Tetrahedron Letters 60 (2019) 151020

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

ipso-Bromination/iodination of arylboronic acids: Poly(4-vinylpyridine)-Br_2/I_2 complexes as safe and efficient reagents

Fang Fu, Laxman Gurung, Miklos Czaun, Thomas Mathew *, G.K. Surya Prakash *

Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, CA 90089-1661, USA

ARTICLE INFO

Article history:
Received 12 June 2019
Revised 1 August 2019
Accepted 5 August 2019
Available online 16 August 2019

Keywords:
Poly(4-vinylpyridine)
ipso-Halogenation
Arylboronic acid
N-Halosuccinimide

ABSTRACT

Poly(4-vinyl pyridine) supported bromine/iodine complexes were prepared and probed for *ipso*-bromination/iodination of arylboronic acids. These solid complexes with catalytic amount of additive are found to be safe and efficient reagent system for the *ipso*-bromination/iodination. The reaction occurs under mild conditions and tolerates various functional groups resulting in products with high selectivity and yields.

Introduction

Aryl halides, in particular, aryl bromide and aryl iodides are valuable synthetic intermediates widely applied in carbon-carbon and carbon-heteroatom bond formation [1]. Another important synthetic application of aryl iodides is to prepare various hypervalent iodine reagents [2]. Moreover, the radiolabeled haloarenes are used as target compounds in biological research and as components of synthetic schemes for diagnostic and therapeutic agents [3].

Traditionally, aryl halides are formed via electrophilic aromatic substitution. While electrophilic aromatic chlorination and bromination work well, due to the low reactivity of iodine and related iodinating agents compared to the corresponding chloro and bromo analogues, the direct iodination of arenes is generally not achievable [4]. A number of general methods for the synthesis of iodoarenes have been developed including: (a) oxidative iodination of arenes by using strong oxidizing agents [5], (b) classic Sandmeyer reaction involving regioselective halogenation of arenes via aryl diazonium salts under acidic condition [6] and organocatalytic variants of Sandmeyer reactions [7], and (c) various methods using highly reactive aromatic mercury [8] and thallium [9] compounds. However, these methods have obvious limitations as they involve hazardous oxidizing agents, harsh reaction conditions, complex and dangerous work up, low regioselectivity and yields. Therefore, most of them don't meet the requirements of safe and environmentally benign methodology.

Organoboron derivatives have drawn considerable attention in *ipso*-substitution reactions, in particular arylboronic acids, by the *ipso*-substitution of boronic acid group can lead to convenient access to arenes bearing important functional groups with good regioselectivity. Arylboronic acids [10] are usually crystalline solids, generally nontoxic and stable to air and moisture. A large number of substituted arylboronic acids are readily prepared via transition metal catalyzed approach and directed borylation of active C—H bonds without using haloarenes [11].

In 1982, Kabalka and his co-workers developed halogenation of organoboranes with halide salts in the presence of chloramine-T [12]. Later, in 1998, *ipso*-halogenation of arylboronic acid was achieved in good yields using *N*-halosuccinimides by Prakash et al. [13] despite some limitations. More related works of *ipso*-halogenation of boronic acid with *N*-halosuccinimides have been reported in the following years [14]. In 2004, Szumigala, Jr. described the synthesis of haloarenes from arylboronic acids using 1,3-dihalo-5,5-dimethylhydantoin (DCDMH or DBDMH) as an effective halogenating agent [15]. In 2011, Chen et al. developed a copper-catalyzed halodeboronation protocol using oxygen as the oxidant [16]. Recently, more methods of boron-iodine exchange have emerged to generate iodoarenes, including copper-catalyzed approaches with iodide salts [17a] or iodine [17b], metal-free methods using iodine [17c], using cetyltrimethyl ammonium bromide (CTAB)/I_2 [17d] or another novel *ipso*-iodination way via *N*-iodomorpholinium iodide (NIMI) [17e]. As compared to *ipso*-substitutions of iodine, the reports on the

* Corresponding authors.
E-mail addresses: tmathew@usc.edu (T. Mathew), gprakash@usc.edu (G.K.S. Prakash).

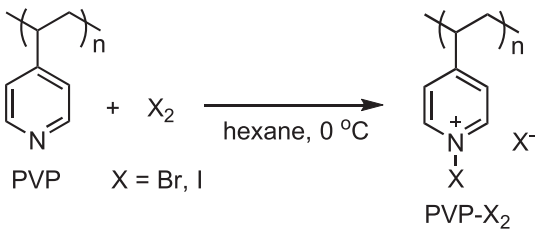
https://doi.org/10.1016/j.tetlet.2019.151020
0040-4039/

ipso-bromination of arylboronic acids are relatively scarce. In addition, many reported methods above are either requiring high temperature, long reaction time, or large excess of additives/special ligand and some of them have limited substrate scope or yields. Therefore, it is very desirable to develop milder, more efficient, less expensive and environmentally benign alternative for preparation of haloarenes.

The recent developments of polymer supported reagents have been growing fast in synthetic organic chemistry [18]. Polymeric reagents are generally macromolecules to which chemical functional groups are connected. They possess the similar potential abilities of the low molecular weight analogues. On the other hand, the main advantages of these polymer-supported species over their monomeric reagents are (a) easier work-up by simple filtration and subsequent washing with the solvent because of their insolubility in the reaction medium, (b) using excess of the reagents to drive the reaction to completion without any concern regarding the separation of the desired products from the unused reagents, (c) recyclability of these polymer supports, (d) lower toxicity which makes them environmentally safer, (e) and fine-tuning the stability and selectivity of the reagents towards different synthetic transformations compared to those carried out on same functional groups by unsupported reagents [19]. Poly(4-vinylpyridine) (PVP) is one of the most frequently used polymer as a solid support for various reagents and catalysts because of its commercial availability, its stability, facile complexation with high loading capacity, fine swelling properties, and good physicochemical characteristics [19]. During the course of our studies, we developed environmentally benign methods via polymer-supported reagents such as PVP-HF, PVP-SO_2 PVP-H_2O_2, PVP-NM (nitrating Mixture), and PVP-CF_3SO_3H in recent decades [20]. In continuation of our efforts using these polymeric complexes for various organic transformations, we decided to explore the application of poly(4-vinylpyridine)- bromine/iodine complexes (PVP-Br_2/I_2) as effective reagents for halogenation of aryl boronic acids. PVP-Br_2 as a polymer-supported solid complex have been previously studied for bromination of aromatic rings, alkenes, alkynes, ketones etc [21]. However, the application of PVP-Br_2/I_2 as polymer supported reagents for *ipso*-halogenation reactions has very rarely been explored in recent years. Herein, we report the preparation and the use of PVP-Br_2/I_2 complexes as green and efficient reagents for *ipso*-bromination/iodination of arylboronic acids with catalytic amount of $NaNO_2$ for the synthesis of the corresponding haloarenes.

Results and discussion

We initiated our investigation by preparing poly(4-vinylpyridine)-bromine/iodine complexes or PVP-Br_2/I_2. Several methods of making PVP-Br_2 had been reported by Zabicky and Mhasalkar [21g]. Accordingly, commercially available poly(4-vinylpyridine), 2% cross linked with divinylbenzene, was stirred with excess hexane as solvent for 24 h so that the polymer was swollen well. Liquid bromine or solid iodine was then carefully added to the swollen polymer support in hexane with efficient cooling and thorough mixing. As complex formation of PVP-Br_2 or PVP-I_2 proceeds, the color of the solution became lighter and lighter and stirring was continued till no further significant change in color was observed (about 24 h). After filtering, washing and drying under the vacuum, a fluffy, free-flowing, fresh orange (PVP-Br_2) or purple black solid (PVP-I_2) was obtained (Scheme 1). The complexes are almost odorless which is ready for use as reagent for bromination/iodination, which are much safer than molecular bromine or iodine. The complex can be stored in well-closed containers for many months. From the



Scheme 1. Preparation of PVP:Br_2 (1:1) and PVP:I_2 (1:1).

weight increment, PVP-Br_2 and PVP-I_2 complexes are found to have a 1:1 M ratio, achieved by the addition of equimolar amounts of bromine or iodine with respect to monomer unit of the polymer. During our initial trials, with direct treatment of the polymer and Br_2/I_2 without swelling for a day, we got PVP-Br_2 and PVP-I_2 complexes with 1.5:1 M ratio and 1.2:1 M ratio respectively. By prior swelling and proper stirring as mentioned we were able to get the complexes with 1:1 M ratio. The changes in morphology of the polymer samples because of the formation of the complexes were further studied through scanning electron microscopy (SEM) (Fig. 1). The surface morphology of the complexes changed significantly compared to that of the precursor PVP polymer. The particle sizes of both PVP-Br_2 and PVP-I_2 were found to be much smaller indicating activities of the complexes with increased reaction surfaces (Fig. 1b, c).

To screen their capabilities as reagents for halogenation, the complexes were subsequently used for *ipso*-bromination or iodination of various arylboronic acids. Preliminary studies showed that the complex is very effective and convenient halogenating reagent (for both bromination and iodination) under mild conditions (Scheme 2).

We began with the screening of reaction conditions such as amount of the reagents, solvent, temperature and time for bromination of *p*-tolylboronic acid with PVP-Br_2 complex with molar ratio 1.5:1 (Table 1). Fortunately, 42% product was formed when 1 equiv. alryboronic acid reacted with 1.5 equiv. PVP-Br_2 (1.5:1) in acetonitrile at room temperature for 17 h (Table 1, entry 1). Increasing the temperature to 80 °C and reducing the reaction time to 3 h, showed significant improvement in yield to 67% though not high as expected (entry 2). Next, we added $NaNO_2$ as additive in different amounts to see whether it has any impact on the reaction. In order to improve the yield of the product, reactions with varying amounts of the complex and the additive with respect to starting materials were further examined (Table 1, entries 3–7). Reaction using 1.5 equivalents of PVP-Br_2 (1.5:1) with 0.25 equiv. sodium nitrite at 80 °C for 3 h yielded the *ipso*-brominated product in 93% yield (Table 1, entry 6). The small amount of sodium nitrite, 0.25 equiv. used in this high yield reaction and much lower yield in its absence reveal its role as a catalyst (Table 1, entry 6).

For the *ipso*-halogenation reaction, acetonitrile (CH_3CN) was found to be the solvent of choice in terms of the yield and selectivity of the reaction (Table 1, entries 3–6, 8). Reaction at a lower temperature led to lower conversion of 4-tolylboronic acid and the yield of the desired product, 4-bromotoluene (Table 1, entry 8).

Next, four different sodium salts were screened in the presence of 1.5 equiv. of PVP-Br_2 (1.5:1) in acetonitrile at 80 °C for 3 h (Table 2). Analytically, catalytic amounts of both sodium nitrite and sodium nitrate provided the products in similar high yields (Table 2, entries 1 and 3). While conducting the reactions under similar conditions, results from sodium nitrite and sodium nitrate did not differ significantly though a slightly better yield was obtained with sodium nitrite (Table 2, entries 2 and 4).

The optimal reaction conditions for *ipso*-bromination reaction using PVP-Br_2 (1.5:1) were found to be: 1.5 equiv. PVP-Br_2 (1.5:1)

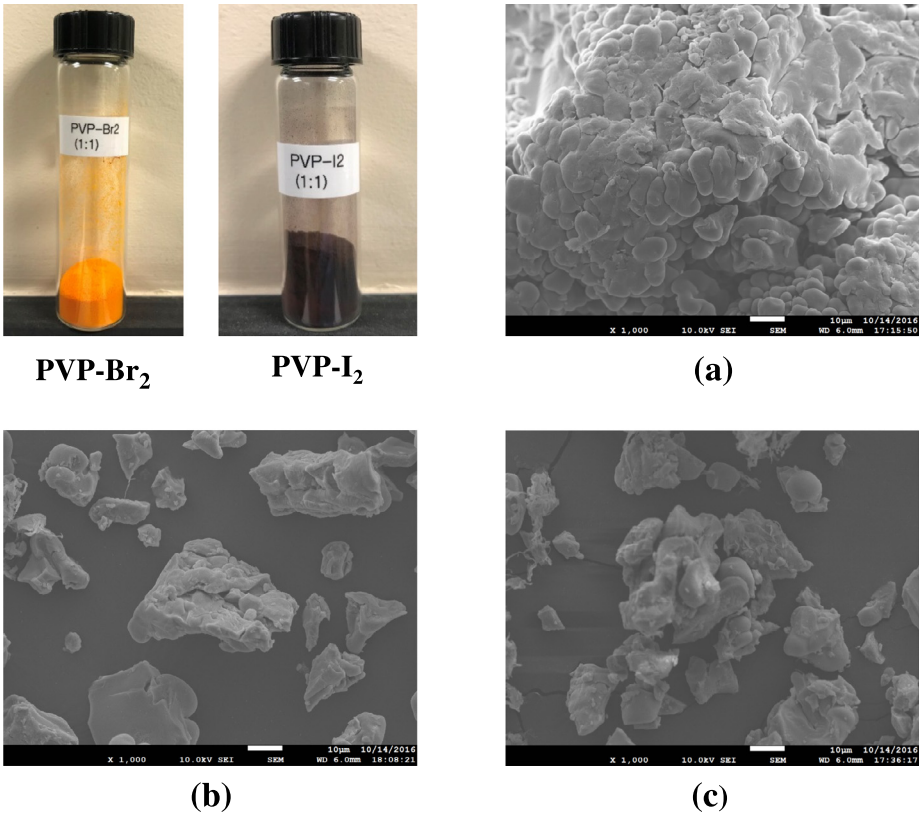
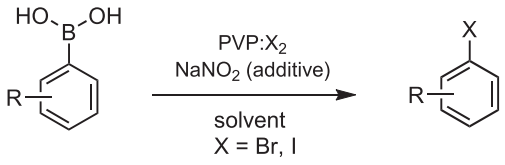


Fig. 1. (a) SEM image of PVP, (b) PVP:Br_2 (1:1) and (c) PVP:I_2 (1:1).

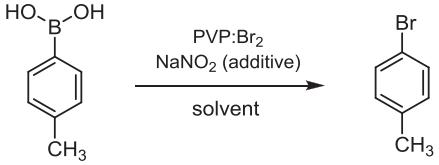


Scheme 2. *ipso*-Halogenation of arylboronic acid using PVP-X_2 complexes.

and 0.25 equiv. $NaNO_2$ in acetonitrile at 80 °C for 3 h. Accordingly, the optimization of reaction conditions for bromination of *p*-tolylboronic acid with PVP-Br_2 (1:1) complex was also studied (Table 3). As PVP-Br_2 (1.5:1) and PVP-Br_2 (1:1) differ in the amount of bromine in the complexes and the particle size of each polymer complex which are contributing factors toward the variance of their reaction activity, greater reactivity was anticipated for PVP-Br_2 (1:1). Therefore, reactions were conducted using PVP-Br_2 (1:1) with the optimized reaction conditions, acetonitrile as solvent and $NaNO_2$ as additive. As shown in Table 3, ratios of PVP-Br_2 (1:1) and $NaNO_2$ display a significant role on the reaction (Table 3, entries 1–4 and 7). The optimum amounts of PVP-Br_2 (1:1) and $NaNO_2$ which provided the best results are 1.35 and 0.25 equivalents respectively. Further screening of the reaction conditions showed that yields dropped with decrease in temperature and time (Table 3, entries 4–6, 7 and 8). In general, the best reaction conditions for *ipso*-bromination using PVP-Br_2 (1:1) are as follows: sodium nitrite (0.25 equiv) as catalyst, PVP-Br_2 (1:1) (1.35 equiv) as the halide source, and acetonitrile as solvent, with the reaction being carried out at 80 °C for one hour.

Furthermore, we also compared the potentials of the two PVP-Br_2 complexes for *ipso*-bromination of arylboronic acids with liquid bromine (Table 4). The results revealed that both PVP-Br_2 complexes are excellent in their ability for *ipso*-bromination of *p*-tolylboronic acid (chosen as the model substrate) in comparison with liquid Br_2. As expected, PVP-Br_2 (1:1) with higher bromine loading was more active than PVP-Br_2 (1.5:1) (Table 4, entries 1–3, and 4–6). Results also show that $NaNO_2$ has more significant effect on reactions with PVP-Br_2, thus making it an essential catalytic component in the reactions to afford the products in high yields.

Table 1
Optimization of the reaction conditions for *ipso*-bromination of arylboronic acids using PVP-Br_2 (1.5:1) complex.[a]



Entry	PVP-Br_2 (equiv)	$NaNO_2$ (equiv)	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	1.5	None	CH_3CN	rt	17	42
2	1.5	None	CH_3CN	80	3	67
3	1.35	1.2	CH_3CN	80	10	100
4	1.8	1.6	CH_3CN	80	3	97
5	1.5	1.2	CH_3CN	80	3	94
6	1.5	0.25	CH_3CN	80	3	93
7	1.5	0.25	CH_2Cl_2	80	3	63
8	1.5	0.25	CH_3CN	60	3	73
9	1.5	0.25	H_2O	80	3	0

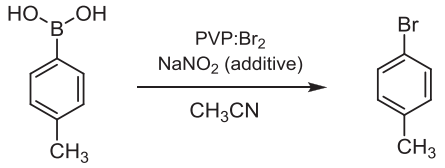
[a] Reaction conditions: 0.25 mmol of 4-tolylboronic acid with 1 equiv. each of PVP-Br_2 (1.5:1) and $NaNO_2$ in 2 mL of the solvent at the temperature and time indicated in the table.
[b] Yield by ^1H NMR.

Table 2
Effect of different sodium salts on the *ipso*-bromination of arylboronic acids using PVP-Br_2 complex (1.5:1).[a]

Entry	Sodium salt	Yield (%)[b]
1	$NaNO_2$	93
2	$NaNO_2$[c]	73
3	$NaNO_3$	92
4	$NaNO_3$[c]	70
5	Na_2CO_3	41
6	NaOH[d]	74
7	None	67

[a] Reaction conditions: 0.25 mmol of 4-tolylboronic acid (1 equiv), 0.38 mmol of PVP-Br_2 (1.5 equiv) in the presence of 0.063 mmol sodium salt (0.25 equiv) in 2 mL of acetonitrile at 80 °C (15 mL pressure tube) for 3 h.
[b] Yield by ^{1}H NMR.
[c] Reaction temperature is 60 °C.
[d] 1.2 equiv of NaOH was used.

Table 3
Optimization of reaction conditions for *ipso*-bromination of *p*-tolylboronic acid with PVP-Br_2 (1:1) complex.[a]



Entry	PVP-Br_2 (equiv)	$NaNO_2$ (equiv)	Temp (°C)	Time (h)	Yield (%)[b]
1	1	1	80	1	86
2	1.5	1.2	80	1	100
3	1.35	1.2	80	1	100
4	1.35	0.25	80	1	97
5	1.35	0.25	60	1	84
6	1.35	0.25	rt	17	91
7	1.35	None	80	1	44
8	1.35	None	80	2	63

[a] Reaction conditions: 0.25 mmol of 4-tolylboronic acid (1 equiv) with PVP-Br_2, $NaNO_2$, 2 mL CH_3CN, temperature and time indicated in table.
[b] Yield by ^{1}H NMR.

Table 4
Activity of the reagents: PVP-Br_2(1.5:1), PVP-Br_2(1:1) and Br_2 for *ipso*-bromination of *p*-tolylboronic acid.[a]

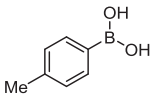
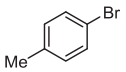
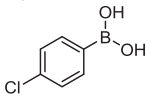
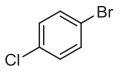
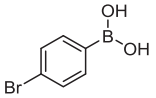
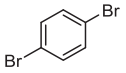
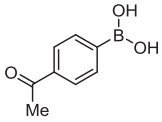
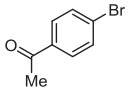
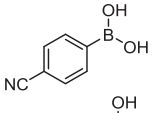
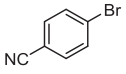
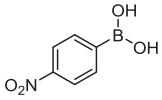
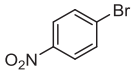
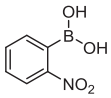
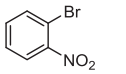
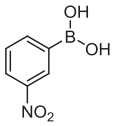
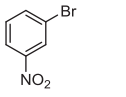
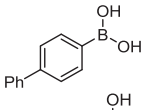
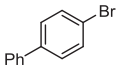
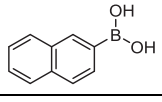
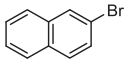
Entry	Bromine source	Additive	Time (h)	Yield (%)[b]
1	Br_2	$NaNO_2$	3	89
2	PVP-Br_2 (1.5:1)	$NaNO_2$	3	93
3	PVP-Br_2 (1:1)	$NaNO_2$	1	97
4	Br_2	None	3	81
5	PVP-Br_2 (1.5:1)	None	3	67
6	PVP-Br_2 (1:1)	None	3	78

[a] Reaction condition: 0.25 mmol of 4-tolylboronic acid (1 equiv), 0.38 mmol PVP-Br_2 (1.5:1) (1.5 equiv), 0.34 mmol of PVP-Br_2 (1:1) (1.35 equiv) or 0.38 mmol Br_2 (1.5 equiv) in the presence of 0.063 mmol sodium salt (0.25 equiv) or no salt in 2 mL of acetonitrile at 80 °C (15 mL pressure tube) for the time indicated.
[b] Yield by ^{1}H NMR.

With optimized reaction conditions of PVP-Br_2 complexes as halide sources for *ipso*-bromination of arlyboronic acid in hand, the scope and functional-group tolerance of this transformation were tested with a variety of representative arylboronic acids, as summarized in Table 5. A series of substrates were smoothly converted into the brominated products with good to excellent yields. Both complexes PVP-Br_2 (1.5:1) and PVP-Br_2 (1:1) exhibited similar trend of reactivity for different functional groups. As the reactions with 1:1 complex resulted in higher yields in shorter time, reactions with 1:1 complex were more focused and the results are displayed in Table 5. Arylboronic acids containing both electron-donating groups as well as electron-withdrawing groups underwent the reaction as expected with precise regioselectivity (at the *ipso* position) though the latter required longer reaction time for achieving satisfactory yields. Various substituents including methyl, halide, acetyl, cyano, nitro and phenyl were safe and tolerant (Table 5, entries 1–9). The bromination of 2-naphthylboronic acid also gave the product in impressive yield (Table 5, entry 10). Notably, reactions with all the three isomeric electron deficient boronic acids, *o*-, *m*-, and *p*-nitro phenylboronic acids resulted in the corresponding *ipso*-brominated products in good yields (Table 5, entries 6–8). The o-nitro phenylboronic acid took the longest time due to the electron withdrawing effect of the nitro group as well as anchimeric resistance (steric hindrance) from its proximity.

To enhance the synthetic utility of this protocol, the iodination reactions of arylboronic acids with PVP-I_2 (1:1) were evaluated in the same way. The results of screening of the reaction conditions for the *ipso*-iodination of *p*-tolylboronic acid with PVP-I_2 (1:1) is

Table 5
ipso-Bromination of arylboronic acids with PVP-Br_2 (1:1) complex.[a]

Entry	Substrate	Time (h)	Product	Yield (%)[b]
1		1		83
2		1		93
3		2		97
4		10		85
5		14		84
6		16		89
7		20		80
8		50		78
9		1		99
10		1		96

[a] Reaction conditions: 0.25 mmol of boronic acid (1 equiv), 0.34 mmol of PVP-Br_2 (1:1) (1.35 equiv) in the presence of 0.063 mmol $NaNO_2$ (0.25 equiv) in 2 mL acetonitrile at 80 °C for the time indicated in the table.
[b] Isolated yields.

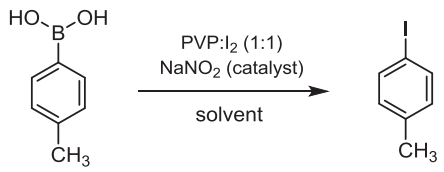
shown in Table 6. When compared to bromination reaction with PVP-Br_2 (1:1), iodination with PVP-I_2 (1:1) was faster (Tables 3 and 6). As in the case of the bromination reactions, catalytic amount of $NaNO_2$ or $NaNO_3$ (0.25 equiv) and CH_3CN as the solvent of choice are key components in the iodination reactions also. Results in Table 6 show that reaction with conditions 1.2 equiv. of PVP-I_2 (1:1) in the presence of 0.25 equiv. $NaNO_2$ in acetonitrile at 80 °C is the most efficient one giving the best yields and therefore, further reactions were conducted under similar conditions. The reaction was also conducted with I_2, in the absence and presence of $NaNO_2$. It is worth mentioning that in the absence of $NaNO_2$ no product was obtained, emphasizing the role of $NaNO_2$ as catalyst. However, reaction of *p*-tolylboronic acid with PVP-I_2 complexes even in the absence of $NaNO_2$ resulted in *p*-iodotoluene in significant amount (39%) showing that complexation improves the reactivity considerably.

After screening various reaction conditions for *ipso*-iodination reaction with PVP-I_2 complexes and finding the optimal conditions, the scope and generality of the reaction were explored using a series of arylboronic acids. The results are summarized in Table 7. As in the case of bromination using PVP-Br_2 complexes, electron rich phenylboronic acids showed much higher reactivity for iodination also (Table 7, entries 1-4, 10 and 11), although electron deficient arylboronic acids required longer reaction time to obtain the products in good yields (Table 7, entries 5–9).

Finally, we investigated the recovery and recycling of the polymer from solid bromine and iodine complexes after the initial course of reactions. At the end of the halogenation reaction of arylboronic acid, the solution containing the product was pipetted out of the pressure tube and the solid polymer residue was rinsed with CH_2Cl_2 to remove the product adhered to the polymer followed by washing the extract with $Na_2S_2O_4$ solution to remove the excess Br_2/I_2 left with the polymer. The solution in CH_2Cl_2 was then washed with water, dried over $MgSO_4$ and product was recovered by evaporating the solvent in a rotary evaporator.

The solid polymer was subsequently washed water, acetone and dried under vacuum. The recovered dry PVP solid was used again to prepare the PVP-Br_2/I_2 (1:1) complexes. The recyclability of this PVP-Br_2/I_2 sample made of recycled PVP was examined by repeating the *ipso*-bromination and *ipso*-iodination of diphenylboronic acid with the sample. The brominated and iodinated products were obtained in 97% and 98% yields respectively (Scheme 3), almost similar to the yields obtained with the PVP-Br_2/I_2 complexes prepared using fresh PVP (Table 5, entry 9; Table 7, entry 10).

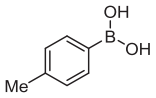
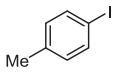
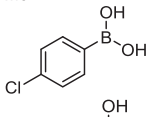
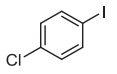
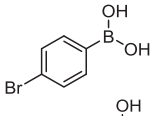
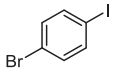
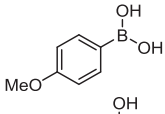
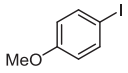
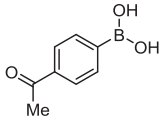
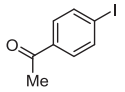
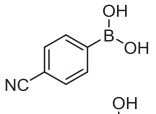
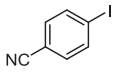
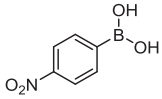
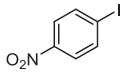
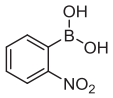
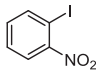
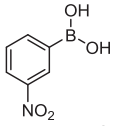
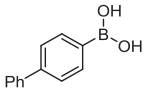
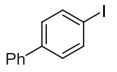
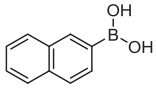
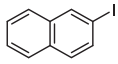
Table 6
Screening the optimal conditions for *ipso*-iodination of p-tolylboronic acid using PVP-I_2 (1:1).[a]



Entry	PVP-I_2 (equiv)	$NaNO_2$ (equiv)	Temp (°C)	Time (h)	Yield (%)[b]
1	1	1	80	0.5	90
2	1.35	1.2	80	0.5	100
3	1.2	1.1	80	0.5	98
4	1.2	0.25	80	0.5	92
5	1.2	0.25	60	0.5	79
6	1.2	0.25	60	1	85
7	1.2	0.25[c]	80	0.5	90
8	1.2	0.25[c]	60	0.5	73
9	1.2	0.25[c]	60	1	79
10	1.2	None	80	0.5	39

[a] Reaction conditions: 0.25 mmol of 4-tolylboronic acid (1 equiv) with PVP-I_2 (1:1), $NaNO_2$, 2 mL acetonitrile, temperature and time indicated in table.
[b] Yield by ^1H NMR.
[c] $NaNO_3$ used as sodium salt.

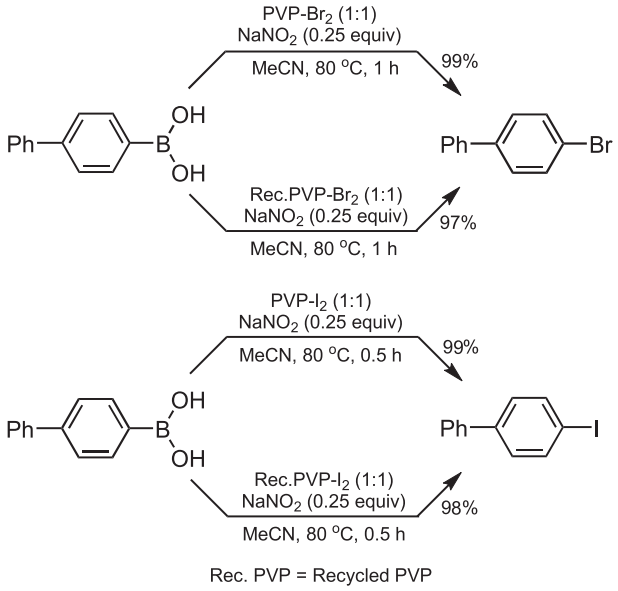
Table 7
ipso-Iodination of arylboronic acids with PVP-I_2 (1:1) complex.[a]

Entry	Substrate	Time (h)	Product	Yield (%)[b]
1		0.5		87
2		1.5		92
3		1.5		94
4		0.5		90
5		5		86
6		8		89
7		8		87
8		9		90
9		25		91
10		0.5		99
11		0.5		99

[a] Reaction conditions: 0.25 mmol of boronic acid, 0.34 mmol of PVP-I_2 (1.2:1) (1.35 equiv) or 0.3 mmol of PVP-I_2 (1:1) (1.2 equiv) in the presence of 0.063 mmol $NaNO_2$ (0.25 equiv) in 2 mL acetonitrile at 80 °C for the time indicated.
[b] Isolated yields.

Conclusions

In summary, we developed a safe and environmentally friendly protocol for the *ipso*-bromination/iodination of arylboronic acids using poly(4-vinylpyridine) supported bromine/iodine complexes. The complexes are free-flowing stable solids and very convenient to handle. Presence of $NaNO_2$ as catalyst promotes the conversion of arylboronic acids bearing various both activated and deactivated functional groups to the corresponding *ipso*-bromo/iodo derivatives with high selectivity and isolated yield. Mild reaction conditions including short reaction times, high yields, easy product-separation as well as purification, and high recyclability of the



Scheme 3. Recycling of poly(4-vinylpyridine) in *ipso*-bromination/iodination reactions using PVP-Br_2/I_2 (1:1).

polymer are the salient features of this methodology. Further studies on the scope of these PVP complexes as safe and efficient "green" reagent system for halogenation in various other synthetic transformations are currently underway.

Acknowledgment

Support by the Loker Hydrocarbon Research Institute, University of Southern California is gratefully acknowledged.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2019.151020.

References

[1] (a) J.F. Hartwig, Angew. Chem. Int. Ed. 37 (1998) 2046–2067;
(b) E. Shirakawa, T. Hayashi, Chem. Lett. 41 (2012) 130–134;
(c) F. Alonso, I.P. Beletskaya, M. Yus, Chem. Rev. 102 (2002) 4009–4091;
(d) G. Cahiez, A. Moyeux, Chem. Rev. 110 (2010) 1435–1462;
(e) N. Miyaura, A. Suzuki, Chem. Rev. 95 (1995) 2457–2483.
[2] (a) T. Wirth, M. Ochiai, A. Varvgolis, V.V. Zhdankin, G.F. Koser, H. Tohma, Y. Kita, Topics in Current Developments in Organic Synthesis, Springer-Verlag, Berlin, 2002;
(b) A. Varvolis, Hypervalent Iodine in Organic Sythesis, Academic Press, London, 1997;
(c) P. Stang, V.V. Zhadankin, Chem. Rev. 96 (1996) 1123;
(d) A. Parra, S. Reboredo, Chem. Eur. J. 19 (2013) 17244–17260.
[3] (a) M.K. Dewanjee, Radioiodination: Theory, Practice, and Biomedical Applications, Kluwer Academic Publishers, Boston, 1992;
(b) R. Weissleder, Science 312 (2006) 1168–1171;
(c) B. Maziere, C. Loch, Appl. Radiat. Isot. 37 (1986) 703–713.
[4] (a) P.B.D. de la Mare, Electrophilic Halogenation, Cambridge University Press, Cambridge, 1976;
(b) J. March, Advance Organic Chemistry, fourth ed., Wiley-Interscience, New York, 2000.
[5] (a) J. Iskra, S. Stavber, M. Zupan, Synthesis (2004) 1869–1873;
(b) N.C. Ganguly, S.K. Barik, S. Dutta, Synthesis (2010) 1467–1472;
(c) K.M. Sosnowski, L. Skulski, Synthesis (2006) 1195–1199;
(d) A.-S. Castanet, F. Colobert, P.-E. Broutin, Tetrahedron Lett. 43 (2002) 5047–5048;
(e) P. Lulinski, L. Skulski, Bull. Chem. Soc. Jpn. 70 (1997) 1665–1669;
(f) P. Lulinski, A. Kryska, M. Sosnowski, L. Skulski, Synthesis (2004) 441–445;
(g) B. Krassowska-Swiebocka, P. Lulinkski, L. Skulski, Synthesis (1995) 926–928;
(h) H.O. Wirth, O. Konigstein, W. Kern, Liebigs Ann. Chem. 42 (1977) 4049;
(i) S. Ahmed, S. Razaq, Tetrahedron 32 (1976) 503;
(j) H. Suzuki, K. Nakamura, R. Goto, Bull. Chem. Soc. Jpn. 39 (1966) 128–131;
(k) H. Suzuki, Bull. Chem. Soc. Jpn. 43 (1970) 481–484;
(l) A. Shimizu, K. Yamataka, T. Isoya, Bull. Chem. Soc. Jpn. 58 (1985) 1611–1612;
(m) A. Bachki, F. Foubelo, M. Yus, Tetrahedron 50 (1994) 5139–5146;
(n) W.-W. Sy, B.A. Lodge, A.W. By, Synth. Commun. 20 (1990) 877–880;
(o) E.B. Merkushev, Synthesis (1988) 923–937.
[6] T. Sandmeyer, Chem. Ber. (1884) 1633–1635.
[7] (a) V.D. Filimonov, N.I. Semenischeva, E.A. Krasnokutskaya, A.N. Tretyakov, H. Y. Hwang, K.-W. Chi, Synthesis (2007) 81–84;
(b) A. Hubbard, T. Okazaki, K.K. Laali, J. Org. Chem. 73 (2008) 316–319.
[8] R.W. Fish, M. Rosenblum, J. Org. Chem. 30 (1965) 1253–1254.
[9] A. McKillop, J.D. Hunt, M.J. Zelesko, J.S. Fowler, E.C. Taylor, G. Mc-Gillivray, F. Kienzle, J. Am. Chem. Soc. 93 (1971) 4841–4844.
[10] E. Negishi, Comprehensive Organometallic Chemistry, G. Wilkinson, F.G.A. Stone, E.W. Abel, ed., Pergamon Press, New York, 1983, Vol. 7, pp 323.
[11] (a) V. Snieckus, Chem. Rev. 90 (1990) 879–933;
(b) S. Dundik, G.C. Fu, J. Am. Chem. Soc. 134 (2012) 10693–10697;
(c) V.J. Olsson, K.J. Szabo, Angew. Chem. Int. Ed. 46 (2007) 6891–6893.
[12] G.W. Kabalka, K.A.R. Sastry, U. Sastry, V. Somayaji, Org. Prep. Proced. Int. 14 (1982) 359–362.
[13] C. Thiebes, G.K.S. Prakash, N.A. Petasis, G.A. Olah, Synlett (1998) 141–142.
[14] (a) J.M. Clough, L.J. Diorazio, D.A. Widdowson, Synlett (1990) 761–762;
(b) N.A. Petasis, I.A. Zavialov, Tetrahedron Lett. 37 (1996) 567–570;
(c) H. Wu, J. Hynes Jr., Org. Lett. 12 (2010) 1192–1195;
(d) W. He, R.-L. Zhang, M.-Z. Cai, RSC Adv. 7 (2017) 764–770.
[15] R.H. Szumigala Jr., P.N. Devine, D.R. Gauthier Jr., R.P. Volante, J. Org. Chem. 69 (2004) 566–569.
[16] G.-Y. Zhang, G.-L. Lv, L.-P. Li, F. Chen, J. Cheng, Tetrahedron Lett. 52 (2011) 1993–1995.
[17] (a) H. Yang, Y. Li, M. Jiang, J. Wang, H. Fu, Chem. Eur. J. 17 (2011) 5652–5660;
(b) Y.L. Ren, X.-Z. Tian, C. Dong, S. Zhao, J. Wang, M. Yan, X. Qi, G. Liu, Catal. Commun. 32 (2013) 15–17;
(c) L. Niu, H. Zhang, H.-J. Yang, H. Fu, Synlett 25 (2014) 995–1000;
(d) R.H. Tale, G.K. Toradmal, V.B. Gopula, A.H. Rodge, R.P. Pawar, K.M. Patil, Tetrahedron Lett. 56 (2015) 2699–2703;
(e) R.H. Tale, G.K. Toradmal, V.B. Gopula, RSC Adv. 5 (2015) 84910–84919.
[18] (a) S.V. Ley, I.R. Baxendale, R.N. Bream, P.S. Jackson, A.G. Leach, D.A. Longbottom, M. Nesi, J.S. Scott, R.I. Storer, S.J. Taylor, J. Chem. Soc. Perkin Trans. I (2000) 3815–4195;
(b) M. Benaglia, A. Puglisi, F. Cozzi, Chem. Rev. 103 (2003) 3401–3427;
(c) A. Kirschning, H. Monenschein, R. Wittenberg, Angew. Chem. Int. Ed. 40 (2001) 650–679;
(d) D.C. Sherington, Polymer-supported Reactions in Organic Synthesis, P. Hodge, D.C. Sherington, ed., Wiley, New York, 1980, pp. 1–82.
[19] B. Tamami, K.P. Borujeni, Iran. Polym. J. 18 (2009) 191–206.
[20] (a) G.A. Olah, T. Mathew, A. Goeppert, B. Torok, I. Bucsi, X.-Y. Li, Q. Wang, E.R. Marinez, P. Batamack, R. Aniszfeld, G.K.S. Prakash, J. Am. Chem. Soc. 127 (2005) 5964–5969;
(b) G.A. Olah, T. Mathew, C. Panja, K. Smith, G.K.S. Prakash, Catal. Lett. 114 (2007) 1–7;
(c) G.K.S. Prakash, S. Chacko, C. Panja, T.E. Thomas, L. Gurung, G. Rasul, T. Mathew, G.A. Olah, Adv. Synth. Catal. 351 (2009) 1567–1574;
(d) G.K.S. Prakash, A. Shakhmin, K.E. Glinton, T. Mathew, G.A. Olah, Green Chem. 16 (2014) 3616–3622;
(e) G.K.S. Prakash, L. Gurung, K.E. Glinton, K. Belligund, T. Mathew, G.A. Olah, Green Chem. 17 (2015) 3446–3451;
(f) G.K.S. Prakash, F. Paknia, A. Kulkarni, A. Narayanan, F. Wang, G. Rasul, T. Mathew, G.A. Olah, J. Fluorine Chem. 171 (2015) 102–112.
[21] (a) L.W. Christensen, D.J. Heacock, Synthesis (1978) 50–51;
(b) Z. Barbara, Z. Marko, Tetrahedron 45 (1989) 7869–7872;
(c) M. Zupan, N. Segatin, Synth. Commun. 24 (1994) 2617–2626;
(d) B. Sket, M. Zupan, Synth. Commun. 19 (1989) 2481–2487;
(e) B. Sket, M. Zupan, J. Org. Chem. 51 (1986) 929–931;
(f) Y. Johar, M. Zupan, B. Sket, J. Chem. Soc. Perkin Trans. I (1982) 2059–2062;
(g) J. Zabicky, M. Mhasalkar, Maromolecules 23 (1990) 3755–3762.