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Preparative Methods for Hypervalent Iodine Reagents

In most cases iodobenzene or some ring-substituted analogues, especially iodobenzoic acid, are the starting materials through which hypervalent iodine reagents are prepared. It is emphasized that most preparations are very convenient, so that it is not necessary to purchase commercially available compounds; these and their suppliers include:

(Diacetoxyiodo)benzene: Aldrich, Fluka, Lancaster, Merck
[Bis(trifluoroacetoxy)iodo]benzene: Aldrich, Fluka
[Bis(trifluoroacetoxy)iodo]pentafluorobenzene: Aldrich, TCI America
Iodosobenzene: ICN, TCI America
2-Iodosobenzoic acid: Aldrich, Fluka
[Hydroxy(tosyloxy)iodo]benzene: Aldrich
Diphenyliodonium-2-carboxylate: Lancaster
Diphenyliodonium chloride, bromide, and iodide: Aldrich, Lancaster
Perfluoroalkyl phenyliodonium salts: TCI America

Because of the multitude and diversity of iodonium salts and zwitterions, some of which are labile or are prepared for specific purposes, their preparative methods are discussed in Chapter 8, for diaryl iodonium salts and related compounds, Chapter 9 for perfluoroalkyl, alkenyl and alkynyl phenyliodonium salts and Chapter 10 for zwitterionic iodonium compounds. In addition, the preparation of some lesser known reagents, including 2-iodosylbenzoic acid, is given in Chapter 12.

2.1 [BIS(ACYLOXY)IODO]ARENES

Although several methods are available for the preparation of the title compounds, in practice the starting material is (diacetoxyiodo)benzene (DIB). The standard method for its preparation is direct oxidation of iodobenzene with either peracetic acid [1] or sodium perborate in acetic acid [2]. The first method appears to be preferable; it requires great care in maintaining temperature at exactly 40°C: at a lower temperature the reaction fails completely, whereas at a higher temperature overoxidation occurs. Also, the reaction fails with old samples of hydrogen peroxide which have lost their original titre. The perborate method is simpler and temperature control needs not be as strict; however, it is more expensive and the yield of DIB is lower. It is considered suitable for small scale preparations of (diacetoxyiodo) arenes.

(Diacetoxyiodo)benzene, DIB [1]

$$PhI \xrightarrow[Ac_2O]{H_2O_2} PhI(OAc)_2$$

A stirred mixture of acetic anhydride (305 ml) and 30% hydrogen peroxide (70 ml) was kept at exactly 40°C for 4 h; the use of a thermostated bath is strongly recommended. To the resulting peracetic acid solution, iodobenzene (52 g, 28.5 ml) was added with stirring over 15 min and the clear reaction mixture was kept overnight at room temperature. A part of DIB crystallized out and was collected; then ice–water (~ 400 ml) was added to the filtrate and a further crop of crystals was obtained. The combined material was washed with cold water and petroleum ether and was dried in a desiccator over sodium hydroxide to yield 55–65 g (67–79%) of crude DIB, m.p. 156–159°C (recrystallized from chloroform, m.p. 163–165°C); this purity is satisfactory in most cases.

DIB is stable in the air; it can be stored at room temperature for long periods, provided it is light-protected. It dissolves in several ordinary solvents, most of which react with it at elevated temperature. A study in some solvents, using iodometric titration for monitoring the loss of oxidation power of DIB with time, showed that benzene is one of the most inert: DIB remained unaltered in it at 25–50°C after 24 h. In contrast, in dimethylsulphoxide (DMSO) at 25°C 97% decomposed after 24 h. Acetone, methanol, methylene chloride, chloroform, acetic acid and acetonitrile are suitable solvents at room temperature even though they are reactive at elevated temperature [3]. Anyway, heating is rarely required in reactions with DIB and in such cases it is for short periods of time, so that the solvent reaction is unimportant.

[Bis(trifluoroacetoxy)iodo]benzene (BTI) [4]

$$PhI(OAc)_2 \xrightarrow{CF_3CO_2H} PhI(O_2CCF_3)_2$$

(Diacetoxyiodo)benzene (20 g) was dissolved in boiling trifluoroacetic acid (25 ml); on cooling to room temperature BTI crystallized out as colourless crystals of good purity (17 g, 60%). The product was washed with petroleum ether and dried in a desiccator over potassium hydroxide. A second crop was obtained by cooling at 0°C; this was contaminated with (diacetoxyiodo)benzene and should be collected separately; when a sufficient quantity accumulated from several batches, it was treated with trifluoroacetic acid as above. Complete removal of the solvent is not recommended because some decomposition occurs at elevated temperature; in the presence of acetic acid the oxygen-bridged *meso* compound $PhI(OOCCF_3)OI(OOCCF_3)Ph$ may also be formed. The filtrate is a mixture of trifluoroacetic acid and acetic acid which differ substantially in their boiling points, so that most of the more volatile (and expensive) trifluoroacetic acid (b.p. 74°C) may be recovered by fractional distillation.

Pure BTI is obtained by recrystallization from acetone–petroleum ether (m.p. 112–120°C with decomposition, depending on the rate of heating). It is soluble in several organic solvents, such as acetone, acetonitrile, chloroform, dichloromethane, ethanol and ether. Most of them react slowly with BTI, even at room temperature; nevertheless, since its reactions do not require heating and are completed in a short time, by-products from reactions with the solvent are minimal and do not pose a problem. The reagent is fairly stable and can be kept without refrigeration for a long period of time, with light protection.

Exchange reactions of DIB with practically any acid is the most convenient method for the preparation of [bis(acyloxy)iodo]benzenes.

[Bis(acyloxy)iodo]benzenes [5]

$$PhI(OAc)_2 \xrightarrow{RCO_2H} PhI(O_2CR)_2$$

A solution of DIB (6 g, 18.6 mmol) and the acid (37.2 mmol) in chlorobenzene (75 ml) was treated in a rotary evaporator to 50–55°C, until the solvent and acetic acid were completely evaporated. The residue obtained was essentially pure [bis(acyloxy)iodo]benzene, in nearly quantitative yield.

Alternative methods involved nucleophilic substitution at iodine in (dichloroiodo)benzene or BTI by the acyloxy group of silver or sodium carboxylates; the latter permits the preparation of mixed [bis(acyloxy)iodo]benzenes with two different acyloxy groups [6]. Also, heating of iodosylbenzene and an acid (molar ratio 1:2) in chloroform results in the formation of [bis(acyloxy)iodo]benzenes quantitatively. A stable (diformyloxyiodo)arene from

2-nitro-4-methyl-iodosylbenzene and formic acid has been prepared in this way in the old literature [7].

Direct oxidation of pentafluoroiodobenzene in fluorotrichloromethane resulted in the preparation of perfluoro DIB, $C_6F_5I(O_2CCF_3)_2$; the oxidant was trifluoroperacetic acid formed *in situ* from 91% hydrogen peroxide and trifluoroacetic anhydride [8]. Heating of $C_6F_5I(O_2CCF_3)_2$ with pentafluorobenzoic acid in carbon tetrachloride resulted in the formation of $C_6F_5I(O_2CC_6F_5)_2$ [9]. Similar methods have been applied for the preparation of [bis(trifluoroacetoxy)iodo]perfluoroalkanes, i.e. either oxidation of perfluoroiodides with trifluoroperacetic acid [10], or reactions of (dichloroiodo)perfluoroalkanes with silver trifluoroacetate [11].

2.2 (DIFLUOROIODO)- AND (DICHLOROIODO)ARENES

The most practical method for the preparation of (difluoroiodo)arenes is from (dichloroiodo)arenes on reaction with mercuric oxide and hydrofluoric acid.

(Difluoroiodo)arenes [12]

$$\mathrm{ArICl_2} \xrightarrow[\mathrm{HgO}]{\mathrm{HF}} \mathrm{ArIF_2}$$

The (dichloroiodo)arene (40 mmol) and finely ground yellow mercuric oxide (10.8 g, 50 mmol) were shaken in a polyethylene bottle with dichloromethane (100 ml). Hydrofluoric acid (48%, 10 ml) was added and the bottle shaken vigorously for about 1 min. The colour of the solution turned from bright yellow to nearly colourless. Then the solvent phase was carefully decanted. The residue was shaken with dichloromethane (50 ml) which was combined with the original solution. The reagent formed was used in this solution for fluorination. In order to find its titre, a portion (1 ml) was analysed by titration of the iodine liberated by reaction with aqueous potassium iodide. The yield was calculated to be in the range 60–90%.

Several (difluoroiodo)arenes are stable at room temperature; when they are pure, they melt without decomposition. However, they present difficulties in handling and usually their preparation *in situ* is preferable. They can be kept in PTFE or polyethylene containers but not in glass containers, since glass is slowly attacked.

The direct chlorination of iodoarenes is a very effective and convenient method to obtain (dichloroiodo)arenes in good yield; this approach was recommended for the purification of arenes. The method described in *Organic Syntheses* [13] is also suitable for a wide number of iodoarenes. An alternative new method involved the oxidation of iodoarenes with a mixture of sodium perborate and hydrochloric acid, in acetonitrile or carbon tetrachloride.

(Dichloroiodo)arenes [14]

$$\mathrm{ArI} \xrightarrow[\mathrm{NaBO_3 \cdot 4\,H_2O}]{\mathrm{HCl}} \mathrm{ArICl_2}$$

Sodium perborate tetrahydrate (770 mg, 5 mmol), was added to a stirred solution of the iodoarene (1 mmol) in a mixture of hydrochloric acid (20 ml) and either acetonitrile or carbon tetrachloride (20 ml); the latter was more effective for all three iodoanisoles. The mixture was stirred at room temperature for 2 h (with the exception of *p*-diiodobenzene which required 3 days) and then was diluted with water (100 ml). The resulting solid which separated was collected, washed with water and light petroleum and dried.

(Dichloroiodo)arenes are yellow crystalline compounds, heat- and light-sensitive. They are stable enough to be handled without special precautions and do not hydrolyse by moisture. Several of them can be kept for long periods of time under refrigeration without any alteration, whereas others should be used as rapidly as possible after preparation. In organic solvents they dissociate partially to iodoarenes and chlorine.

2.3 IODOSYLARENES

With the exception of cyclic '*o*-iodosylbenzoic acid' (Section 12.1), unsubstituted iodosylbenzene is normally the reagent of choice. The best methods for its preparation involve hydrolysis of either (dichloroiodo)- or (diacetoxyiodo)benzene. Both have been described but the latter is more convenient and has a better yield.

Iodosylbenzene [15]

$$\mathrm{PhI(OAc)_2} \xrightarrow[\mathrm{H_2O}]{\mathrm{NaOH}} \mathrm{PhIO}$$

Finely ground DIB (32.2 g, 10 mmol) was placed in a 250 ml beaker, and 150 ml of 3N sodium hydroxide was added over 5 min with vigorous stirring. The mixture was triturated with a spatula for 15 min in order to become homogeneous. After standing for 45 min, water was added (100 ml) with vigorous stirring and the solid collected on a Buchner funnel; it was returned to the beaker and triturated in water (200 ml), collected again, washed with water (3 × 200 ml) and dried by maintaining suction. Further purification was effected by triturating this solid in chloroform (75 ml). After air-drying, iodosylbenzene (18.7–20.5 g, 85–93%) was obtained, m.p. 210°C. HAZARD: the compound explodes at its m.p. In some reactions best results were obtained when it was well-crushed and kept over P_4O_{10} for 2–3 weeks. When left at room temperature for long periods of time, iodosylbenzene disproportionates to iodobenzene and iodylbenzene.

2.4 [HYDROXY(TOSYLOXY)IODO]BENZENE AND ITS ANALOGUES

The standard method for the preparation of [hydroxy(tosyloxy)iodo]benzene (HTI) is the reaction of (diacetoxyiodo)benzene (DIB) with *p*-toluenesulphonic acid hydrate.

[Hydroxy(tosyloxy)iodo]benzene, HTI [16]

$$\mathrm{PhI(OAc)_2} \xrightarrow[\mathrm{MeCN}]{\mathrm{TsOH.\,H_2O}} \mathrm{PhI(OH)OTs}$$

p-Toluenesulphonic acid monohydrate (7.61 g, 40 mmol) dissolved in a minimum amount of acetonitrile was added to a suspension of DIB (6.44 g, 20 mmol) in acetonitrile (45 ml) at room temperature. The reaction mixture was allowed to stand for a few hours; crystals of HTI separated (two crops may be collected) in a total yield of 93% (7.62 g). The crude product was washed with acetone (removes *p*-toluenesulphonic acid) and ether (removes acetic acid). It may be recrystallized from acetonitrile or methanol–ether; m.p. 140–142°C.

HTI is a stable crystalline compound, which may be stored at room temperature. It is slightly soluble in dichloromethane (5.3 mg/ml) and moderately soluble in water (1 g/42 ml); in most ordinary solvents it is practically insoluble and it usually enters into reactions from suspensions.

The preparation of HTI analogues, for example with a camphorsulphonyloxy group in the place of the tosyloxy group, was effected similarly [17]. Also, phenyl substituted analogues have been obtained by this procedure or through metathetical reactions between HTI and iodoarenes [18].

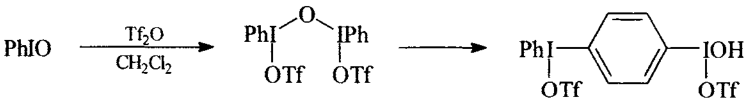
[Methoxy(tosyloxy)iodo]benzene was prepared by simply dissolving HTI in trimethyl orthoformate [19]:

$$\mathrm{PhI(OH)OTs} \xrightarrow[86\%]{\mathrm{HC(OMe)_3}} \mathrm{PhI(OMe)OTs}$$

An exchange reaction between HTI and some optically active alcohols (R*OH) was used for the preparation of compounds of the general formula PhI(OR*)OTs [20].

1,4-Bis(iodosyl)benzene reacted with triflic anhydride to afford a bis iodine (III) derivative [21]. DIB or iodosylbenzene, however, do not afford with triflic acid, or its anhydride, the expected analogues of HTI, although these are initially formed. The reaction of iodosylbenzene and triflic anhydride leads to two different products, depending on reaction time. When triflic acid was allowed to react with iodosylbenzene in dichloromethane for about 20 min the yellow μ-compound **1** (m.p. 100–110°C) was obtained; it was the same with the so-called Zefirov's reagent, which was originally prepared from DIB and triflic acid in chloroform. When the reaction time was extended to 12 h, then **1** isomerized to the slightly pale yellow compound **2** (m.p. 125–132°C). For preparative purposes the direct reaction of iodosylbenzene with triflic acid was preferable for **2**, since it was isolated in 94% yield.

μ-Oxo-bis[(trifyloxy)(phenyl)]iodine, 1 [22]



1 **2**

Triflic anhydride (1.17 g, 4.14 mmol) in dry dichloromethane (5 ml) was added slowly at room temperature to a stirred mixture of freshly prepared and carefully dried iodosylbenzene (1.77 g, 8.05 mmol), in dichloromethane (5 ml). The reaction was carried out in a flame-dried 50 ml three-neck flask under nitrogen. The solution became homogeneous after 5 min and a yellow solid precipitated after another 20 min. This was collected on a Schlenk filter under nitrogen, rinsed with dichloromethane (3 × 5 ml) and dried *in vacuo*, affording **1** (1.64 g, 93%), mildly air-sensitive but thermally stable.

1-[Hydroxy(trifyloxy)iodo]-4-[(phenyl)(trifyloxy)iodo]benzene, 2 [23]

$$\mathrm{PhIO} \xrightarrow[\mathrm{CH_2Cl_2}]{\mathrm{TfOH}} \mathbf{2}$$

To a stirred suspension of iodosylbenzene (10 mmol) in dry dichloromethane (20 ml) was slowly added, dropwise, triflic acid (3 g, 20 mmol) at 0°C. The reaction mixture was stirred for 4 h at room temperature, concentrated and dry ether was added to the residue. Compound **2** crystallized upon trituration, was washed with dry ether and dried *in vacuo*; it could be handled at room temperature without any special precaution.

2.5 REAGENTS OF IODINE (V)

The preparation of iodylbenzene has been described in *Organic Syntheses* from (dichloroiodo)benzene [24]; an alternative simpler method involved the direct oxidation of iodobenzene using aqueous hypochlorite and phase transfer catalysis.

Iodylbenzene [25]

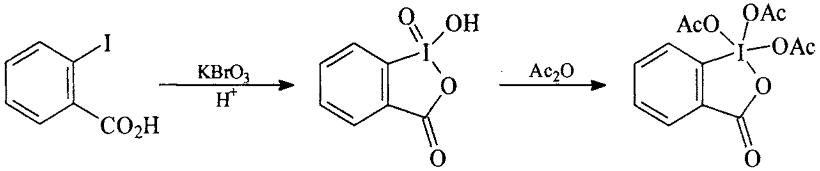
$$\mathrm{PhI} \xrightarrow[\mathrm{cat.}]{\mathrm{HOCl\ /\ H_2O}} \mathrm{PhIO_2}$$

Iodobenzene (1.01 g, 4.9 mmol) was dissolved in dichloromethane (75 ml) and stirred vigorously with hypochlorite solution (200 ml of commercial laundry bleach adjusted to pH 8.2 and containing 200 mg of tetrabutylammonium hydrogen sulphate) at room temperature for 45 min. The reaction mixture was allowed to stand for 1 h; then the precipitate was filtered to give crude iodylbenzene (0.69–0.94 g, 59–81%). Purification may be effected by crystallization from water or acetic acid.

HAZARD: the melting point of iodylbenzene (231–240°C) is also its decomposition point, accompanied by explosion. Generally, all iodylbenzenes are potentially explosive when heated; a violent decomposition of iodylbenzene (dry sample) has been induced by scraping with a spatula.

The Dess–Martin reagent was prepared in two steps from *o*-iodobenzoic acid which was first converted into the isolable '*o*-iodylbenzoic acid', of cyclic structure. The original procedure for the second step was substantially improved.

a. *1-Oxido-1-hydroxybenziodoxol-3*(1H)*-one* (*o-iodylbenzoic acid)* [26]
b. *1,1,1-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3*(1H)*-one* [27,28]
(Dess-Martin reagent)



a. Potassium bromate (76 g, 0.45 mol) was added to a vigorously stirred mixture of 2-iodobenzoic acid (85.2 g, 0.34 mol) and sulphuric acid (730 ml of 0.73 M) over 30 min, in a 55°C bath. The mixture was warmed to 68°C with stirring for 3.6 h. The precipitate formed on cooling in an ice bath was filtered and washed with water (11 ml) and ethanol (2 × 50 ml) to give the intermediate *o*-iodylbenzoic acid (89 g, 93%) m.p. 232–233°C.

b. This compound (100 g, 0.235 mol) was added to a 1-l flask containing acetic anhydride (400 ml) and *p*-toluenesulphonic acid hydrate (0.5 g) and the mixture was stirred for 2 h in an oil bath at 80°C, with protection from humidity with a drying tube. The reaction mixture was cooled in an ice bath and the precipitate was filtered through a fritted glass funnel, followed by rinsing with anhydrous ether (5 × 50 ml). The resulting title compound (138 g, 91%) was quickly transferred to an argon flushed amber-glass bottle and stored in the cold (m.p. 134°C).

HAZARD: the intermediate *o*-iodylbenzoic acid is explosive on heating above 200°C and also upon impact; the Dess–Martin reagent explodes violently on heating under confinement, at 130°C.

The mono-acetylated form of the above *o*-iodylbenzoic acid, i.e. 1-acetoxy-1,2-benziodoxol-3(1*H*)-one-1-oxide, is probably the actual oxidizing species [28].

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