A Simple, Two-Step Conversion of Various Iodoarenes to (Diacetoxyiodo)arenes with Chromium(VI) Oxide as the Oxidant[†]

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Received 18 March 1998; revised 9 May 1998

Abstract: Chromium(VI) oxide, an inexpensive and easily handled oxidant, dissolved in the anhydrous acetic acid/acetic anhydride/concentrated H_2SO_4 liquid system effectively oxidizes various iodoarenes ArI to the respective iodine(III) intermediates $ArISO_4$ and/or $ArI(OSO_3H)_2$. The resulting solutions were mixed with excess 20% aqueous ammonium acetate solution to give, after filtration and purification, (diacetoxyiodo)arenes $ArI(OAc)_2$ in 58–82% yields.

Key words: chromium(VI) oxide, iodoarenes, (diacetoxyiodo)arenes, diacetoxylation

(Diacetoxyiodo)arenes, and particularly the parent (diacetoxyiodo)benzene, have been known for a long time.[1, 2] They are potent, often selective, oxidizing agents, hence the interest in (diacetoxyiodo)arenes and (diacetoxyiodo)benzene is growing rapidly, as demonstrated by a number of recent reviews.[3, 4] They are also used for the facile syntheses of, for example, [bis(trifluoroacetoxy)iodo]arenes, [hydroxy(tosyloxy)iodo]arenes (selective oxidants), and aromatic iodonium salts (arylating reagents).[3] There are several preparative methods for these compounds. So far the substrates have generally been:[1–4] (i) iodosylarenes dissolved in glacial acetic acid; (ii) (dichloroiodo)arenes in which chloride is exchanged by acetoxy groups coming either from silver, lead(II) or sodium acetate, or from acetic acid in the presence of mercury(II) oxide in chlorinated solvents.[5] (iii) iodoarenes are oxidized in warm glacial acetic acid by either peracetic acid, or sodium perborate,[6] or electrolytically. The standard, and most general, method for the synthesis of (diacetoxyiodo)arenes (the oxidative diacetoxylation of ArI by warm peracetic acid) is, in fact, a very prolonged reaction (12–16 h), and the utmost care should be taken to maintain the exact temperature.[3] (Diacetoxyiodo)arenes are generally crystalline compounds, fairly stable in the air, which may be stored for long periods by avoiding light.

We have previously reported[7–11] many short-cut syntheses of diaryliodonium salts. We have oxidized various iodoarenes ArI (excluding those substituted solely with stronger electron-donating groups, e.g. OMe), with the anhydrous $CrO_3/AcOH/Ac_2O$/concd H_2SO_4 liquid mixture, immediately followed by the acidic coupling of the in situ formed iodine(III) intermediates, $ArISO_4$ and/or $ArI(OSO_3H)_2$, with many activated arenes, Ar'H. The soluble diaryliodonium hydrosulfates thus obtained, $Ar(Ar')I^+HSO_4^-$, were precipitated in the form of insoluble diaryliodonium bromides, iodides, or perchlorates. We also established[12] that by pouring the deep-green solutions containing chromium(III) salts and $ArISO_4$ and/or $ArI(OSO_3H)_2$ into excess aqueous Na_2SO_3 solution buffered with $(NH_4)_2CO_3$ to neutralize H_2SO_4, the respective iodoarenes ArI were immediately obtained (Equation 1).

$$\begin{aligned} &ArISO_4 + Na_2SO_3 + H_2O \longrightarrow ArI + Na_2SO_4 + H_2SO_4 \\ &ArI(OSO_3H)_2 + Na_2SO_3 + H_2O \longrightarrow ArI + Na_2SO_4 + 2\,H_2SO_4 \end{aligned} \qquad (1)$$

In this work we applied this method to the oxidation of seventeen iodoarenes (Table 1) with the $CrO_3/AcOH/Ac_2O$/concd H_2SO_4 liquid system, followed by mixing the resulting deep-green reaction mixtures with excess 20% aqueous ammonium acetate solution. Crude crystalline (diacetoxyiodo)arenes, obtained according to Equations 2 and 3, were mixed with a little of the hydrolyzed yellowish side products (Equation 4).

$$3\,ArI + 2\,CrO_3 + 6\,H_2SO_4 + 6\,Ac_2O \xrightarrow{30\text{ min, }40\,^{\circ}C} 3\,ArISO_4 + Cr_2(SO_4)_3 + 12\,AcOH \qquad (2)$$

$$\underset{\textit{(not isolated)}}{3\,ArISO_4} + 6\,AcONH_4 \xrightarrow{\text{fast reaction, }5\,^{\circ}C} 3\,ArI(OAc)_2 + 3\,(NH_4)_2SO_4 \qquad (3)$$

Subsequently, the crude (diacetoxyiodo)arenes, washed on the filter with cold 10% aqueous acetic acid,[13] were dried and recrystallized from either ethyl acetate or acetic acid mixed with acetic anhydride (9:1) to acetylate the yellowish product mixture (Equation 4) to (diacetoxyiodo)arenes. Then, to the cooled solutions either hexane or diethyl ether were added in excess (Table 1) to improve the crystallization yields. After washing the (diacetoxyiodo)arenes on the filter with hexane or diethyl ether, followed by air drying, the final yields of pure (diacetoxyiodo)arenes were 58–82% (Table 1). Their purity and ho-

$$\begin{aligned} &ArI(OAc)_2 \xrightarrow[-\,AcOH]{H_2O} ArI(OH)OAc \xrightarrow[-\,AcOH]{H_2O} ArIO \\ &2\,ArI(OH)OAc \xrightarrow[-\,H_2O]{} [ArI(OAc)]_2O \end{aligned} \qquad (4)$$

Table 1. Preparative Details and Melting Points (Uncorrected) of the (Diacetoxyiodo)arenes Obtained

Entry	Substrate	Product[a]	Yield[b] (%)	Crystallization Solvent[c]	mp (dec) (°C); (Lit.)
1	C_6H_5-I	C_6H_5-I$(OAc)_2$	79[d]	OAcEt/hexane (1:1)	159–161 (161.1–162.2)[14]
2	4-FC_6H_4-I	4-FC_6H_4-I$(OAc)_2$	79	OAcEt/hexane (1:2)	177–178 (177.0–179.8)[14]
3	2-ClC_6H_4-I	2-ClC_6H_4-I$(OAc)_2$	82	OAcEt/hexane (1:2)	140–142 (140)[2]
4	3-ClC_6H_4-I	3-ClC_6H_4-I$(OAc)_2$	82	OAcEt/hexane (1:1)	154–156 (153.1–154.7)[14]
5	4-ClC_6H_4-I	4-ClC_6H_4-I$(OAc)_2$	76	OAcEt/hexane (1:2)	112–115 (109.8–113.2)[14]
6	4-BrC_6H_4-I	4-BrC_6H_4-I$(OAc)_2$	77	OAcEt/hexane (1:2)	120–122
7	2,4-$Cl_2C_6H_3$-I	2,4-$Cl_2C_6H_3$-I$(OAc)_2$	75	AcOH/Et_2O (1:3)	160–162
8	2,4,6-$Cl_3C_6H_2$-I	2,4,6-$Cl_3C_6H_2$-I$(OAc)_2$	68	AcOH/Et_2O (1:3)	166–167 (166.8)[2]
9	3-$NO_2C_6H_4$-I	3-$NO_2C_6H_4$-I$(OAc)_2$	79	OAcEt/hexane (1:1)	148–150 (151.0–154.2)[14]
10	4-$NO_2C_6H_4$-I	4-$NO_2C_6H_4$-I$(OAc)_2$	60	AcOH/Et_2O (1:3)	117–121 (167–168)[15,e]
11	2-MeO; 5-$NO_2C_6H_3$-I	2-MeO; 5-$NO_2C_6H_3$-I$(OAc)_2$	82	AcOH/Et_2O (1:2)	182–183
12	4-MeO; 3-$NO_2C_6H_3$-I	4-MeO; 3-$NO_2C_6H_3$-I$(OAc)_2$	65	AcOH/Et_2O (1:2)	153–156
13	2-Me; 5-$NO_2C_6H_3$-I	2-Me; 5-$NO_2C_6H_3$-I$(OAc)_2$	58	AcOH/Et_2O (1:2)	175–177
14	4-$MeO_2CC_6H_4$-I	4-$MeO_2CC_6H_4$-I$(OAc)_2$	78	OAcEt/hexane (1:2)	149–151 (150.0–153.3)[14]
15	3-CNC_6H_4-I[f]	3-CNC_6H_4-I$(OAc)_2$[f]	80	AcOH/Et_2O (1:2)	188–189
16	4-CNC_6H_4-I[f]	4-CNC_6H_4-I$(OAc)_2$[f]	79	AcOH/Et_2O (1:2)	172–173
17	5-CN; 2-$MeOC_6H_3$-I[f]	5-CN; 2-$MeOC_6H_3$-I$(OAc)_2$[f]	74	AcOH/Et_2O (1:2)	207–208

[a] Satisfactory microanalyses obtained for the purified products: C ± 0.2, H ± 0.2, I ± 0.2, N ± 0.2%; other halogens were found qualitatively.

[b] For the purified products.

[c] EtOAc and glacial AcOH were admixtured with Ac_2O (9:1).

[d] When we enlarged tenfold the preparative scale, the final yield for pure (diacetoxyiodo)benzene was the same.

[e] For $C_{10}H_{10}INO_6$: calcd C, 32.72; H, 2.75; I, 34.57; N, 3.82. Found C, 32.6; H, 2.9; I, 34.5; N 3.7.

[f] CN = cyano group.

Table 2. Spectroscopic ^1H NMR Data (r.t.) of Purified (Diacetoxyiodo)arenes

Entry[a]	^1H NMR ($CDCl_3$/TMS) δ
1	2.01 (s, 6H, $MeCO_2$), 7.45–8.13 (m, 5H, ArH)
2	2.01 (s, 6H, $MeCO_2$), 7.12–8.14 (sym. m, 4H, ArH)
3	2.00 (s, 6H, $MeCO_2$), 7.32–8.27 (m, 4H, ArH)
4	2.02 (s, 6H, $MeCO_2$), 7.41–8.10 (m, 4H, ArH)
5	2.01 (s, 6H, $MeCO_2$), 7.43–8.06 (sym. m, 4H, ArH)
6	2.01 (s, 6H, $MeCO_2$), 7.59–7.99 (sym. m, 4H, ArH)
7	2.00 (s, 6H, $MeCO_2$), 7.31–8.19 (m, 3H, ArH)
8	2.01 (s, 6H, $MeCO_2$), 7.60 (s, 2H, ArH)
9	2.04 (s, 6H, $MeCO_2$), 7.70–8.96 (m, 4H, ArH)
10	2.04 (s, 6H, $MeCO_2$), 8.32 (s, 4H, ArH)
11	1.99 (s, 6H, $MeCO_2$), 4.13 (s, 3H, OMe), 7.23–9.04 (m, 3H, ArH)
12	2.02 (s, 6H, $MeCO_2$), 4.06 (s, 3H, OMe), 7.18–8.56 (m, 3H, ArH)
13	2.02 (s, 6H, $MeCO_2$), 2.86 (s, 3H, Me), 7.70–9.03 (m, 3H,ArH)
14	2.02 (s, 6H, $MeCO_2$), 3.97 (s, 3H, CO_2Me), 8.10–8.20 (sym. m, 4H, ArH)
15	2.04 (s, 6H, $MeCO_2$), 7.61–8.39 (m, 4H, ArH)
16	2.03 (s, 6H, $MeCO_2$), 7.76–8.26 (sym. m, 4H, ArH)
17	1.98 (s, 6H, $MeCO_2$), 7.21–8.42 (m, 3H, ArH)

[a] Entries 1–17 correspond to those in Table 1.

mogeneity were checked by TLC, their structures were supported by their melting points, if previously published, correct elemental analyses (C, H, I, N), and integrated ^1H NMR spectra (Table 2).

The present method is suitable for the seventeen iodoarenes, for which the corresponding (diacetoxyiodo)arenes are listed in Table 1. As in the previous case,[7–11] iodoanisoles and iodoacetanilides were unsuitable for this method, since they were quickly oxidized in the solution by CrO_3, with the evolution of iodine vapors, and the formation of tarry products. 4-Iodotoluene gave 4-(diacetoxyiodo)toluene only in 20% yield; as side products we identified by TLC 4-iodobenzoic acid (40%), the unreacted 4-iodotoluene as well as 4-tolyl acetate. Iodobenzaldehydes were smoothly oxidized to iodobenzoic acids which, in turn, were converted to crude (diacetoxyiodo)arenes, which rapidly decomposed on heating during recrystallization to form CO_2 (barium hydroxide test) and the substrate. 1-(Diacetoxyiodo)-2-nitrobenzene could not be obtained in its pure crystalline form, though the corresponding iodine(III) intermediate, 2-$NO_2C_6H_4$-ISO_4, was formed from 1-Iodo-2-nitrobenzene in the acidic CrO_3 solution, which was evidenced by its coupling in situ with e.g. anisole to form the respective iodonium salt (86%).[8] Lower crude yields (20–60%) of diaryliodonium salts were obtained, when the previously oxidized 4-iodotoluene[8–11] and 4-iodobenzoic acid[11] were coupled in situ with several activated arenes.

In conclusion, we reported a new, quick and inexpensive method for the effective conversion of various iodoarenes to the corresponding (diacetoxyiodo)arenes, including (diacetoxyiodo)benzene obtained from iodobenzene in 79% yield. When (diacetoxyiodo)arenes are prepared from appropriate iodoarenes (Table 1), our novel method is 8–16 times faster (30 min as compared with 4–8 h) and ca. 5 times less expensive (taking into account total amounts, and the respective costs, of all the reagents and solvents applied) than the method of McKillop and Kemp.[6]

The starting iodoarenes ArI were either obtained commercially or by the reported methods. They were freshly purified prior to use, and analyzed (C, H, I). ^{1}H NMR spectra of pure (diacetoxyiodo)arenes (Table 2) were taken with a VARIAN (200 MHz) spectrometer in $CDCl_3$ solutions, at r.t. Microanalyses were carried out at the Institute of Organic Chemistry, the Polish Academy of Sciences, Warsaw.

The toxic residues left after the acetoxylation reactions were disposed of according to the local safety measures. We did not recover chromium(III) salts from the residues. This should be taken into account, when the preparations in larger quantities are intended.

(Diacetoxyiodo)arenes; General Procedure:

Powdered CrO_3 (0.67 g, 6.7 mmol; 0% excess) was slowly added portionwise to a stirred mixture of glacial AcOH (5 mL) with Ac_2O (3 mL), keeping the temperature below 40 °C. The deep-orange solution was cooled to 10 °C, and the appropriate iodoarene (10.2 mmol; 2% excess to consume all the CrO_3, otherwise the final (diacetoxyiodo)arenes were contaminated with inseparable Ar-$ICrO_4$[1, 2]) was added with stirring. Concentrated (98%) H_2SO_4 (1.32 mL, 24 mmol; 20% excess) was slowly added dropwise, keeping the temperature below 30 °C. Next, the mixture was stirred at 40 °C for a further 30 min, then cooled to 5 °C. Cold (0–5 °C) 20% aq $AcONH_4$ (20 mL; 150% excess) was rapidly added to the stirred deep-green mixture, which precipitated out the crude product (sometimes it was oily, but quickly solidified). The flask was left in a refrigerator for a few hours. The crystals were collected by filtration, washed with cold (5 °C) 10% aq AcOH (2 × 10 mL),[13] until the washings became colorless [all chromium(III) salts, $AcONH_4$, and $(NH_4)_2SO_4$ were washed off into the filtrate], and air dried. The yellowish crude products were recrystallized from either AcOH/Ac_2O or EtOAc/Ac_2O (9:1). After short boiling, the yellowish solutions faded and, after cooling, either hexane or Et_2O were added in excess (Table 1) with stirring. After 30 min, the crystals were collected by filtration, washed with hexane or Et_2O and air dried. See Table 1 for more details.

† These results were presented at a Meeting of the Polish Chemical Society, Poznań, September 23–26, 1996. They are a part of the future dissertation of P. Kaźmierczak, M. Sc.

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