A facile acid-promoted protodeboronation of arylboronic acids in the absence of metal catalysts or any other additives is described. This protodeboronation is general for a range of arylboronic acids with both electron-donating and electron-withdrawing groups in good to excellent yields under air atmosphere. Density functional theory mechanistic studies showed that the protodeboronation of arylboronic acids followed an intermolecular metathesis via a four-membered ring transition state. The effect of the substituent of arylboronic acids in protodeboronation is also theoretically studied.

**Results and discussion**

In our attempted Knoevenagel condensation mentioned above, the protodeboronation product was afforded. Since a good yield (71%) was obtained, we decided to expand this conversion to other substrates. The screen of the reaction conditions was

![Scheme 1](image)

**Scheme 1** The unexpected protodeboronation rather than condensation.
still required before we started our study. In the original Knoevenagel, NH₄OAc was used as a weakly basic catalyst to capture the reactive hydrogen. In order to check whether NH₄OAc played a role in the protodeboronation, we conducted a control experiment where 2-formylthiophene (3) was still obtained in a yield of 72% without using NH₄OAc (Scheme 2). This proved that AcOH alone could promote this reaction and therefore the following studies was performed in AcOH in the absence of NH₄OAc. Although the protodeboronation of organoboronic acid by acids was known, but only with formic acid and several inorganic acids.¹⁶ No systematic studies were found in the literatures using AcOH. In addition, the early study was focused mainly on the kinetics of the protodeboronation.¹⁶ This inspired us to explore a mild and an efficient acid-promoted protodeboronation universale for various arylboronic acid.

The optimization of reaction conditions for the acid-mediated protodeboronation was performed first, and 4-hydroxyphenylboronic acid (4a) was chosen as a substrate. The examination of the solvent indicated that acetic acid is the best acidic medium for the protodeboronation process (yield of 70%), followed by HCOOH with a lower yield of 45%, mixed solvents of AcOH/H₂O and HCl/H₂O with further decreased yields of no more than 30% (23% and 26%, respectively), and CF₃COOH being totally inactive (Table 1, entries 1–5). The influence of the temperature was also investigated. As shown in the same table, the yield of the phenol increased steadily with increasing temperature (Table 1, entries 6–9). Finally, 130 °C was determined as the best temperature for the reaction.

Under these optimized conditions, different arylboronic acids were used as substrates to confirm the usefulness of the acid-promoted protodeboronation, except for several cases where the conversions were conducted at 110 °C due to the lower boiling point of the corresponding protodeboronation products (Table 2, entries 7–11, for 5g, 5h, 5j). The results are summarized in Table 2. Electron-donating groups exhibited a better effect on both rate and yield than electron-withdrawing groups. The protodeboronation of arylboronic acids with electron-donating groups, such as –OH, –OCH₃, –Ph, –CH₃, were completed in 1–4 h with yields between 78–92% (Table 2, entries 1–7). The position of the groups on the phenyl ring had no obvious effect on the reaction (Table 2, entries 2 vs. 3, 8 vs. 9, 10 vs. 11 and 15 vs. 12). In addition, both the arylboronic acid 4d with the strong steric hindrance of two 2-CH₃O and the polycyclic arylboronic acid 4f could afford excellent yields of 88% and 92% (Table 2, entries 4 and 6). Conversely, as expected, electron-withdrawing groups (such as –Br, –Cl, –NO₂, –COCH₃, –CHO, –COOH, –COOCH₃), decreased the yield of the protodeboronation, furnishing yields of 52–71%, except for 4-Cl (85%), 3-COCH₃ (80%) and 4-CHO (84%), in a reaction time of 5–20 h (Table 2, entries 8–19). Although no difference was observed in the yields between weaker electron-withdrawing groups such as –Br and –Cl (55–85%) and stronger electron-

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**Table 1** Influence of solvent and temperature

| Entry | Solvent       | T (°C) | Yield (%) |
|-------|---------------|--------|-----------|
| 1     | AcOH          | 110    | 70        |
| 2     | HCOOH         | 110    | 45        |
| 3     | AcOH/H₂O      | 110    | 23        |
| 4     | HCl/H₂O       | 110    | 26        |
| 5     | CF₃COOH       | 110    | 0         |
| 6     | AcOH          | 25     | 8         |
| 7     | AcOH          | 50     | 58        |
| 8     | AcOH          | 80     | 63        |
| 9     | AcOH          | 130    | 81        |

*a Reaction conditions: arylboronic acids (0.5 mmol), AcOH (10 mL), under air, 1 h. b Isolated yields.

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**Table 2** Protodeboronation of arylboronic acids in acetic acid

| Entry | Ar Compound | Time(h) | Product | Yield (%) |
|-------|-------------|---------|---------|-----------|
| 1     | 4-HO-C₆H₄  | 4a      | 1       | 54        |
| 2     | 4-CH₃O-C₆H₄ | 4b     | 4       | 54        |
| 3     | 3-CH₃O-C₆H₄ | 4c     | 4       | 54        |
| 4     | 2,6-(CH₃O)₂-C₆H₄ | 4d | 3     | 5d       |
| 5     | 4-Ph-C₆H₄   | 4e     | 3       | 5e       |
| 6     | 9-Anthryl   | 4f     | 3       | 5f       |
| 7     | 4-CH₃-C₆H₄  | 4g     | 3       | 5g       |
| 8     | 3-Br-C₆H₄  | 4h     | 5       | 5h       |
| 9     | 3-Br-C₆H₄  | 4i     | 5       | 5h       |
| 10    | 4-Cl-C₆H₄  | 4j     | 5       | 5j       |
| 11    | 3-Cl-C₆H₄  | 4k     | 5       | 5j       |
| 12    | 3-NO₂-C₆H₄ | 4l     | 10      | 5l       |
| 13    | 3-CH₃CO-C₆H₄ | 4m | 8     | 5m       |
| 14    | 3-CHO-C₆H₄ | 4n     | 8       | 5n       |
| 15    | 4-NO₂-C₆H₄ | 4o     | 10      | 5l       |
| 16    | 4-CH₃CO-C₆H₄ | 4p | 16     | 5m       |
| 17    | 4-CHO-C₆H₄ | 4q     | 8       | 5n       |
| 18    | 4-COOH-C₆H₄ | 4r    | 8       | 5r       |
| 19    | 4-CH₃COO-C₆H₄ | 4s | 20     | 5s       |
| 20    | 2-CH₃COO-C₆H₄ | 4t | 2     | 5r       |
| 21    | OHC         | 1       | 2       | 3        |
| 22    | OHC         | 1       | 2       | 3        |

*a Reaction condition: arylboronic acids (0.5 mmol), AcOH (10 mL). The reactions were conducted at 130 °C under air. b Isolated yields. c The reactions were conducted at 110 °C, GC yields. d The product was benzoic acid rather than the expected methyl benzoate.
withdrawing groups such as –NO₂, –COCH₃, –CHO, –COOH and –COOCH₃ (52–84%), the reaction rates clearly differed. Protodeboronation of arylboronic acids with strong electron-donating groups required longer reaction times of 8–20 h (Table 2, entries 12–19). This proved that electron deficiency of the C–B bond did not favor the reaction. Extraordinarily, arylboronic acid substituted with –COOCH₃ on the ortho-position did not give the protodeboronated methyl benzoate, but was directly hydrolyzed to benzoic acid 5r in just 2 h (Table 2, entry 20). Heterocyclic boronic acids (4u and 1) could also easily provide the protodeboronation product in excellent yields of 96% and 84% under these conditions (Table 2, entries 21 and 22). In general, the results above demonstrate the universality of this reaction.

To further explore the scope of the substrates, the protodeboronation of other surrogates such as 4-hydroxyphenylboronic acid pinacol ester (4v) and potassium 4-carboxyphenyltrifluoroborate (4w) were studied. The protodeboronation of 4v and 4w still proceeded although longer reaction time was required (24 h) (Scheme 3). 4v gave the protodeboronation product in a yield of 77%, while 4w afforded a lower yield of 36%. The arylboronic acid pinacol ester and potassium aryltrifluoroborate display enhanced chemical stability compared with arylboronic acids. The slower protodeboronation rates may be due to the decreased Lewis acidity of the boron atom from arylboronic acid pinacol ester and potassium aryltrifluoroborate, which is consistent with Cheon’s studies. ¹⁴,¹⁵

Aryl iodides, important building blocks in forming C–C and C–X (X = heteroatom) bond, are widely used in organic synthesis. ¹⁰ As we know, the regioselective iodination of arenes is usually difficult. ¹⁶ While the 4-iodoanisole (8) was successfully formed in a total yield of 61% through the AcOH-promoted protodeboronation in which the –B(OH)₂ motif acted as a directing group (Scheme 4).

For the protodeboronation of arylboronic acids, as shown in Scheme 5, there are two scenarios to address the aryl–H bond formation: (1) arylboronic acids A react with AcOH to form aryl complex B via a four-membered ring transition state ATS (path 1); (2) arylboronic acids A can be attack by H⁺ reagent to form complex C, and then OAc⁻ attack the –B(OH)₂ motif through B–C bond cleavage and form aryl complex B (path 2). With the help of DFT calculations, the energy profiles of the protodeboronation of arylboronic acids are calculated in Fig. 1. Fig. 1 shows that the arylboronic acids react directly with AcOH to form aryl–H bond via an intermolecular metathesis process. We failed to locate the complex C in path 2, which means the complex C is unlikely to be involved as the stable intermediate in the protodeboronation.

In order to understand the effect of the substituent of arylboronic acids in protodeboronation, we compared the reaction profiles starting from the arylboronic acids A₁ with electron-donating group (entry 2 in Table 2) and arylboronic acids A₂ with electron-withdrawing group (entry 16 in Table 2). From the energy profiles shown in Fig. 1, we can clearly see that protodeboronation of A₁ (Fig. 1a, with an energy barrier of 37.5 kcal mol⁻¹) has lower energy barrier than that of A₂ (Fig. 1b, with an energy barrier of 43.4 kcal mol⁻¹). Electronically, the boron-bonded carbon in A₁ is electron-rich when compared with that in A₂ because of the electron property of substituent of arylboronic acids. The natural bond orbital (NBO) analysis shows that the natural atomic charges of the boron-bonded carbon are calculated to be –0.468 in A₁ and –0.409 in A₂, respectively, suggesting that the AcOH reagent favors attack of

![Scheme 3 Protodeboronation of 4-hydroxyphenylboronic acid pinacol ester and potassium 4-carboxyphenyltrifluoroborate.](image)

![Scheme 4 The protodeboronation of arylboronic acid was applied in the synthesis of 4-idoanisole.](image)

![Scheme 5 The proposed mechanism for protodeboronation of arylboronic acids.](image)

![Fig. 1 The energy profiles calculated for the protodeboronation of A₁ and A₂.](image)
the boron-bonded carbon in A1 over that in A2. These results are consistent with the experimental observation that arylboronic acids with electron-donating group have high yield with short reaction time than that with electron-withdrawing group.

Conclusions

In conclusion, we have achieved an acid-mediated protodeboronation from a wide variety of arylboronic acid substrates. Compared to other methods reported before, it is a greener process in that no any metal catalysts and additives are needed. The only use of acetic acid is highly practical. In addition, the electron-withdrawing groups can also be tolerated in the protodeboronation. This method could be an attractive complement to the case in which substituents of the arylboronic acids are susceptible to alkaline medium. An intermolecular metathesis reaction mechanism was developed based on DFT calculations. Additionally, the NBO analysis provided information on the effect of the substituent of arylboronic acids.

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