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Efficient iodination of aromatic compounds using potassium ferrate supported on montmorillonite

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Abstract

Potassium ferrate impregnated on montmorillonite is a mild, cheap, and non-toxic reagent for the iodination of phenols, including naphthol, aromatic amines, and heterocyclic substrates in fair to excellent yields by a simple isolation procedure.

Keywords: Iodination; Heterocyclic and aromatic compounds; Potassium ferrate

Aromatic iodo compounds are widely employed as important chemicals or intermediates in organic synthesis [1]. Iodoarenes are useful intermediates for pharmaceuticals [2] natural products [3] and in carbon–carbon and carbon–heteroatom bond formation *via* cross-coupling reactions [4].

Because of the low reactivity of molecular iodine toward electrophilic reactions, direct iodination of aromatic compounds is more difficult than other halogens. This problem is overcome by activating iodine for electrophilic substitution by the use of iodonium equivalents (I^+) or catalysts and oxidants in conjunction with iodine that generate electrophilic iodine (I) species [5].

Many methods have been reported for efficient nuclear iodination of aromatic compounds, however, most of them involve the use of toxic elements such as, I_2/CrO_3 [6], $I_2/Hg(NO_3)_2$ [7], $I_2/Pb(OAc)_4$ [8] and $I_2/Ce(OTf)_4$ [9].

It has been reported that efficiency of potassium ferrate could be increased when it was supported on clay mineral or silica gel [10,11]. The solid-supported reagent was used for variety of organic transformation in an effective manner [11]. Due to the attributes described above for the use of supported potassium ferrate and our current interest in developing new iodination procedures we reveal herein for the first time, using potassium ferrate impregnated on montmorillonite, as a safe, inexpensive, easy to handle, and convenient oxidative source. In this note we wish to report that K_2FeO_4 supported on montmorillonite (K-10) allows the iodination reaction of several activated aromatics, including anilines, alkyl benzenes and phenols to yield the corresponding iodinated products in good to excellent yields. Our results are summarized in Table 2. The reagent is prepared by simple mixing of commercially available montmorillonite and potassium ferrate in a weight ratio of 1:2 by mortar.

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Table 1
Optimization of anisole iodination using 1 mmol K_2FeO_4 and different ratio of K-10/I_2 under various conditions at reflux temperature.

Entry	Solvent	K-10 (g)	Time (h)	GC yield[a](%)
1	dichloromethane	0.4	3	15
2	chloroform	0.4	3	20
3	diethyl ether	0.4	3	–
4	acetonitrile	0.4	3	–
5	benzene	0.4	3	60[b]
6	*n*-pentane	0.4	3	93
7	*n*-hexane	0.2	8	36
8	*n*-hexane	0.4	3	95
9	*n*-hexane	0.6	2.5	93

[a] Isolated yields.
[b] Iodobenzene was monitored.

In initial studies, we examined anisole as a model substrate (Table 1). For establishing the best reaction conditions, an optimization study was performed using the reaction of anisole in the presence of varying amounts of potassium ferrate and K-10. Along this line, potassium ferrate (1 mmol) and montmorillonite (0.4 g) in hexane gave the best yield of the desired product within 3 h (GC analysis). Workup of the reaction mixture resulted in the corresponding 4-iodoanisole with excellent regioselectivity and in excellent isolated yield (95%).

The amount of potassium ferrate can greatly affect the yield of 4-iodoanisole, and improves by increasing the equivalents of potassium ferrate, and reaches to the maximum level on 0.5 mmol. Study about the effect of K_2FeO_4 to the K-10 weight ratio, the iodination reaction was carried out with increasing amounts of K_2FeO_4, however, a 1:2 potassium ferrate: K-10 weight ratio was required in order to achieve a quantitative conversion of anisole within a few hours. It is noteworthy that with increasing the K-10 to K_2FeO_4 weight ratio, the yield of 4-iodoanisole was not significantly affected. The effects of solvents were examined and further improved rates of conversion were achieved when the reactions were carried out in pentane or hexane.

The generality of this approach was established on a series of activated aromatics along with some heterocyclic compounds as presented in Table 2. It is important to notice that trace amounts of water accelerates the transformation

Table 2
Iodination of various aromatic compounds with K_2FeO_4/K-10/I_2 in *n*-hexane.

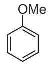
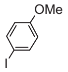
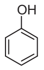
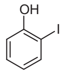
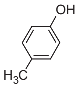
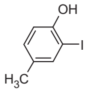
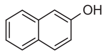
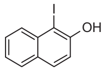
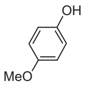
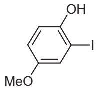
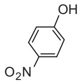
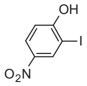
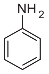
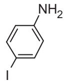
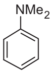
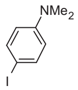
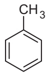
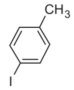
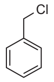
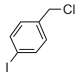
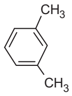
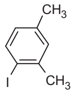
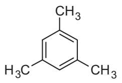
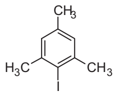
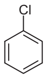
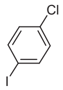
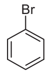
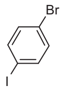
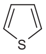
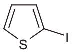
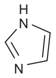
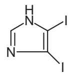
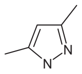
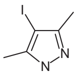
Entry	Substrate	Product	Time (min)	Yield (%)	mp (litre) (°C)
1			110	95	48–49 (53–54) [12a]
2			140	85[a]	40–41 (43–44) [12b]
3			120	95	Oil (oil) [12c]
4			120	77	88–90 (91–92) [12d]
5			110	92	61–62 (63.5–64.5) [12e]
6			150	81	85–87 (90–91.5) [12f]
7			90	88	62–63 (64–65) [12g]

Table 2 (*Continued*)

Entry	Substrate	Product	Time (min)	Yield (%)	mp (litre) (°C)
8			100	82	77–78 (76.5–78.5) [12d]
9			140	95	Oil (oil) [12h]
10			190	76	52–53 (53) [12i]
11			150	85	Oil (oil) [12j]
12			180	95	30–31 (30–31) [12k]
13			600	25	54–55 (54.5) [12l]
14			600	40	90–91 (90) [12l]
15			360	73	bp 180–182 (bp 180–182) [12m]
16			520	50	190–191 (191–192) [12n]
17			150	85	133–135 (134–136) [12o]

[a] The ratio of *ortho*: *para* is about 90:10.

and improves its efficiency and in some cases iodination was not occurred in the absence of water (Table 2, entries 4, 8, 14 and 15). These results are consistent with Laszlo's and Caddick's observations that the presence of water is important [10,11]. In all cases the reaction proceeds to completion in a short period affording good to excellent yield with a higher preference for monosubstitution, which occurs mainly on the *para* position. Interestingly, regioselective iodination was observed in the case of phenol to give 2-iodophenol in 85% yield (Table 2, entry 2). Other phenolic compounds were also iodinated under similar conditions (entries 3–6). The reagent was also successful in converting 4-nitrophenol to the corresponding iodo derivative (entry 6). In the case of *p*-methoxyphenol (entry 5) where this *para* substitution is prohibited, it is worth noticing that the regioselectivity is governed by the hydroxy group.

Iodinations of aniline, *N*, *N*-dimethylaniline were also completed in a short reaction time (90 and 100 min, respectively) and the mono-iodinated *para* isomers were obtained in 88 and 82% isolated yields plus their corresponding *ortho* isomers, which were isolated in 10–15% yields (entries 7–8). The present method can be applicable to alkylbenzenes, and the corresponding monoiodination product was obtained in good yield (entries 9 and 10). Di- or tri-substituted benzenes such as 1,3-dimethylbenzene (entry 11) and 1,3,5-trimethylbenzene (entry 12) also reacted to give the corresponding monoiodination products. Iodinations of chlorobenzene and bromobenzene as less reactive arenes were also studied. Progress of the reactions was monitored by GC analysis whereby, after 10 h only 25 and 40% yields were observed, respectively (entries 13 and 14).

Also, monoiodination of an activated heterocycle, thiophene (entry 15) was obtained, while, imidazole was mostly diiodinated by this system (entry 16). The iodination of 3,5-dimethylpyrazole produced 4-iodo-3,5-dimethylpyrazole in 85% isolated yield as the sole product after 2.5 h together with unreacted starting material (entry 17). Attempted iodination of nitrobenzene with K_2FeO_4/K-10 under similar reaction conditions failed and the starting material was isolated intact after 12 h.

The other unusual results were observed when 1-naphthol and 2-naphthol used as substrates. Surprisingly, 1-naphthol was remained almost unchanged under same protocol while 2-naphthol converted to desired product 1-iodo-2-naphthol in good yield. These results encouraged us to carry out a competition experiment and we found that iodination of a mixture of 1-naphthol and 2-naphthol led to almost exclusive formation of 1-iodo-2-naphthol (70%) with very little 4-iodo-1-naphthol formed (5%).

In conclusion, we have established potassium ferrate impregnated on K-10 as an efficient and eco-friendly oxidant for regioselective monoiodination under mild conditions. The ease of this present protocol is expected to make this methodology a good alternative to well-known methods, since the iodination proceeds in high yields. To develop the synthetic utility of this method, its applications to other heterocycles are being pursued.

Typical procedure for iodination of anisole: To a mixture of Iodine (0.127 g, 0.5 mmol) and K-10 (0.4 g) in *n*-hexane (10 mL), K_2FeO_4 (0.5 mmol), anisole (0.108 g, 1 mmol) was added and the mixture was heated to reflux temperature for the time specified in Table 2. The progress of the reaction was monitored by GC or TLC. The reaction mixture was filtered and treated with 10% aqueous sodium thiosulfate solution (10 mL). The resulting mixture was dried over anhydrous $MgSO_4$ and filtered. Evaporation of the solvent resulted in the crude product was further purified by column chromatography to afford 4-iodoanisole in 95% yield (Table 2, entry 1). Then similar reaction conditions were applied for the iodination at reflux temperature.

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