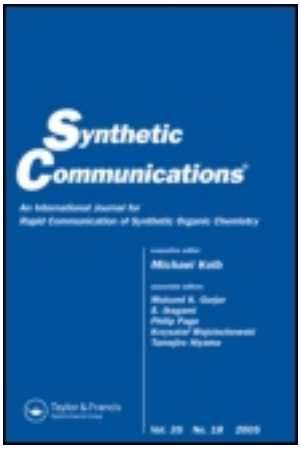

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Convenient and Efficient Method for the Iodination of Aromatic Amines by Pyridinium Iodochloride

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Convenient and Efficient Method for the Iodination of Aromatic Amines by Pyridinium Iodochloride

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Abstract: A simple and efficient method for the iodination of aromatic amines using pyridinium iodochloride (PyICl) in methanol as solvent is reported. Mild reaction conditions, short reaction time, and good to excellent yields of the product are the noteworthy advantages of the method. Pyridinium iodochloride is an efficient solid iodinating reagent and can be handled safely.

INTRODUCTION

Aromatic iodides have long been used in organic synthesis as versatile intermediates that can be transformed to variety of functional groups.[1] They can be easily functionalized through metal-catalyzed cross-coupling reactions[2] in the synthesis of many interesting natural products[3] and also bioactive material.[4] Iodoaromatic compounds are used in medicine as drug or diagnostic aids, contractors,[5] and radioactively labelled markers.[6] They also have importance in medicinal and pharmaceutical research.[7]

In recent years, direct iodination methods have been intensively developed using iodinium donating systems, such as iodine nitrogen dioxide,[8] iodine-F-TEDA-[1-chloromethyl-4-fluoro-1, 4-diazoniabicyclo [2,2,2] octane-bis-(tetrafluoroborate)][9] bis-*N*-iodosuccinimide,[10] iodine-di-iodine pentaoxide,[11] mercury(II)-oxide-iodine,[12] iodine monochloride,[13] bis(pyridine)iodonium(I)

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tetrafluorobrate CF_3SO_3H,[14] NIS-CF_3SO_3H,[15] iodine silver sulfate,[16] iodine-mercury salts,[17] NaOCl-NaI,[18] iodine/$Na_2S_2O_8$,[19] and iodine-$(NH_4)_2S_2O_8$-$CuCl_2$-Ag_2SO_4.[20]

Recently, in our previous communication, iodination of aromatic compounds has been done by iodine and iodine acid as iodinating agents.[21,22] We report here iodination of several aromatic amines using pyridiuium iodochioride as iodinating agent.

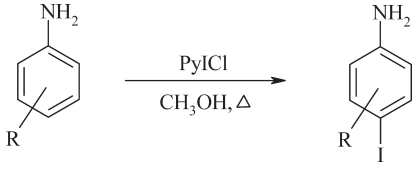
The advantages of this method are easy preparation of reagent, no need of catalyst, mild conditions, simple operation, and short reaction time with excellent yield of product. Because the reagent is solid, it can be easily weighted, has no hazardous effect, and is ecofriendly.

To illustrate the advantage of the proposed reagent, we chose several reactive aromatic amines (Scheme 1). These reactions were carried out by heating amines with pyridinium iodichloride on a water bath for 1 h using methanol as solvent. A variety of reactive aromatic amines were investigated for a reaction with PyICl (Table 1). The product was obtained in a regioselective manner, with iodination occurring at the electron-rich *ortho* or *para* positions. When the *ortho* position was blocked with substituent, only iodination took place at the *para* position.

EXPERIMENTAL

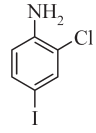
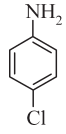
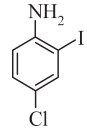
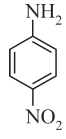
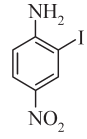
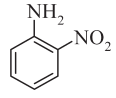
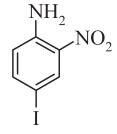
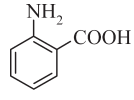
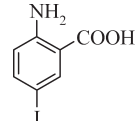
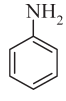
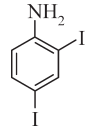
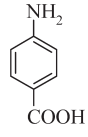
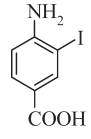
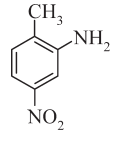
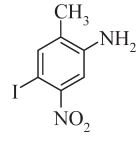
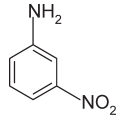
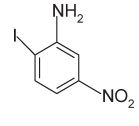
General Procedures

Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer spectrometer. ^{1}H NMR spectra were recorded on a Gemini 300-MHz instrument in $CDCl_3$ as solvent and TMS as an internal standard. Elemental analysis was carried out on a Carlo Erba 1108 analyzer. All the products were identified by comparison of their spectral and physical data with those of the known sample. The purity of products was checked by thin-layer chromatography (TLC) on silica-gel on silica gel polygram SIL UV 254 plates. All amines and other chemicals were purchased from Merck Chemical Company.



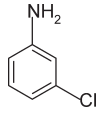
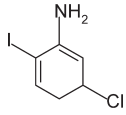
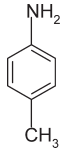
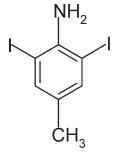
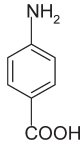
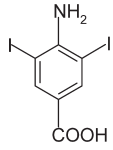
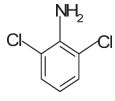
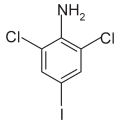
Scheme 1.

Table 1. Physical and analytical data of iodoanilines

Sr. no.	Substrate	Product	Yield	Mp (°C) found (reported)
1			75	70 (70–73)[23]
2			90	40 (39–43)[24]
3			85	116 (115)[25]
4			83	122 (123)[26]
5			80	207 (208)[27]
6			85	95 (95–96)[23]
7			92	254 (259)[28]
8			78	77 (78)[29]
9			84	120

(*continued*)

Table 1. Continued

Sr. no.	Substrate	Product	Yield	Mp (°C) found (reported)
10			89	58
11			76	120
12			77	255
13			81	80

Preparation of Pyridinium Iodochloride

To a solution of pyridine (7.9 g, 0.1 mol) in acetic acid, a solution of iodine monochloride (16 g, 0.1 mol) in acetic acid was added slowly at 0 °C with continuous stirring. The pale yellow solid obtained was filtered, dried, and recrystallised by ethyl alcohol. The purity of reagent was checked by thin-layer chromatography (TLC).

General Procedure for Iodination of Aromatic Amines by Pyridinium Iodochloride

Aromatic amine (1 mmol) and pyridinium iodochloride (1 mmol) were dissolved in methanol (15 mL) and refluxed on a water bath for 1 h. The dark yellow colors appeared in reaction mixture; the content was poured in ice-cold water. The solid thus obtained was filtered and recrystallized from ethanol.

IR and ^{1}H NMR Data of the Iodinated Products

2-Iodo, 5-nitroaniline: IR (cm^{-1}): 3355 (NH); 1611, 1550 (C═C). ^{1}H NMR ($CDCl_3$) δ: 4 (dd, 1H, 4 Ar-H), 7 (dd, 1H, 4 Ar-H). Anal. calcd. for

$C_6H_5IN_2O_2$: C, 27.26; H, 1.89; I, 48.10; N, 5.33. Found: C, 27.20; H, 1.81; I, 48.23; N, 5.25.

2-Iodo, 5-chloroaniline: IR (cm^{-1}): 3311 (NH); 1604, 1518 (C═C). ^1H NMR ($CDCl_3$) δ: 4 (s, 2H, NH_2), 7.4 (s, 1H, 2 Ar-H). Anal. calcd. for C_6H_5ICIN: C, 2845; H, 1.97; I, 50.19; N, 5.33. Found: C, 2834; H, 1.88; I, 50.30; N, 5.19.

2,5-Diodo, 4-methylaniline: IR (cm^{-1}): 3319 (NH), 1610, 1578 (C═C). ^1H NMR ($CDCl_3$) δ: 2.2 (S, 3H, CH_3), 4.25 (S, 2H, NH_2), 7.5 (S, 2H, 2 and 6 Ar-H). Anal. calcd. for $C_7H_7I_2N$: C, 23.39; H, 1.94; I, 70.75; N, 3.59. Found: C, 23.49; H, 1.82; I, 70.67; N, 3.48.

4-Amino, 3-5-Diiodobenzoic acid: IR (cm^{-1}): 3345 (NH); 1609, 1546 (C═C). ^1H NMR ($CDCl_3$) δ: 4.65 (S, 2H, NH), 7.85 (S, 2H, 3,5 Ar-H). Anal. calcd. for $C_7H_5I_2NO_2$: C, 23.59; H, 1.28; I, 65.29; N, 3.59 Found: C, 23.47; H, 1.22; I, 65.34; N, 3.42.

2,5-Dichloro, 4-Iodoaniline: IR (cm^{-1}): 3355 (NH); 1611, 1550 (C═C). ^1H NMR ($CDCl_3$) δ: 7.2 (dd, 1H, 4 Ar-H), 7 (dd, 1H, 4 Ar-H). Anal. Calcd. for $C_6H_4ICl_2N$: C, 25.01; H, 1.38; I, 44.09; N, 4.86. Found: C, 25.15; H, 1.43; I, 44.11; N, 4.73.

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