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Chinese Chemical Letters 20 (2009) 1439–1443
CHINESE CHEMICAL LETTERS
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A mild, efficient and selective iodination of aromatic compounds using iodine and 1,4-bis(triphenylphosphonium)-2-butene peroxodisulfate

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Received 21 April 2009

Abstract

A simple and efficient method for the iodination of aromatic compounds has been achieved in the presence of iodine and 1,4-bis(triphenylphosphonium)-2-butene peroxodisulfate.

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Keywords: Iodoaromatic compounds; Aromatic compounds; Iodine; 1,4-Bis(triphenylphosphonium)-2-butene peroxodisulfate

Iodination of aromatic compounds intrigued chemists for many years and was the subject of numerous investigations due to the interest of iodoaromatics as pivotal precursor in organic synthesis and their roles as bacterial and fungicidal agents [1–5]. Because of the low reactivity of iodine, iodination of aromatic substrates require the presence of a mediator such as a strong oxidizing agent [6–13], i.e. (IO_3 anions, silver complexes, H_2O_2, nitric acid, sulfuric acid, iodic acid, sulfur trioxide and hydrogen peroxide and NaOCl). It was also reported that the aromatic iodination with molecular iodine was catalyzed by stoichiometric amounts of metal halides, such as $AlCl_3$–$CuCl_2$ [14], $SbCl_5$ [15] or most of them imply the use of strong acidic [16,17] or basic conditions [18,19] such as (CF_3COOH, H_2SO_4 and KOH). Unfortunately, some of these methods are not always fully satisfactory and suffer from disadvantages such as long reaction times, low regioselectivity, over iodination, using of expensive or sensitive reagents and poor yields. In this article we wish to report that the 1,4-bis(triphenylphosphonium)-2-butene peroxodisulfate/I_2 is an excellent system for the iodination of both activated and deactivated aromatic rings. For the synthesis of this new peroxodisulfate reagent, cis 1,4-dichloro-2-butene was treated with triphenylphosphine in refluxing $CHCl_3$ for 2.5 h to produce 1,4-bis(triphenylphosphonium)-2-butene dichloride (**1**), upon cooling and treatment with diethyl ether and then with acetone, as a white solid in 80% yield. Stirring a mixture of **1** and $K_2S_2O_8$ in water at ambient temperature for 1 h, yielded after filtration, washing with acetone and drying, 1,4-bis(triphenylphosphonium)-2-buteneperoxodisulfate (**2**) as a white solid in 78% yield (Scheme 1).

Structures **1** and **2** were confirmed by IR, ^{1}H NMR and ^{13}C NMR. 1,4-Bis(triphenylphosphonium)-2-butene peroxodisulfate **2** is stable for long periods without losing its activity. The readily prepared reagent **2** in contrast to

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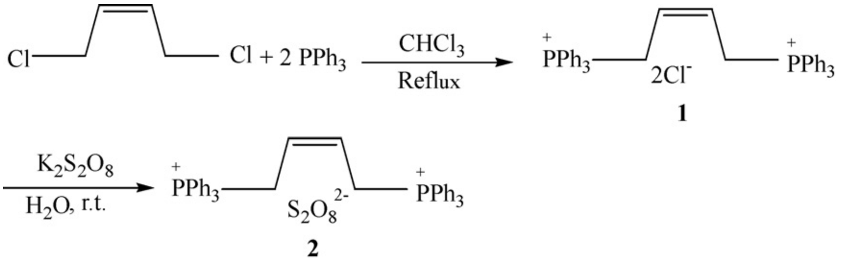
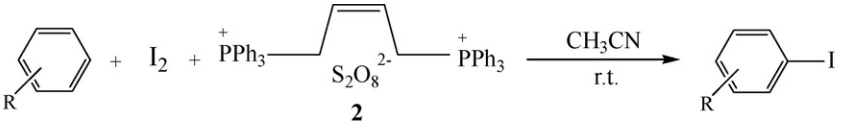
doi:10.1016/j.cclet.2009.06.017



Scheme 1.



Scheme 2.

$K_2S_2O_8$, $Na_2S_2O_8$ and $(NH_4)_2S_2O_8$ is easily soluble in various organic solvents such as acetonitrile, methanol, dichloromethane, chloroform and ethyl acetate, therefore it can be used in general organic reactions. Simple stirring of a mixture of compound **2**, iodine and aromatic substrates in acetonitrile at ambient temperature gave, after work-up and isolation, the desired iodoaromatic compounds in high yields (Scheme 2). The obtained results are summarized in Table 1.

1. Experimental

1.1. General

All products were characterized by comparison of their physical data, IR, ^{1}H NMR and ^{13}C NMR spectra with authentic samples [20–25]. The IR spectra were recorded on Bomem FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were taken on a 400 MHz Brucker spectrometer. 1,4-Bis(triphenylphosphonium)-2-butene peroxodisulfate was prepared and other chemicals were purchased from the Merck chemical company Darmstadt, Germany. The purity determination of the products and reaction monitoring were accomplished by TLC on polygram SILG/UV 254 plates.

Table 1
Iodination of aromatic compounds with 1,4-bis(triphenylphosphonium)-2-butene peroxo-disulfate/I_2 system in acetonitrile.

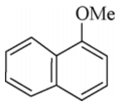
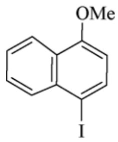
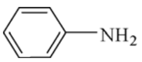
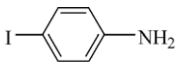
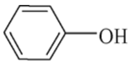
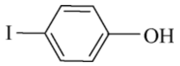
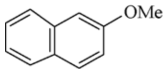
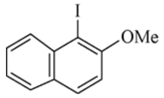
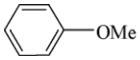
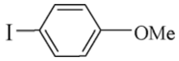
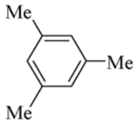
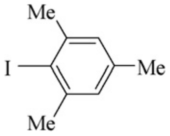
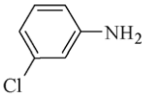
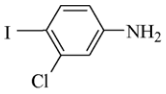
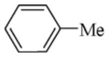
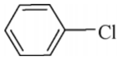
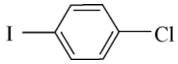
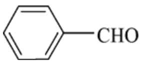
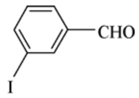
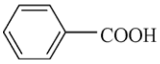
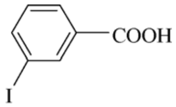
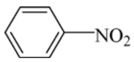
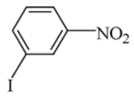
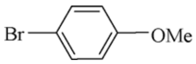
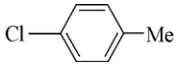
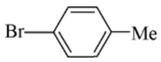
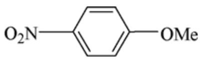
No.	Substrate	Product	Time (h)	Yield[a] (%)	mp [b.p] (°C)	Lit. mp [b.p] (°C)
1			0.4	87	124–125	–
2			0.5	88	63–65	(62.5–63) [12]
3			0.6	91	92–93	(93–94) [13]

Table 1 (*Continued*)

No.	Substrate	Product	Time (h)	Yield[a] (%)	mp [b.p] (°C)	Lit. mp [b.p] (°C)
4			0.6	88	88–89	(87–88) [14]
5			0.8	91	50–53	(51–52) [15]
6			0.8	91	30–31	(29–30) [16]
7			1	89	65–66	(64–66) [16]
8			1.2	88	31–32	(33–35) [13]
9			1.5	94	57–59	(56–57) [13]
10			2.8	87	54–57	(54–56) [17]
11			3.5	84	187–189	(188–189) [17]
12			4	82	35–36	(34–36) [17]
13		–	10	–	–	–
14		–	10	–	–	–
15		–	10	–	–	–
16		–	10	–	–	–

[a] Isolated yields in acetonitrile.

1.2. *Preparation of 1,4-bis(triphenylphosphonium)-2-butene dichloride (**1**)*

To a solution of 1,4-dichlorobutene (0.63 g, 5 mmol) in $CHCl_3$ (10 mL) in a 50 mL round-bottomed flask equipped with a magnetic stirrer and a reflux condenser was added triphenylphosphine (10 mmol). The reaction mixture was refluxed for 2.5 h. The solution was cooled to room temperature and then diethyl ether was added drop wise until an oily product was separated. The ether was removed by decantation and acetone (40 mL) was added. Stirring the acetone solution for 40 min afforded a white precipitate which was filtered, washed with acetone and then dried. Yield (80%), mp 278–279 °C.

IR (KBr): 3053, 2755, 1613, 1575, 1478, 1437, 754, 693, 556 (cm^{-1}). ^{13}C NMR ($CDCl_3$, δ ppm): 20.7, 120.8, 132.15, 134.2, 137.01, 140.17. ^1H NMR ($CDCl_3$, δ ppm): 5.7 (dd, 4H), 6.3 (m, 2H), 7.79–8 (m, 30H).

1.3. *Preparation of 1,4-bis(triphenylphosphonium)-2-butene peroxodisulfate (**2**)*

In a 25 mL round-bottomed flask equipped with a magnetic stirrer, a solution of $K_2S_2O_8$ (0.54 g, 2 mmol) in H_2O (5 mL) was prepared. Compound **1** (1.298 g, 2 mmol) was added to this solution and the reaction mixture was stirred at ambient temperature for 3 h. The resulting white precipitate was filtered, washed with distilled water (10 mL) and dried *in vacuo*; Yield (78%), mp 205–208 °C.

IR (KBr): 3053, 2750, 1623, 1585, 1472, 1437, 1258, 750, 724, 689, 556 (cm^{-1}). ^{13}C NMR ($CDCl_3$, δ ppm): 19.04, 119.45, 130.05, 133.98, 136.91, 138.8. ^1H NMR ($CDCl_3$, δ ppm): 4.7 (dd, 4H), 5.8 (m, 2H), 7.68–8 (m, 30H).

1.4. *General procedure for iodination of aromatic compounds*

To a solution of aromatic compound (1 mmol) in CH_3CN/H_2O (5/1:30 mL) in a 50 mL round-bottomed flask with a magnetic stirrer was added 1,4-bis(triphenylphosphonium)-2-butene peroxodisulfate (1 mmol) and iodine (1 mmol). The reaction mixture was stirred magnetically at ambient temperature for the appropriate time indicated in Table 1. The progress of the reaction was monitored by TLC. The reaction mixture was poured into an aqueous sodium thiosulfate solution (1 mol/L) and extracted with diethyl ether (3× 15 mL). The ethereal layer is dried over anhydrous calcium chloride. Evaporation of the solvent followed by column chromatography on silica gel gave the corresponding iodinated compounds.

2. Results and discussions

To gain some preliminary information on this synthetically useful reaction, we studied the influence of different factors: solvent, molar ratio and temperature on the reaction kinetics. Thus, the effect of various solvents such as $CHCl_3$, CH_2Cl_2, CCl_4 and CH_3CN on the reaction rate and yield were investigated. The experimental results showed that acetonitrile was the best choice for our procedure. Also our observations revealed that the molar ratio of 1.0:1.0:1.0 for aromatic substrate, iodine and oxidant, was the most effective, giving a short reaction times and clean products. When the same reaction was performed at reflux temperature, using anisole as a substrate, along with the formation of the major *p*-iodoanisole, amount of *o*-iodoanisole was also obtained. This result prompted us to carry out all further investigations at room temperature, as it was found to favor the iodination reaction.

As indicates in Table 1 iodination of aromatic substrates with ($2/I_2$) system gave only monoiodination products in which iodine appears at para-position with activated aromatic rings and at meta-position with deactivated rings. The lack of any ortho-isomers in the case of former substrate or ortho-and para-isomers in the case of later substrates clearly shows that in each case the iodination occurs at the position which is more electron rich and is almost free of steric effect. As shown in Table 1 (Entries 10–12), our procedure is a convenient method for the meta-iodination of benzene derivatives containing a single deactivating substituent. When the para-position of substituted benzene is not free, iodination did not occur at all even at reflux temperature and for a long period of time (Entries 13–16). As it is expected, the time of the iodination reaction increases as we go from more activated compound towards the least one (Table 1). With 1-methoxynaphthalene and 2-methoxynaphthalene iodination occurred at 4 and 1 positions, respectively (Entries 1 and 4). It is noteworthy that careful investigation shows that with all substrates used in this procedure no polyiodinated products have been found. This makes our procedure a suitable method for preparation of monoiodo derivatives of aromatics in high yields. Since we observed the iodination of aromatic ring with both electron donating and electron withdrawing groups therefore a possible mechanism might be as followed in which the sulfate anion radical gain an electron from aromatic ring, oxidizes the ring to a cation radical which then react with iodine to form the products [26]. By conducting a few of the reactions in the presence of acrylonitrile, the yields of the iodination products dropped sharply due to formation of poly acrylonitrile. This evidence clearly established the radical mechanism for our procedure.

In conclusion, we have developed a simple procedure for the iodination of activated and deactivated aromatic compounds under ambient conditions using ($2/I_2$) system as a mild and selective iodinating agent.

The ^{1}H NMR and ^{13}C NMR spectra data of the products are listed below:

*4-$IC_{10}H_6OMe$ (**1**)*: ^{1}H NMR (δ ppm): 3.97 (s, 3H, OCH_3), 6.8 (d, 1H, $J = 8.1$ Hz, 2H), 7.38 (dd, 1H, $J = 8.2$, 6.9 Hz, 7H), 7.69 (d, 1H, $J = 8.1$ Hz, 3H), 7.71 (dd, 1H, $J = 8.3$, 6.9 Hz, 6H), 7.82 (d, 1H, $J = 8.3$ Hz, 5H), 8.17 (d, 1H, $J = 8.2$ Hz, 8H). ^{13}C NMR (δ ppm): 48, 85.2, 107.2, 122.6, 123.8, 125.6, 127.3, 129.3, 131.2, 135.3, 159.4
*4-$IC_6H_4NH_2$ (**2**)*: ^{1}H NMR(δ ppm): 4.9 (brs, 2H, NH_2), 6.67 (d, 2H, $J = 8.5$ Hz, 2, 6H), 7.52 (d, 2H, $J = 8.5$ Hz, 3, 5-H). ^{13}C NMR (δ ppm): 83.2, 120.2, 139.1, 145.8
*2-I-1, 3,5-$C_6H_2(CH_3)_3$ (**6**)*: ^{1}H NMR (δ ppm): 1.85 (s, 3H, CH_3), 2.53 (s, 6H, $2CH_3$), 6.71 (s, 2H, 4, 6H), ^{13}C NMR (δ ppm): 25.2, 28.6, 88.5, 132.8, 140.4, 147.2
*4-I-3-$ClC_6H_3NH_2$ (**7**)*: ^{1}H NMR (δ ppm): 5.09 (brs, 2H, NH_2), 6.14 (d, 1H, $J = 8.4$ Hz, 6H), 7.34 (s, 1H, 2H), 7.39 (d, 1H, $J = 8.4$ Hz, 5H), ^{13}C NMR (δ ppm): 91.7, 114.4, 117.6, 144.3, 145.7, 147.6
*3-IC_6H_4CHO (**10**)*: ^{1}H NMR (δ ppm): 6.9 (dd, 1H, $J = 7.9$, 7.6 Hz, 5H), 7.38 (d, 1H, $J = 7.9$ Hz, 4H), 7.95 (d, 1H, $J = 7.6$ Hz, 6H), 8.42 (s, 2H), 10.2 (s, 1H, CHO). ^{13}C NMR (δ ppm): 92.2, 129.5, 130.1, 140.9, 141, 142.8, 193.2.

Acknowledgment

We thank Chamran University for financial support of this work.

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