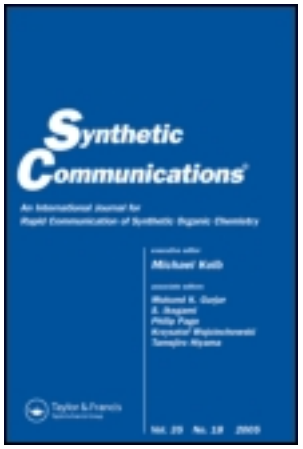

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A PRACTICAL IODINATION OF AROMATIC COMPOUNDS BY USING IODINE AND IODIC ACID

Avinash T. Shinde,[1] Sainath B. Zangade,[2] Shivaji B. Chavan,[2] Archana Y. Vibhute,[2] Yogesh S. Nalwar,[2] and Yeshwant B. Vibhute[2]

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This article describes simple and efficient method for the iodination of different aromatic amines, hydroxy aromatic aldehydes, hydroxy acetophenones and phenols using iodine and iodic acid in ethanol as a solvent. Notable advantages include mild reaction condition, no need of catalyst, short reaction time, simple practical procedure, giving excellent yield of the product.

Keywords: Aromatic compounds; iodination; iodine and iodic acid

INTRODUCTION

The different aromatic compounds have been the subject of numerous studies due to their organic synthesis as versatile intermediate that can be transformed to variety of functional groups.[1] Aromatic iodo compounds can be easily functionalized through metal-catalyzed cross-coupling reactions[2] in the synthesis of many interesting natural products[3] and bioactive material.[4] Iodoaromatic compounds are used in medicine as drug or diagnostic aids, contractors,[5] and radioactively labeled markets.[6] They also have important in medicinal and pharmaceutical research.[7] The chemistry dealing with selective introduction of an iodine atom into organic molecules thus attracted broad interest in the wider specific community.

Recently direct iodination methods have been intensively developed using iodonium donating system, 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] trichloroisocyanuric acid/I_2/Wet SiO_2,[11] mercury(II)–oxide-iodine,[12] iodine-monochloride,[13] bis(pyridine)iodonium(I), tetrafluoroborate CF_3SO_3H,[14] NIS-CF_3SO_3H,[15] iodine silver sulfate,[16] iodine-mercury salts,[17] NaOCl-NaI.[18] However, most of these methods are hazardous or toxic, involve costly reagents, require high reaction temperatures or demand a long reaction time.

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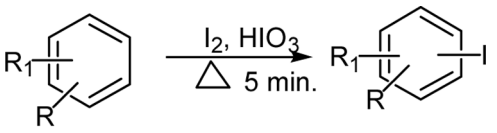


R = NH_2, CHO, $COCH_3$, OH
R1 = Cl, F, NO_2, COOH, OH,
Br, C_6H_5, OC_2H_5, CH_3

Scheme 1. Iodination of aromatics.

In our recent communication, iodination of aromatic compounds has been done using iodine and iodic acid as iodinating agent in solvent ethanol by stirring method,[19,20] requiring nearly 2 h for complete iodination. Therefore, there is a need for a method that may be more effective, safer, and faster, giving quantitative yield of Iodo compound.

We report here in a simple practical procedure of iodination. An advantages of this method are procedural simplicity, no need of catalyst, clean work up, short reaction time, and nearly quantitative yield.

To illustrate the advantages of the present method, we have chosen different reactive hydroxy aromatic aldehydes, hydroxy acetophenones and phenols. Substrate and iodine were dissolved in 95% ethanol, added to it iodic acid dissolved in minimum amount of water, and refluxed on a water bath for 5 min. on cooling crystalline product separated out. Iodination occurs at the electron-rich center.

Structures of the compounds were confirmed by taking mixed melting points with authentic sample or by spectral and elemental analysis (Scheme 1).

EXPERIMENTAL

General Procedure

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. The purity of products was checked by thin-layer chromatography (TLC) on silica-gel.

General Procedures for Iodination of Aromatic Amines, Hydroxy Aromatic Aldehydes, Hydroxy Acetophenones, and Phenols

Aromatic Compounds (50 mmol), iodine (20 mmol) dissolved in ethanol (20 ml) by warming, iodic acid (10 mmol) dissolved in water (1 ml) was added with shaking and refluxed on boiling water bath for 5 min. on cooling solid separated out. Obtained solid product was filtered and crystallized from ethanol. Purity of compound was checked by TLC. Physical and analytical data are given in Tables 1–4.

Table 1. Physical and analytical data of iodo amines

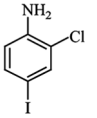
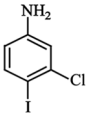
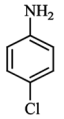
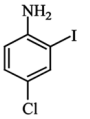
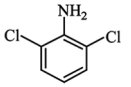
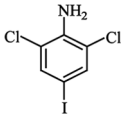
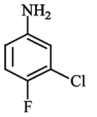
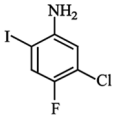
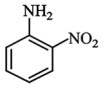
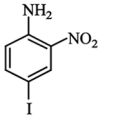
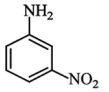
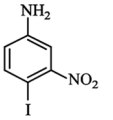
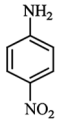
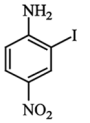
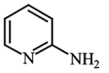
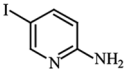
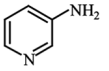
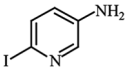
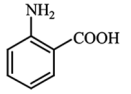
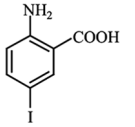
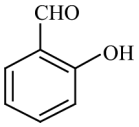
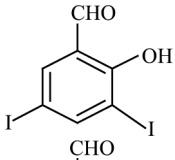
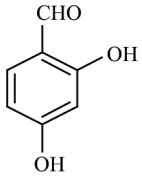
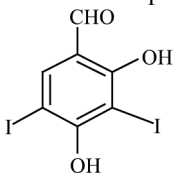
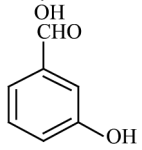
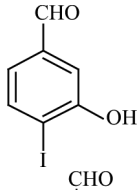
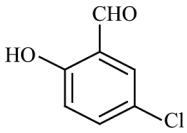
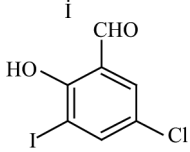
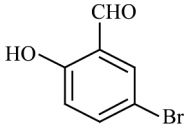
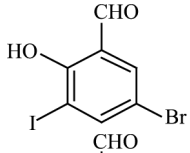
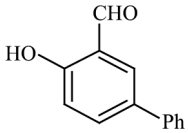
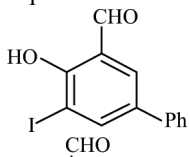
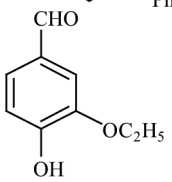
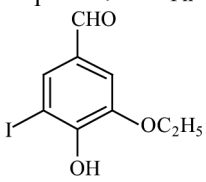
Sr. No.	Substrate	Product	Yield	Mp (°C) Found (Reported)
1.			75	65 (65)[21]
2.			80	60 (58)[21]
3.			75	39 (39–41)[21]
4.			81	87 (80)[21]
5.			75	180 (180)[22]
6.			85	120 (122–123)[21]
7.			80	122[21]
8.			85	115 (116)[21]
9.			85	130 (128–131)[22]
10.			75	67 (65–70)[22]
11.			60	220 (220–225)[21]

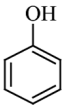
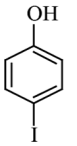
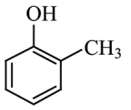
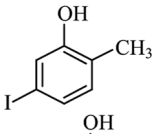
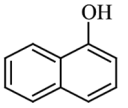
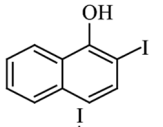
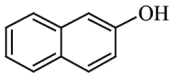
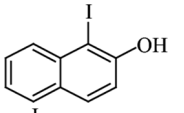
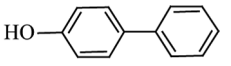
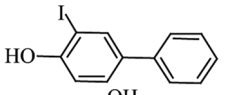
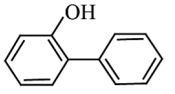
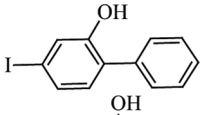
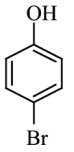
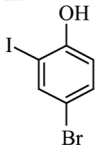
Table 2. Physical and analytical data of iodo hydroxy aromatic aldehydes

Sr. No.	Substrate	Product	Yield	Mp (°C) Found (Reported)
1.			82	110 (110)[23]
2.			70	172 (172)[23]
3.			78	182 (180)[24]
4.			85	76 (78)[23]
5.			68	80 (81)[23]
6.			57	135 (136)[24]
7.			75	184 (185)[25]

Spectral Data of Selected Compounds

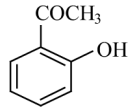
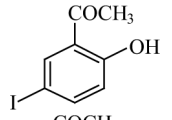
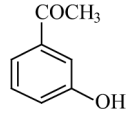
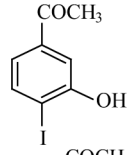
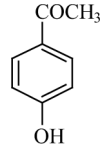
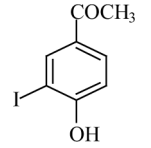
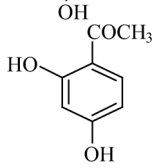
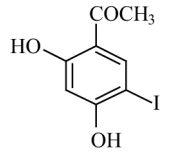
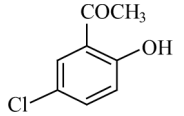
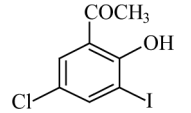
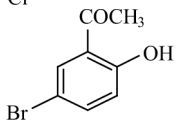
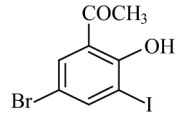
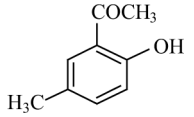
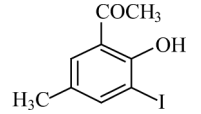
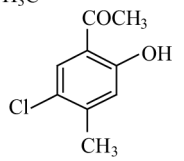
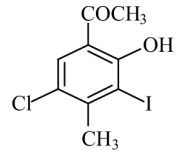
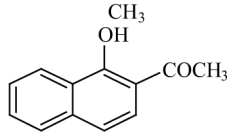
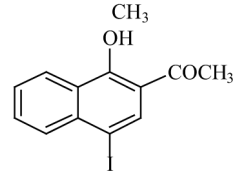
1. **2-Iodo-4-nitroanline:** IR (cm^{-1}): 3355 (NH); 1611, 1550 (C=C) ^1H NMR($CDCl_3$) δ: 4(s, 2H, NH_2), 7.39 (dd, 1H, 3Ar-H). Anal. calcd. for $C_6H_5IN_2O_2$: C, 27.26; H, 1.89; I, 48.10; N, 5.33. Found: C, 27.20; H, 1.81; I 48.23; N, 5.25.
2. **2-Iodo-4-chloroaniline:** IR (cm^{-1}) 3311 (NH); 1604, 1518 (C=C) ^1H NMR ($CDCl_3$) δ: 4 (S, 2H, NH_2), 7.42 (S, 1H, 3Ar-H). Anal. calcd. for C_6H_5ICIN: C, 28.45; H, 1.97; I, 50.19; N, 5.33. Found: C, 28.34; H, 1.88; I, 50.30; N, 5.19.

Table 3. Physical and analytical data of iodo-phenols

Sr. No.	Substrate	Product	Yield	Mp (°C) Found (Reported)
1.			72	43 (42–44)[22]
2.			78	100 (105–110)[22]
3.			76	103 (103)[22]
4.			82	108–110[22]
5.			84	125 (115–119)[22]
6.			76	120–122[22]
7.			85	90[22]

3. **2,6-Dichloro-4-iodoaniline**: IR (cm^{-1}) 3355 (NH); 1611, 1550 (C=C).^{1}H NMR ($CDCl_3$) δ: 4.05 (s, 2H, NH_2), 7.3 (s, 2H, 3 and 5Ar-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, 4.730.
4. **2-Hydroxy-3,5-diiodobenzaldehyde**: IR (cm^{-1}) 2845 (C-H of CHO), 2719 (C-H of CHO); 1658 (C=O); 1587 (C=C);^{1}H NMR ($CDCl_3$) δ: 8.01 (s, 1H; 6Ar-H), 8.13 (S, 1H; 4Ar-H); 9.97 (s, 1H, CHO), 11.82 (s, 1H, OH). Anal. calcd. for $C_7H_4I_2O_2$: C, 22.45; H, 1.06; I, 67.91; Found: C, 22.34; H, 1.72; I, 67.83.
5. **2,4-Dihydroxy-3,5-diiodobenzaldehyde**: IR (cm^{-1}) 2811 (C-H of CHO); 1648 (C=O); 1575 (C-C); ^{1}H NMR ($CDCl_3$) δ: 7.86 (s, 1H, 6ArH), 8.38 (s, 1H, OH), 11.85 (s, 1H, OH), 10.05 (s, 1H, CHO), Anal. Calcd. for $C_7H_4I_2O_3$, C, 21.53; H, 1.02; I, 65.12. Found: C, 21.49; H, 1.12; I, 65.19.
6. **4-Hydroxy-5-iodo-3-methoxybenzaldehyde:** IR (cm^{-1}) 2827 (C-H of CHO); 2739 (C-H of CHO); 1666 (-C=O); 1585 (C=C); ^{1}H NMR ($CDCl_3$) δ: 3.98 (s, 3H, OCH_3), 7.34 (s1H, 2Ar-H), 7.58 (s, 1H, 6Ar-H), 8.06 (s, 1H, OH), 9.98 (s, 1H, CHO). Anal. calcd. for $C_8H_7IO_3$; C, 34.53; H, 2.51; I, 45.68. Found: C, 34.48; H, 2.41; I, 45.72.

Table 4. Physical and analytical data of iodo hydroxy acetophenones

Sr. No.	Substrate	Product	Yield	Mp (°C) Found (Reported)
1.			84	140 (132)[23]
2.			85	155
3.			80	165 162[23]
4.			85	177 178[23]
5.			82	89 90[23]
6.			78	105 104[23]
7.			86	90[23]
8.			92	76[23]
9.			90	156

7. **5-Bromo-2-hydroxy-3-iodoacetophenone:** IR (cm^{-1}) 1635 (C=O); 1580 (C=C); ^1H NMR ($CDCl_3$) δ: 6.93 (s, 1H, 4Ar-H), 7.28 (s, 1H, 6Ar-H), 12.85 (s, 1H, OH). Anal. Calcd. for $C_8H_6BrIO_2$: C, 28.15; H, 1.75; X, 59.65. Found: C, 28.07; H, 1.62; X, 60.31.

8. **2,4-Dihydroxy-3,5-diiodoacetophenone**: IR (cm^{-1}) 1640 (C=O); 1570 (C-C); ^1H NMR ($CDCl_3$) δ:2.68 (s, 3H, $COCH_3$), 8.68 (s, 1H, 6Ar-H), 8.35 (s, 1H, OH), 11.82 (s, 1H, OH). Anal. Calcd. for: $C_8H_6I_2O_3$: C, 23.76; H, 1.48; X, 62.87. Found: C, 23.69; H, 1.71; X, 62.89.
9. **5-Chloro-2-hydroxy-3-iodo-4-methylacetophenone:** IR (cm^{-1}) 1645 (C=O), 1570 (C-C). ^1H NMR ($CDCl_3$) δ: 2.15 (s, 3H, CH_3), 2.68 (s, 3H, $COCH_3$), 8.69 (s, 6H, Ar-H), 11.85 (s, 1H, OH). Anal. Calcd. for $C_9H_8ClIO_2$: C, 34.83; H, 2.5; X, 52.33. Found: C, 34.79; H, 2.41; X, 51.94.

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