A Direct and Convenient Synthesis of Periodoarenes Using Molecular Iodine

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Received 5 August 2009; revised 3 September 2009

Abstract: Molecular iodine exhaustively iodinates aromatic hydrocarbons in the presence of potassium peroxodisulfate, concentrated sulfuric acid, and trifluoroacetic acid to give the periodinated aromatic compounds. Benzene and other moderately activated and deactivated arenes are readily converted into the corresponding periodinated derivatives in good to high yields.

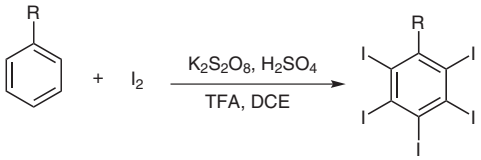
Key words: arenes, molecular iodine, periodoarenes, iodination, potassium persulfate

Poly- and periodinated aromatic compounds are traditionally prepared by time-consuming multi-step procedures from the corresponding amines involving acetylation, nitration, diazotization, and reduction.[1] Another method for the preparation of polyiodinated aromatic compounds directly from commercially available iodo compounds using sulfuric acid is based on the migration of iodine atoms present in the nucleus of the aromatic iodo compounds (Jacobsen reaction).[2] The scope of this method is very limited. The preparation of periodinated aromatic compounds through mercuration followed by iododemercuration with potassium triiodide has been reported.[3–5] Molecular iodine is not commonly used for iodination of aromatic compounds due to its low electrophilic property. To carry out the direct iodination reaction using molecular iodine requires an appropriate oxidizing agent to convert molecular iodine into a powerful electrophile.[6,7] Preparation of periodinated aromatic compounds using molecular iodine in the presence of fuming sulfuric acid as an oxidizing agent was reported.[8,9] Recently, Mattern[10] reported the preparation of periodinated aromatic compounds using molecular iodine in the presence of H_5IO_6 in sulfuric acid. Although such reported methods for the preparation of periodinated aromatic compounds are excellent and powerful in most cases, these methods have drawbacks such as the need for longer reaction time and strong acidic or severe reaction conditions to carry out the reaction. Therefore, it is desirable to seek a convenient and milder method for the preparation of periodinated aromatic compounds.

In the iodination reaction of arenes with molecular iodine, we have found that the reaction of arenes with molecular iodine occurs very easily in the presence of $K_2S_2O_8$ as an oxidant and give iodoarenes in good yields.[11] This reagent system is convenient and powerful even in the case of deactivated arenes. Thus, we extended this method to periodination of aromatic compounds.

Our present periodination method is quite different from the previously reported methods.[8–10] The present periodination method is effective for the arenes bearing moderately deactivating groups as well as moderately activating groups. Moreover, the reaction conditions are milder than those of the reported periodination methods.

We have studied the direct periodination reaction to apply it to a wide variety of aromatic compounds. Table 1 shows the results of direct periodination of different aromatic compounds with molecular iodine in the presence of $K_2S_2O_8$ and sulfuric acid in trifluoroacetic acid (TFA) and 1,2-dichloroethane (DCE). The outline of the periodination is illustrated in Scheme 1. Aromatic compounds bearing weakly deactivating groups such as chloro, bromo, fluoro, and iodo groups gave periodination products in good to high yields. Moderately activated aromatic compounds such as toluene, *o*-, *m*- and *p*-xylenes also gave periodination products in good to high yields. This method is not applicable for highly electron-rich aromatic compounds as well as for aromatic compounds bearing strongly electron-withdrawing groups.



Scheme 1

During the periodination of different aromatic compounds an excess of iodine was used to obtain the completely iodinated products. Benzene, iodobenzene, and 1,4-diiodobenzene were easily converted into hexaiodobenzene (**1**) in high yields (Table 1, entries 1–3). The moderately activated arenes such as toluene, *o*- and *p*-iodotoluenes, *p*-xylene, ethylbenzene, and butylbenzene were smoothly periodinated to give the products **2**, **5**, **6**, and **7** in high yields (entries 4–6, 9, 11), except for ethylbenzene (entry 10). Ethylbenzene gave 36% of periodinated product **6**. *o*-Xylene and *m*-xylene readily underwent periodination at low temperature, but the yields were relatively lower than those of the periodination products of toluene, *p*-xylene and butylbenzene (entries 7 and 8). The moderately deactivated aromatic compounds such as chlorobenzene,

SYNTHESIS 2010, No. 1, pp 0027–0029
Advanced online publication: 22.10.2009
DOI: 10.1055/s-0029-1217072; Art ID: F15409SS

Table 1 Direct Periodination of Arenes[a]

Entry	Arene	Temp (°C)	Time (h)	Product	Yield (%)[b]
1	benzene	60	48	hexaiodobenzene (**1**)	89
2	iodobenzene	60	48	**1**	87
3	*p*-diiodobenzene	60	48	**1**	90
4	toluene	30	36	pentaiodotoluene (**2**)	79
5	*o*-iodotoluene	r.t.	36	**2**	82
6	*p*-iodotoluene	r.t.	36	**2**	80
7	*o*-xylene	0–5	48	1,2,3,4-tetraiodo-5,6-dimethylbenzene (**3**)	53
8	*m*-xylene	0–5	48	1,2,3,5-tetraiodo-4,6-dimethylbenzene (**4**)	31
9	*p*-xylene	r.t.	14	1,2,4,5-tetraiodo-3,6-dimethylbenzene (**5**)	70
10	ethylbenzene	30	78	ethylpentaiodobenzene (**6**)	36
11	butylbenzene	r.t.	48	butylpentaiodobenzene (**7**)	65
12	chlorobenzene	60	48	chloropentaiodobenzene (**8**)	86
13	1-chloro-4-iodobenzene	60	24	**8**	88
14	*o*-dichlorobenzene	60	48	1,2-dichloro-3,4,5,6-tetraiodobenzene (**9**)	60
15	*m*-dichlorobenzene	60	48	1,3-dichloro-2,4,5,6-tetraiodobenzene (**10**)	87
16	*p*-dichlorobenzene	60	36	1,4-dichloro-2,3,5,6-tetraiodobenzene (**11**)	54
17	bromobenzene	60	18	bromopentaiodobenzene (**12**)	97
18	1-bromo-4-iodobenzene	60	36	**12**	87
19	*o*-dibromobenzene	60	18	1,2-dibromo-3,4,5,6-tetraiodobenzene (**13**)	84
20	*p*-dibromobenzene	60	08	1,4-dibromo-2,3,5,6-tetraiodobenzene (**14**)	86
21	fluorobenzene	45	60	fluoropentaiodobenzene (**15**)	71
22	1-fluoro-4-iodobenzene	60	18	**15**	51

[a] Reaction conditions: arene (1.0 mmol), I_2 (5.0 mmol), $K_2S_2O_8$ (5.0 mmol), H_2SO_4 (1.0 mmol), TFA (4.0 mL), and DCE (10 mL).
[b] Isolated yields.

1-chloro-4-iodobenzene, *o*-dichlorobenzene, *m*-dichlorobenzene, *p*-dichlorobenzene, bromobenzene, 1-bromo-4-iodobenzene, *o*-dibromobenzene, *p*-dibromobenzene, fluorobenzene, and 4-fluroiodobenzene were easily converted into the corresponding periodination products **8**–**15** (entries 12–22) in good to high yields.

In summary, we have demonstrated a direct and convenient preparation of periodoarenes using molecular iodine. This method covers many aromatic substrates including from moderately activated alkylbenzenes to deactivated halobenzenes. Moreover, the periodination reaction proceeds under the mildest conditions among the procedures reported so far. Therefore, the present periodination method is a suitable process for the synthesis of polyfunctionalized materials.

All solvents and starting materials were used during the research works as received without further purification, unless otherwise indicated. ^{1}H NMR and ^{13}C NMR were recorded on a Jeol JNM-AL-300FT-NMR spectrometer in DMSO-d_6 solution (TMS as an internal standard). Melting points of the pure compounds were recorded on a Yanaco melting point apparatus and are uncorrected. Elemental analysis was performed by the Service Center of the Elemental Analysis of Organic Compounds, Faculty of Science, Kyushu University, Japan.

Direct Periodination of Aromatic Compounds; General Procedure

Required molar amount of arene (1.0 mmol), molecular I_2 (1.27 g, 5.0 mmol), and $K_2S_2O_8$ (1.35 g, 5.0 mmol) were dissolved in DCE (10 mL). The reaction mixture was stirred in an ice bath for about 5 min, and then TFA (4 mL) and aq concd H_2SO_4 (0.18 mL, 1 mmol) were gradually added with constant stirring. The mixture was stirred for about 10 min in the ice bath and stirred further for 15 min at r.t. The temperature of the mixture was then gradually increased to the required temperature and stirred until the completion of the

reaction. The mixture was cooled and poured into ice-cold H_2O (40–50 mL). The precipitated solid was collected by suction, washed with H_2O (30–40 mL), and CH_2Cl_2 (20–25 mL) or CH_2Cl_2–hexane (1:1, 20–30 mL) to remove the unreacted I_2 (Table 1).

Hexaiodobenzene (1)
Yellow crystalline solid; mp 355–375 °C (dec.) [Lit.[10] mp 380–419 °C (dec.)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 121.65.

Pentaiodotoluene (2)
Yellow crystalline solid; mp 289–304 °C (dec.) [Lit.[10] mp 310–313 °C (dec.)].

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.29 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 147.06, 125.39, 119.52, 112.53, 47.05.

1,2,3,4-Tetraiodo-5,6-dimethylbenzene (3)
Pale yellow crystalline solid; mp 254–262 °C (Lit.[5] mp 263–264 °C).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.70 (s, 6 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 141.24, 121.69, 116.94, 33.78.

1,2,3,5-Tetraiodo-4,6-dimethylbenzene (4)
Pale yellow crystalline solid; mp 253–255 °C (dec.) (Lit.[5] mp 252–254 °C).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.08 (s, 6 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 145.77, 126.93, 110.38, 104.42, 42.61.

1,2,4,5-Tetraiodo-3,6-dimethylbenzene (5)
Light purple crystalline solid; mp 237–243 °C (Lit.[5] mp 245–248 °C).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.23 (s, 6 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 145.29, 116.81, 46.02.

Ethylpentaiodobenzene (6)
Yellow crystalline solid; mp 262–266 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.67 (q, J = 7.5 Hz, 2 H, CH_2), 1.02 (t, J = 7.5 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 151.58, 126.38, 120.20, 111.80, 50.86, 11.89.

Anal. Calcd for $C_8H_5I_5$: C, 13.06; H, 0.69. Found: C, 13.50; H, 0.78.

Butylpentaiodobenzene (7)
Pale yellow crystalline solid; mp 157–159 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.75 (t, J = 7.5 Hz, 2 H, CH_2), 1.60–1.39 (m, 4 H, CH_2CH_2), 0.98 (t, J = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 152.02, 125.12, 117.65, 110.34, 58.89, 29.36, 22.56, 13.71.

Anal. Calcd for $C_{10}H_9I_5$: C, 15.73; H, 1.19. Found: C, 15.89; H, 1.13.

Chloropentaiodobenzene (8)
Yellow crystalline solid; mp 323–331 °C (dec.) (Lit.[10] mp 356–358 °C).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 140.02, 124.83, 120.90, 111.70.

1,2-Dichloro-3,4,5,6-tetraiodobenzene (9)
Yellow crystalline solid; mp 275–308 °C.

^{13}C NMR (75 MHz, DMSO-d_6): δ = 133.74, 123.53, 115.04.

Anal. Calcd for $C_6Cl_2I_4$: C, 11.08. Found: C, 11.49.

1,3-Dichloro-2,4,5,6-tetraiodobenzene (10)
Yellow crystalline solid; mp 258–262 °C.

^{13}C NMR (75 MHz, DMSO-d_6): δ = 142.74, 126.96, 111.18, 101.71.

Anal. Calcd for $C_6Cl_2I_4$: C, 11.08. Found: C, 11.34.

1,4-Dichloro-2,3,5,6-tetraiodobenzene (11)[12]
Pale yellow crystalline solid; mp 248–275 °C.

^{13}C NMR (75 MHz, DMSO-d_6): δ = 139.27, 114.91.

Bromopentaiodobenzene (12)
Yellow crystalline solid; mp 316–325 °C (dec.) [Lit.[4] mp 340 °C (dec.)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 134.29, 124.26, 121.34, 114.99.

1,2-Dibromo-3,4,5,6-tetraiodobenzene (13)
Yellow crystalline solid; mp 260–272 °C.

^{13}C NMR (75 MHz, DMSO-d_6): δ = 129.28, 123.67, 117.58.

Anal. Calcd for $C_6Br_2I_4$: C, 9.75. Found: C, 10.15.

1,4-Dibromo-2,3,5,6-tetraiodobenzene (14)[12]
Pale yellow crystalline solid; mp 271–285 °C (dec.).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 133.86, 117.55.

Fluoropentaiodobenzene (15)
Yellow crystalline solid; mp 261–263 °C (Lit.[4] mp 262–264 °C).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.78 (J = 239.9 Hz), 123.89, 117.58 (J = 3.8 Hz), 96.41 (J = 30.9 Hz).

References

(1) *Houben–Weyl Methoden der Organischen Chemie*, Vol. V/4; Muller, E., Ed.; Thieme Verlag: Stuttgart, **1960**, 639–647.
(2) Suzuki, H.; Goto, R. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 389.
(3) Conley, N. R.; Lagowski, J. J. *Synth. React. Inorg., Met-Org. Chem.* **2003**, *33*, 1741.
(4) Deacon, G. B.; Farquharson, G. J. *Aust. J. Chem.* **1977**, *30*, 1701.
(5) Yagupol'skii, L. M.; Popov, V. I.; Kondratenko, N. V. *Zh. Org. Khim.* **1976**, *12*, 916; *Chem. Abstr.* **1976**, *85*, 446115.
(6) Butler, A. R. *J. Chem. Ed.* **1971**, *48*, 508.
(7) Durand, J. F.; Mancet, M. *Bull. Soc. Chim. Fr.* **1935**, *2*, 665.
(8) Arotsky, J.; Butler, R.; Darby, A. C. *J. Chem. Soc. C* **1970**, 1480.
(9) Suzuki, H. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2871.
(10) Mattern, D. L. *J. Org. Chem.* **1984**, *49*, 3051.
(11) Hossain, Md. D.; Oyamada, J.; Kitamura, T. *Synthesis* **2008**, 690.
(12) Reddy, C. M.; Kirchner, M. T.; Gundakaram, R. C.; Padmanabhan, K. A.; Desiraju, G. R. *Chem. Eur. J.* **2006**, *12*, 2222.