Oligomeric Iodosylbenzene Sulfate: A Convenient Hypervalent Iodine Reagent for Oxidation of Organic Sulfides and Alkenes

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Abstract: Oligomeric iodosylbenzene sulfate, (PhIO)₃·SO₃, which can be formally considered as a partially depolymerized activated iodosylbenzene, is a readily available, stable, and water-soluble hypervalent iodine reagent that is useful for the oxidation of sulfides or alkenes. Furthermore, this reagent can be conveniently generated in situ from (diacetoxyiodo)benzene and sodium bisulfate and used without isolation in oxidations in aqueous solution or under solventfree conditions. The reaction of iodosylbenzene sulfate in situ with organic sulfides at room temperature affords sulfoxides in high yields without over-oxidation to sulfones, and this reaction is compatible with the presence in the substrate molecule of hydroxy groups, double bonds, benzylic carbon atoms, carboxylate groups, and various substituted phenyl rings. The reaction of an alkene with iodosylbenzene sulfate generated in situ results in oxidative rearrangement to form a ketone or aldehyde.

Key words: oxidations, iodine, sulfoxides, iodosylbenzene, (diacetoxyiodo)benzene, hypervalent iodine

Hypervalent iodine compounds are used extensively in organic synthesis as highly selective and environmentally friendly oxidizing reagents.¹ Among these reagents, iodosylbenzene, $(PhIO)_n$, is especially important as an oxygen-transfer agent that has found widespread application in various oxidation reactions.^{2,3} In particular, iodosylbenzene is the most efficient source of oxygen atoms for oxidations catalyzed by cytochrome P-450 or discrete transition-metal complexes.² Despite its usefulness as an oxidant, practical applications of iodosylbenzene are hampered by its low solubility in nonreactive media,³ its low thermal stability, and its tendency to explode violently upon moderate heating.⁴ The low solubility of iodosylbenzene is explained by its existence as a zigzag, polymeric, asymmetrically bridged structure in which monomeric units of iodosylbenzene (PhIO) are linked by intermolecular I···O secondary bonds.³ An explanation of the oxo-bridged zigzag polymer structure of $(PhIO)_n$ on the basis of the trans-effects of the ligands has recently been provided.5

Iodosylbenzene can be depolymerized by protonation or by treatment with a Lewis acid. Ochiai and co-workers have reported the preparation, X-ray crystal structures, and useful oxidizing reactions of activated complexes of

SYNTHESIS 2009, No. 15, pp 2505–2508 Advanced online publication: 26.06.2009 DOI: 10.1055/s-0029-1216870; Art ID: M01009SS © Georg Thieme Verlag Stuttgart · New York iodosylbenzene monomer with 18-crown-6 (18C6), for example, complex $1.^6$ The depolymerized protonated iodosylbenzene complex 1 is an efficient oxidizing agent that has moderate solubility and excellent stability in water.^{6a}

[Hydroxy(tosyloxy)iodo]benzene (HTIB, **2**) and similar phenyliodine(III) organosulfonates, PhI(OH)OSO₂R, represent an important class of hypervalent iodine reagents that are commonly used as versatile mild oxidants and electrophiles in organic synthesis.^{1,3,7} In contrast to phenyliodine(III) organosulfonates, the corresponding derivatives of sulfuric acid have not been extensively investigated. The formation of a highly hygroscopic sulfate **4** in the reaction of (dichloroiodo)benzene and silver sulfate was briefly described by Alcock and Waddington in 1963,⁸ and the unstable and extremely hygroscopic sulfates **3** (PhIO·SO₃) and **5** [(PhIO)₂·SO₃] are generated from iodosylbenzene and sulfur trioxide or trimethylsilyl chlorosulfonate under absolutely dry conditions.⁹



Figure 1 Known phenyliodine(III) organosulfonates and sulfates

We recently reported the preparation and X-ray structure of a new, stable, and water-soluble oligomeric iodosylbenzene sulfate (PhIO)₃·SO₃ (**6**; Scheme 1), which can be considered as a partially depolymerized and activated form of iodosylbenzene.¹⁰ Compound **6** can be prepared by treatment of (diacetoxyiodo)benzene with one equivalent of sodium bisulfate, and isolated by crystallization from water as a stable yellow crystalline product (Scheme 1).

We have found that sulfate 6 is a highly reactive oxidant towards organic sulfides and alkenes, with a reactivity pattern that is similar to that of activated iodosylbenzene complexes, such as complex 1. In particular, the oxidation of the aryl alkyl sulfide 7 proceeds at room temperature

3 Phl(OAc)₂ + 2 NaHSO₄
$$\xrightarrow{H_2O}$$
 (PhIO)₃SO₃
- 6 AcOH
- Na₂SO₄ 6

Scheme 1 Preparation of oligomeric iodosylbenzene sulfate (6)

within 10 minutes, thereby demonstrating the high oxidizing ability of reagent 6. This oxidation leads to the formation of the corresponding sulfoxide 8 in high yield without over-oxidation to the sulfone (Scheme 2). A similar oxidation with iodosylbenzene proceeds under the same conditions (water, room temperature), but only in the presence of a catalytic bromide anion, which is required for the depolymerization of (PhIO)_n.¹¹ The oxidation of cyclohexene with sulfate 6 results in ring contraction with the formation of cyclopentanecarbaldehyde (9).¹² Likewise, the oxidation of 1,1-diphenylethylene leads to oxidative rearrangement with formation of ketone 10 (Scheme 2).¹³ This pattern of reactivity is similar to that of iodosylbenzene activated by a Brønsted or Lewis acid. In particular, the reaction of (PhIO)_n with cyclohexene in aqueous sulfuric acid affords ketone 9 in 44% yield.^{12a} The formation of the same product in low yield was also reported for the reactions of cyclohexene with phenyl-



Scheme 2 Oxidations by using oligomeric iodosylbenzene sulfate 6

iodosyl sulfate and iodosylbenzene-trifluoroborane complex.^{12b}

A further study of these reactions (Scheme 2) showed that reagent 6 can be conveniently generated in situ from (diacetoxyiodo)benzene and sodium bisulfate, and used without isolation for subsequent oxidations in aqueous solution or under solvent-free conditions.¹⁴ In particular, the reaction of sulfide 7 with (diacetoxyiodo)benzene and so-

Sulfide	Product ^a	MeCN-H ₂ O (5:1)		H ₂ O		Solid state	
		Time (min)	Yield (%) ^b	Time (h)	Yield (%) ^b	Time (min)	Yield (%)
PhSMe	PhSOMe	10	86	1.25	88	1.0	93
4-BrC ₆ H ₄ SMe	4-BrC ₆ H ₄ SOMe	15	98	1.0	96	1.0	99
4-MeOC ₆ H ₄ SMe	4-MeOC ₆ H ₄ SOMe	5.0	67	1.75 ^c	88	1.0	89
PhSCH ₂ CN	PhSOCH ₂ CN	2.0	45	2.0	d	2.0	d
CH ₂ =CHCH ₂ SPh	CH ₂ =CHCH ₂ SOPh	2.0	_e	3.0	66	1.0	68
(<i>t</i> -Bu) ₂ S	(t-Bu) ₂ SO	0.5	47	f	_f	_f	_f
MeS(CH ₂) ₂ OH	MeSO(CH ₂) ₂ OH	2.0	_e	1.25	47	1.0	82
(CH ₂) ₅ S	(CH ₂) ₅ SO	_f	_f	1.30	46	_f	_f
PhSBn	PhSOBn	5.0	95	5.0	80	1.0	90
4-ClC ₆ H ₄ SCH ₂ CO ₂ H	4-ClC ₆ H ₄ SOCH ₂ CO ₂ H	d	_d	3.0 ^g	19	d	d
4-O ₂ NC ₆ H ₄ SMe	4-O ₂ NC ₆ H ₄ SOMe	360	84	_h	_h	5.0	90
4-NCC ₆ H ₄ SMe	4-NCC ₆ H ₄ SOMe	10	92	_h	_h	3.0	94
3-O ₂ NC ₆ H ₄ SMe	3-O ₂ NC ₆ H ₄ SOMe	10	_i	10	_i	5.0	47
[Me(CH ₂) ₇] ₂ S	[Me(CH ₂) ₇] ₂ SO	20	97	_h	_h	2.0	95

^a All products were identified by comparison of their physical and spectral (IR, NMR, and MS) properites with those reported in the literature.¹⁵ ^b Isolated yield (column chromatography).

° The reaction was started out at 0 °C and then gradually warmed to r.t.

^d The reaction was too slow at r.t., and significant decomposition was observed upon heating.

^e Nonselective reaction with the formation of a complex mixture was observed under these conditions

^f The reaction was not performed in a mortar because of the extremely strong smell of the substrate.

^g The reaction was carried out at 90 °C.

^h The reaction was not performed because the substrate was insoluble in H₂O.

ⁱ A black tar was formed under these reaction conditions.

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dium bisulfate in aqueous acetonitrile proceeds at room temperature within 10 minutes and affords the corresponding sulfoxide 8 in 92% isolated yield, which is almost identical to that obtained with purified reagent 6 (Scheme 2). The results of oxidations of various sulfides with reagent 6 generated in situ from (diacetoxyiodo)benzene and sodium bisulfate in aqueous acetonitrile, water, or under solvent-free conditions are summarized in Table 1. The final products were isolated and their identity was confirmed by GC-MS and NMR spectroscopy through comparison with known sulfoxides.¹⁵ In general, the best yields of sulfoxides were achieved and the reaction was fastest under solvent-free conditions. No overoxidation to sulfones was observed, and the reaction is compatible with the presence of a hydroxy group, a double bond, a benzylic carbon, a carboxylic function, or various substituted phenyl rings in the molecule of the substrate (Table 1).

Reactions of alkenes 11 and 14 with (diacetoxyiodo)benzene and sodium bisulfate under solvent-free conditions afforded the corresponding products of oxidative rearrangements 9, 10, 12, 13, and 15 (Scheme 3). The yields of these products were almost identical to those obtained with the pure reagent 6 (Scheme 2). The formation of the rearranged aldehyde 12 in the reaction of styrene with activated iodosylbenzene monomer complex 1 has been previously reported.^{6a}



Scheme 3 Oxidations of alkenes with reagent 6 generated in situ from (diacetoxyiodo)benzene and sodium bisulfate

In conclusion, our study showed that oligomeric iodosylbenzene sulfate **6** is a readily available, stable, and versatile water-soluble reagent for the oxidation of sulfides and alkenes. The reactivity pattern of this reagent is similar to that of relatively unstable activated monomeric iodosylbenzene complexes, such as **1**. Furthermore, reagent **6** can be conveniently generated in situ from (diacetoxy-iodo)benzene and sodium bisulfate, and used without isolation for subsequent oxidations in aqueous solution or under solvent-free conditions.

All melting points were determined by using a Boetius melting point apparatus and are uncorrected. ¹H and ¹³C NMR spectra were recorded on a Bruker AM-200 NMR spectrometer (200 and 50 MHz) with TMS as the internal standard; chemical shifts are reported in parts per million (ppm). GC-MS spectra were obtained by us-

ing a gas chromatograph equipped with a quadrupole mass spectrometer (Hewlett Packard 5890/II) as the detector (EI, 70 eV). Microanalyses were carried out by using a 1106 Carlo Erba CHNS-O analyzer. Flash column chromatography was performed on silica gel (L40/100 μ m; Chemapol). TLC was performed on silica gel plates (Sorbfil, Russia). All commercial reagents were of ACS reagent grade and used without further purification. Oligomeric iodo-sylbenzene sulfate (**6**) was prepared according to the previously reported procedure.¹⁰

Oxidation of 4-(Methylthio)benzonitrile (7) with Oligomeric Iodosylbenzene Sulfate (6)

Solid reagent **6** (130 mg, 0.175 mmol) was added to a stirred soln of sulfide **7** (82.5 mg, 0.5 mmol) in 5:1 MeCN–H₂O (1 mL), and the soln was stirred at r.t. for 10 min. The solvent was evaporated and the residue was separated by column chromatography [hexanes–EtOAc (2:1)]; yield: 76 mg (92%). The purity and identity of product **8** were confirmed by GC-MS and by comparison of its NMR spectra with literature data.^{15b}

Oxidation of Sulfides to Sulfoxides with Oligomeric Iodosylbenzene Sulfate (6) Generated In Situ: General Procedures

Oxidation in Aqueous Acetonitrile: Solid PhI(OAc)₂ (169 mg, 0.525 mmol) and NaHSO₄·H₂O (73 mg, 0.525 mmol) were added to a stirred soln of the organic sulfide (0.5 mmol) in 5:1 MeCN–H₂O (1 mL), and the mixture was magnetically stirred until the reagent was consumed (TLC; see Table 1). The mixture was then concentrated in vacuo, and the organic products were extracted with CH₂Cl₂ (2 mL) and separated by column chromatography [EtOAc–hexanes (1:2) followed by EtOAc] to give the analytically pure sulfoxide.

Oxidation in Water: Solid PhI(OAc)₂ (169 mg, 0.525 mmol) and NaHSO₄·H₂O (73 mg, 0.525 mmol) were added to a stirred soln of the organic sulfide (0.5 mmol) in H₂O (1 mL), and the mixture was magnetically stirred until the reagent was consumed (TLC; see Table 1). The mixture was then extracted with CH₂Cl₂ (2 mL), and the organic products were separated by column chromatography [EtOAc–hexanes (1:2) followed by EtOAc] to give the analytically pure sulfoxide.

Solvent-Free Oxidation: Solid PhI(OAc)₂ (169 mg, 0.525 mmol), NaHSO₄·H₂O (73 mg, 0.525 mmol), and an organic sulfide (0.5 mmol) were mixed in a mortar, and the mixture was intensively ground for 1–5 min (see Table 1). The mixture was then extracted with CH₂Cl₂ (2 mL), and the organic products were separated by column chromatography [EtOAc–hexanes (1:2) followed by EtOAc] to give the analytically pure sulfoxide.

Oxidation of Alkenes with Oligomeric Iodosylbenzene Sulfate (6) Generated In Situ: General Procedure

Solid PhI(OAc)₂ (161 mg, 0.5 mmol), NaHSO₄·H₂O (69 mg, 0.5 mmol), the alkene (0.5 mmol), and two drops of H₂O (about 34 mg) were mixed in a mortar, and the mixture was intensively ground for 0.5–1 min. The mixture was then extracted with Et₂O, and the organic products were separated by column chromatography [hexanes then EtOAc–hexanes (1:5)]. Products **9**, **12**, **13**, and **15** were isolated as their 2,4-dinitrophenylhydrazones by adding 4–5 mL of a standard soln of 2,4-dinitrophenylhydrazine [prepared from 2,4-dinitrophenylhydrazine (3 g), concd H₂SO₄ (15 mL), EtOH (70 mL), and H₂O (20 mL)]. The crystals that formed were filtered off, washed with EtOH, dried, and recrystallized (EtOH).

Phenylacetaldehyde (12)

Yield: 86% [isolated as 2,4-dinitrophenylhydrazone; mp 120–121 °C (Lit.¹⁶ 121 °C)].

1-Phenylacetone (13)

Yield: 83% [isolated as 2,4-dinitrophenylhydrazone, mp 157–158 $^{\circ}C$ (Lit. 16 156 $^{\circ}C$)].

1,2-Diphenylethanone (10)

Yield: 97%; mp 59-60 °C (Lit.16 60 °C).

¹H NMR (200 MHz, CDCl₃): δ = 4.24 (s, 2 H, CH₂), 7.27 (m, 5 H), 7.43 (m, 3 H), 8.00 (dd, J = 1.6, 7.0 Hz, 2 H, H_{aron}).

¹³C NMR (50 MHz, CDCl₃): δ = 45.26 (CH₂), 126.63, 128.34, 128.44, 129.04, 129.22, 132.66, 134.43, 126.60 (C arom.), 196.32 (CO).

Cyclopentanecarbaldehyde (9)

Yield: 39% [isolated as 2,4-dinitrophenylhydrazone, mp 154–156 °C (Lit.¹⁷ 156–157 °C)].

1-Cyclopentylethanone (15)

Yield: 45% [isolated as 2,4-dinitrophenylhydrazone, mp 115–116 °C (EtOH)].

Anal. Calcd. for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.17. Found: C, 53.15; H, 5.76; N, 20.01.

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