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Direct, easy, and scalable preparation of (diacetoxyiodo)arenes from arenes using potassium peroxodisulfate as the oxidant

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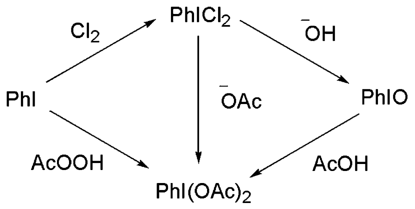
Abstract—The reaction of arenes with potassium peroxodisulfate, elemental iodine, and acetic acid in the presence of concd sulfuric acid, efficiently generates the corresponding (diacetoxyiodo)arenes in good yields, providing an easy, safe, and effective method for preparing (diacetoxyiodo)arenes from arenes and iodine.

Over the past decade, the use of hypervalent iodine reagents has gained importance as mild oxidants and as a safe alternative to heavy-metal reagents for performing a variety of organic transformations. (Diacetoxyiodo)arenes, [$ArI(OAc)_2$], and the parent compound, (diacetoxyiodo)benzene [$PhI(OAc)_2$], have been known for a long time.[1–5] Particularly the parent (diacetoxyiodo)benzene is a crystalline compound and is fairly stable in air, which can be stored for long periods in the dark. It is a potent, often chemoselective oxidant, and is widely used in modern organic synthesis. (Diacetoxyiodo)benzene is also used for the facile synthesis of, for example, iodosylbenzene, [bis(trifluoroacetoxy)iodo]benzene, [hydroxyl(tosyloxy)iodo]benzene (Koser's salt, *selective oxidants*), and aromatic iodonium salts (*arylating reagents*).[2–6] Several methods are available for the preparation of (diacetoxyiodo)benzene. Historically, the first member, (diacetoxyiodo)benzene was synthesized by Willgerodt in 1892, by dissolving iodosylbenzene in hot acetic acid.[7] The representative methods, as shown in Scheme 1, involve the reaction of iodosylbenzene with acetic acid,[7] the direct oxidation of iodobenzene in acetic acid,[3–5,8–12] and the reaction of (dichloroiodo)benzene with metal acetates or acetic acid.[13,14] In most of the above methods, iodobenzene is used as a starting material to prepare (diacetoxyiodo)benzene. Iodobenzene is readily available but expensive.



Scheme 1.

The most ideal procedure for (diacetoxyiodo)benzene should involve a straightforward synthesis from benzene and iodine. This procedure gives a direct and efficient method that does not contain the step via iodobenzene synthesis. However, to the best of our knowledge, there are no methods for preparing (diacetoxyiodo)benzene directly from benzene and iodine. Very recently, Shreeve and co-workers reported a direct synthesis of (diacetoxyiodo)arenes mediated by Selectflour.[15] In the Selectfluor-mediated method, electron-rich di- and tri-substituted benzenes were used as starting materials to obtain the corresponding $ArI(OAc)_2$ in good yields. However, it seems that this method cannot be applied for benzene, mono-substituted benzenes, and electron-deficient arenes, judging from the Selectfluor-mediated iodination of arenes.[16] During the course of our systematic studies on effective and easy preparations of $ArI(OAc)_2$, we have already devised two methods for their synthesis from iodoarenes.[17] Herein, we wish to

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Keywords: (Diacetoxyiodo)arenes; Arenes; Elemental iodine; Potassium peroxodisulfate; Hypervalent iodine; Oxidation.

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report a direct, easy method for the preparation of (diacetoxyiodo)benzene from benzene. Also we describe the application to toluene and less reactive halobenzenes.

In our laboratory, we found a direct and efficient method for preparing $ArI(OAc)_2$ in good yield from the corresponding arenes with iodine in AcOH, using commercial potassium peroxodisulfate, $K_2S_2O_8$, as the oxidant.[18] The results are given in Table 1. Addition of concd H_2SO_4 is essential to generate (diacetoxyiodo)arenes. Trifluoromethanesulfonic acid was also effective but H_2SO_4 was convenient for handling and workup. $K_2S_2O_8$ is used as a strong oxidizing agent in many applications. It has the particular advantages of being almost non-hygroscopic, a particularly good storage stability, and is easy and safe to handle. The oxidation of arenes to (diacetoxyiodo)arenes can be easily scaled up, given the advantages of $K_2S_2O_8$ outlined above, together with the complete absence of effluent or byproduct problems. The essence of our novel method is described in Scheme 2.

The oxidative reactions shown in Scheme 2 were carried out at 40 °C, in a mixture of AcOH, $C_2H_4Cl_2$, iodine, and concd H_2SO_4. The presence of $K_2S_2O_8$ (in stoichiometric quantities) in the reaction mixture was indispensable because without its addition the oxidation reactions did not proceed. When $K_2S_2O_8$ was replaced for sodium peroxodisulfate, $Na_2S_2O_8$, the final yields of $ArI(OAc)_2$ were lowered by ca. 20–25%. Attempt to use $NaBO_3$ for this preparation was unsuccessful. Decrease in the amount of AcOH did not affect the yield of (diacetoxyiodo)benzene. The reaction of 10- or 50-fold scale to that in entry 2 did not lead to the decrease in the yield (entries 3 and 4). Toluene also gave 4-(diacetoxyiodo)toluene in good yield. Interestingly, arenes bearing weakly deactivated groups such as chloro, bromo, and fluoro groups gave (diacetoxyiodo)arenes in good yields. In order to broaden the scope of this reaction, we conducted the oxidation of xylene, mesitylene, and *tert*-butylbenzene. Actually these substrates underwent the oxidation reaction. However, we found that these reactions resulted in the formation of iodosylbenzene derivatives, respectively. Therefore, it is considered that relatively electron-rich property of these compounds causes hydrolysis of (diacetoxyiodo)arenes during the reaction or the workup procedure. This method was not applicable for arenes with strong electron-donating groups. For example, naphthalene and anisoles were quickly oxidized in the reaction mixtures, but the reaction resulted in the decomposition and the formation of tarry products. This method was also unaffected for arenes with strong electron-withdrawing groups such as trifluoromethyl and nitro groups due to their decreased reactivity.

Table 1. Direct synthesis of (diacetoxyiodo)arenes from arenes[a]

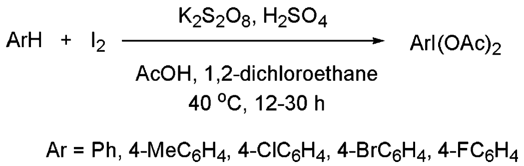
Entry	Arene	Time (h)	Product	Yield (%)
1	Benzene	20	$PhI(OAc)_2$	73
2[b]	Benzene	24	$PhI(OAc)_2$	70
3[c]	Benzene	28	$PhI(OAc)_2$	66
4[d]	Benzene	30	$PhI(OAc)_2$	64
5	Toluene	12	$4\text{-}MeC_6H_4I(OAc)_2$	70
6	Chlorobenzene	20	$4\text{-}ClC_6H_4I(OAc)_2$	71
7	Bromobenzene	20	$4\text{-}BrC_6H_4I(OAc)_2$	70
8	Fluorobenzene	20	$4\text{-}FC_6H_4I(OAc)_2$	69

[a] The reaction of an arene (1.18 mmol) was carried out in AcOH (5 mL), I_2 (0.5 mmol), $C_2H_4Cl_2$ (2 mL), and H_2SO_4 (4 mmol) in the presence of $K_2S_2O_8$ (5 mmol) at 40 °C.

[b] Benzene (1.18 mmol), AcOH (2 mL), I_2 (0.5 mmol), $C_2H_4Cl_2$ (2 mL), H_2SO_4 (4 mmol), and $K_2S_2O_8$ (5 mmol).

[c] Benzene (11.8 mmol), AcOH (20 mL), I_2 (5 mmol), $C_2H_4Cl_2$ (20 mL), H_2SO_4 (40 mmol), and $K_2S_2O_8$ (50 mmol).

[d] Benzene (59.0 mmol), AcOH (100 mL), I_2 (25 mmol), $C_2H_4Cl_2$ (100 mL), H_2SO_4 (200 mmol), and $K_2S_2O_8$ (250 mmol).



Scheme 2.

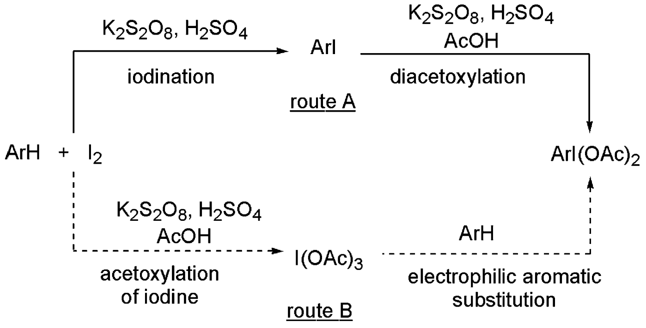
Mechanistically, there are two possible routes for generating (diacetoxyiodo)arenes, as shown in Scheme 3:

Route A: iodination of arenes, followed by diacetoxylation leading to (diacetoxyiodo)arenes;

Route B: generation of triacetoxyiodine(III), followed by electrophilic aromatic substitution to give (diacetoxyiodo)arenes.

The latter route may be suitable because $I(OAc)_3$ is a reactive electrophile and reacts with aromatics. According to Shreeve's result,[15] $I(OAc)_3$ is only effective for trisubstituted electron-rich aromatics such as mesitylene and 1-*tert*-butyl-3,5-dimethylbenzene. In our case, however, our method is effective for benzene and electron-deficient, less reactive halobenzenes. Therefore, a plausible route is the former one.

In order to detect the intermediate iodoarene in route A, we examined the reaction with a less amount of $K_2S_2O_8$. When benzene was reacted with iodine in the presence of 2 equiv of $K_2S_2O_8$ under the same conditions, iodobenzene was formed in 66% yield, together with 21% yield



Scheme 3.

of $PhI(OAc)_2$. We have already obtained the evidence that the reaction of iodobenzene with $K_2S_2O_8/H_2SO_4$ in AcOH effectively proceeds to give (diacetoxyiodo)benzene. Therefore, it is considered that, once iodoarenes are formed, they are immediately oxidized to give $ArI(OAc)_2$ under the reaction conditions.

In summary, our easy, cheap, and possibly environmentally benign one-pot procedure reported in this paper gave (diacetoxyiodo)arenes in good yields by the reaction of arenes with $K_2S_2O_8$, iodine, $C_2H_4Cl_2$, and AcOH in the presence of concd H_2SO_4 at 40 °C. In our opinion, the herein presented (diacetoxyiodo)arenes can be safely scaled up.

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18. *General procedure (Table 1, Scheme 2)*: A solution of an appropriate arene (1.18 mmol) in a mixture of AcOH (5 mL), $C_2H_4Cl_2$ (2 mL), concd H_2SO_4 (4 mmol), and I_2 (0.5 mmol) was heated with stirring to 40 °C for 15 min. Next, $K_2S_2O_8$ (5 mmol) was added portionwise during 10 min and the stirring was continued until TLC analysis indicated completion of reaction. The reaction needed 12–30 h. After the reaction was completed, water (10 mL) was added. The precipitated solid was collected by filtration under reduced pressure, washed with CH_2Cl_2 (10 mL), and discarded. The crude product was obtained by extraction of the filtrate with dichloromethane (3 × 10 mL) and finally washed with H_2O (10 mL) followed by drying (anhydrous Na_2SO_4), filtration, and removal of the solvent by evaporation under reduced pressure. The crude product was purified by washing with hexane (20 mL) or recrystallized from AcOH. Large-scale (Table 1, entry 4) synthesis was conducted for (diacetoxyiodo)benzene in a similar manner. A solution of benzene (4.62 g, 59 mmol) in a mixture of AcOH (100 mL), $C_2H_4Cl_2$ (100 mL), concd H_2SO_4 (200 mmol), and I_2 (6.34 g, 25 mmol) was heated with stirring to 40 °C. Next, $K_2S_2O_8$ (250 mmol) was added portionwise over 20 min and the stirring was continued for 30 h. Workup of the reaction mixture gave the purified product (10.79 g, 64%).