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Catalytic and Chemoselective Oxidation of Activated Alcohols and Direct Conversion of Diols to Lactones with In Situ-Generated Bis-IBX Catalyst

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Dedicated to Professor Mariappan Periasamy (University of Hyderabad) on the occasion of his 60th birthday

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The *twisted* 3,3'-diiodo-2,2',6,6'-tetramethoxybiphenyl-4,4'dicarboxylic acid (**DIDA**) was designed and synthesized for the in situ generation of **Bis-IBX** and catalytic oxidations. The seemingly better solubility of the in situ-generated **Bis-IBX** and the attenuated reactivity arising from its unique structural features and methoxy substituents allowed the catalytic

Introduction

Over the past decade or so, o-iodoxybenzoic acid (IBX) has emerged as a very powerful oxidation reagent.^[1] Aside from advantages such as its low cost and ready availability, environmentally-benign characteristics, non-toxicity, etc., a myriad of facile transformations that continue to be reported render this reagent virtually indispensable in contemporary organic oxidation chemistry.^[1] Unfortunately, IBX is explosive^[2] and highly insoluble in common organic solvents, so that solvents such as DMSO are normally used for oxidations using this reagent.^[3] Considerable efforts have been directed towards devising modified reagents that would overcome these serious drawbacks.^[4] The development of catalytic oxidation protocols using precursor iodoacids that allow the in situ generation of hypervalent I^V species in the presence of a terminal oxidant such as oxone is a new dimension to the oxidation chemistry based on IBX.^[5]

It was Vinod et al. who first developed a catalytic protocol for the oxidation of alcohols using the oxidant-precursor, *o*-iodobenzoic acid, as a catalyst (30 mol-%) in the presence of oxone in a water/acetonitrile biphasic mixture.^[5a] Giannis et al. subsequently reported similar catalytic oxidations with *o*-iodobenzoic acid in water/EtOAc mixtures.^[5b] These studies highlight the possibility of avoiding the isolation of explosive IBX. Ishihara et al. demonstrated oxidation of activated alcohols selectively using **DIDA**/ oxone. Chemoselective oxidations were demonstrated for substrates containing two different hydroxy groups. Furthermore, the unique reactivity of **DIDA** was demonstrated for sequential oxidation reactions of 1,4- and 1,6-diols to give lactones catalytically in respectable yields.

the remarkable reactivity of o-iodoxybenzenesulfonic acid (IBS, Scheme 1), generated in situ from o-iodobenzenesulfonic acid and oxone.^[5d] Recently, we showed that TetMe-IBX (Scheme 1), generated in situ from its precursor tetramethyl-o-iodobenzoic acid, is a good reagent for the oxidation of a variety of primary and secondary aliphatic and benzylic alcohols.^[5e] The non-planarity introduced into the structure by a steric relay between four consecutive methyl groups results in an enhancement of the reactivity and solubility of this reagent over IBX. In a continuation of these investigations, we surmised that o-iodobenzoic acids that lead, upon oxidation with oxone, to pentavalent iodanes with enhanced solubility and attenuated reactivity should be appealing from the point of view of achieving chemoselectivity in oxidations.^[4b] In particular, we envisaged that the oxidation of activated benzylic alcohols in the presence of aliphatic alcohols could possibly be accomplished catalytically. We thus designed tetramethoxysubstituted bis-iodoxybenzoic acid (Scheme 1), referred to as **Bis-IBX** for convenience, as a modified IBX derivative, whose precursor, i.e., 3,3'-diiodo-2,2',6,6'-tetramethoxybiphenyl-4,4'-dicarboxylic acid (DIDA), could be used catalytically in the oxidations. The rationale behind the design of **Bis-IBX** are as follows: i) the methoxy groups at the *ortho* positions render the two aryl rings orthogonal; in general, the molecular systems characterized by orthogonal planes lead to packing difficulties in the solid state such that one may expect better solubility; ii) the four methoxy groups may aid solubility in common organic solvents; and iii) while the electron-rich methoxy groups in each of the iodobenzene rings may promote oxidation in the presence of oxone for ready generation of I^V species, they decelerate

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the rate of oxidation of alcohols, as is evident from mechanistic studies.^[4,5] This latter point is an important criterion for chemoselective oxidations. In this paper, we show that the precursor of **Bis-IBX**, i.e., **DIDA**, can indeed be used catalytically in the presence of oxone for the oxidation of primary alcohols either to the corresponding aldehydes or to the acids, and of secondary alcohols to ketones. Capitalizing on the ability of the in situ generated hypervalent iodine species to oxidize only activated alcohols, i.e., benzylic alcohols, we demonstrate chemoselective oxidation at the benzylic site for substrates containing two hydroxy functionalities. Furthermore, we show that **DIDA** uniquely brings about the conversion of 1,4- and 1,6-diols into the corresponding lactones by two consecutive oxidation reactions.



Scheme 1. Structures of the in situ-generated modified IBXs and **Bis-IBX**.

Results and Discussion

Synthesis of 3,3'-Diiodo-2,2',6,6'-tetramethoxybiphenyl-4,4'-dicarboxylic Acid, DIDA

Synthesis of the target twisted **Bis-IBX** was approached starting from 5-methylresorcinol dimethyl ether, which was subjected to *o*-lithiation with BuLi, followed by treatment with iodine to give the mono-iodinated product (Scheme 2). Ullmann coupling of this product, followed by double iodination of the biphenyl with NIS under acidic conditions, and subsequent oxidation of the two methyl groups using KMnO₄ in basic medium, led to the target diiodo-diacid, i.e., **DIDA**. Persistent efforts to isolate **Bis-IBX** by oxidation either with oxone or with KBrO₃/dilute H₂SO₄ were unsuccessful.

Catalytic Oxidation of Alcohols

In light of our failure to isolate the **Bis-IBX**, the oxidation of alcohols using in situ generated IBX from **DIDA** in the presence of oxone was attempted with *p*-bromobenzyl alcohol as a representative case in a range of solvents and with different catalyst loadings in the presence of oxone



Scheme 2. Synthetic route to 3,3'-diiodo-2,2',6,6'-tetramethoxybiphenyl-4,4'-dicarboxylic acid (**DIDA**).

(2 equiv.) (Table 1). The solvents tested included tert-butanol, ethyl acetate, ethyl formate, acetonitrile, acetonitrile/ water, DMF, nitromethane, etc., and the catalyst loading was between 1 and 5 mol-%. The reaction conditions involving acetonitrile/water (1:1, v/v) at 50 °C and using 5 mol-% of the catalyst were judged to be best for the oxidation of alcohols to the corresponding acids; of course, it is well known that oxone oxidizes aldehydes to acids in DMF at room temperature.^[6] Furthermore, the screening results also revealed that the oxidation with DIDA (5 mol-%) in nitromethane led selectively to the aldehyde at room temp. (Table 1). Encouraged by these results, the oxidation of a variety of primary and secondary alcohols was examined using DIDA (5 mol-%) and oxone (2 equiv.) in acetonitrile/water (1:1) (Table 2). While the reactions were carried out at 50 °C for primary alcohols, the oxidation of secondary alcohols was performed at room temp. The oxidation reactions of primary alcohols were carried out at elevated temperature to reduce the reaction times; the primary alcohols could be converted into the carboxylic acids at room temperature when the reactions were run for a longer duration (Table 1).

As can be seen from Table 2, the reaction yields were excellent for all the benzylic alcohols examined (Table 2, entries 1–5). The secondary alcohols were found to undergo smooth oxidation at room temp. to give the ketones in very good yields (Table 2, entries 6–8, 11, 15–16), with the exception of some ketones that underwent complicated reactions. Although 1-indanol gave the expected oxidation product,

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Catalytic Oxidation of Activated Alcohols



Table 1. Optimization of the conditions for the oxidation of p-bromobenzyl alcohol with **DIDA** as a catalyst in the presence of oxone.

Entry	Solvent	Temp. [°C]	Catalyst [mol-%]	Time [h]	Conversion [%]	Aldehyde [%]	Acid [%]
1	MeCN (dry)	r.t.	1	24	88	85	3
2	MeCN (dry)	r.t.	2.5	24	100	90	4
3	MeCN/H ₂ O (9:1)	r.t.	2.5	24	88	16	66
4	MeCN/H ₂ O (1:1)	r.t.	5	60	100	-	96
5	MeCN/H ₂ O (1:1)	50	5	7.5	100	-	93
6	MeCN/H ₂ O (1:1)	50	2.5	10	100	-	95
7	DMF (dry)	r.t.	2.5	24	82	10	69
8	<i>t</i> BuOH	r.t.	1	24	75	65	10
9	CH ₃ NO ₂	r.t.	1	24	97	93	trace
10	CH ₃ NO ₂	r.t.	5	10.2	100	96	0
11	DME	r.t.	1	24	trace	-	-
12	EtOAc	r.t.	1	24	90	85	trace
13	dioxane	r.t.	1	24	trace	-	-
14	HCO ₂ Et	r.t.	1	24	100	85	3

the yield was poor (Table 2, entry 9). A possible reason for this is the known reactivity of oxone towards benzylic C– H bonds.^[7] A vicinal diol, 1,2-diphenylethane-1,2-diol, gave benzil as the major oxidation product (Table 2, entry 10). Aliphatic alcohols were found not to undergo oxidation. Consequently, cholestanol was recovered quantitatively, and 3-phenylpropanol was recovered in 84% yield after 24 h (Table 2, entries 12 and 13). The small loss of the starting material in the latter case is attributed to reactions induced by oxone.^[7] Notably, 2-hydroxy-2-phenylacetic acid underwent decarboxylative oxidation to give benzoic acid in quantitative yield (Table 2, entry 14).

Based on the selective conversion of *p*-bromobenzyl alcohol to the corresponding aldehyde in nitromethane during the screening experiments (Table 1, entry 10), the oxidation of primary and secondary alcohols was investigated with **DIDA** at room temp. in the presence of oxone. The oxidation of benzylic alcohols occurred selectively to give the corresponding aldehydes in 10–20 h (Table 3, entries 1–5), while primary and secondary aliphatic alcohols such as cholestanol and 3-phenylpropanol remained unreactive. An allylic alcohol, cinnamyl alcohol, was found to undergo oxidation rather slowly (Table 3, entry 6). The unreactivity of aliphatic alcohols under the conditions used for the oxidation of benzylic alcohols prompted us to investigate the possibility of chemoselectivity in oxidations. Thus, the chemoselective benzylic oxidation of diols such as 1-phen-

ylbutane-1,3-diol and *p*-bromophenylethylene glycol was examined. Remarkable selectively was observed in both cases, and β -hydroxybutyrophenone and 4-bromo- α -hydroxyacetophenone, respectively, were formed in very good isolated yields (Table 3, entries 7 and 8). In contrast, 1,2diphenylethane-1,2-diol gave a mixture of benzoin and benzil, which suggests that the selective oxidation of benzylic vicinal diols to the corresponding acyloin is difficult to control (Table 3, entry 9).

During our attempts to oxidize 1,2-phenylenedimethanol to the corresponding dialdehyde^[4b] using **DIDA**/oxone in nitromethane at room temp., we stumbled on the observation that the corresponding lactone, namely, isobenzofuran-1(3H)-one, was formed in excellent yield (Table 4, entry 1). Buoyed by this observation, the oxidation of a number of aryldimethanols with **DIDA** (5 mol-%) and oxone (2 equiv.) was examined. As can be seen from the results in Table 4, increasing the number of electron-withdrawing groups led to reduced yields of the lactones, and virtually no reaction at all was seen (Table 4, entries 1, 4, and 7). Significantly, 2,2'-biphenyldimethanol was found to undergo lactonization to give the product in 82% isolated yield (Table 4, entry 5). Inexplicably, naphthalene-1,8-dimethanol was found to be unreactive, even after heating at 100 °C (Table 4, entry 8). It is noteworthy that the catalytic conversion of diols into lactones using I^V reagents is unprecedented.[8]

Table 2. Oxidation of primary^[a] and secondary^[b] alcohols using **DIDA**/oxone in CH₃CN/H₂O (1:1).

Entry	Substrate	Time [h]	Product	Yield ^[c] [%]
1 2 3 4 5	X X = H Br NO ₂ CN CI	5.5 7.5 9.5 10.0 6.0	х-<>>-<>OH	97 93 ^[d] 96 97 97
6	OH Me	11.5	Me	98
7	OH Meo	7.5	Meo	91
8	OH Ph Ph	6.5	Ph	97
9	OH C	13		60 ^[e]
10	OH OH	13		60 ^[1]
11		5.8		96
12	cholestanol	24	_[9]	
13	ОН	24	_[h]	
14	ОН	14	Соон	98
15 16	x	6 6.3	x-	90 92

[a] At 50 °C. [b] At room temp. [c] Isolated yields. [d] Oxidation with o-iodobenzoic acid (10 mol-%) as the catalyst led to the acid and aldehyde in 83 and 12% yields, respectively after 36 h. [e] The formation of an unidentified polar compound was observed, which seemed to account for the poor yield. [f] Benzoic acid (23%) and benzoin (10%) were isolated as by-products. [g] The starting material was recovered quantitatively. [h] Starting material (82%) was recovered, the remainder was an intractable material.

Catalytic Activity and Mechanistic Implications

The results of the oxidations shown in Tables 2, 3, and 4 clearly demonstrate the new catalytic activity of **DIDA**. Thus, the selective oxidation of activated primary alcohols to aldehydes, as well as over-oxidation to acids, can be readily performed depending on the choice of solvent. Furthermore, the catalytic protocol is amenable to the chemoselective oxidation of substrates that contain two or more hydroxy functionalities, in that only the hydroxy groups at the benzylic positions are oxidized under very mild reaction conditions. It should be noted that *catalytic* chemoselective oxidation based on IBX is unprecedented. Furthermore, it was shown that **DIDA** can be used catalytically to accomplish the conversion of diols into lactones by consecutive oxidations involving an initial alcohol-to-aldehyde conversion followed by a lactol-to-lactone oxidation.^[9] This latter result is remarkable in the light of the reported failure of this conversion by Corey et al. using IBX in stoichiometric amounts.[10]

To establish the fact that the structural attributes inherent to **DIDA** impart superior reactivity, control experiments were performed using o-iodobenzoic acid under identical conditions. Such control experiments are pertinent to evaluating the efficacy of the catalytic oxidations with **DIDA** in the light of the following considerations: i) oxone is known to oxidize benzylic alcohols, albeit at higher temperatures;^[7] and ii) simple *o*-iodobenzoic acid (20-40 mol-%) has also been reported to be an effective catalyst for the oxidation of benzylic alcohols in the presence of oxone



Table 3. Catalytic oxidation of primary and secondary alcohols using DIDA/oxone in CH₃NO₂ at room temp. (30-35 °C).



[a] Isolated yields. [b] Oxidation with o-iodobenzoic acid led to the aldehyde in 73% yield after 36 h. [c] Benzil (39%) was isolated.

(0.8–1.5 equiv.) in acetonitrile/water medium.^[5a] Thus, the catalytic oxidation of p-bromobenzyl alcohol, a representative case, was carried out with o-iodobenzoic acid (10 mol-%) and DIDA (5 mol-%) under identical experimental conditions by using oxone (2 equiv.) in CH₃CN/H₂O (1:1) and nitromethane solvents at 50 °C and room temp., respectively. In acetonitrile/water, the reaction with **DIDA** was complete within 7.5 h, leading to p-bromobenzoic acid in 93% isolated yield, whereas the reaction with o-iodobenzoic acid as the catalyst went on for 36 h, providing the acid in 83% yield together with the aldehyde in 12% yield. For the oxidation in nitromethane at room temp., the aldehyde was obtained in 96% isolated yield with DIDA after 10.2 h, whereas it was isolated in only 73% yield after 36 h with oiodobenzoic acid. Furthermore, a similar control experiment using o-iodobenzoic acid for the oxidation of benzene-1,2-dimethanol led to the corresponding lactone in 72% yield after 48 h, while the same reaction was accomplished with **DIDA** in 15 h, providing the lactone in 96% isolated yield. Indeed, this oxidation was incomplete when o-iodobenzoic acid was used as the catalyst, even after 48 h. These results clearly attest to the unique reactivity of **DIDA** for catalytic oxidations.

To explain the reactivity of **DIDA**, let us first focus on the nature of the in situ generated species that is responsible for the observed oxidations. As mentioned at the outset, the pentavalent λ^5 -iodane, i.e., **Bis-IBX**, could not be isolated when either oxone or KBrO₃ was used as an oxidant. Thus, one wonders what the species is that is responsible for the oxidation of the alcohols to the corresponding aldehydes or ketones. To gain some insight into this, the oxidation of **DIDA** in the presence of oxone in a D_2O/CD_3CN (2:1) mixture was monitored by 500 MHz ¹H NMR spectroscopy. The initially turbid solution gradually turned clear over a period of 24 h. The multiple substitution of the aromatic rings of **DIDA** greatly simplifies the spectral analysis. Thus, the singlet for the equivalent aromatic protons at δ = 7.16 ppm gradually disappeared, with concomitant appearance of several signals. These in turn disappeared with time, leading finally to a singlet at $\delta = 7.58$ ppm (Figure 1). The number of singlets that appeared as the oxidation progressed can be accounted for by assuming sequential oxidation of the two iodines initially to I^{III} and eventually to $I^{\rm V}$ species. Attempts to isolate the presumed $I^{\rm V}$ compound led to the recovery of the starting material, which suggests that it is too labile to be isolated. Similar monitoring of the oxidation by ¹³C NMR spectroscopy was thwarted by the concentration being too low to allow rapid spectral acquisition. Although the ¹H NMR analysis does point towards the in situ generation of the I^V species, unambiguous evidence was unfortunately not obtained. Nonetheless, the fact that the species is indeed Bis-IBX can be substantiated from the following considerations. Zhdankin et al. have shown that an o-methoxy group stabilizes IV iodyl species, i.e., -IO2, with weak I···O interactions leading to so-called pseudocyclic IBX-ethers;^[11] indeed, such species have been shown to be effective for the oxidation of alcohols when used in stoichiometric amounts in refluxing chloroform.^[11] FULL PAPER

Table 4. Oxidation of diols to lactones using **DIDA**/oxone in CH_3NO_2 at room temp. (30–35 °C).



[a] Isolated yields. [b] Oxidation with *o*-iodobenzoic acid as the catalyst led to the corresponding lactone in 72% yield after 48 h. [c] Isolated as a mixture of 5-bromoisobenzofuran-1(3*H*)-one and 6-bromoisobenzofuran-1(3*H*)-one in a 1:2.5 ratio, as determined by ¹H NMR spectroscopy. [d] The starting material was recovered in 30% yield. [e] The starting material was recovered quantitatively.

Notably, they are very much less reactive than IBX. Catalytic oxidations with iodo compounds that yield pseudocyclic IBX-ethers/esters/amides by in situ oxidations using oxone/KBrO₃ are unknown before now. Based on the established reactivity pattern of the pseudocyclic IBX-ethers, the reasonably rapid oxidations observed in our work with catalytic amounts of **DIDA** (5 mol-%) should be better understood based on the formation of **Bis-IBX** species. After all, why such a **Bis-IBX** should not be formed is incomprehensible. The fact that the iodyl species is unlikely to be involved is further supported from the absence of any reactivity of an analogous derivative, i.e., 3,3'-diiodo-2,2',6,6'-tetramethoxybiphenyl, which is devoid of the carboxy groups. This convincingly points to the operation of λ^5 -iodane species in the observed oxidations. Of course, the

mechanism of the oxidation of alcohols with IBX reagents has been thoroughly established in several investigations,^[5d,5e] and is not considered by us any further.



Figure 1. ¹H NMR (500 MHz) spectroscopic monitoring of the oxidation of **DIDA** in CD_3CN/D_2O (1:2): (a) at the beginning of the reaction, (b) after 2 h, (c) after 4 h, and (d) after 24 h.

The questions that still remain are: why is the **Bis-IBX** unstable, and why do the oxidations occur more rapidly with **DIDA** than with the simple *o*-iodobenzoic acid. We believe that the o-methoxy group in some way imparts steric constraints to destabilize the λ^5 -iodane species. The reason why oxidations occur more rapidly must be to do with the better solubility of the in situ generated Bis-IBX in the reaction medium than that of the parent IBX. Otherwise, faster reactions with the reagent with attenuated reactivity cannot be rationalized. We believe that the presence of orthogonal aromatic planes precludes aggregation of in situ formed Bis-IBX, and thus improves its solubility. In the realm of supramolecular chemistry, molecules with such features function effectively as inclusion host compounds by virtue of the fact that they cannot pack efficiently except in the presence of guest molecules of suitable shape and size.^[12]

Conclusions

A variety of modified IBXs with improved attributes that address the disadvantages associated with poor solubility and explosive characteristics continue to be reported. The development of catalytic oxidation protocols based on the in situ generation of IBX is appealing from the point of view of cost economy and simplicity. To the best of our knowledge, only a few instances of catalytic oxidations are known to date,^[5a–5e] and protocols that permit modulation

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Catalytic Oxidation of Activated Alcohols

of the reactivity of in situ-generated IBX for catalytic chemoselective oxidations are virtually unprecedented. We have designed a tetramethoxybiphenyl-based molecular system that leads, upon in situ oxidation, to Bis-IBX, which is characterized by perpendicular aromatic planes. Bis-IBX derived from such a twisted biphenyl scaffold presumably undergoes inefficient aggregation, which results in good solubility and facile oxidation. The solubility, in conjunction with the attenuated reactivity arising from the presence of the methoxy groups, allows the catalytic oxidation of reactive activated alcohols only. Primary alcohols are converted catalytically to the corresponding aldehydes selectively (in CH₃NO₂ at room temp.), or to the acids (in CH₃CN/H₂O (1:1) at 50 °C). These results are remarkably different from those reported with other reagents^[5a-5e] used catalytically, in the sense that aliphatic alcohols are untouched under the reaction conditions, which means that the oxidation of benzylic alcohols can occur selectively. The diiodo-diacid, i.e., DIDA, can also be used for cascade oxidations in which diols are sequentially converted to lactones.

Experimental Section

4-Iodo-3,5-dimethoxytoluene (2): nBuLi (1.4 M in hexane; 8.5 mL, 11.84 mmol) was added dropwise to a solution of 3,5-dimethoxytoluene (1.5 g, 9.87 mmol) in dry THF (20 mL) at 0 °C over a period of 15 min. The reaction mixture was stirred for 1.5 h at 0 °C, by which time the reaction mixture had turned yellow. A solution of of iodine (3.01 g, 11.84 mmol) in dry THF (20 mL) was added using a dropping funnel. The resulting reaction mixture was allowed to reach room temp. slowly, and was allowed to stir at this temperature for another 30 min. At the end of this period, the reaction mixture was quenched with ice, the THF was removed under reduced pressure, and the product was extracted with chloroform. The combined chloroform extracts were washed with sodium thiosulfate solution and dried with anhydrous Na₂SO₄. The solvent was removed in vacuo to give the crude product, which was further purified by column chromatography to give 2 (2.6 g, 95%), m.p. 87–89 °C. ¹H NMR (500 MHz, CDCl₃): δ = 2.35 (s, 3 H), 3.86 (s, 6 H), 6.34 (s, 2 H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 21.9, 56.4, 73.5, 105.2, 140.3, 159.1 ppm. HRMS (EI⁺): calcd. for C₉H₁₁IO₂ [M]⁺ 277.9804; found 277.9809.

2,2',6,6'-Tetramethoxy-4,4'-dimethylbiphenyl (3): This compound was prepared following a modified Ullmann reaction reported for the synthesis of 2,2',6,6'-tetramethoxybiphenyl.^[13] Accordingly, 3,5-dimethoxytoluene (0.28 g, 1.80 mmol) was subjected to ortholithiation in THF as described above. After 1.5 h, cuprous iodide (0.38 g, 1.98 mmol) was introduced in 2-3 portions. The resulting reaction mixture was allowed to stir at 0 °C for 1 h, during which time the reaction mixture turned grayish-black. Subsequently, a solution of 4-iodo-3,5-dimethoxytoluene (0.5 g, 1.80 mmol) in dry pyridine (7 mL) was added dropwise to the reaction mixture, which was then heated at reflux for 72 h. At the end of this period, the pyridine and THF were removed under reduced pressure, the residue was neutralized with dilute HCl, and the organic matter was extracted with chloroform three times. The combined organic extracts were washed with brine and dried with anhydrous Na₂SO₄, and the solvent was removed in vacuo. The crude residue was purified by column chromatography to obtain biphenyl product 3 (0.41 g, 75%) as a colorless solid, m.p. 136–138 °C. ¹H NMR

(500 MHz, CDCl₃): δ = 2.39 (s, 6 H), 3.71 (s, 12 H), 6.48 (s, 4 H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 22.3, 56.1, 105.5, 109.5, 138.6, 158.2 ppm. HRMS (EI⁺): calcd. for C₁₈H₂₂O₄ [M]⁺ 302.1518; found 302.1517.

3,3'-Diiodo-2,2',6,6'-tetramethoxy-4,4'-dimethylbiphenyl (4): TFA (0.2 mL) was added slowly to a mixture of 2,2',6,6'-tetramethoxy-4,4'dimethylbiphenyl (0.50 g, 1.65 mmol) and NIS (0.81 g, 3.64 mmol) in CH₃CN (8 mL). The resulting reaction mixture was stirred at room temp. for 3 h, and was subsequently quenched by the addition of crushed ice. The colorless solid that formed was filtered off to give **4** (0.89 g, 98%); m.p. 201–212 °C. ¹H NMR (500 MHz, CDCl₃): δ = 2.53 (s, 6 H), 3.47 (s, 6 H), 3.72 (s, 6 H), 6.72 (s, 2 H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 29.3, 56.0, 60.4, 88.6, 108.6, 115.4, 142.9, 158.17, 158.21 ppm. HRMS (EI⁺): calcd. for C₁₈H₂₀I₂O₄ [M]⁺ 553.9451; found 553.9459.

3,3'-Diiodo-2,2',6,6'-tetramethoxy-4,4'-biphenyldicarboxylic Acid (DIDA): KMnO₄ (19.1 g, 120.8 mmol) was added in several portions at regular intervals over a period of 5 d to a solution of 3,3'-diiodo-2,2',6,6'-tetramethoxy-4,4'-dimethylbiphenyl (5.58 g, 10.07 mmol) in pyridine/water (4:1 v/v; 100 mL) heated at reflux. After completion of the reaction, the pyridine and most of the water were removed in vacuo, and the brown solid was filtered off. The filtrate was acidified with concd. HCl and the resulting precipitate was collected by filtration to give DIDA (3.68 g, 60%) as a colorless solid, which was stable up to 250 °C, but decomposed at 256–258 °C with the liberation of iodine. IR (KBr): $\tilde{v} = 2939$, 1705 cm⁻¹. ¹H NMR (500 MHz, [D₆]acetone): $\delta = 3.49$ (s, 6 H), 3.81 (s, 6 H), 7.27 (s, 2 H) ppm. ¹³C NMR (125 MHz, [D₆]DMSO): δ = 56.6, 60.6, 81.4, 108.4, 119.6, 141.0, 158.34, 158.38, 169.3 ppm. HRMS (ESI⁻): calcd for $C_{18}H_{15}I_2O_8$ [M - H]⁻ 612.8856; found 612.8857.

Procedure for the Catalytic Oxidation of Alcohols: In a typical experiment, the alcohol (0.5-1.0 mmol), **DIDA** (5 mol-%), and oxone (2 equiv.) were added to CH₃CN/water (1:1; 4–6 mL). The resulting mixture was stirred at room temp. for the oxidation of secondary benzylic alcohols, or heated at 50 °C for primary benzylic alcohols. After completion of the reaction, as judged from TLC analysis, a little water was added to dissolve the inorganic salts, and then the organic matter was extracted with ethyl acetate. The combined extracts were washed with brine, dried with anhydrous Na₂SO₄, and concentrated in vacuo. Filtration over a short pad of silica gel gave the pure oxidation product.

For oxidations in CH_3NO_2 , a procedure similar to that described above was followed, with the reactions all being conducted at room temp.

Supporting Information (see footnote on the first page of this article): ¹H and ¹³C NMR spectra for the intermediates, target compound, and the products of oxidations.

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Catalytic Oxidations

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The *twisted* 3,3'-diiodo-2,2',6,6'-tetramethoxybiphenyl-4,4'-dicarboxylic acid (**DIDA**), used catalytically, permits the in situ generation of a **Bis-IBX**, and promotes the chemoselective oxidation of activated alcohols.

Catalytic Oxidation of Activated Alcohols



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Catalytic and Chemoselective Oxidation of Activated Alcohols and Direct Conversion of Diols to Lactones with In Situ-Generated Bis-IBX Catalyst

Keywords: Hypervalent compounds / Oxidation / Alcohols / Lactones / Chemoselectivity / Homogeneous catalysis