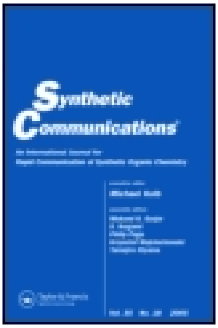

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Oxidative Bromination of Aromatic Compounds Using O-Iodoxybenzoic Acid with Tetraethylammonium Bromide

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Oxidative Bromination of Aromatic Compounds Using *O*-Iodoxybenzoic Acid with Tetraethylammonium Bromide

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Abstract: A mild and selective procedure for the bromination of activated arenes using *o*-iodoxybenzoic acid and tetraethylammonium bromide is presented. The reactions were carried out at room temperature and gave moderate to excellent yields.

Keywords: Bromoarenes, *o*-iodoxybenzoic acid, oxidative bromination, tetraethylammonium bromide

Aryl halides are important synthetic intermediates for a variety of transformations including carbon–carbon bond formation via cross-coupling reactions such as Stille–Suzuki, Heck, and Sonogashira and carbon–heteroatom bond formation via aromatic functionalization protocols.[1] The traditional method for aromatic bromination is electrophilic substitution with molecular bromine.[2] However, despite the widespread use of molecular bromine as an electrophilic reagent, it is a toxic, difficult to handle, low-boiling lachrymatory liquid that causes severe burns on contact with skin.[3] Other reagents used for aromatic brominations are N-halo succinamides, HBr/TBHP (t-butylhydroperoxide) or H_2O_2, quaternaryammonium tribromide, PHP (pyridinium hydrobromide perbromide), $KBr/NaBO_3$, $NaBr/NaClO_2/Mn(acac)_3$/moist montmorillonite, LiBr/CAN (ceric ammoniumnitrate), BuOBr/zeolite, benzyltriphenylphosphonium tribromide, NaBr/dimethyl dioxirane,[4] and bromodimethylsulfonium bromide

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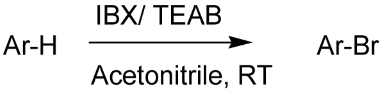


Scheme 1.

(BDMS).[5] Recently, using bromine–dioxane complex under solvent-free conditions, hypervalent iodine reagents[6] such as polymer-supported *o*-iodoxybenzoic acid (IBX) amide with TEAB and $PhI(OAc)_2$ with KBr have been used for aromatic bromination. Despite the many halogenation methods that are available, additional methods for this transformation are still valuable.

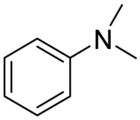
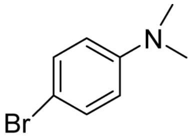
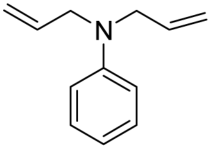
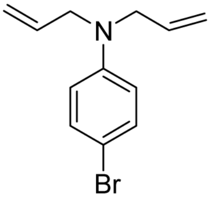
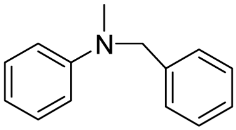
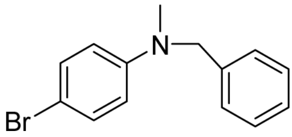
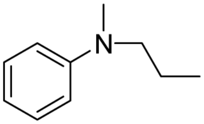
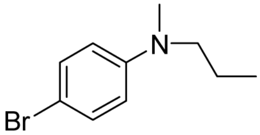
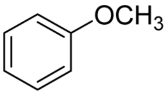
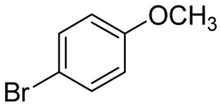
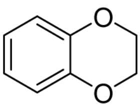
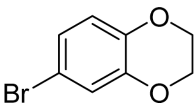
Hypervalent iodine reagents have found widespread applications in organic synthesis because of their selectivity and simplicity in use. Our group has been extensively working on the development of novel methodologies using hypervalent iodine reagents,[7] mainly IBX and Dess–Martin periodinane (DMP). In continuation of our studies on the development of newer applications of hypervalent iodine (λ^5) compounds, herein we report the application of IBX with TEAB for oxidative bromination of aromatic compounds under neutral conditions (Scheme 1).

The method is simple and selective, giving good to excellent yields of brominated products. A series of arenes was selected for attempted bromination. Stoichiometric combination of IBX with TEAB in acetonitrile smoothly brominated a variety of substrates at room temperature (Table 1). Inspection of the results gathered in Table 1 reveals that this combination of reagents is effective for the monobromination of electron-rich aromatics (entries 1–10) and thiophene (entry 11). Additionally, this combination of reagents is capable for the transformation of an *N*,*N*-diallylbenzenamine into the corresponding *N*,*N*-diallyl-4-bromobenzenamine while the alkene group remained unaffected, showing the chemoselectivity of the method (entry 2). When the reaction was performed on *N*-benzyl-*N*-methylbenzenamine, bromination occured at the *para* position of aniline (entry 3). When phenol and aniline were subjected to the reaction conditions, it led to a complex mixture (entries 12 and 13). The substrates containing electron-withdrawing groups such as nitro, ester, and nitrile did not react, indicating the need of electron-donating groups (entries 14–16).

Among the pentavalent iodine reagents, DMP was also studied for this transformation. IBX was found to be the most effective in terms of conversions and reaction rates.

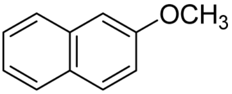
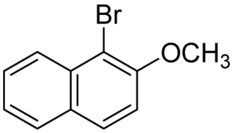
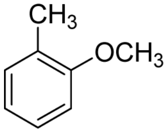
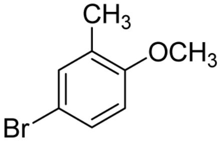
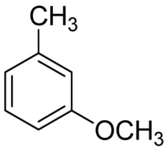
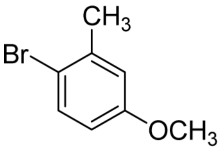
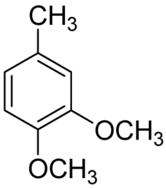
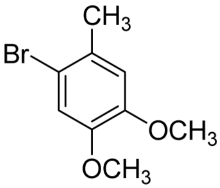
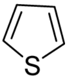
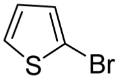
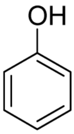
In summary, a simple, chemoselective, and mild method has been developed for oxidative bromination of aromatic compounds by using a combination of IBX with TEAB.

Table 1. Aromatic bromination using IBX with TEAB[a]

Entry	Substrate	Product	Time (min)	yield (%)[b]	Mp
1			10	96	54–55 °C[4b]
2			10	96	Oil[9]
3			10	96	Oil[10]
4			10	95	Oil[10]
5			600	85	Oil[4b]
6			300	92	Oil[6a]

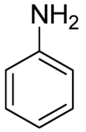
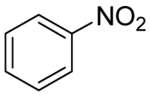
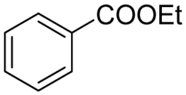
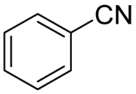
(*Continued*)

Table 1. Continued

Entry	Substrate	Product	Time (min)	yield (%)^b	Mp
7			720	80	80–82 °C[4b]
8			300	92	65–67 °C[5]
9			300	90	Oil[5]
10			60	94	Oil[11]
11			180	92	Oil[8]
12		Complex mixture	5	—	—

(*Continued*)

Table 1. Continued

Entry	Substrate	Product	Time (min)	yield (%)[b]	Mp
13		Complex mixture	5	—	—
14		NR	—	—	—
15		NR	—	—	—
16		NR	—	—	—

[a] Reactions were performed on a 5 mmol scale using 1.1 equiv. of IBX with TEAB. Reactions were monitored by TLC and GC analysis on 5% OV-17 (6′, 1/8″) column and FID detector.

[b] Isolated yields.

EXPERIMENTAL

General Experimental Procedure for Aromatic Bromination

To a stirred suspension of IBX (1.54 g, 5.5 mmol) in CH_3CN (20 ml), TEAB (1.16 g, 5.5 mmol) was added. A yellow suspension was observed to which substrate (5 mmol) was added in one portion after 5 min. The reaction mixture was stirred at room temperature until complete consumption of starting material was observed by thin-layer chromatography (TLC). Acetonitrile was removed under reduced pressure, and the resultant residue was washed with ethyl acetate (25 ml) followed by 10% sodium bisulfite solution (25 ml), saturated sodium carbonate (25 ml), and brine (25 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give the crude product. The pure product was isolated after column chromatography (silica-gel mesh size 60–120, eluent *n*-hexane).

ACKNOWLEDGMENT

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