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Preparation and structure of 2-iodoxybenzoate esters: soluble and stable periodinane oxidizing reagents†

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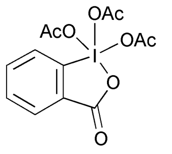
Esters of 2-iodoxybenzoic acid (IBX-esters) are potentially valuable oxidizing reagents belonging to a new class of pentavalent iodine compounds with a pseudo benziodoxole structure.

Organic derivatives of pentavalent iodine (λ^5-iodanes) have found wide applications as versatile oxidizing reagents in the synthesis of complex organic molecules.[1] Dess–Martin periodinane (DMP, **1**) and its precursor 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one 1-oxide (IBX, **2**) are the most recognizable members of this class of compounds.[1,2] Solid state analysis of **2** shows an extended series of intermolecular secondary bonding interactions, dominated by two I$\cdots$O contacts, an O–H$\cdots$O hydrogen bond, and π-stacking. This affords a three dimensional polymeric network in the solid state that substantially limits the solubility of IBX in common organic solvents.[3] We reasoned that a partial disruption of the polymeric nature of IBX could be achieved through manipulation of the *intra*molecular I$\cdots$O bonding interaction of the benziodoxole substructure, and this would be a mechanism toward enhancing reagent solubility. This concept has been initially explored with 2-iodoxybenzamides, which do indeed show improved solubility and stability in comparison to IBX.[4] We now report on the facile preparation of a new class of I(V) oxidants, the IBX-esters **4**. These stable, soluble reagents show oxidizing properties similar to IBX and DMP. X-Ray crystallographic analyses show that **4a·DMSO**, **4c** and **4d** share a common, pseudocyclic benziodoxole configuration and suggest that this structural characteristic is sufficient for increasing the solubility of I(V) oxidants.



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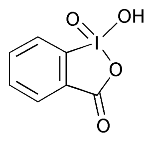

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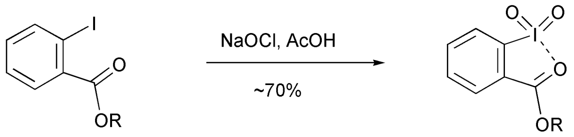
Iodoxyarenes **4** were prepared from the esters of 2-iodobenzoic acid **3** using hypochlorite oxidation[5] (Scheme 1), and the products are isolated by filtration in the form of stable, white, microcrystalline solids. This facile procedure allows for the preparation of reagents **4** derived from a wide variety of precursors, including primary, secondary, and tertiary alcohols, adamantanols, as well as optically active menthols and borneol.



3a-j **4a-j**

a: R = Me; **b:** R = Et; **c:** R = *i*-Pr; **d:** R = *tert*-Bu;
e: R = (–)-menthyl; **f:** R = (+)-menthyl; **g:** R = (±)-menthyl;
h: R = [(1*S*)-*endo*]-(–)-bornyl; **i:** R = 2-adamantyl; **j:** R = 1-adamantyl

Scheme 1

The structure and constitution of compounds **4a–j** were established through a combination of elemental analysis, spectroscopic data, ESI mass spectrometry, and single crystal X-ray analysis.[6] All products have moderate to good solubility in common organic solvents, such as chloroform, dichloromethane, and acetonitrile. In CH$_2$Cl$_2$, for example, the solubilities of **4c**, **4d** and **4e** are 2.9, 0.2, and 1.7 M, respectively. The solubility of crystalline **4a** at 0.003 M, however, is considerably less.

A broad range of solubility, *i.e.*, **4c** *vs.* **4a**, suggested that molecular structure was not the only factor, but that secondary bonding interactions in the solid-state (*i.e.*, polymeric *vs.* non-polymeric) might also play a significant role. Several derivatives **4** have therefore been characterized by X-ray crystallography (Fig. 1). The structure of **4c** shows a unit cell consisting of two crystallographically independent molecules (Fig. 1A). Strong secondary I$\cdots$O bonding interactions between neighboring molecules afford dimeric pairs (dashed lines). These dimers are then linked together by a combination of strong and weak (dotted lines) interactions, forming a polymeric motif. Within each molecule, an intramolecular close contact between the I(V) center and the oxygen atom of the ester group (I1–O13 2.8185(17) and I2–O23 2.6979(16) Å) affords the pseudo-benziodoxole ring.[3,7]

X-Ray crystallographic analysis of **4d** shows a centrosymmetric arrangement of four molecules (Fig. 1B). As observed for **4c**, the secondary I$\cdots$O bonding interactions that link neighboring molecules are present, as is the intramolecular close contact between the iodine center and the oxygen atom of the ester group (I1–O13 2.688(2) and I2–O23 2.673(3) Å). Unlike **4c**, however, there are no additional interactions present to connect discrete tetramers into a polymeric structure, and as a result O22 remains uncoordinated.

Whereas crystals of **4c** and **4d** could be grown from CH$_3$CN, the more sparingly soluble **4a** provided X-ray quality crystals only from DMSO.[8] Analysis of the crystals shows a dimeric structure between two inversion related molecules. The remaining close contact to the I(V) center, however, occurs with oxygen from a DMSO molecule. As found in the structures of **4c** and **4d**, the *intra*molecular I$\cdots$O interaction center involving the iodonium center and ester oxygen is again significant, with I–O1 2.6979(15) Å. Like **4d**, there are no repeating, polymeric interactions, and O4 is uncoordinated.

The *intra*molecular I$\cdots$O bonding motif with the carbonyl oxygen is common to the structures of IBX-esters **4a**, **4c** and **4·DMSO**, and suggests that the presence of an ester moiety in the *ortho*-position is vital for improved solubility.[9,10] This results from a disruption of *inter*molecular I$\cdots$O bonds and a concurrent reduction of the polymeric interactions found in some iodyl and iodosyl derivatives.[10] In comparison to the IBX-esters, IBX shows a stronger *intra*molecular I–O interaction with the carboxylate oxygen (2.263(2) Å),[3] as well as a three-dimensional network based on a combination of intermolecular O–H$\cdots$O and I$\cdots$O secondary bonding. It is, therefore, the absence of the hydrogen bonding interactions in the IBX-esters that appears sufficient to enhance

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† Electronic Supplementary Information (ESI) available: synthetic and characterization data for all new compounds; general procedures for the oxidation of alcohols with reagent **4c**. See http://www.rsc.org/suppdata/cc/b3/b312961f/

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solubility *vs.* IBX. The consequence of this effect can be appreciated by considering the structure of **4c**, which shows that even with partial oligomeric nature on the basis of I···O bonding, considerable solubility can be maintained.

According to literature data,[1] iodylbenzene ($PhIO_2$) as well as other non-cyclic iodylarenes are not effective oxidants toward alcohols, due in part to decreased solubility. In agreement with their structural features, the oxidizing reactivity of IBX-esters **4** is closer to the benziodoxole-based pentavalent iodine reagents such as IBX, in contrast to the non-cyclic iodylarenes.

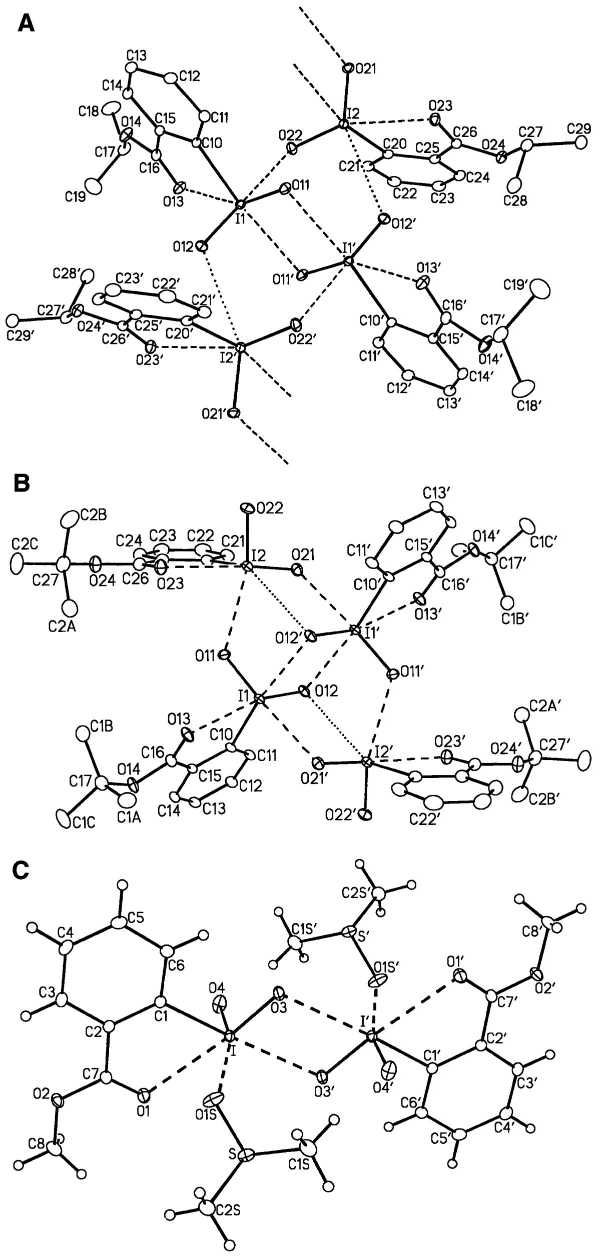

Fig. 1 ORTEP representations of molecules **4c** (top), **4d** (middle) and **4a** (bottom). Selected distances [Å] for **4c**: I1–O11 1.8170(15), I1–O12 1.8033(17), I1–O13 2.8185(17), I1–O11′ 2.6285(16), I1–O22 2.6711(17), I2–O21 1.8164(16), I2–O22 1.8088(16), I2–O23 2.6979(16), I2–O12′ 3.0510(17), I2–O21″ 2.5597(17); **4d**: I1–O11 1.804(2), I1–O12 1.816(2), I1–O12′ 2.698(2), I1–O13 2.688(2), I1–O21′ 2.710(3), I2–O11 2.838(3), I2–O12′ 3.021(3), I2–O21 1.811(3), I2–O22 1.781(3), I2–O23 2.673(3); **4a**: I–O1 2.6979(15), I–O3 1.8061(14), I–O3′ 2.7805(15), I–O4 1.7940(15), I–O1S 2.7560(16). Primed atoms are related to unprimed ones *via* crystallographic inversion centers at the following positions: **4c** (1/2, 0, 0), **4d** (0, 1/2, 1/2) and **4a** (1/2, 0, 0). Thermal ellipsoids shown at the 20% probability level.

A range of alcohols can be oxidized by reagents **4** to the respective carbonyl compounds under mild conditions in the presence of trifluoroacetic acid, BF_3-etherate, or KBr as a catalyst. For example, oxidation of benzyl alcohol in the presence of KBr[11] in chloroform at 50 °C cleanly gives benzaldehyde as the only product detected by ^1H NMR spectroscopy. A variety of secondary alcohols, such as cyclohexanol and cycloheptanol, are converted to the corresponding ketones in 95–98% yields as determined by GC analysis. Furthermore, the increased solubility of, *e.g.*, **4c** greatly expands the range of solvents that can be utilized in comparison to IBX. The oxidation of 1-phenylethanol to acetophenone, for example, proceeds in good yield ($>65\%$) using CH_3CN, $CHCl_3$, CH_2Cl_2, and benzene.

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6 Crystal data for **4a**: $C_{10}H_{13}IO_5S$, M = 372.16, triclinic, space group $P\bar{1}$ (No. 2), a = 8.0364(4), b = 9.0124(5), c = 10.0969(6) Å; α = 81.281(1), β = 76.595(1), γ = 67.422(1)°; V = 655.25(6) Å^3, T = 193 K; μ = 2.609 mm^{-1}, Z = 2, 4571 reflections measured, 2632 unique (R_{int} = 0.0140); final R_1 = 0.0160. For **4c**: $C_{10}H_{11}IO_4$, M = 322.09, triclinic, space group $P\bar{1}$ (No. 2); a = 9.6939(6), b = 10.5225(7), c = 11.2574(7) Å; α = 96.658(1), β = 94.913(1), γ = 105.585(1)°; V = 1090.40(12) Å^3, T = 193 K; μ = 2.928 mm^{-1}, Z = 4, 8154 reflections measured, 4428 unique (R_{int} = 0.0160); final R_1 = 0.0199. For **4d**: $C_{11}H_{13}IO_4$, M = 336.11, triclinic, space group $P\bar{1}$ (No. 2), a = 10.8981(9), b = 11.3827(10), c = 11.5247(10) Å; α = 83.3624(17), β = 62.3591(16), γ = 89.6303(17)°; V = 1256.18(19) Å^3, T = 193 K; μ = 2.546 mm^{-1}, Z = 4, 7149 reflections measured, 5063 unique (R_{int} = 0.0198); final R_1 = 0.0324. CCDC 222124–222126. See http://www.rsc.org/suppdata/cc/b3/b312961f/ for crystallographic data in .cif or other electronic format.

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