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Iodination of industrially important aromatic compounds using N-iodosuccinimide by grinding method

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Abstract: Iodination of various industrially and pharmaceutically important substituted aromatics has been achieved using N-iodosuccinimide (NIS) in solid state by grinding at room temperature. This method provides several advantages such as short reaction time (5–8 min), high yields (94–99%), and nonhazardous and simple work-up procedure. High gas chromatography (GC) purity (95–99.9%) suggests that the reaction is highly selective. Substrates which are sensitive to oxidation, viz aniline and phenols are iodinated smoothly in high yield.

Keywords: aromatic; catalysis; iodoarenes; regiospecific.

1 Introduction

Aromatic iodides are important intermediates for the synthesis of various pharmaceutical and bio-active materials [1]. However, the low electrophilic nature of molecular iodine compared to molecular bromine and chlorine makes direct iodination difficult [2]. Thus, iodination of aromatic substrates requires the presence of a mediator such as a strong oxidizing agent [3–10], i.e. (IO_3^- anions, silver complexes, nitric acid, sulfuric acid, iodic acid, sulfur trioxide, H_2O_2 and NaOCl), and use of activators such as toxic heavy metals [11] (lead, mercury and chromium). Iodination of organic compounds has been reviewed by Frota et al. [12]. However, most of these procedures have the drawback of poor yields, long reaction time, harsh reaction conditions, and use of hazardous or toxic reagents, hence questioning the suitability for commercial production. N-iodosuccinimide (NIS) is a potential source of iodonium ions, and has been used

along with p-toluenesulfonic acid, trifluoromethanesulfonic acid and trifluoroacetic acid [13–15]. The presence of p-toluenesulfonic acid needs a low temperature, long reaction time (14 h) and leads to a mixture of isomeric products. The use of trifluoromethanesulfonic acid results in low yield (17–79%). The trifluoroacetic acid in acetonitrile takes 1.5–6 h. These procedures require the use of expensive and toxic acids and acetonitrile as solvent. It is also known that NIS exhibits maximal activity in strongly acidic medium [16]. However, the system $\text{NIS}-\text{H}_2\text{SO}_4$ shows lower yield and low selectivity [17, 18]. Keeping the aforesaid literature data in mind, a new system using substrate, NIS (1:1 ratio) in acetic acid, at room temperature has been evaluated. This reaction gave 91–99% yield in 30–240 min. It is a clean organic reaction process which does not use harmful organic solvents and hence is in great demand today [19]. Recently, the grinding technique has been tried in synthetic organic chemistry [20]. This is because molecules in the crystals are arranged tightly and regularly [21]. Furthermore, the solid state reaction has many advantages: little pollution, low cost, and simplicity in progress and handling [22]. In the present method we report a simple and clean method for iodination of organic compounds of industrial significance at room temperature, short duration (5–7 min) and high yields (94–99%). Acetic acid was used as a catalyst.

2 Materials and methods

2.1 General

Products were characterized by comparison with standard samples using spectral techniques, Fourier-transform infrared (FTIR) spectroscopy, ^1H nuclear magnetic resonance (NMR) and gas chromatography-mass spectrometry (GC-MS). The ^1H NMR spectra were recorded using a 400 MHz Bruker Avance II 400 NMR spectrometer in $\text{CDCl}_3/\text{DMSO}$ and are reported in ppm using tetramethylsilane as an internal standard. The FTIR spectra were recorded on a Prestige 21 FTIR spectrometer (Shimadzu). The FTIR spectra were recorded in the range 4000–450 cm^{-1} in KBr. The UV spectra were recorded on a UV-1800 double beam UV-visible spectrometer (Shimadzu) in the wavelength range 190–1100 nm. GC-MS analyses were recorded on a GCMS QP 2010 plus (Shimadzu, Japan). The column used was

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Rtx-5 Sil. The GC-MS and mass scanned in the range 5–350 amu. The GC-MS purity is reported by area percentage (%).

2.2 General procedure for iodination

2.2.1 Preparation of 2,6-diiodo-4-nitrophenol (1.n) (conventional method): NIS (0.0039 mol) in AcOH (5 ml) was added into a 100 ml round bottom flask, and to the resulting solution, 4-nitrophenol (4-NP) (0.0019 mol) was added rapidly. Finally, the reaction mixture was stirred at 25°C and the reaction was monitored using thin-layer chromatography (TLC). After completion of the reaction (240 min) the mixture was poured into ice-cold water to precipitate the product. The precipitated mass was separated from the mother liquid by vacuum filtration utilizing a Buchner funnel and then washed twice with deionized water and dried. The total isolated yield was 0.72 g (97%).

2.2.2 Preparation of 2,6-diiodo-4-nitrophenol (1.n) (grinding method): 4-NP (0.0019 mol), NIS (0.0039 mol) and 0.5 ml of AcOH as a catalyst were mixed in a mortar. Finally, the reaction mixture was grounded together in a mortar using a pestle at room temperature (25°C) and monitored by TLC. After completion of the reaction (5 min) the mixture was poured into ice-cold water to precipitate the product. The precipitated mass was separated from the mother liquid by vacuum filtration utilizing a Buchner funnel and then washed twice with deionized water and dried. The total isolated yield was 0.725 g (98%) with a GC-MS purity of 98.06%.

2.2.3 Preparation of 2-iodo-4-nitroaniline (1.a): The procedure was the same as given in general procedure (2.2.2). The reactant NIS (1 mol) with 4-nitroaniline (0.27 g, 0.0019 mol) and 0.5 ml of AcOH was used as a catalyst. The reaction was monitored by TLC. The isolated yield was 0.515 g (99%).

2.2.4 Preparation of 2,4,6-triiodoaniline (1.i): Here, 3 mol equivalent of NIS was taken wrt 1 mol equivalent of aniline and the reaction procedure was the same as general procedure (B). The total isolated yield was 0.913 g (97%) with GC purity of 95.33%.

2.3 Spectral data of different compounds

2.3.1 2,6-Diiodo-4-nitrophenol (1.n): Yellow crystal, mp 155°C, lit. 154–157°C [23]. ¹H NMR (400 MHz, CDCl₃) δ: 8.60(s, 2H). MS (APCI): calcd. for C₆H₂NO₃I₂ [M] + 390.90; found, 391.

2.3.2 2-Iodo-4-nitroaniline (1.a): Orange powder, mp 106°C, lit. 106–107°C [24]. IR (KBr) cm⁻¹: 3477, 3371, 1608, 1579, 1489, 1303, 1257, 1151, 1114, 1029. ¹H NMR (400 MHz, DMSO) δ: 8.50(d, 1H, Ar-H), 8.00(dd, 1H, Ar-H), 6.7(d, 1H, Ar-H) ppm. MS (APCI): calcd. for C₆H₆N₂O₂I [M] + 264.022; found, 264.

2.3.3 2,4,6-Triiodoaniline (1.i): Dark powder, mp 185°C, lit. 185°C [25]. IR (KBr) cm⁻¹: 3305, 1753, 1606, 1514, 1436, 1396, 1367, 1051, 536. ¹H NMR (400 MHz, DMSO) δ: 7.83(s, 2H, ArH), 2.22(s, 1H, CH) ppm. MS (APCI): calcd. for C₆H₃I₃N [M] + 470; found, 470.

2.3.4 5-Iodovanillin (1.b): 0.532 g (97%). Reddish brown, mp 183–185°C, lit. 181–182°C [26] IR (KBr) cm⁻¹: 3153, 2980, 2846, 1664, 1585,

1571, 1490, 1460, 1417, 1354, 1296, 1259, 1246, 1166, 1143, 1039, 854, 785, 669. ¹H NMR (400 MHz, DMSO) δ: 3.94(s, 3, OCH₃), 7.34 (d, 1, C-2H), 7.81 (d, 1, C-6H), 9.73 (s, 1, CHO) ppm. MS (APCI): calcd. for C₈H₇IO₃ [M] + 278.04; found, 278.

2.3.5 5,7-Diiodo-8-hydroxyquinoline (1.f): 0.738 g (97%). Greenish powder, mp 212–214°C, lit. 214–215°C [23] IR (KBr) cm⁻¹: 3061, 2883, 1483, 1454, 1388, 1328, 1201. ¹H NMR (400 MHz, CDCl₃) δ: 7.61(1H, dd) 8.29(1H, dd), 8.31 (1H,s), 8.81 (1H, dd) ppm, MS (APCI): calcd. for C₉H₆NOI₂ [M] + 396.95; found, 397.

2.3.6 4-Iodo-2-nitroaniline (1.h): 0.49 g (98%). Orange solid, mp 120–121°C, lit. 122°C [26] IR (KBr) cm⁻¹: 2877, 1598, 1529, 1444, 1317, 1246, 1155, 1087, 877, 752, 665. ¹H NMR (400 MHz, CDCl₃) δ: 8.42(d, H-3) 7.57(dd, H-5), 7.26 (s, NH₂), 6.62 (d, H-6) ppm. MS (APCI): calcd. for C₆H₅IN₂O₂ [M] + 264.02; found, 264.

2.3.7 3,5-Diiodo-4-hydroxybenzaldehyde (1.e): 0.688 g (98%). White solid, mp 200–202°C, lit. 199–200°C [24] IR (KBr) cm⁻¹: 3192, 1707, 1666, 1456, 1408. ¹H NMR (400 MHz, DMSO) δ: 8.20(s, 2H) 9.73(s, 1H, CHO) ppm. MS (APCI): calcd. for C₇H₄I₂O₂ [M] + 373.91; found, 374.

2.3.8 3,5-Diiodosalicylic acid (1.c): 0.751 g (98%). White powder, mp 232°C, lit. 232–234°C [26] IR (KBr) cm⁻¹: 3500, 1699, 1616, 1581, 1558, 1436, 1417, 1392, 1274, 1222, 881. ¹H NMR (400 MHz, DMSO) δ: 7.33(d, H-3) 2.66(d, H-2), 2.15 (s, 1H), MS (APCI): calcd. for C₇H₄I₂O₃ [M] + 471; found, 471.

2.3.9 4-Iodoacetanilide (1.j): 0.466 g (94%). Off white solid, mp 184°C, lit. mp 184°C [24] IR (KBr) cm⁻¹: 3290, 3253, 1666, 1529, 1483, 1383, 1307, 1253, 1002, 817, 738, 503. ¹H NMR (400 MHz, DMSO) δ: 2.15(s, H-3, COCH₃) 7.34(d, H-2), 7.58 (d, H-2), ppm. MS (APCI): calcd. for C₈H₈INO [M] + 261.06; found, 261.

2.3.10 3,5-Diiodosalicylaldehyde (1.l): 0.708 g (99%). Pale yellow, mp 109°C, lit. mp 109–110°C [24] ¹H NMR (400 MHz, CDCl₃) δ: 11.73(s, 1H) 9.70(s, 1H) 8.23(d, 1H) 7.83(d, 1H). MS (APCI): calcd. for C₇H₄I₂O₂ [M] + 374; found, 374.

2.3.11 2,4-Diiodo-6-nitrophenol (1.m): 0.725 g (98%). Yellow crystal, mp 99°C, lit. 98°C [24] ¹H NMR (400 MHz, DMSO) δ: 8.32(d, 1H, Ar-H), 8.40(d, 1H) ppm. MS (APCI): calcd. for C₆H₂NO₃I₂ [M] + 391; found, 391.

2.3.12 2,4-Diiodoaniline (1.g): 0.642 g (98%). Dark powder, mp 95°C, lit. 95°C [25] ¹H NMR (400 MHz, CDCl₃) δ: 7.30(dd, 1H), 7.86(d, 1H), 2.17(s, 2H) ppm.

2.3.13 2,4,6-Triiodophenol (1.d): 0.912 g (96%). Light brown, mp, 159°C, lit. 156–159°C [23] IR (KBr) cm⁻¹: 3441, 3053, 1732, 1539, 1433, 1230, 858, 700. ¹H NMR (400 MHz, DMSO) δ: 7.93 (s 2 H, ArH) 5.76 (s 1H, OH) ppm. MS (APCI): calcd. for C₆H₃I₃O [M] + 471.80; found, 472.

2.3.14 3,5-Diiodo-4-hydroxybenzonitrile (1.k): 0.694 g (99%). Beige, mp, 204°C, lit. 202–204°C [24] ¹H NMR (400 MHz, DMSO) δ: 7.98 (s 1 H, CH) 2.17 (s 1H, CH) ppm. MS (APCI): calcd. for C₇H₃I₂NO [M] + 370.91; found, 371.

3 Results and discussion

The present paper reports a convenient and highly selective method for the iodination of activated aromatic compounds. A variety of ortho/para hydroxyl substituted aromatic aldehydes and highly activated arenes, such as

aniline and phenol, were selected for the iodination reaction using NIS by the grinding method in a mortar and pestle at room temperature. Iodination was achieved in a shorter period (5–7 min) with excellent yield (94–99%, Tables 1 and 2) and selectivity (95–99.9%, Table 3). After completion of the reaction, water was added to separate

Table 1: Iodination of aromatic compounds using N-iodosuccinimide (NIS) by grinding and with solvent, a comparison.

Entry	Substrate	Product	By grinding		With solvent ^b	
			Time (min)	Yield (%)	Time (min)	Yield (%)
1.a			5	99	120	96
1.b			5	97	120	95
1.c			5	98	120	94
1.d			5	96	30	93
1.e			5	98	120	98
1.f			7	97	180	95
1.g			5	98	120	95
1.h			5	98	120	98
1.i			5	97	240	93
1.j			8	94	240	91
1.k			5	99	240	99
1.l			5	99	120	98
1.m			7	98	240	96
1.n			5	98	240	97
1.o			7	97	240	94
1.p			7	97	240	93

^aReaction conditions: substrate: NIS, 1:1 (monomer), 1:2 (dimer), 1:3 (trimer); AcOH, 0.5 ml, temperature at 25°C.

^bReaction conditions: substrate: NIS, 1:1 (monomer), 1:2 (dimer), 1:3 (trimer); AcOH, 5 ml, temperature at 25°C. NIS, N-iodosuccinimide.

Table 2: Product selectivity wrt starting material in the iodination of various aromatics using N-iodosuccinimide (NIS).

Entry	Substrate	Substrate: NIS	Product	Yield ^a (%)	Product purity ^b (%)	
					Main product	Others
I.h		1:1		98	99.9	—
I.k		1:2		99	99.9	—
I.l		1:2		99	99.9	—
I.e		1:2		98	99.9	—
I.m		1:2		98	99.9	—
I.d		1:3		96	99.9	—
I.j		1:1		94	99.9	—
I.n		1:2		98	98.06	1.94
I.b		1:1		97	98.87	1.13
I.i		1:3		97	95.33	4.67

^aIsolated yields.^bPurity determined by gas chromatography-mass spectrometry (GC-MS).

the product. The end product does not require further purification. This method has an advantage in that substrates like anilines and phenol do not get oxidized. The products were identified by comparing melting points, FTIR, GC-MS, and ¹H NMR spectral data with that reported in literature. The system has been successfully applied to a variety of industrially important substrates (Table 1). Initially, the diiodination of 4-NP as a model compound using a combination of NIS (2 equivalent) and AcOH (0.5 ml) has been used as a catalyst by grinding has proved to be an excellent reagent at room temperature, to give 2,6-diiodo-4-nitrophenol in excellent yield of 98% (Table 1, entry **1.n**) in 5 min. Gallo et al. [43] reported the formation of 2,6-diiodo-4-nitrophenol at higher temperature (50°C), using longer duration (24 h) and with lower yield (80%). Zielinska and Skulski [41] also reported that 2,6-diiodo-4-nitrophenol can be prepared at higher temperature (50°C), with lower yield (72%). The effects of the concentration of NIS on the yield of **1.n** were examined. Figure 1 suggests that the quality of the product is

strongly dependent on the mole ratio of NIS/4-NP. It has been found that the optimum yield (98%) of 2,6-diiodo-4-nitrophenol is obtained at the mole ratio of NIS/4-NP 2/1. No effect on the yield of the product was observed when we further increased the mole ratio of NIS/4-NP from 2.0 to 2.2 (98%). When the mole ratio of NIS/4-NP was decreased from 2.0 to 1.8, the yield of 2,6-diiodo-4-nitrophenol decreased (64%). Further decrease in the mole ratio from 1.5 to 1 leads to formation of 2-iodo-4-nitrophenol (**1.o**) which melts at 86°C (mp of 2-iodo-4-nitrophenol is 86–87°C [26]). Thus, from the above observations, it is concluded that the optimum mole ratios of 4-NP to NIS (1:2 and 1:1) were found to be ideal for diiodination (**1.n**) and monoiodination, respectively. It has been observed that GC-MS analysis of the final product obtained at the above mole ratio shows 98.06% purity for 2,6-diiodo-4-nitrophenol (see Table 3, entry **1.n**). The iodination of vanillin (**1.b**) resulted in 5-iodovaniline with excellent selectivity and yield of 98%, 97% with no detectable ortho or para compounds. Gary and Doxsee [28] reported preparation

Table 3: Comparison of iodination of aromatic compounds using N-iodosuccinimide (NIS) by grinding method with other reported systems.

Entry	Substrate	Product	Present study (by grinding)		Literature results		
			Time (min)	yield (%)	Time (min)	yield (%)	Application
1.a			5	99	180	69 [1]	Hyper proliferative disorder [27]
1.b			5	97	180	83 [28]	In ink jet printer [29]
1.c			5	98	1,200	80 [30]	Intermediate for veterinary anthelmintic agents [26]
1.d			5	96	480	64 [31]	Antiinflammatory, analgesic, antiatherosclerotic [23]
1.e			5	98	840	68 [32]	Herbicide [33]
1.f			7	97	240	50 [34]	Drug, anti-corrosion and chelating agent [26]
1.g			5	98	180	57 [35]	Anti-microbial agent [24]
1.h			5	98	480	98 [36]	In fuel cell [37]
1.i			5	97	240	87 [35]	Intermediates for drugs, pesticides and fungicides [38]
1.j			8	94	1,440	47 [34]	Intermediate for drugs, chemical, and dyestuff [39]
1.k			5	99	480	80 [35]	Used in herbicide [40]
1.l			5	99	50–70°C,	82 [30]	A potent antibacterial [31]
1.m			7	98	50°C	72 [41]	Used in treatment of hookworm infection [42]
1.n			5	98	1,440	80 [43]	Used in treatment of hookworm infection [44]
1.o			7	97	0°C	70 [45]	Used in medicine, and pharmaceuticals [41]
1.p			7	97	0°C	72 [45]	Used as intermediates for drugs, pesticides [38]

^aReaction conditions: substrate: NIS, 1:1 (monoiodination), 1:2 (diiodination), 1:3 (triiodination); AcOH, 0.5 ml, temperature at 25°C.

^bReaction conditions: substrate: NIS, 1:1 (monoiodination), 1:2 (diiodination), 1:3 (triiodination); AcOH, 5 ml, temperature at 25°C and gave 91–99% yield.

NIS, N-iodosuccinimide.

of 5-iodovanillin at 0°C and lower yield (83%). Phenol and aniline were instantaneously triiodinated (**1.d**, **1.i**) to their corresponding iododerivatives with excellent selectivity and yield (99.9%, 95.33%, and 96%, 97%, respectively).

Triiodination formation requires 1:3 molar ratio of substrate/NIS. Reddy et al. [31] reported synthesis of 2,4,6-triiodophenol using longer duration (8 h), with lower yield (64%) and poor GC purity (66%). Bell et al. [32] reported

Figure 1: Effect of mole ratio of N-iodosuccinimide/4-nitrophenol on the yield in the iodination of 4-nitrophenol to 2,6-diiodo-4-nitrophenol.

synthesis of 2,4,6-triiodoaniline under severe reaction conditions, with poor yield (87%, 3 h). The iodination of p-hydroxybenzaldehyde (**1.e**) resulted in 3,5-diiodo-4-hydroxybenzaldehyde with excellent yield (98%) and purity (99.9%). Ping et al. [36] reported preparation of 3,5-diiodo-4-hydroxybenzaldehyde using longer duration (14 h), with poor yield (68%). Another industrially important aldehyde, 3,5-diiodosalicylaldehyde (**1.l**), shows high selectivity (99.9%) and excellent yield (99%). Janson [30] reported the formation of 3,5-diiodosalicylaldehyde at higher temperature (50–70°C) and low yield (82%). The iodination of 3,5-diiodo-4-hydroxybenzonitrile (**1.k**) shows high regioselectivity (99.9%) and excellent yield

(99%). The potential antimicrobial agent 2,4-diiodoaniline (**1.g**) can also be obtained using the same reaction conditions with excellent yield 98%. Bell et al. [32] reported the synthesis of 2,4-diiodoaniline under severe reaction conditions, with poor yield (57%, 3 h). Deactivated anilines (**1.h**, **1.c**) were smoothly iodinated to their iodo derivatives with excellent yield. Another industrially important compound, 3,5-diiodosalicylic acid (**1.c**), was also prepared from salicylic acid in excellent yield (98%) in 5 min at room temperature. This substrate undergoes iodination at high temperature and a longer reaction time [34]. The iodination of acetanilide (**1.j**) under similar conditions was achieved with good selectivity and yield (99%, 94%), respectively. Sket et al. [37] reported synthesis of 4-iodoacetanilide under very harsh conditions (105°C) with poor yield (47%). 8-Hydroxyquinoline (oxime) (**1.f**) also underwent clean iodination to yield 5,7-diiodo-8-hydroxyquinoline in good yield (97%). Previous procedures for the iodination of 8-hydroxyquinoline were more costly and cumbersome, relying, e.g. on the use of cross linked polystyrene-[4-vinylpyridinium dichloroiodate (I)] [46] or MeOCONCl₂ and NaI [45]. Acid-sensitive substrates like aromatic amines (entries **1.a**, **1.h** and **1.p**), including notably 4-nitroaniline (**1.a**), lead to iodination at vacant ortho position to give 2-iodo-4-nitroaniline in 99% yield. Boothe et al. [7] reported the formation of 2-iodo-4-nitroaniline at 0°C with a reported yield of 70%. The iodination of 2-nitroaniline (**1.h**) gave excellent selectivity (99.9%) and yield (98%). Emmanuvel et al. [35] reported the formation of 4-iodo-2-nitroaniline in a longer duration (8 h). There was no effect of electron withdrawing -NO₂ group in the case of o-nitrophenol (**1.m**) which gave excellent purity (99.9%) and yield

Scheme 1: A possible mechanism of iodination for aromatic compounds.

(98%). Zielinska and Skulski [41] reported the formation of 2,4-diiodo-6-nitrophenol at higher temperature (50°C) with lower yields (80%).

A possible mechanism of iodination for aromatic compounds is shown in Scheme 1. NIS is activated by AcOH. It is proposed that the active species for this iodination is

Spectrum Peak Pick Report

Data Set: 4-Hydroxybenzonitrile- in Acetic Acid.spc

Figure 2: UV spectra of N-iodosuccinimide.

probably the *in situ* formed “I⁺” which can act as a very reactive electrophile, allowing iodination in a short reaction time at room temperature. As far the mechanism of

iodination of organic compounds using NIS is concerned, UV-visible spectroscopy was carried out. The absorption spectra of NIS exhibit maximum absorption at 469 nm

Spectrum Peak Pick Report

Data Set: NIS in Acetic Acid.spc - Dataset 224042

[Measurement Properties]
Wavelength Range (nm.): 190.00 to 1100.00
Scan Speed: Medium
Sampling Interval: 1.00
Auto Sampling Interval: Enabled
Scan Mode: Auto

No.	Wavelength	Absorbance	Description
1	469.00	0.931	469 nm
2	300.00	3.763	300 nm

[Instrument Properties]
Instrument Type: UV-1800 Series
Measuring Mode: Absorbance
Slit Width: 1.0 nm
Light Source Change Wavelength: 340.0 nm
S/R Exchange: Normal

[Attachment Properties]
Attachment: None

[Operation]
Threshold: 0.0010000
Points: 4
InterPolate: Disabled
Average: Disabled

[Sample Preparation Properties]
Weight:
Volume:
Dilution:
Path Length:
Additional Information:

Figure 3: UV spectra of hydroxybenzonitrile.

and another peak at 300 nm (Figure 2). When substrate 4-hydroxybenzonitrile with maximum absorption at 250 nm (Figure 3) was added to the reaction mixture, the

peak due to NIS disappears at 469 nm completely and a peak at 230 nm (Figure 4) appears, suggesting the formation of succinimide. There was no peak at 420 nm and

Spectrum Peak Pick Report

Data Set: Rxn Mix 15 min.spc

[Measurement Properties]

Wavelength Range (nm.): 190.00 to 1100.00
 Scan Speed: Medium
 Sampling Interval: 1.00
 Auto Sampling Interval: Enabled
 Scan Mode: Auto

No.	Wavelength	Absorbance	Description
1	230.00	1.794	230 nm

[Instrument Properties]

Instrument Type: UV-1800 Series
 Measuring Mode: Absorbance
 Slit Width: 1.0 nm
 Light Source Change Wavelength: 340.0 nm
 S/R Exchange: Normal

[Attachment Properties]

Attachment: None

[Operation]

Threshold: 0.0010000
 Points: 4
 InterPolate: Disabled
 Average: Disabled

[Sample Preparation Properties]

Weight:
 Volume:
 Dilution:
 Path Length:
 Additional Information:

Figure 4: UV spectra of reaction mixture.

366 nm, which are attributed to I_2 and I_3^- , respectively, in the literature [47]. This shows that these intermediate species of iodine are not formed during this iodination process. These observations support the mechanism.

4 Conclusion

It can be concluded that this is a simple, highly regioselective and efficient method for iodination of activated aromatic compounds, aldehydes, phenol and aniline using NIS by the grinding method. This method providing a practical alternative to other procedures by avoiding the use of harsh reaction conditions like high temperature, long reaction time, costly metal catalysts, and problematic halogenated solvents. Furthermore, ambient conditions and simple work-up procedure, shorter reaction time (5–7 min) and commercially viable route for synthesis of iodo-organics make the present method an attractive procedure in comparison to other iodination protocols.

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