give the corresponding bicyclic boronic esters **3b** and **3c** in 88 and 85% yield, respectively (Table 2, entries 2 and 3). Dihydropyran **2b**, a dimer of ethyl vinyl ketone, also worked well to give boronic ester **3d** (entry 4). Dihydropyrans **2c** and **2d** gave the corresponding bicyclic boronic esters **3e** and **3f** in good yields (entries 5 and 6). In the case of **2e** having a terminal alkene moiety, the carbon–carbon double bond was tolerated to give boronic ester **3g** in 66% yield (entry 7).

To gain some mechanistic insight into the present ring contraction, we examined some control experiments. When the reaction of **2a** was carried out in the absence of boronic acid, 2-hydroxy-1,6-diketone **5** was obtained in a 33% yield, whereas cyclic diol **4** was not formed (Scheme 2). The reaction of isolated **5** with phenylboronic acid (**1a**) was tested with or without $Et_2MeN{\cdot}HI$

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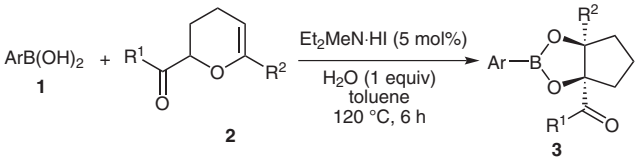
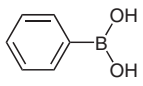
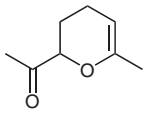
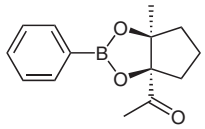
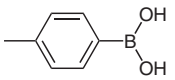
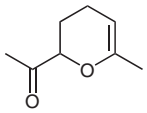
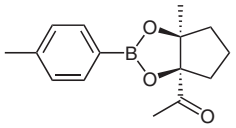
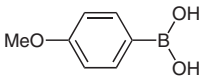
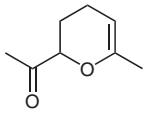
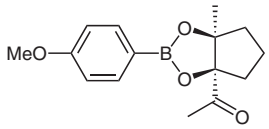
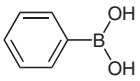
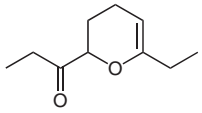
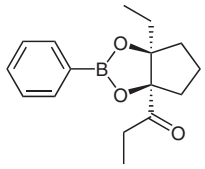
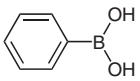
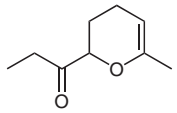
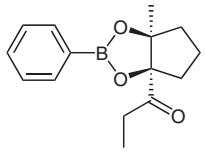
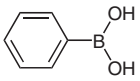
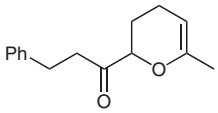
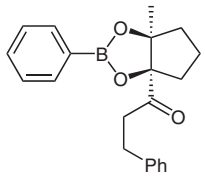
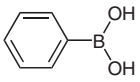
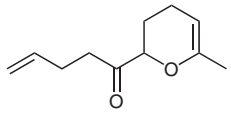
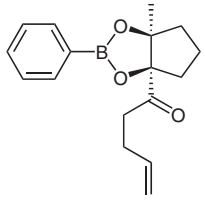
(Scheme 3). In both cases, boronic ester **3a** was obtained, which strongly suggests the intermediacy of **5**.

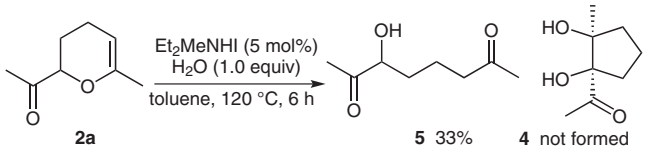
Taking this observation into consideration, we propose a mechanism for the present reaction, which is shown in Scheme 4. An acid-catalyzed hydrative ring-opening reaction would give 2-hydroxy-1,6-diketone **5**. An intramolecular aldol reaction of diol **6**, the enol form of **5**, would give *cis*- and *trans*-cyclic diols **4**. The *trans*-diol cannot

Table 2 $Et_2MeN{\cdot}HI$-Catalyzed Ring Contraction of 2-Acyl-Substituted Dihydropyrans **2** with Arylboronic Acids **1**[a]

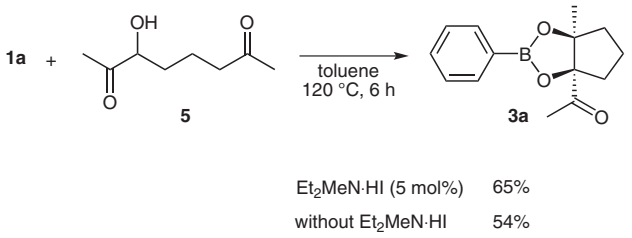


Entry	1	2	3	Yield (%)[b]
1	 **1a**	 **2a**	 **3a**	95
2	 **1b**	 **2a**	 **3b**	88
3	 **1c**	 **2a**	 **3c**	85
4	 **1a**	 **2b**	 **3d**	70
5	 **1a**	 **2c**	 **3e**	75
6	 **1a**	 **2d**	 **3f**	81
7	 **1a**	 **2e**	 **3g**	66

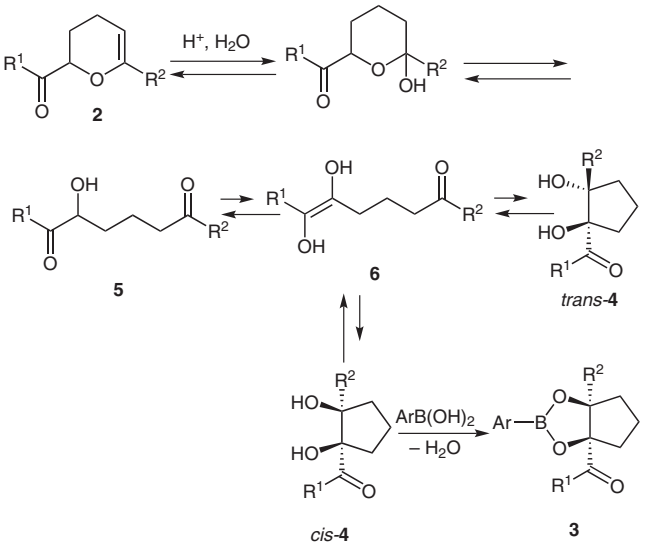
[a] Conditions: **1** (0.5 mmol), **2** (0.5 mmol), $Et_2MeN{\cdot}HI$ (5 mol%), H_2O (0.5 mmol), toluene (2 mL), 120 °C.
[b] Isolated yield after flash chromatography on SiO_2.
[c] The reaction was conducted for 10 h.



Scheme 2 Reaction of **2a** with $Et_2MeN{\cdot}HI$ in the absence of boronic acid



Scheme 3 Reaction of **5** with phenylboronic acid



Scheme 4 Possible mechanism for the $Et_2MeN{\cdot}HI$-catalyzed ring contraction

undergo condensation with boronic acids; hence, it reverts back to **6**. Eventually, the *cis*-diol would undergo condensation with boronic acids to give *cis*-boronic esters **3**.

In conclusion, we have developed a novel $Et_2MeN{\cdot}HI$-catalyzed ring contraction of 2-acyl-substituted 2,3-dihydropyrans **2** in the presence of arylboronic acids **1** leading to arylboronic acid *cis*-cyclopentanediol esters **3**. A variety of boronic esters can be obtained from easily available starting materials. The reaction would involve an acid-catalyzed ring opening followed by an intramolecular aldol reaction and condensation with boronic acids.

The ^1H NMR spectra were recorded with a JEOL JMN-500 (500 MHz) spectrometer in $CDCl_3$, and are referenced at 0.00 ppm for TMS. Chemical shifts (δ) are reported in ppm. ^{13}C NMR spectra were recorded with a JEOL JMN-500 (125 MHz) spectrometer in $CDCl_3$ and are referenced at 77 ppm for $CDCl_3$. IR spectra were obtained on a JASCO FT/IR-4100 spectrometer; absorptions were reported in cm^{-1}. Both conventional and high resolution mass spectra were recorded on a JEOL MS700 spectrometer. Dihydropyrans **2a** and **2b** were prepared from methyl vinyl ketone and ethyl vinyl ketone, respectively. Dihydropyrans **2c**, **2d**, and **2e** were prepared from **2a** according to the reported method.[7] The products were purified by flash chromatography on silica gel (Nacalai Tesque Inc., Silica Gel 60, 230–400 mesh).

3a-Acetyl-6a-methyl-2-phenyl-4*H*-tetrahydrocyclopenta[1,3,2]dioxaborole (3a); Typical Procedure

Phenylboronic acid (**1a**; 0.5 mmol, 60.9 mg), dihydropyran (**2a**; 0.5 mmol, 70.4 mg), $Et_2MeN{\cdot}HI$ (5 mol%, 5.2 mg), H_2O (0.5 mmol, 9 mg), and toluene (2 mL) were placed in a screw-capped test tube. The test tube was purged with argon and sealed. The mixture was stirred at 120 °C for 6 h. After the reaction, the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane–EtOAc, 15:1) to give the boronic ester **3a** as a colorless oil; yield: 115.8 mg (95%), R_f = 0.30 (hexane–EtOAc, 15:1) (Table 2).

IR (neat): 1714 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.36 (s, 3 H), 1.63–1.80 (m, 3 H), 1.90–1.97 (m, 1 H), 2.06–2.10 (m, 1 H), 2.26–2.34 (m, 1 H), 2.35 (s, 3 H), 7.42 (t, *J* = 7.5 Hz, 2 H), 7.50–7.54 (m, 1 H), 7.85–7.89 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.38, 23.35, 28.14, 38.45, 41.77, 94.52, 98.55, 127.87, 127.91, 134.95, 211.62.

MS (EI): *m*/*z* (%) = 244 (M^+, 20), 201 (100), 186 (41), 97 (71).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{17}BO_3$ (M^+): 244.1271; found: 244.1269.

3a-Acetyl-6a-methyl-2-(4-methylphenyl)-4*H*-tetrahydrocyclopenta[1,3,2]dioxaborole (3b)

White solid; mp 69–70 °C; R_f = 0.25 (hexane–EtOAc, 20:1).

IR (KBr): 1712 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.34 (s, 3 H), 1.61–1.76 (m, 3 H), 1.90–1.94 (m, 1 H), 2.04–2.06 (m, 1 H), 2.25–2.30 (m, 1 H), 2.32 (s, 3 H), 2.40 (s, 3 H), 7.24 (d, *J* = 7.5 Hz, 2 H), 7.75 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.73, 22.38, 23.34, 28.09, 38.43, 41.80, 94.37, 98.47, 128.64, 128.74, 134.99, 141.94, 211.72.

MS (EI): *m*/*z* (%) = 258 (M^+, 37), 215 (100), 200 (42), 187 (21), 119 (25), 97 (92), 69 (22).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{19}BO_3$ (M^+): 258.1427; found: 258.1426.

3a-Acetyl-6a-methyl-2-(4-methoxyphenyl)-4*H*-tetrahydrocyclopenta[1,3,2]dioxaborole (3c)

White solid; mp 92–93 °C; R_f = 0.24 (hexane–EtOAc, 20:1).

IR (KBr): 1710 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.33 (s, 3 H), 1.60–1.74 (m, 3 H), 1.88–1.92 (m, 1 H), 2.03–2.08 (m, 1 H), 2.24–2.31 (m, 1 H), 2.32 (s, 3 H), 3.84 (s, 3 H), 6.93 (d, *J* = 7.4 Hz, 2 H), 7.79 (d, *J* = 7.4 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.38, 23.34, 28.03, 38.40, 41.79, 55.10, 94.28, 98.41, 113.42, 113.53, 136.74, 162.45, 211.77.

MS (EI): *m*/*z* (%) = 274 (M^+, 46), 231 (46), 216 (100), 135 (25), 97 (71).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{19}BO_4$ (M^+): 274.1376; found: 274.1372.

6a-Ethyl-2-phenyl-3a-propanoyl-4*H*-tetrahydrocyclopenta[1,3,2]dioxaborole (3d)

Colorless oil; R_f = 0.30 (hexane–EtOAc, 20:1).

IR (neat): 1713 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 6.7 Hz, 3 H), 1.06 (t, *J* = 6.4 Hz, 3 H), 1.47–1.58 (m, 1 H), 1.57–1.64 (m, 4 H), 1.67–1.72 (m, 1 H), 1.75–1.79 (m, 1 H), 1.91–1.95 (m, 1 H), 2.06–2.11 (m, 1 H), 2.17–2.23 (m, 1 H), 2.67 (dq, *J* = 19.3, 6.4 Hz, 1 H), 2.84 (dq, *J* = 19.3, 6.4 Hz, 1 H), 7.43 (t, *J* = 7.5 Hz, 2 H), 7.51 (t, *J* = 7.4 Hz, 1 H), 7.86 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.07, 8.55, 22.25, 29.57, 33.50, 39.32, 39.46, 97.82, 98.53, 127.75, 126.78, 131.54, 134.93, 213.86.

MS (EI): *m*/*z* (%) = 272 (M^+, 26), 215 (100), 200 (34), 111 (52).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{21}BO_3$ (M^+): 272.1584; found: 272.1583.

6a-Methyl-2-phenyl-3a-propanoyl-4*H*-tetrahydrocyclopenta[1,3,2]dioxaborole (3e)

Colorless oil; R_f = 0.30 (hexane–EtOAc, 20:1).

IR (neat): 1713 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.06 (t, *J* = 6.78 Hz, 3 H), 1.31 (s, 3 H), 1.68–1.78 (m, 3 H), 1.90–1.96 (m, 1 H), 2.03–2.10 (m, 1 H), 2.27–2.34 (m, 1 H), 2.58 (dq, *J* = 19.3, 6.8 Hz, 1 H), 2.88 (dq, *J* = 19.3, 6.8 Hz, 1 H), 7.41 (t, *J* = 7.4 Hz, 2 H), 7.52 (t, *J* = 7.4 Hz, 1 H), 7.86 (d, *J* = 7.3 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.10, 22.37, 23.39, 23.42, 33.34, 38.65, 41.77, 94.53, 98.58, 127.81, 127.88, 131.60, 134.93, 213.54.

MS (EI): *m*/*z* (%) = 258 (M^+, 42), 201 (100), 200 (69), 105 (25), 97 (94).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{19}BO_3$ (M^+): 258.1427; found: 258.1423.

6a-Methyl-2-phenyl-3a-(3-phenylpropanoyl)-4*H*-tetrahydrocyclopenta[1,3,2]dioxaborole (3f)

Colorless oil; R_f = 0.30 (hexane–EtOAc, 20:1).

IR (neat): 1712 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.17 (s, 3 H), 1.58–1.70 (m, 3 H), 1.83–1.87 (m, 1 H), 1.97–2.02 (m, 1 H), 2.18–2.28 (m, 1 H), 2.75–2.90 (m, 3 H), 3.10–3.16 (m, 1 H), 7.07–7.15 (m, 3 H), 7.17–7.22 (m, 3 H), 7.33 (t, *J* = 7.4 Hz, 2 H), 7.43 (t, *J* = 7.9 Hz, 1 H), 7.76 (d, *J* = 7.9 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.98, 22.34, 23.23, 29.14, 38.84, 41.80, 94.64, 98.40, 126.00, 127.82, 128.35, 128.42, 131.64, 134.95, 141.00, 212.06.

MS (EI): *m*/*z* (%) = 334 (M^+, 18), 201 (100), 97 (64).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{23}BO_3$ (M^+): 334.1740; found: 334.1737.

3a-(But-4-enoyl)-6a-methyl-2-phenyl-4*H*-tetrahydrocyclopenta[1,3,2]dioxaborole (3g)

Colorless oil; R_f = 0.30 (hexane–EtOAc, 20:1).

IR (neat): 1713 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.25 (s, 3 H), 1.59–1.74 (m, 3 H), 1.85–1.88 (m, 1 H), 1.97–2.04 (m, 1 H), 2.17–2.34 (m, 3 H), 2.57 (ddd, *J* = 18.8, 8.3, 6.4 Hz, 1 H), 2.92 (ddd, *J* = 18.8, 8.3, 6.0 Hz, 1 H), 4.90 (d, *J* = 10.5 Hz, 1 H), 4.98 (d, *J* = 17.0 Hz, 1 H), 5.75 (ddt, *J* = 17.0, 10.5, 6.4 Hz, 1 H), 7.35 (t, *J* = 7.3 Hz, 2 H), 7.42–7.48 (m, 1 H), 7.79 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.37, 23.44, 27.11, 38.81, 39.33, 41.80, 94.66, 98.44, 115.31, 127.86, 131.66, 134.95, 137.14, 212.26.

MS (EI): *m*/*z* (%) = 284 (M^+, 22), 201 (100), 97 (59).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{21}BO_3$ (M^+): 284.1584; found: 284.1587.

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