

# Improved, Acid-catalyzed Iodinating Procedures for Activated Aromatics with (Diacetoxyiodo)benzene as the Oxidant

Anna Kryska and Lech Skulski\*

Chair and Laboratory of Organic Chemistry, Faculty of Pharmacy, Medical Academy, 1, Banacha Street, PL 02-097 Warsaw, Poland

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Activated aromatics are effectively converted, at room temperature and within 15 min, into the corresponding mono-, di- or tri-iodinated products in anhydrous  $I_2$ –PhI(OAc) $_2$ –AcOH–Ac $_2$ O systems, acidified with catalytic amounts of conc. H $_2$ SO $_4$ .

Although a considerable number of halogenation reactions of aromatics have been reported,<sup>1–3</sup> it is still desirable to seek better, *i.e.* quick, inexpensive, easy, and environmentally benign methods. Organic hypervalent iodine reagents nowadays play an important role in organic synthesis,<sup>5,6</sup> hence they have also been applied as oxidants for aromatic halogenation. So far, eight organic iodine(III) compounds, *viz.*: iodobenzene **1**, (diacetoxyiodo)benzene **2**, poly[styrene(iodoso diacetate)] **3**, iodine(III) *tris*(trifluoroacetate) **4**, [bis(trifluoroacetoxy)iodo]benzene **5**, [hydroxy(tosyloxy)iodo]benzene **6** (Koser's reagent), 1-(*p*-toluenesulfonyloxy)-1,2-benziodoxol-3(1*H*)-one **7**, and diphenyliodonium tetrafluoroborate **8** have been used as the oxidants for this purpose; see our review given in a full-text version of this paper. None of these reagents, however, permit aromatic fluorination. In view of the electron density on the aromatic ring, it seems that halogenation of chlorobenzene represents the limit of the scope of the reactions with reagents **1–3** and **5–8**; more deactivated aromatics cannot be halogenated with these reagents. The evident advantages of these *solid* reagents are:<sup>7</sup> (1) low toxicity, (2) easy handling and simple

experimental operations, (3) usually high yields of halogenation products, (4) possibility of recovery of iodobenzene from the final reaction mixtures (for the used reagents **1**, **2**, **5**, **6** and **8**), which may be recycled after its oxidative conversion into the initial iodine(III) reagents, according to known procedures.<sup>6,44</sup> Similarly, the polymeric reagent **3** can be recovered in good yield by simple filtration as poly(iodostyrene) and **3** can easily be regenerated and reused.<sup>8</sup> However, all the hypervalent iodine reagents are more or less light- and heat-sensitive, while **4** and **5** are additionally moisture-sensitive.

In our laboratory, we are particularly interested in developing novel (or modified) and effective iodinating procedures for both activated<sup>40–42</sup> and deactivated<sup>41,42</sup> aromatic systems. Reagents **2**, **5** and **6** are commercially available with a notably low cost<sup>39</sup> of **2**. Hence, in the present work we attempted to considerably improve reaction conditions for the iodination of benzene, iodobenzene, ten activated arenes and three hetarenes in 40–82% yields (Table 1) with reagent **2** as a relatively cheap,<sup>39</sup> fairly stable, and readily available<sup>6,44</sup> oxidant. It was possible to mono-, di-, or even tri-iodinate the studied aromatics at or near

**Table 1** Pure halogenated products prepared at room temperature (checked with TLC)

Substrate	Product	X $_2$ (t/min) <sup>a</sup>	H $_2$ SO $_4$ added	Yield (%)	Mp/ $^{\circ}$ C (solvent) <sup>b</sup>	Lit. <sup>c</sup> mp/ $^{\circ}$ C	Analysis (%X) Calc./Found
Benzene	Iodobenzene	I $_2$ (15)	5 drops	52	bp 78–80/20	bp 63–64/8	62.20/61.9
Iodobenzene	1,4-Diiodobenzene	I $_2$ (15)	5 drops	72	125.5–126( <b>E</b> )	125	76.93/76.8
1,2-Xylene	4,5-Diiodo-1,2-xylene	I $_2$ (15)	1 ml	45	89–90( <b>E</b> )	90	70.90/70.4
1,3-Xylene	4,6-Diiodo-1,3-xylene	I $_2$ (15)	1 ml	40	71.0–71.5( <b>E</b> )	71–72	70.90/70.8
1,4-Xylene	2,5-Diiodo-1,4-xylene	I $_2$ (15)	1 ml	68	104–104.5( <b>E</b> )	103–104	70.90/70.6
Mesitylene	Triiodomesitylene	I $_2$ (15)	5 drops	80	207.5–208( <b>E</b> )	206–206.5	76.47/76.3
Mesitylene	Tribromomesitylene	Br $_2$ (15)	1 drop	65	225–226( <b>F</b> )	225.5–226	54.73/54.6
Durene	Diiododurene	I $_2$ (15)	2 drops	78	137–138( <b>F</b> )	140	65.75/65.8
Durene	Dibromodurene	Br $_2$ (15)	1 drop	62	200–202( <b>E</b> )	202–203	54.73/54.6
Biphenyl	4,4'-Diiodobiphenyl	I $_2$ (15)	3 drops	75	204–205( <b>B</b> )	205	62.51/62.4
Diphenylmethane	4,4'-Diiododiphenylmethane	I $_2$ (15)	1 ml	45	93–94( <b>M</b> )	93–94	60.43/60.3
Triphenylmethane	4,4',4''-Triiodotriphenylmethane	I $_2$ (15)	5 drops	55	127–128( <b>H</b> )	131–132 <sup>d</sup>	61.21/61.3
Fluorene	2,7-Diiodofluorene	I $_2$ (15)	None	78	215–216( <b>E</b> )	215	60.72/60.5
Fluoren-9-one	2-Iodofluoren-9-one	I $_2$ (15)	5 drops	70	150–151( <b>E</b> )	151–152	41.46/41.0
Fluoren-9-one	2,7-Diiodofluoren-9-one	I $_2$ (15)	7 drops	80	203–204( <b>E</b> )	203–204	58.75/58.7
Fluoren-9-one	2,7-Dibromofluoren-9-one	Br $_2$ (15)	1 drop	73	192 (subl.), 201–202( <b>I</b> )	199–200	47.28/47.8
Dibenzofuran	2-Iododibenzofuran <sup>e</sup>	I $_2$ (15)	5 drops	72	112–113( <b>E</b> )	112–113	43.15/43.3
Dibenzofuran	2,8-Diiododibenzofuran <sup>e</sup>	I $_2$ (15)	3 drops	80	172.5–173( <b>G</b> )	172.5–173	60.43/60.6
Xanth-9-one	2,7-Diiodoxanth-9-one	I $_2$ (15)	1 drop	70	239–241( <b>A</b> )	240–242	56.65/56.9
Uracil	5-Iodouracil	I $_2$ (30) <sup>f</sup>	1 ml	82	269–272( <b>E</b> )	272	53.32/53.4

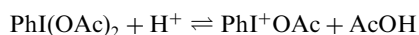
<sup>a</sup>Halogen applied (I $_2$  or Br $_2$ ) and time for each oxidative halogenation reaction at room temperature. <sup>b</sup>Solvents used for recrystallization: **A**, Me $_2$ CO; **B**, benzene; **C**, CCl $_4$ ; **D**, DMF; **E**, EtOH; **F**, AcOH; **G**, CHCl $_3$ ; **H**, heptane; **I**, AcOEt; **M**, MeOH. <sup>c</sup>*Dictionary of Organic Compounds*, Chapman and Hall, London, 6th edn., 1996. <sup>d</sup>O. Fischer and W. Hess, *Ber. Dtsch. Chem. Ges.*, 1905, **38**, 335. <sup>e</sup>**CAUTION**: these compounds are irritating to the eyes and cause dizziness. <sup>f</sup>At 40  $^{\circ}$ C the iodination was complete within 15 min.

\*To receive any correspondence (*e-mail*: lskulski@farm.amwaw.edu.pl).

room temperature and within at most 15 min, except for uracil which, however, was readily monoiodinated within 15 min at 40  $^{\circ}$ C.

Ogata and Aoki<sup>15</sup> first iodinated 1,3-xylene to 4-iodo-1,3-xylene (96%) in warm (60 °C) 99.5% acetic acid, with reagent **2** as the oxidant, with iodobenzene, produced as the side-product, being recovered. Next,<sup>3</sup> several activated arenes were iodinated in warm (50 °C) acetic acid with I<sub>2</sub>-**2** to give monoiodinated products, within 1–5 h, in 56–89% yields. It had been concluded<sup>3</sup> that for the introduction of an iodine atom into alkyl benzenes it is convenient to use the I<sub>2</sub>-**2** system in warm acetic acid. Quite recently, Togo *et al.*<sup>8</sup> have compared the reagent **2** and polymer-supported **3** in the oxidative iodination reactions of activated aromatics and obtained fairly similar results. With I<sub>2</sub>-**2** (in ethyl acetate, at room temp. or at 60 °C) they monoiodinated nine activated arenes in 4–99% yields and within 4–16 h; they also diiodinated mesitylene (96%), biphenyl (87%) and diphenyl ether (70%) at 60 °C after 16 h. Since 1980, however, mono- di-, and tri-iodinated derivatives of activated arenes and hetarenes have instead been prepared with I<sub>2</sub>-**5** (in chlorinated solvents) in good or excellent yields, mainly at room temp. and within 0.25–2 h.<sup>3</sup> The other hypervalent iodine reagents have, so far, been used to a lesser extent.

In earlier work<sup>40–42</sup> we deliberately applied anhydrous, strongly acidic iodinating systems, since water (owing to its high hydration power) considerably diminishes the iodinating activity of some transient iodine(I) species. When reagent **2** is applied as the oxidant to iodinate aromatics, transient acetyl hypoiodite (MeCO<sub>2</sub>I) was suggested as the iodinating species.<sup>3</sup> In the presence of strong acids, the reactivity of **2** is enhanced, because of its dissociation to more reactive cationic species:<sup>6</sup>



We established experimentally that the addition of varying catalytic amounts of conc. (98%) H<sub>2</sub>SO<sub>4</sub> (one drop up to 1 ml) considerably accelerated the iodination reactions studied, carried out in anhydrous systems, arene or heteroarene-I<sub>2</sub>-**2**-glacial MeCO<sub>2</sub>H-(MeCO)<sub>2</sub>O; only fluorene was effectively iodinated in the absence of H<sub>2</sub>SO<sub>4</sub> (Table 1). The reactions proceeded fairly quickly, until the coloration of iodine faded. Then, the resulting reaction mixtures were poured into excess aq. Na<sub>2</sub>SO<sub>3</sub> (or K<sub>2</sub>S<sub>2</sub>O<sub>5</sub>) solutions buffered with (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> to neutralize the H<sub>2</sub>SO<sub>4</sub>. The iodinated liquid or (mostly) solid products were isolated and purified by common preparative methods. The purified products, checked with TLC, were analyzed (Table 1). From the filtrates the iodobenzene was recovered in 40–75% yields; see Experimental section.

For comparison, the oxidative bromination of mesitylene, durene and fluoren-9-one were similarly carried out in the anhydrous systems, arene-Br<sub>2</sub>-**2**-glacial MeCO<sub>2</sub>H-(MeCO)<sub>2</sub>O with only one drop of conc. (98%) H<sub>2</sub>SO<sub>4</sub> added. Generally, the reactions proceeded much faster than

the corresponding iodination reactions to give tribromomesitylene (65%), dibromodurene (62%) and 2,7-dibromofluoren-9-one (73%).

In conclusion, we present here, considerably improved, easy, quick and effective iodinating procedures, producing mono-, di-, or even tri-iodinated products from the substrates listed in Table 1; these procedures seem to be applicable also for the aromatic bromination of activated aromatics. The oxidative reagent **2** applied in this work is less expensive,<sup>39</sup> somewhat more stable, and preparatively more accessible<sup>6,44</sup> than the moisture-sensitive<sup>39</sup> reagent **5**.

## Experimental

*Typical Diiodination Procedure.*—The reagent **2** (11 mmol; 10% excess), powdered diiodine (10.3 mmol; 3% excess), and appropriate arene (10 mmol) were dissolved or suspended in a stirred mixture of glacial acetic acid (15 ml) with acetic anhydride (15 ml). Then, conc. (98%) H<sub>2</sub>SO<sub>4</sub> was slowly added dropwise, (one drop up to 1.0 ml, Table 1). The stirring was continued until the iodine coloration faded fully, or nearly so, within at most 15 min. The mixture was poured into a stirred 5% aq. Na<sub>2</sub>SO<sub>3</sub> (or K<sub>2</sub>S<sub>2</sub>O<sub>5</sub>) solution (100 ml) to destroy the excess of **2** and any unreacted iodine, buffered with (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> to neutralize H<sub>2</sub>SO<sub>4</sub> (foaming). The precipitates were washed on the filter with water, air-dried, and recrystallized from appropriate organic solvents (Table 1). From the filtrates the iodobenzene was recovered in 40–75% yields by extraction with CHCl<sub>3</sub>.

Techniques used: TLC, microanalysis, mp/bp determination

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