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Comparative Reactivity of Hypervalent Iodine Oxidants in Metalloporphyrin-Catalyzed Oxygenation of Hydrocarbons: Iodosylbenzene Sulfate and 2-Iodylbenzoic Acid Ester as Safe and Convenient Alternatives to Iodosylbenzene

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Abstract: A comparative study of the reactivity of 2-iodylbenzoic acid isopropyl ester (IBX-ester), oligomeric iodosylbenzene sulfate $[(PhIO)_3{\cdot}SO_3]_n$, and iodosylbenzene in the oxygenation of anthracene in the presence of metal porphyrin or phthalocyanine complexes is reported. Results of this study demonstrate that oligomeric iodosylbenzene sulfate and the IBX-ester are the most reactive oxygenating reagents that can be used as a safe and convenient alternative to the thermally unstable and potentially explosive iodosylbenzene.

Keywords: iodine; iodosylbenzene; 2-iodylbenzoic acid isopropyl ester (IBX-ester); oxygenation; porphyrins

Hypervalent iodine compounds are versatile, selective oxidants that have the added advantage of being biodegradable and low in toxicity.[1,2] Among these reagents, iodosylbenzene, $(PhIO)_n$, is particularly important as an efficient oxygen transfer agent that has found widespread application in various oxygenation reactions.[2] In 1979 Groves and co-workers reported that iodosylbenzene is the most efficient source of oxygen for the oxygenation of hydrocarbons in the presence of iron(III) porphyrin complexes,[3a] and since then $(PhIO)_n$ has been widely used as a terminal oxidant in the reactions mimicking natural oxidations performed by the heme-containing cytochrome P-450 class of enzymes.[3] Despite its usefulness as an oxidant, practical applications of iodosylbenzene are hampered by its low solubility in non-reactive media,[2] as well as low thermal stability and explosive properties upon moderate heating.[4]

In this communication, we report preliminary results on the use of the new and convenient hypervalent iodine reagents **1** and **2** (Figure 1) as terminal oxidants in the biomimetic oxidation of anthracene to anthraquinone catalyzed by Fe(III) phthalocyanine complex **3** (Figure 2), Co(II) tetraphenylporphyrin (**4**) or Ru(II) tetraphenylporphyrin (**5**).

The oligomeric iodosylbenzene sulfate $[(PhIO)_3{\cdot}SO_3]_n$ (**2**) was prepared by simple treatment of commercially available (diacetoxyiodo)benzene with aqueous hydrogen sulfate and isolated as a thermally stable, yellow crystalline solid.[5] The isopropyl ester of 2-iodylbenzoic acid (IBX-ester) (**1**) was prepared by the hypochlorite oxidation of the readily available isopropyl ester of 2-iodobenzoic acid and isolated in the form of a stable, white, microcrystalline solid.[6a,b] Reagent **1** is also commercially available from several chemical companies.[6c] Complex **3** was prepared using the direct high-temperature reaction between 4-*tert*-butylphthalonitrile and iron(II) acetate as described previously,[7] while Co(II) tetraphenylporphyrin **4** and Ru(II) carbonyl tetraphenylporphyrin **5** were obtained from commercial sources. The heterogenized phthalocyanine catalysts similar to complex **3** were previously reported in the C–H activation reactions using H_2O_2 or organic peroxides as source of oxygen.[8] Recently, we have reported the use of complexes **3–5** in the catalytic oxidations of alcohols.[9]

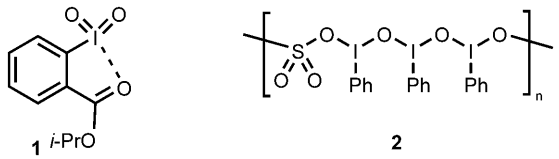


Figure 1. Hypervalent iodine oxidants: isopropyl 2-iodylbenzoate (**1**) and oligomeric iodosylbenzene sulfate (**2**).

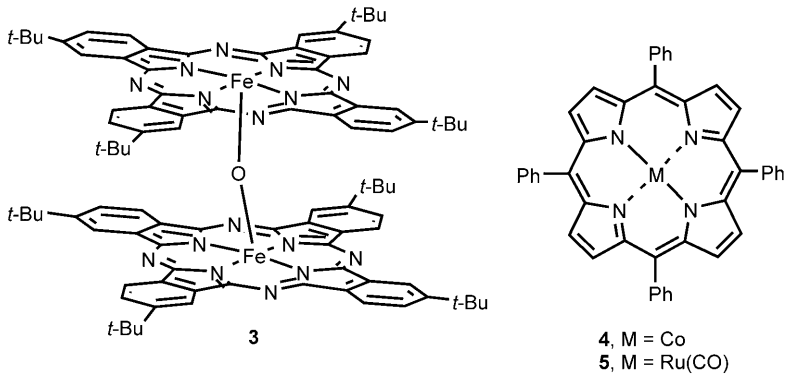
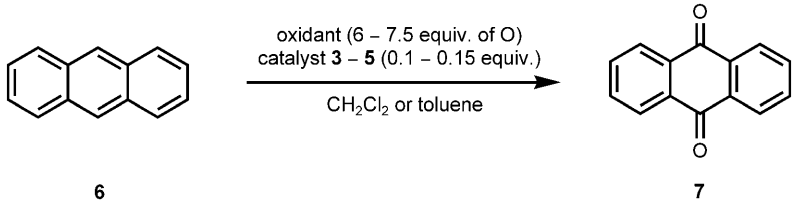


Figure 2. Iron(III) phthalocyanine (**3**) and metal porphyrin complexes **4** and **5**.



Scheme 1. Catalytic oxidation of anthracene (**6**) to anthraquinone (**7**).

We have investigated the catalytic oxidation of anthracene (**6**) to anthraquinone (**7**) using oxidants **1**, **2** and complexes **3–5** (Scheme 1) in comparison with iodosylbenzene as the common oxygenating reagent. The use of iodosylbenzene in this reaction in the presence of transition metal complexes was previously reported in the literature.[10]

The oxidation of anthracene was carried out in dry dichloromethane or in toluene using a 2.0–2.5-fold excess (6.0–7.5 mol. equiv. of active oxygen per 1 molecule of anthracene **6**) with 0.10–0.15 equiv of the appropriate catalyst (Table 1). After the indicated time, the catalyst was removed by flash chromatography and the obtained solution was analyzed by GC-MS to

Table 1. Catalytic oxidations of anthracene (**6**) to anthraquinone (**7**) using hypervalent iodine reagents.

Entry	Reagent (mol equiv.)		Temperature [°C]	Catalyst (mol%)		Solvent	Conversion [%]	Time [h]
1	**1**	3	r.t.	none	0	toluene	0	24
2	**1**	3	40	none	0	CH_2Cl_2	0	24
3	**1**	3	110	none	0	toluene	14	3.5
4	**1**	3	110	none	0	toluene	86	24
5	**1**	3	r.t.	**3**	15	toluene	0	24
6	**1**	3	110	**3**	15	toluene	100	2.5
7	**1**	3	110	**4**	15	toluene	14	3.5
8	**1**	3	110	**5**	15	toluene	0	21
9	**1**	3	40	**5**	15	CH_2Cl_2	100	0.5
10	**1**	3	r.t.	**5**	10	CH_2Cl_2	100	3.5
11	**2**	2.5	r.t.	none	0	toluene	0	24
12	**2**	2.5	r.t.	**3**	10	toluene	100	2
13	**2**	2.5	r.t.	**4**	10	CH_2Cl_2	100	2
14	**2**	2.5	r.t.	**5**	10	CH_2Cl_2	100	1
15	PhIO	7.5	r.t.	none	0	toluene	0	24
16	PhIO	7.5	r.t.	**3**	10	toluene	100	5
17	PhIO	7.5	r.t.	**5**	15	CH_2Cl_2	7	3
18	PhIO	7.5	r.t.	**5**	15	CH_2Cl_2	100	24
19	PhIO	7.5	r.t.	**4**	15	CH_2Cl_2	26	2

determine the conversion of anthracene (**6**) to anthraquinone (**7**). According to the GC-MS and NMR data, **7** and the appropriate iodides resulting from the reduction of hypervalent iodine reagents were the only products formed under these reaction conditions. Dichloromethane was found to be the best solvent for the oxidations in the presence of metal porphyrins **4** and **5**. Toluene was used for the reactions catalyzed by Fe(III) phthalocyanine **3** due to the instability of complex **3** in dichloromethane solutions. The results of the oxidations are summarized in Table 1.

First of all, we have found that the oxidation of anthracene with hypervalent iodine reagents **1** and **2** in the absence of catalysts at room temperature in toluene or at 40 °C in dichloromethane proceeds extremely slowly and does not show any measurable conversion to anthraquinone after 24 h (entries 1, 2, and 11). Reagent **1**, however, slowly oxidizes anthracene in toluene under reflux conditions (110 °C) with a 14% conversion after 3.5 h and 86% conversion after 24 h (entries 3 and 4). The addition of 0.15 mol equiv of Fe(III) phthalocyanine **3** leads to a significant increase in the reaction rate with a 100% conversion being reached in 2.5 h at 110 °C (entry 6). The graphical representation of the conversion in this reaction *vs.* time is shown in Figure 3. Lowering the reaction temperature leads to a slower conversion rate in the reaction in the presence of Fe(III) phthalocyanine **3** (entry 5).

The use of Co(II) tetraphenylporphyrin **4** and Ru(II) carbonyl tetraphenylporphyrin **5** as catalysts in this oxidation under the same reaction conditions (110 °C, toluene) leads to a significantly lower conversion (14%, entry 7 and 0%, entry 8, respectively), which is even lower than the conversion in the absense of a catalyst (entries 3 and 4). This result is probably explained by the low thermal stability of the intermediate high-valent oxo-metal complexes generated from the initial interaction of metal porphyrins **4** and **5** and the oxidant. Lowering the reaction temperature leads to a fast and efficient oxidation in the presence of catalyst **5** (entry 9: 100% conversion in 0.5 h at 40 °C; entry 10: 100% conversion in 3.5 h at room temperature). It should be emphasized that IBX-ester **1** is more reactive in this reaction than the commonly used iodosylbenzene, which shows only 7% conversion after 3 h and 100% conversion only afer 24 hour of the reaction in the presence of Ru(II) porphyrin **5** (entries 17 and 18, respectively). The Co(II) porphyrin **4** shows slightly lower catalytic activity in these oxidations (entries 13 and 19).

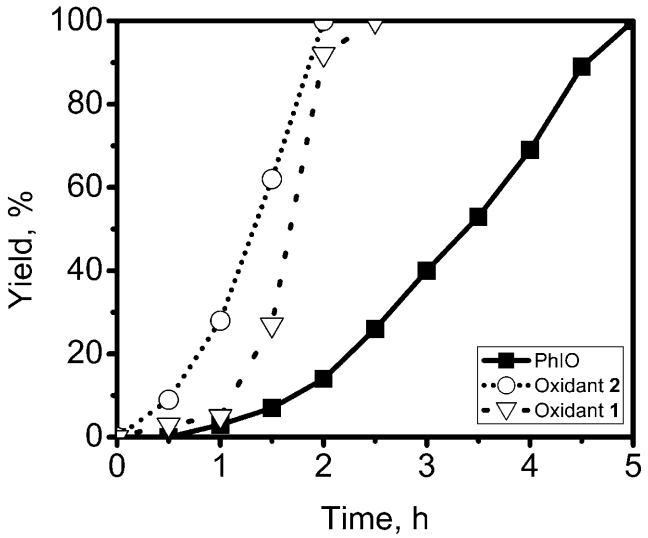
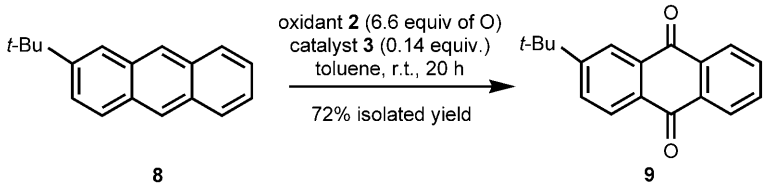


Figure 3. Conversion in catalytic oxidation of anthracene (**6**) to anthraquinone (**7**) using oxidants **1**, **2** and iodosylbenzene in the presence of the Fe(III) phthalocyanine complex **3**. Oxidations using IBX-ester **1** were performed at 110 °C in toluene, while oxidant **2** and PhIO were used in dichloromethane at room temperature.

In contrast to IBX-ester **1**, the oligomeric iodosylbenzene sulfate **2** shows high reactivity in catalytic oxidations at room temperature in the presence of any of the catalysts **3–5** (10 mol%), while the reaction in the absence of catalysts at room temperature does not occur (entry 11). The best catalytic effect is observed in the presence of Ru(II) porphyrin **5** (entry 14; 100% conversion in 1 hour). The reactivity of oxidant **2** in the presence of catalysts **3** and **4** is slightly lower (entries 12 and 13; 100% conversion in 2 h). The graphical representation of the conversion in the oxidations using reagents **1** and **2** catalyzed by the Fe(III) phthalocyanine complex **3** *vs.* time is shown in Figure 3 in comparison with the analogous oxidation using iodosylbenzene.

The data presented in Table 1 and Figure 3 clearly indicate that the oligomeric iodosylbenzene sulfate **2** is the best oxidant, significantly more reactive than the commonly used iodosylbenzene. The slower reaction with iodosylbenzene can partially be explained by its polymeric structure, $(PhIO)_n$, requiring initial depolymerization, while the structure of sulfate **2** consists of smaller trimeric units of PhIO. The presence of the initial period of activation in the reaction of $(PhIO)_n$ is clearly observed on its reactivity curve (Figure 3). The reaction of IBX-ester **1** in the presence of the Fe(III) phthalocyanine complex **3** requires heating to 110 °C; the need for higher temperature can be explained by the low solubility of reagent **1** in toluene, which is the preferable solvent for the reactions involving catalyst **3**. The reactivity of both oxidants **1** and **2** is similar when a more stable Ru(II) complex **5** is used in dichloromethane solution (entries 9, 10 and 14). Overall, ruthenium(II) complex **5** shows the highest catalytic activity; however, the availability and low cost of iron(III) complex **3** as compared to the ruthenium porphyrin **5** make it a po-



Scheme 2. Catalytic oxidation of 2-*tert*-butylanthracene (**8**) to 2-*tert*-butylanthraquinone (**9**) using oligomeric iodosylbenzene sulfate **2** as the oxidant.

tentially useful reagent for biomimetic catalytic transformations.

In order to demonstrate the general character of the optimized reaction conditions, we performed the oxidation of 2-*tert*-butylanthracene (**8**) using oxidant **2** in the presence of the Fe(III) phthalocyanine complex **3** (Scheme 2). Compared to the oxidation of anthracene (**6**) the reaction of 2-*tert*-butylanthracene (**8**) was slower, probably due to steric hindrance caused by the *tert*-butyl group, with a 100% conversion reached only after 20 h at room temperature. The GC analysis of the reaction mixture indicated the presence of a single product of oxidation, 2-*tert*-butylanthraquinone (**9**), along with iodobenzene resulting from the reduction of reagent **2**. 2-*tert*-Butylanthraquinone (**9**) was isolated from the reaction mixture by preparative column chromatography on silica gel as yellow needles in 72% yield and identified by comparison with an authentic sample.[11]

In summary, the results of our study show that IBX-ester **1** and oligomeric iodosylbenzene sulfate **2** are efficient oxygenating agents in the biomimetic catalytic oxidation of aromatic hydrocarbons in the presence of metal porphyrin or phthalocyanine complexes. These two reagents can be used as safe and convenient alternative to the potentially explosive iodosylbenzene. Reagents **1** and **2** can be conveniently prepared from common precursors and in contrast to the thermally unstable iodosylbenzene, they can be stored for extended periods at room temperature and are not explosive.

Experimental Section

General Methods

All reactions were performed under a dry nitrogen atmosphere with flame-dried glassware. All commercial reagents were ACS reagent grade and used without further purification. Dichloromethane was distilled from CaH_2 and stored over molecular sieves (4 Å). Co(II) tetraphenylporphyrin **4** and Ru(II) carbonyl tetraphenylporphyrin **5** were obtained from commercial sources. Iodosylbenzene sulfate **2** and isopropyl ester of 2-iodylbenzoic acid (IBX-ester) **1** were prepared according to previously reported procedures.[5,6a] Iodosylbenzene was prepared by a known method involving the alkaline hydrolysis of (diacetoxyiodo)benzene.[2a] GC-MS analysis was carried out with an HP 5890 A Gas Chromatograph using a 5970 Series mass selective detector.

Typical Pocedure for Catalytic Oxidation of Anthracene

A solution of anthracene (**6**; 0.10–0.15 mmol) in toluene or dichloromethane (3–5 mL) was mixed with the appropriate catalyst (0.010–0.015 mmol) and the hypervalent iodine oxidant (6–7.5 equiv. of O), with stirring, at indicated temperature (see Table 1). Samples of the reaction mixture (50 μL) were collected every 30 min, filtered through 2–3 cm of silica gel suspended in a Pasteur pipet, washed with a mixture of ethyl acetate and hexane (2:3 v:v), and analyzed using GC-MS.

Catalytic Oxidation of 2-*tert*-Butylanthracene

A solution of 2-*tert*-butylanthracene (**8**; 16 mg, 0.068 mmol) in toluene (2.5 mL) was mixed with Fe(III) phthalocyanine complex **3** (15 mg, 0.0094 mmol) and reagent **2** (110 mg, 0.15 mmol) and was stirred 24 h at room temperature. The solvent was removed and the residue was separated by column chromatography on silica gel (ethyl acetate/hexane, 1:20) to give 2-*tert*-butylanthraquinone **9** as yellow needles; yield:13 mg (72%); mp 101–102.5 °C (Lit.[11] mp 103–104 °C).

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