Iodination of Both Deactivated and Activated Arenes with Sodium Periodate or Sodium Iodate as the Oxidants

Piotr Luliński and Lech Skulski*

Chair and Laboratory of Organic Chemistry, Medical University of Warsaw, Banacha 1, PL 02-097 Warsaw, Poland

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Five easy, relatively inexpensive, and environmentally-safe aromatic oxidative iodination procedures are presented; three of them are particularly suitable for *deactivated* arenes. Nine deactivated arenes, four halobenzenes, benzene, toluene, and *N,N*-dimethylaniline were reacted upon with the following *anhydrous* systems: diiodine/**$NaIO_4$** or (in four cases) **$NaIO_3$**/acetic anhydride/glacial acetic acid, acidified with varying amounts of concd (98%) sulfuric acid; the following workups are explained. The aromatic oxidative iodination reactions proceeded mostly at room temperature and within 1—8 h to give fifteen mono- and two diiodinated purified products (sometimes obtained in 2—3 different ways) in 51—95% yields.

Aromatic iodides are generally more reactive than the respective chlorides and bromides; hence, they have found many applications in organic syntheses (see e.g. Ref. 1, p. 924). Moreover, they are suitable to form stable polyvalent iodine derivatives, which are versatile reagents in organic synthesis.[2] Many different methods, and their improvements, have been reported for the effective preparation of aromatic iodides,[1,3,4] but it is still desirable to seek *better*, i.e. quick, inexpensive, easy, and *environmentally benign* methods. In our former papers[5—8] we reported simple and efficient laboratory methods for the oxidative iodination of: (i) some highly activated arenes with molecular iodine (diiodine) in the presence of lead(IV) acetate in glacial acetic acid,[5] (ii—iv) both activated and deactivated arenes in the *anhydrous*, strongly acidic systems, viz. $I_2/CrO_3/Ac_2O/AcOH$/concd H_2SO_4,[6] I_2/activated $MnO_2/Ac_2O/AcOH$/concd H_2SO_4 or $I_2/KMnO_4/Ac_2O/AcOH$/concd H_2SO_4.[7] However, these reactions demanded the use of more or less *toxic*, though readily available and inexpensive, oxidants; hence the wastes left after the oxidative iodination reactions were unavoidably contaminated with Pb(II), Cr(III), or Mn(II) salts, respectively. Recently, we have reported[8] some improved, acid-catalyzed iodinating (and brominating) procedures for *activated* aromatics with (diacetoxyiodo)benzene as the fairly *non-toxic*, relatively cheap, and readily available[9] oxidant; these effective procedures (in which acetic acid/acetic anhydride *anhydrous* mixtures were used as the solvents) allowed us to mono-, di-, and even triiodinate several arenes, more reactive than chlorobenzene, at room temperature and within 15 min. In our opinion, the particular emphasis should be put now on seeking some much better oxidative iodination procedures, applicable for various **deactivated** aromatics. This was just the main aim of the present work.

Taking into account the environmental safety as well as the total costs of all the iodine consumed, very promising have been, and still are, the aromatic oxidative iodination reactions with inorganic iodine(VII) and iodine(V) reagents used as the oxidants, viz. periodic acid or its salts, iodic acid or its salts, as well as diiodine pentaoxide. In acidic media, often containing an amount of *water*, most of the reported aromatic iodination reactions proceeded according to the following general stoichiometries and mechanisms:

$3I_2 + I(VII) \rightarrow 7I^+$ (various electrophilic transient *iodine(I)* species)

$2I_2 + I(V) \rightarrow 5I^+$ (as above)

H–Ar–H (activated) + 1 or $2I^+ \rightarrow$ **H–Ar–I** or **I–Ar–I** + 1 or $2H^+$

The characteristic feature of all these reactions is that diiodine is oxidized by the aforementioned oxidants to form some transient *iodine(I)* species, I^+, whereas all the above oxidants are reduced by diiodine to form the same transient I^+ species, which next react with an aromatic compound, eventually leading to the formation of only the desired iodination product, **Ar–I** or **I–Ar–I**, and *water* (as well as e.g. Na_2SO_4 and/or $NaHSO_4$, if $NaIO_4$ or $NaIO_3$ are used as the oxidants in liquid media acidified with concd H_2SO_4)—hence without any strongly toxic residues.

So far, periodic acid or its salts,[1,10—12] and iodic acid or its salts[1,12,13] have been used as the oxidants by a number of authors to iodinate oxidatively a variety of **activated** aromatics, but with including also halobenzenes.[13] Only I_2O_5 has scarcely ever been used until recently.[14,15] Periodic acid is a strong oxidant:[10] the standard potential E° for the periodate–iodate couple in acid solution is above 1.6 V; the oxidation power of free iodic acid is only slightly lower. Condensed polynuclear aromatic compounds were readily iodinated oxidatively with diiodine in the presence of iodic or periodic acid, but the latter sometimes oxidized the substrates.[12,16] Suzuki[17] concluded his extensive studies as follows: The oxidative iodination with periodic acid is

"the most convenient method for preparation of mono- or diiodo derivatives from various polyalkylbenzenes in high yields;" see Table 2 in Ref. 1. Merkushev[1] summarized the literature results as follows: "the iodination in the presence of iodic acid and periodic acid is accelerated considerably by the addition of sulfuric acid and, in some cases, of *water*. These ***mild oxidants*** are widely used in the iodination of aromatic compounds *activated* to electrophilic substitution reactions as well as in iodination reactions of polynuclear aromatic compounds." 1,2,4,5-Tetraiodobenzene (60%) or hexaiodobenzene (73%) were obtained from benzene by the treatment with solutions of periodic acid and potassium iodide in concd H_2SO_4.[18] There is also evidence that for some aromatic oxidative iodinations I_3^+ may be the attacking entity, when SO_3 or HIO_3 is the oxidizing agent.[3a,3d] Finally, the treatment of halobenzenes, benzoic acid, or nitrobenzene, dissolved in various solvents, with HIO_3 and concd H_2SO_4 possibly resulted in the formation of the respective iodylarenes, Ar–IO_2; next, they may be reduced to the corresponding iodides, Ar–I.[12,19]

Periodic acid, $NaIO_4$, I_2O_5, iodic acid, and $NaIO_3$ are commercially available with notably *lower costs*[20] for the two sodium salts. These salts in solutions or suspensions acidified with excess concd H_2SO_4 would momentarily form in situ either HIO_4 or HIO_3, respectively. For example, German chemists[13] made the following remark (p. 90, footnote): "We always applied in our (oxidative iodination) reactions the large-grained iodic acid from Merck; no pretreatment of it was neccesary. Also *alkali metal iodates* may be used in the reactions, if appropriate amounts of a mineral acid are added."

However, it is necessary to recall that iodates *alone*, e.g. KIO_3, can effectively react with benzene and activated arenes in *anhydrous* Ac_2O/AcOH/H_2SO_4 mixtures to afford symmetrical diaryliodonium salts, viz.[21]

$$2\text{Ar–H} + IO_3^- + 2H_2SO_4 + 2Ac_2O \rightarrow Ar_2I^+ + 2HSO_4^- + 4\text{AcOH} + [\text{O}]$$

Results and Discussion

For benzene, toluene, four halobenzenes, 4-nitroanisole, and *N,N*-dimethylaniline their oxidative iodination reactions were carried out by us according to the following stoichiometry (improved Procedure **1**):

$$14\text{Ar–H} + 6I_2 + 2NaIO_4 + 8Ac_2O + H_2SO_4 \xrightarrow[4\text{—}5\text{ h; mostly r.t.}]{\text{AcOH/Ac}_2\text{O}} 14\textbf{Ar–I} + Na_2SO_4 + 16\text{AcOH} \quad (1)$$

Supposedly, only some transient *iodine(I)* species are acting there (as *weaker* electrophiles) upon the eight reacted arenes. After one suspends $NaIO_4$ and powdered diiodine in a cooled (5—10 °C) *anhydrous* mixture of glacial acetic acid with acetic anhydride, the following concentrated (98%) H_2SO_4 should be added dropwise very slowly, with stirring, to keep the temperature **below 10 °C** (strongly exothermic reaction).[22] Then, an appropriate activated arene was added, and after its dissolving, the main iodination reaction was started. The reaction mixtures were usually stirred for 4—5 h, mostly at room temperature (Table 1). The least reactive 4-nitroanisole was at first stirred at room temperature for one hour, but its iodination was completed by a further stirring for one hour at 45 °C. The most reactive *N,N*-dimethylaniline was iodinated in 65% yield by stirring at +5 °C for only one hour.[23] Then, all the reaction mixtures were quenched by pouring them into excess aqueous Na_2SO_3 solutions (*under a fume hood !*); the following simple workups and good yields (55—76%) of the purified products are explained in the Experimental Section and listed in Table 1, respectively.

In improved Procedure **2** we halved the amount of the benzene added to the reaction mixture (in respect to that used in Procedure **1**) to obtain finally, after the workup and recrystallization from ethanol, the purified 1,4-diiodobenzene in 85% yield.

In our former papers[6,7] we have expressed the opinion that in the ***anhydrous***, strongly acidic media, such strong oxidants as CrO_3, activated MnO_2, or $KMnO_4$ [as well as *metaperiodic* or *iodic acid* produced in situ in the present work from $NaIO_4$ or $NaIO_3$] may readily oxidize diiodine to some transient *iodine(III)* species, acting upon deactivated aromatics as *stronger* electrophiles than I^+, viz.

$$2I_2 + 3\text{I(VII)} \rightarrow 7I^{3+} \text{ (various strongly electrophilic transient } \textit{iodine(III)} \text{ species)}$$

$$I_2 + 3\text{I(V)} \rightarrow 5I^{3+} \text{ (as above)}$$

$$\text{H–Ar–H (deactivated)} + 1 \text{ or } 2I^{3+} \rightarrow \text{H–Ar–I}^{2+} \text{or } I^{2+}\text{–Ar–I}^{2+} + 1 \text{ or } 2H^+$$

We have observed during our numerous experiments that in the presence of **water** (which always considerably diminishes the activity of all electrophilic iodinating species, owing to its high hydration power) the assumed transient *iodine(III)* species (denoted above as I^{3+}) are *unstable* and very quickly vanish to form some less reactive and more stable *hydrated* species, probably I–$O^{\oplus}H_2$. Assumingly, these transformations would undergo as follows:

$$I_2^{3+}(SO_4)_3 + 2H_2O \rightarrow I_2^{1+}(SO_4) + 2H_2SO_5$$
$$I^{3+}(SO_4)OSO_3H + H_2O \rightarrow I^{1+}OSO_3H + H_2SO_5$$
$$I^{3+}(OSO_3H)_3 + H_2O \rightarrow I^{1+}OSO_3H + H_2SO_5 + H_2SO_4$$
$$I_2(SO_4) + 2H_2O + H_2SO_4 \rightarrow 2\text{I–O}^{\oplus}H_2 + 2HSO_4^{\ominus}$$
$$IOSO_3H + H_2O \rightarrow \text{I–O}^{\oplus}H_2 + HSO_4^{\ominus}$$
$$H_2SO_5 + H_2O \rightarrow H_2SO_4 + H_2O_2$$

Hence, the *anhydrous* and strongly acidic conditions are indispensable to attain the possible highest yields of the assumed organic *iodine(III)* intermediates, Ar–ISO_4 or O_4SI–Ar–ISO_4,[24] derived from the reacted deactivated arenes by their electrophilic substitution with I^{3+}. After completing the main iodination reactions, the resulting reaction mixtures were poured into excess aqueous Na_2SO_3 solutions [which also destroyed unreacted diiodine and any oxidizing species]:

Table 1. Iodinated Pure Products Prepared (Checked with TLC)

Substrate	Procedure	Product	Yield %	Time/h (Temp/°C)	Analysis/I% Calcd (Found)	Mp/°C/ **solvent**[a] (lit)[25]
C_6H_6	**1b**	PhI	65	4 (r.t.)	62.23 (62.08)	bp 73—77/34 (bp 63—64/8; 188/760)
C_6H_6	**2**	1,4-$I_2C_6H_4$	85	4 (r.t.)	76.95 (76.20)	129—131/**E** (129)
PhI	**1c**	1,4-$I_2C_6H_4$	67	5 (r.t.)	76.95 (76.40)	129—131/**E** (129)
PhI	**3b**	1,4-$I_2C_6H_4$	82	3 (r.t.)	76.95 (76.63)	129—131/**E** (129)
PhBr	**1c**	4-BrC_6H_4I	76	5 (r.t.)	44.86 (44.80)	92—94/**E** (91—92)
PhBr	**3a**	4-BrC_6H_4I	85	3 (r.t.)	44.86 (44.62)	92—94/**E** (91—92)
PhBr	**5a**	4-BrC_6H_4I	87	3 (r.t.)	44.86 (44.44)	92—94/**E** (91—92)
PhCl	**1c**	4-ClC_6H_4I	73	5 (r.t.)	53.22 (52.67)	54—55/**E** (57)
PhCl	**3a**	4-ClC_6H_4I	56	3 (r.t.)	53.22 (52.90)	54—55/**E** (57)
PhF	**1c**	4-FC_6H_4I	70	5 (r.t.)	57.18 (56.87)	bp 78—80/25 (bp 182—184/760)
PhMe	**1b**	4-IC_6H_4Me[b]	55	4 (r.t.)	58.22 (57.75)	bp 84—88/15 (bp 100/25; 36—37)
$PhN(Me)_2$	**1a**	4-$IC_6H_4N(Me)_2$	65	1 (5)	51.36 (50.48)	80—81/**E** (82)
4-$NO_2C_6H_4OMe$	**1d**	2-MeO-5-NO_2-C_6H_3I	68	1 (r.t.) 1 (45)	45.48 (45.06)	92—93/**E** (97)
PhCOOH	**3c**	3-IC_6H_4COOH	95	4 (r.t.)	51.17 (50.92)	189—190/**C** (187—188)
PhCOOH	**5a**	3-IC_6H_4COOH	93	4 (r.t.)	51.17 (50.97)	188—189/**C** (187—188)
PhCOOMe	**3c**	3-IC_6H_4COOMe	87	4 (r.t.)	48.43 (48.36)	50—52/**P** (54—55)
PhCOOEt	**3c**	3-IC_6H_4COOEt	68	4 (r.t.)	45.97 (46.17)	bp 161—162/30 (bp 150.5/15)
$PhNO_2$	**3f**	3-$IC_6H_4NO_2$	86	4 (r.t.) 3 (65)	50.96 (50.49)	37—38/**P** (38)
$PhNO_2$	**5c**	3-$IC_6H_4NO_2$	92	4 (r.t.) 3 (65)	50.96 (50.50)	37—38/**P** (38)
4-$NO_2C_6H_4Me$	**3d**	2-Me-5-NO_2-C_6H_3I	88	1 (r.t.) 2 (50)	48.25 (47.78)	53—54/**E** (61)
$PhCF_3$	**3e**	3-$IC_6H_4CF_3$	64	1 (r.t.) 3 (65)	46.65 (46.18)	bp 84—88/40 (bp 182—183/760)
4-ClC_6H_4CHO	**3d**	4-Cl-3-IC_6H_3CHO	91	8 (r.t.)	47.63 (47.48)	114—116/**E** (117)
4-MeC_6H_4COOH	**3d**	3-I-4-Me-C_6H_3COOH	92	1 (r.t.) 3 (45)	48.43 (47.37)	210—211/**C** (210—212)
4-MeC_6H_4COOH	**5b**	3-I-4-Me-C_6H_3COOH	83	5 (r.t.)	48.43 (48.01)	210—211/**C** (210—212)
PhCOPh	**4**	3-$IC_6H_4COC_6H_4I$-3′	51	4 (r.t.)	58.48 (58.58)	140—142/**A** (152.5—153.5)

a) Solvents used for recrystallization: **A:** Me_2CO; **C:** CCl_4; **E:** EtOH; **P:** petroleum ether. b) There is a mixture of *o*- and *p*-isomers (ratio 1 : 5; ^1H NMR).

$$Ar\text{–}ISO_4 + Na_2SO_3 + H_2O \rightarrow \mathbf{Ar\text{–}I} + Na_2SO_4 + H_2SO_4$$

$$O_4SI\text{–}Ar\text{–}ISO_4 + 2Na_2SO_3 + 2H_2O \rightarrow \mathbf{I\text{–}Ar\text{–}I} + 2Na_2SO_4 + 2H_2SO_4$$

Thus, for the following eight *deactivated* arenes iodinated oxidatively with the appropriate $I_2/NaIO_4/Ac_2O/AcOH/$ concd H_2SO_4 system, viz. nitrobenzene, 4-nitroanisole, α,α,α-trifluorotoluene, benzoic acid and its methyl and ethyl esters, 4-toluic acid, 4-chlorobenzaldehyde [however, *we failed* to iodinate benzaldehyde, benzonitrile, and benzamide] as well as (for comparison) iodobenzene, bromobenzene, and chlorobenzene, we carried out their iodination reactions according to the considerably changed (as compared

with Procedure **1**) general reaction stoichiometry as follows (novel Procedure **3**):

$$14\text{Ar–H} + 4\text{I}_2 + 6\text{NaIO}_4 + 24\text{Ac}_2\text{O} + 17\text{H}_2\text{SO}_4 \xrightarrow[3\text{—}8\text{ h; mostly r.t.}]{\text{AcOH/Ac}_2\text{O}} 14\text{Ar–ISO}_4 + 3\text{Na}_2\text{SO}_4 + 48\text{AcOH} \quad (2)$$

After the main iodination reactions were completed within 3—8 h and mostly at room temperature (unless otherwise stated in Table 1), the strongly acidic final reaction mixtures were poured into excess aqueous Na_2SO_3 solutions. After the crude aryl iodides, **Ar–I**, were collected by filtration, they were recrystallized from appropriate organic solvents (Table 1) to give the eleven purified monoiodinated products in good or excellent yields (56—95%). Due to the presence of the aldehyde group in 4-chlorobenzaldehyde, we avoided the use of aqueous Na_2SO_3 solution for quenching the final reaction mixture; see Experimental for the alternative method applied, which worked well. However, when *benzene* was monoiodinated according to Procedure **3**, rather impure iodobenzene, bp 70—78 °C/35, was obtained in only 43% yield.

In novel Procedure **4**, suitable for the oxidative diiodination of *deactivated* arenes, the amount of the benzophenone added to the reaction mixture was halved (in respect to that used for the monoiodination of Ar–H in Procedure **3**) to obtain finally, after the workup and recrystallization from acetone, the purified 3,3′-diiodobenzophenone in only 51% yield; for more details see Experimental.

Finally, using the appropriate $I_2/NaIO_3/Ac_2O/AcOH/$ concd H_2SO_4 system—equally suitable for the oxidative monoiodination of *deactivated* arenes as that used in Procedure **3**—we monoiodinated nitrobenzene, benzoic acid, and 4-toluic acid, as well as (for comparison) bromobenzene, according to the general reaction stoichiometry shown below (novel Procedure **5**):

$$10\text{Ar–H} + 2\text{I}_2 + 6\text{NaIO}_3 + 18\text{Ac}_2\text{O} + 13\text{H}_2\text{SO}_4 \xrightarrow[3\text{—}7\text{ h; mostly r.t.}]{\text{AcOH/Ac}_2\text{O}} 10\text{Ar–ISO}_4 + 3\text{Na}_2\text{SO}_4 + 36\text{AcOH} \quad (3)$$

After completing, as above, the main iodination reactions within 3—5 h at room temperature (except for nitrobenzene, see Table 1), the strongly acidic final reaction mixtures were poured into excess aqueous Na_2SO_3 solutions. The crude aryl iodides, **Ar–I**, were collected by filtration and recrystallized from appropriate organic solvents (Table 1) to give the four purified monoiodinated products in excellent yields (83—93%).

Summing up, our easy and relatively inexpensive Procedures **1**—**5** presented in this paper gave mono- or diiodinated products from both activated and deactivated arenes in good or excellent yields (51—95%). In our opinion, particularly interesting are our iodination results obtained with *deactivated* arenes (novel Procedures **3**—**5**). There has been a general opinion that inorganic iodine(VII) and iodine(V) oxidants are ***mild***[1]-hence they can hardly be appropriate for the effective oxidative iodination of deactivated aromatic substrates. Our present experimental results show clearly that this opinion should be denied, if acidic and anhydrous conditions are maintained in the reactions. It is also of importance that no strongly toxic wastes are left after completing the oxidative iodination reactions with using Procedures **1**—**5**.

The structures of the *purified* iodinated products (their purity was also checked by TLC), all known in the literature, were supported by their melting points (or boiling points) compared with those submitted in the literature (Table 1) as well as by mixed melting points with authentic specimens obtained by reported methods. The structures were also supported by elemental analyses (Table 1).

Experimental

Melting or boiling points in Table 1 are uncorrected. The commercial reagents and solvents were purified or dried, if necessary, prior to use. Sodium metaperiodate and sodium iodate were commercial reagents (Aldrich).[20] Molecular iodine (diiodine) should be ***finely powdered*** in order to facilitate its dissolution. Elemental analyses were carried out at the Institute of Organic Chemistry, the Polish Academy of Sciences, Warsaw.

Procedure 1: The Monoiodination of Some More Active Arenes with $NaIO_4$ as Oxidant: $NaIO_4$ (0.43 g, 2.0 mmol; 0% excess) [for halobenzenes: 0.47 g, 2.2 mmol; 10% excess] and diiodine (1.52 g, 6.0 mmol; 0% excess) [for *N*,*N*-dimethylaniline: 1.68 g, 6.6 mmol; 10% excess] were suspended in a stirred mixture of glacial AcOH (10 ml) with Ac_2O (5 ml) cooled to 5—10 °C. Alternatively, *varied quantities*[22] (see below) of concentrated (98%) H_2SO_4 were very slowly added dropwise, with vigorous stirring while keeping the temperature at 5—10 °C (*exothermic reaction*), viz.

(a) for *N*,*N*-dimethylaniline, 0.27 ml (0.49 g; 5 mmol) of concd H_2SO_4 was added;

(b) for benzene and toluene, 1.07 ml (1.96 g; 20 mmol) of concd H_2SO_4 was added;

(c) for four halobenzenes, 5.33 ml (9.80 g; 100 mmol) of concd H_2SO_4 was added;

(d) for 4-nitroanisole, 8.52 ml (15.68 g; 160 mmol) of concd H_2SO_4 was added.

An appropriate *arene* (14.0 mmol; 0% excess) [for benzene, toluene, *N*,*N*-dimethylaniline, and 4-nitroanisole: 15.4 mmol; 10% excess] was added portionwise or dropwise with stirring, and the stirring was continued for 1—5 h, mostly at room temperature (Table 1). The reaction mixture was poured into ice-water containing the previously dissolved Na_2SO_3 [0.5 g, 3.96 mmol in Procedures **1** and **2**; 2.5 g, 19.8 mmol in Procedures **3**—**5**] (*under a fume hood!*). After ca. 15 min, the *solid* products were collected by filtration, washed well with water, air-dried, and recrystallized from appropriate solvents (Table 1). The *oily* products were extracted with $CHCl_3$ (3×10 ml), the collected extracts were dried ($MgSO_4$), the solvent was distilled off, and the residues were fractionated under vacuum (Table 1).

Procedure 2: The Diiodination of Benzene with $NaIO_4$ as Oxidant: $NaIO_4$ (0.60 g, 2.8 mmol; 40% excess) and diiodine (2.13 g, 8.4 mmol; 40% excess) were suspended in a stirred mixture of glacial AcOH (10 ml) with Ac_2O (5 ml) cooled to 5—10 °C. Concentrated (98%) H_2SO_4 (2.66 ml, 4.90 g; 50 mmol) was very slowly added dropwise, with vigorous stirring while keeping the temperature at 5—10 °C (*exothermic reaction*). Then *benzene* (0.55 g, 7.0 mmol; 0% excess) was added, and the stirring was continued for 4 h at room temperature. The reaction mixture was poured into ice-water containing the previously dissolved Na_2SO_3 (*fume hood*). After ca. 15 min, the collected precipitate was worked

up as above in Procedure **1** (Table 1).

Procedure 3: The Monoiodination of Some Deactivated Arenes with $NaIO_4$ as Oxidant: $NaIO_4$ (1.54 g, 7.2 mmol; 20% excess) and diiodine (1.22 g, 4.8 mmol; 20% excess) [for α,α,α-trifluorotoluene: $NaIO_4$ (1.28 g, 6.0 mmol; 0% excess) and diiodine (1.02 g, 4.0 mmol; 0% excess)] were suspended in a stirred mixture of glacial AcOH (10 ml) with Ac_2O (5 ml) cooled to 5—10 °C. Alternatively, *varied quantities*[22] (see below) of concentrated (98%) H_2SO_4 were very slowly added dropwise, with vigorous stirring while keeping the temperature at 5—10 °C (*exothermic reaction*), viz.

(a) for chlorobenzene and bromobenzene, 2.13 ml (3.92 g; 40 mmol) of concd H_2SO_4 was added;

(b) for iodobenzene, 3.20 ml (5.88 g; 60 mmol) of concd H_2SO_4 was added;

(c) for benzoic acid, and its methyl and ethyl esthers, 4.26 ml (7.84 g; 80 mmol) of concd H_2SO_4 was added;

(d) for 4-nitrotoluene, 4-toluic acid, and 4-chlorobenzaldehyde, 5.33 ml (9.80 g; 100 mmol) of concd H_2SO_4 was added;

(e) for α,α,α-trifluorotoluene, 10.65 ml (19.6 g; 200 mmol) of concd H_2SO_4 was added;

(f) for nitrobenzene, 15.98 ml (29.4 g; 300 mmol) of concd H_2SO_4 was added.

An appropriate *arene* (14 mmol; 0% excess) [for α,α,α-trifluorotoluene: 15.4 mmol; 10% excess] was added portionwise or dropwise with stirring, and the stirring was continued for 3—8 h, mostly at room temperature (Table 1). The reaction mixture was poured into ice-water containing the previously dissolved Na_2SO_3 (*fume hood*) [**Note:** for *4-chlorobenzaldehyde* its main iodination reaction was quenched by a very slow addition of concd aq HCl (10 ml) to the externally cooled reaction mixture, followed by pouring into 200 ml of ice-water]. After ca. 15 min, the collected crude products were worked up as above in Procedure **1** (Table 1).

Procedure 4: The Diiodination of Benzophenone with $NaIO_4$ as Oxidant: $NaIO_4$ (1.80 g, 8.4 mmol; 40% excess) and diiodine (1.42 g, 5.6 mmol; 40% excess) were suspended in a stirred mixture of glacial AcOH (10 ml) with Ac_2O (5 ml) cooled to 5—10 °C. Concentrated (98%) H_2SO_4 (3.20 ml, 5.88 g; 60 mmol) was very slowly added dropwise, with vigorous stirring while keeping the temperature at 5—10 °C (*exothermic reaction*). Then *benzophenone* (1.27 g, 7.0 mmol; 0% excess) was added, and the stirring was continued for 4 h at room temperature. The reaction mixture was poured into ice-water containing the previously dissolved Na_2SO_3 (*fume hood*). After ca. 15 min, the collected precipitate was worked up as above in Procedure **1** (Table 1).

Procedure 5: The Monoiodination of Some Deactivated Arenes with $NaIO_3$ as Oxidant: $NaIO_3$ (1.43 g, 7.2 mmol; 20% excess) and diiodine (0.61 g, 2.4 mmol; 20% excess) were suspended in a stirred mixture of glacial AcOH (10 ml) with Ac_2O (5 ml) cooled to 5—10 °C. Alternatively, *varied quantities*[22] (see below) of concentrated (98%) H_2SO_4 were very slowly added dropwise, with vigorous stirring while keeping the temperature at 5—10 °C (*exothermic reaction*), viz.

(a) for bromobenzene and benzoic acid, 4.26 ml (7.84 g; 80 mmol) of concd H_2SO_4 was added;

(b) for 4-toluic acid, 5.33 ml (9.80 g; 100 mmol) of concd H_2SO_4 was added;

(c) for nitrobenzene, 15.98 ml (29.4 g; 300 mmol) of concd H_2SO_4 was added.

An appropriate *arene* (10.0 mmol; 0% excess) was added portionwise or dropwise with stirring, and the stirring was continued for 3—7 h, mostly at room temperature (Table 1). The reaction mixture was poured into ice-water containing the previously dissolved Na_2SO_3 (*fume hood*). After ca. 15 min, the collected precipitates were worked up as above in Procedure **1** (Table 1).

In the above Procedures **1**—**5**, the yields of mono- or diiodinated products given in Table 1 were calculated from the total amounts of those reagents (diiodine or arenes) which were used in the reactions in *strictly* stoichiometric quantities (0% excess).

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20 Aldrich Catalogue Handbook of Fine Chemicals 1999—2000: a) periodic acid, 98%, 90.80 DM/100 g; b) $NaIO_4$, 99%, 53.00 DM/100 g; c) I_2O_5, 98+%, 160.90 DM/100 g; d) iodic acid, 99.5%, A.C.S. reagent, 94.20 DM/2×50 g; e) $NaIO_3$, 98+%, 61.50 DM/100 g. The potassium salts are also low-priced: f) KIO_4, 99.8%, A.C.S. reagent, 55.00 DM/100 g; g) KIO_3, 98%, 34.30 DM/100 g.

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22 Varied quantities of concd H_2SO_4 added to the reaction mixtures (established by us experimentally and given in Experimental for each of the arenes iodinated) clearly depended on related reactivities (and basicities) of the arenes investigated. More deactivated was arene, more concd H_2SO_4 had to be added to catalyze better the iodination reaction and to increase possibly the concentration of still *more reactive* either *iodine(I)* (in Procedures **1** and **2**) or *iodine(III)* transient species (in Procedures **3**—**5**):

$$I_2(SO_4) \xrightleftharpoons{+H_2SO_4} 2IOSO_3H \rightleftharpoons 2I^{\oplus} + 2HSO_4^{\ominus}$$

$$I_2(SO_4)_3 \xrightleftharpoons{+H_2SO_4} 2I(SO_4)OSO_3H \rightleftharpoons 2I^{\oplus}(SO_4) + 2HSO_4^{\ominus} \xrightleftharpoons{+H_2SO_4} 2I^{\oplus}(OSO_3H)_2 + 2HSO_4^{\ominus}$$

However, the amount of H_2SO_4 added is always growing to some optimum extent, different for particular arenes. When this extent is considerably exceeded, then the iodination yield may drop strikingly, due to the predominant *protonation* of the reacted aromatic molecules. For example, the most reactive (and basic) *N,N*-dimethylaniline was quickly and effectively iodinated (at +5 °C) only in the least acidic reaction mixture (Experimental). Previously, in a very brief communication, without an experimental part, Soviet authors [Yu. A. Serguchev, V. G. Davydova, D. I. Makhon'kov, A. V. Cheprakov, and I. P. Beletskaya, *Zh. Org. Khim.*, **21**, 2010 (1985); *J. Org. Chem. USSR*, **21**, 1841 (1985)] have reported that on treating PhR (R = H, halogens, CH_3, CF_3) with $I_2/Pb(OAc)_4$ in trifluoroacetic acid, the corresponding aryl iodides were formed in 85—99% yields, determined by GLC. Both *iodine(I)* and ***iodine(III)*** species were assumed to be there the iodination agents. A possibility of intermediate formation of $ArI(OCOCF_3)_2$ from ArH was claimed to be evidenced solely for chlorobenzene (no yield given) reacted upon with a Pb^{4+}–I_2 (3 : 1) system, in which the following stoichiometry is obeyed:

$$3Pb^{4+} + I_2 \rightarrow 3Pb^{2+} + 2I^{3+}.$$

This iodination method has never been published in a more detailed form.

23 For some reasons, *we failed* to iodinate likewise aniline and *N,N*-diethylaniline. It is necessary to recall that *N,N*-dimethylaniline was previously iodinated with I_2/HIO_3 in acetic acid to give, besides 4-iodo-*N,N*-dimethylaniline, a mixture of three other products; for more details see: S. Ghosal, *J. Indian Chem. Soc.*, **42**, 799 (1965); see also Ref. 10 above, p. 242.

24 In the discussed, strongly acidic reaction mixtures, the assumed organic *iodine(III)* intermediates, Ar–ISO_4, are, probably, quickly equilibrating with some other intermediates, viz. Ar–I–$(OSO_3H)_2$. For the sake of simplicity, only the Ar–ISO_4 intermediates are shown and discussed in the text. Their presence in the investigated solutions may be supported experimentally as follows. Evidently, the same fairly stable intermediates were produced, when *aryl iodides* were oxidized by CrO_3 dissolved in strongly acidified solutions: $3Ar\text{–}I + 2Cr^{6+} \rightarrow 3Ar\text{–}I^{2+} + 2Cr^{3+}$. When the resulting solutions were poured into excess aq ammonium acetate solutions, then the respective purified (diacetoxyiodo)arenes were attained in 58—82% yields, viz.[9] $Ar\text{–}ISO_4 + 2AcONH_4 \rightarrow Ar\text{–}I(OAc)_2 + (NH_4)_2SO_4$.

25 "Dictionary of Organic Compounds," 6th ed, Chapman & Hall, London (1996).

Note. Quite recently, Russian chemists [V. K. Chaikovskii, T. S. Kharlova, V. D. Filimonov, and T. A. Saryucheva, *Synthesis*, **1999**, 748] have developed easy and effective procedures for iodination of *deactivated* aromatics, without casual oxidation of CH_3 or even CHO groups (e.g. they iodinated benzaldehyde in 61% yield). The reactions were carried out in 90% concd H_2SO_4 with some superactive iodine reagent "I^+" prepared on a base of *toxic* iodine chloride and silver sulfate, at 0—20 °C and within 15—150 min. Also, nearly all the former iodinating procedures suitable for *deactivated* aromatics are briefly reviewed therein—with excluding, however, Refs. 6 and 7.