Oxidative cleavage of vicinal diols: IBX can do what Dess–Martin periodinane (DMP) can†

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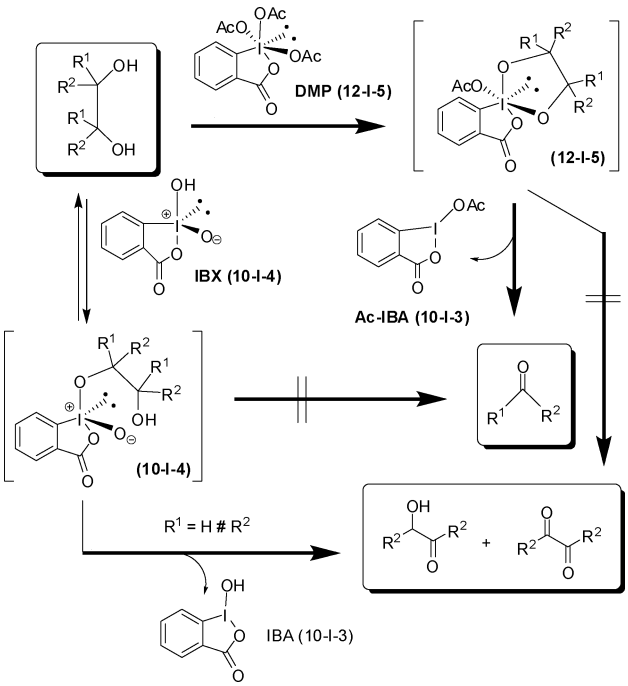
Received 12th December 2006, Accepted 16th January 2007
First published as an Advance Article on the web 30th January 2007
DOI: 10.1039/b618135j

The fact that IBX exhibits reactivity akin to DMP is demonstrated from the results observed with strained and sterically hindered *syn* 1,2-diols, which undergo oxidative cleavage *via* a 12-I-5 spirobicyclic periodinane. The use of TFA, a protonating solvent, promotes the formation of the 12-I-5 intermediate for 1,2-diols of all types (*sec*,*sec*, *sec*,*tert* and *tert*,*tert*), leading to efficient oxidative fragmentation.

The oxidizing agent *o*-iodoxybenzoic acid, popularly known as IBX, has recently grown in importance in oxidation chemistry due to its easy synthesis and hence cheap availability, environmentally-benign attributes, and more importantly a multitude of transformations that may be readily accomplished with it in a facile manner.[1] Strangely, it was only after a century that the extremely useful oxidation properties of IBX were uncovered. In 1994, Frigerio and co-workers[2] showed for the first time that IBX is soluble in DMSO and that it oxidizes alcohols to carbonyl compounds in this medium. The recent demonstration by Nicolaou and co-workers of a variety of IBX-mediated transformations at elevated temperatures in DMSO has spurred a renewed interest in IBX oxidation chemistry.[3] Thus, the kaleidoscopic ability of IBX to accomplish a myriad of transformations continues to be uncovered even a decade after its oxidation properties were revealed.[4]

In the course of our studies on IBX oxidations,[5] we were intrigued by the reported results that IBX oxidizes *sec*,*sec*-1,2-diols to the corresponding α-ketols and/or α-diketones without cleaving the glycolic C–C bond,[2] and that it does not react with *tert*,*tert*-1,2-diols to afford oxidative fragmentation products, namely ketones.[6] In contrast, DMP has long been known to accomplish the same transformation rather easily (Scheme 1).[6,7] This difference in the reactivities of IBX and DMP with respect to 1,2-diols was shown to be a consequence of *reversible* formation of a 10-I-4 species with IBX and *irreversible* formation of a 12-I-5 species with DMP;[6] the latter decomposes rapidly into dicarbonyl compounds, while the former cannot undergo cleavage. In the present investigation, we have examined IBX-mediated oxidative cleavage of *tert*,*tert*-1,2-diols and have also discovered pathways that favor fragmentation of *sec*,*sec*-1,2-diols, which otherwise yield non-cleavage products. Herein, we report that IBX can be employed to accomplish oxidative cleavage of 1,2-diols in the manner of DMP by simple variation of solvent and/or temperature, and present our results that attest to the formation of a modified 12-I-5 species.



Scheme 1

In our initial experiments, we found that benzpinacol ($Ph_2C(OH)C(OH)Ph_2$) underwent C–C bond cleavage when heated with IBX in DMSO at 80 °C. Evidently, the elevated temperature drives the reaction over activation barriers necessary for the observed fragmentation. Encouraged by this result, the oxidative cleavage of a variety of 1,2-diols was examined at 70–80 °C in DMSO. Four different *tert*,*tert*-1,2-diols were found to undergo fragmentation to ketones (both aliphatic and aromatic) in excellent isolated yields (entries 1, 3, 5 and 7, Table 1).‡ However, a range of *sec*,*sec* as well as *sec*,*tert*-1,2-diols was found to be oxidized, under same conditions, to the corresponding ketols and/or 1,2-diketones (entries 9, 12, 14, 16, 24, 30, 32, 34 and 36); clearly, in these cases the oxidation of hydroxyl group/s to ketol and/or diketone competes with oxidative fragmentation. However, strained *syn*-1,2-diols (at rt) and sterically-hindered *sec*,*sec*-1,2-diols (at 65 °C) were found to undergo cleavage to the corresponding dialdehyde/aldehydes in varying yields (entries 18, 20 and 22), as well as being converted to the non-cleavage oxdiation products, *viz.*, diketones and ketols. Indeed, *sec*,*tert*-1,2-diols also exhibited moderate cleavage in DMSO as the solvent (entries 26 and 28).

Mechanistically, the oxidative fragmentation of *tert*,*tert*-1,2-diols with IBX in DMSO at 80 °C should be reconciled based on the formation of a spirobicyclic periodinane 12-I-5 species

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† Electronic supplementary information (ESI) available: Experimental procedures and characterization data for products. See DOI: 10.1039/b618135j

Table 1 Results of oxidative cleavage of 1,2-diols to carbonyl compounds with IBX in DMSO and TFA

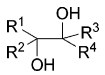
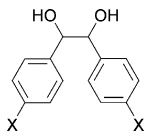
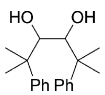
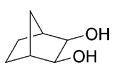
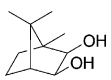
			Reaction conditions					
Entry	Substrate		Solvent	Equiv.[a]	Temp./°C	Time/h	Oxidation products	Yield (%)[b]
1		$R^1 = R^2 = R^3 = R^4 = Ph$	DMSO	2.0	80	4.0	Cleavage	90
2			TFA	2.0	30	3.0	Cleavage	75[c]
3		$R^1 = R^3 = Ph$; $R^2 = R^4 = Me$	DMSO	1.5	80	1.5	Cleavage	86
4			TFA	1.5	30	0.1	Cleavage	88
5		$R^1 = R^2 = R^3 = R^4 = Et$	DMSO	1.2	80	1.2	Cleavage	>80[d,e]
6			TFA	1.2	30	0.1	Cleavage	>90[d,e]
7		$R^1 = R^2 = -(CH_2)_5-$; $R^3 = R^4 = -(CH_2)_5-$	DMSO	1.2	80	5.0	Cleavage	>90[c,d,e]
8			TFA	1.2	30	0.1	Cleavage	>90[d,e,f]
9		X = H	DMSO	2.5	30	0.5	Non-cleavage	86
10			TFA	1.5	30	0.1	Cleavage	85
11			TFA	2.0	30	0.1	Cleavage	80
12		$X = CH_3$	DMSO	2.5	30	0.5	Non-cleavage	88
13			TFA	1.5	30	0.1	Cleavage	85
14		X = F	DMSO	2.5	30	0.5	Non-cleavage	>80
15			TFA	1.5	30	0.1	Cleavage	80
16		X = Br	DMSO	2.5	30	0.5	Non-cleavage	70
17			TFA	1.5	30	0.1	Cleavage	82
18			DMSO	2.5	65	3.0	Cleavage + non-cleavage	88
19			TFA	1.2	30	0.3	(70 : 30) Cleavage	80
20			DMSO	1.2	30	2.0	Cleavage	70
21			TFA	1.2	30	0.1	—[g]	—
22			DMSO	1.2	30	2.0	Cleavage + non-cleavage (66 : 34)[d]	—
23			TFA	1.2	30	0.1	Cleavage[d]	—
24			DMSO	1.5	30	0.5	Non-cleavage	>90
25			TFA	1.5	30	0.1	Cleavage	>90[d]
26			DMSO	2.0	80	7.0	Cleavage + non-cleavage (60 : 40)[d]	—[h]
27			TFA	1.1	30	0.1	Cleavage	90
28			DMSO	1.1	rt	—	Cleavage (27%)[i]	—
29			TFA	1.1	30	0.1	Cleavage	80

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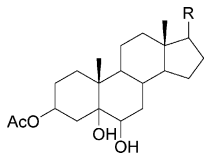
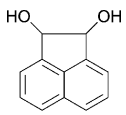
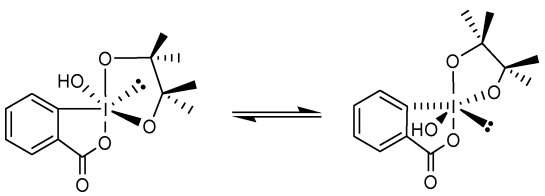
Table 1 (*Contd.*)

Entry	Substrate		Reaction conditions				Oxidation products	Yield (%)[b]
			Solvent	Equiv.[a]	Temp./°C	Time/h		
30		R = -$CH(CH_3)CH_2CH_2$-$CH_2CH(CH_3)_2$	DMSO	6.0	rt	1.0	Non-cleavage[j]	—
31			TFA	1.2	30	0.1	Cleavage	90
32		R = -$COCH_3$	DMSO	6.0	rt	1.0	Non-cleavage[j]	—
33			TFA	1.2	30	0.1	Cleavage	85
34		*Syn*	DMSO	2.5	30	1.0	Non-cleavage	85
35			TFA	1.2	30	0.2	Cleavage	—[g]
36		*Anti*	DMSO	2.5	30	1.0	Non-cleavage	82
37			TFA	2.5	30	0.2	Non-cleavage	76

[a] Molar equivalent of IBX. [b] Isolated yields, unless mentioned otherwise. [c] Conversion 75%. [d] Based on ^{1}H NMR (400 MHz) analysis of the reaction mixture. [e] With 2.0 equiv. of IBX, α,β-unsaturated ketone was also observed. [f] Based on GC analysis. [g] A complex mixture of products was observed. [h] Conversion 85%. [i] Ref. 6. [j] Ref. 2.

(as formed in DMP oxidation), while non-cleavage oxidation must occur *via* a 10-I-4 species. In order to characterize the 12-I-5 intermediate formed during the oxidative cleavage of *tert*,*tert*-1,2-diols, the progress of the reaction of pinacol, a representative case, with IBX was monitored by ^{1}H NMR spectroscopy. The NMR profiles for the reaction of pinacol with IBX in a sealed NMR tube after different reaction durations are shown in Fig. 1. The appearance of 4 methyl signals at rt suggests that IBX reacts with pinacol to form an alkoxyiodinane oxide (**A**), which has been previously characterized.[6] Upon heating at 80 °C, 2 new methyl signals with equal intensity appear, with concomitant disappearance of the signals of **A** (see **B** → **C** → **D**). Further, one observes the formation of a fragmentation product, acetone (**C**). We attribute these two new signals to the formation of a spirobicyclic 12-I-5 species, *cf.* Scheme 2. A rapid equilibrium on the NMR time scale between two *enantiomeric* species, as shown in eqn (1), presumably occurs, and accounts for the appearance of only two methyl signals.[8]



(1)

How is the formation of 12-I-5 species, responsible for oxidative cleavage, facilitated at a high temperature in DMSO? Based upon ^{1}H NMR studies, Nicolaou and co-workers showed recently that DMSO forms an adduct with IBX at higher temperatures (Scheme 2).[9] The formation of such an adduct may increase the reactivity of IBX toward alcohols. Thus, the formation of a 12-I-5 spirobicyclic periodinane intermediate must be promoted (Scheme 2) by initial attack of the 1,2-diol on the DMSO–IBX

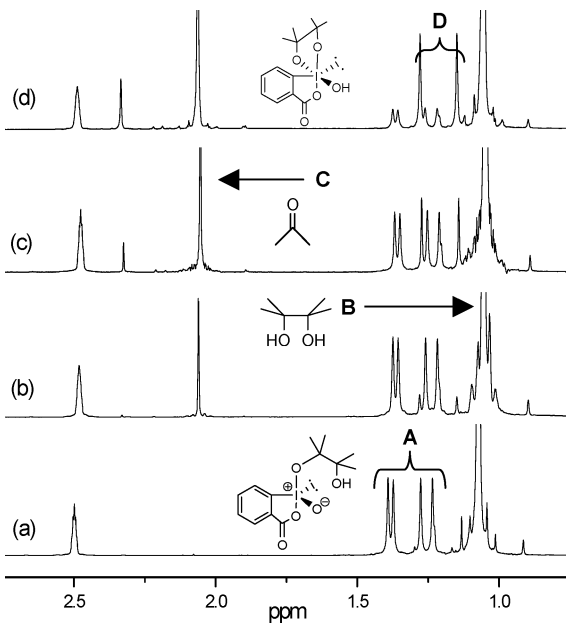
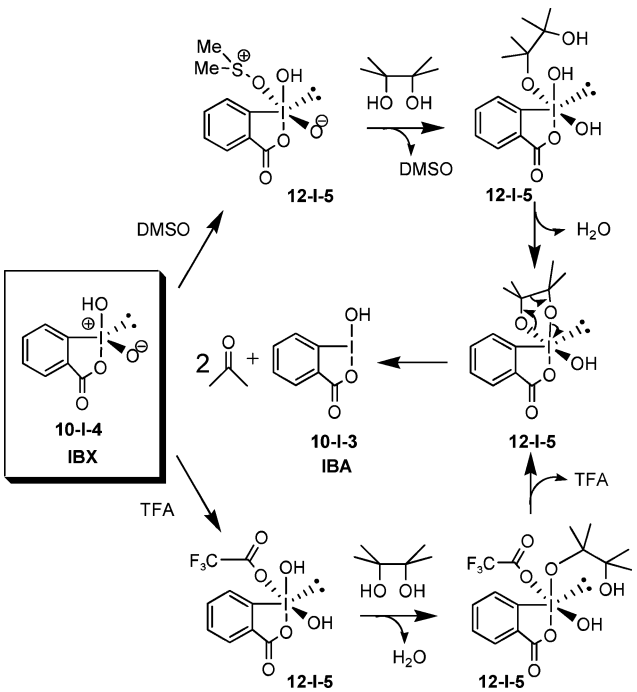


Fig. 1 ^{1}H NMR monitoring of the reaction of IBX with pinacol in DMSO in a sealed NMR tube: (a) 0.5 h, 30 °C; (b) 1 h, 80 °C; (c) 2 h, 80 °C and (d) 4 h, 80 °C.

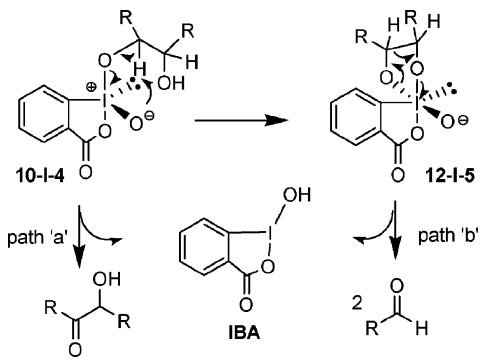
adduct followed by dehydration of the monoalkoxy periodinane;[6] DMSO may initially depart as a good leaving group, akin to that of the acetoxy group in DMP. These considerations do not appear to apply for cyclic strained *syn*-1,2-diols, as reflected in their reactivity at rt; the formation of 12-I-5 species should be facile for conformationally predisposed cyclic *syn*-1,2-diols.

To achieve oxidative cleavage of *sec*,*sec*-1,2-diols which yield non-cleavage products with IBX in DMSO, we envisaged that protonation of 10-I-4 species may suppress the nucleophilic attack



Scheme 2

leading to the ketol (path 'a', Scheme 3). It was soon realized from preliminary experiments that TFA not only serves as a proton source, but is also an extremely good solvent for IBX. Thus, with neat TFA as solvent, a variety of *sec*,*sec*, *tert*,*tert* and *sec*,*tert syn*-1,2-diols were found to undergo oxidative cleavage in very short reaction times (5–30 min) and in respectable isolated yields (Table 1).‡ Surprisingly, addition of the diol to TFA, followed by IBX, led to an intractable mixture of products.



Scheme 3

Insofar as the mechanism of fragmentation is concerned, we believe that IBX is converted to a 12-I-5 spirobicyclic periodinane species in TFA much more rapidly than for DMP, because CF_3COO^- is a much better leaving group than CH_3COO^- (Scheme 2). The rapidity with which the reaction is completed (within 10–30 min after the addition of the diol) appears to suggest that the formation of the 12-I-5 species is rate-determining.[10] In line with this mechanism, one molar equivalent of IBX suffices for oxidative cleavage. The reduction product of IBX was confirmed to be iodosobenzoic acid (IBA, Schemes 1–3) by isolation and characterization by ^{1}H NMR studies (see ESI†).

The results of oxidation of acenaphthylen-1,2-diols with IBX in TFA are quite instructive. The *syn* diol (entry 35, Table 1) gave a complex mixture of products (presumably due to the dialdehyde undergoing further reactions in the acidic medium), whereas the *anti* diastereomer (entry 37, Table 1) yielded non-cleavage products in 76% isolated yield—clearly suggestive of the difficulty associated with the formation of spirobicyclic 12-I-5 periodinane intermediate, which is responsible for oxidative cleavage.

In summary, the fact that IBX does exhibit reactivity akin to DMP is revealed from the results observed with strained and sterically-hindered *syn*-1,2-diols. The relief of strain in the 12-I-5 intermediate (path 'b', Scheme 3) and the difficulty of hydrogen transfer in the 10-I-4 intermediate (path a) facilitate the cleavage. When the use of DMSO does not result in the cleavage of 1,2-diols, TFA serves as a solvent as well as a proton source to effect rapid oxidative cleavage. The drawback with the protocol involving the use of the TFA is that it cannot be employed for acid-sensitive diols, *e.g.*, protected mannitols, cyclic *sec*,*sec*-1,2-diols (for which the resultant dialdehydes may undergo rapid acid-catalyzed aldol chemistry), *etc.* Given that IBX is an excellent eco-friendly oxidation reagent, the above-described reactivity of IBX in a protic solvent is expected to further enhance the breadth of its applications in organic oxidation chemistry. As far as vicinal diols are concerned, simple variation of experimental conditions permits oxidation of choice, *i.e.*, oxidative cleavage or non-cleavage.

Acknowledgements

We are thankful to DST, India, for financial support. NS and KS are grateful to CSIR and UGC, respectively for their research fellowships. We thank one of the referees for invaluable suggestions.

Notes and references

‡ **General procedure for oxidation of 1,2-diols to the corresponding carbonyl compounds with IBX in DMSO.** In a representative case, 1.2–2.5 equiv. of IBX in 1.0 mL of DMSO was stirred for *ca.* 10 min, and to this mixture 1–2 mmol of 1,2-diol was introduced. The reaction mixture was stirred at the appropriate temperature (see Table 1). The progress of the reaction was monitored by TLC analysis. After completion of the reaction, the reaction mixture was quenched with water and the organic matter was extracted with diethyl ether or CH_2Cl_2. The organic layer was washed with sodium bicarbonate and brine solution, dried over anhyd. Na_2SO_4 and the solvent concentrated *in vacuo.* Silica-gel column chromatography of the crude reaction mixture yielded the products, which were characterized spectroscopically. **General procedure for oxidation of 1,2-diols to the corresponding carbonyl compounds with IBX in TFA.** In a typical experiment, 1.2–2.0 equiv. of IBX in 1.5–2.0 mL of TFA was stirred for 5 min, and to this mixture 1–2 mmol of 1,2-diol was introduced. The reaction mixture was stirred at appropriate temperature (see Table 1). The progress of the reaction was monitored by TLC analysis. After completion of the reaction, the reaction mixture was quenched with water and the organic matter was extracted with diethyl ether or CH_2Cl_2. The organic layer was washed with sodium bicarbonate and brine solution, dried over anhyd. Na_2SO_4 and the solvent removed *in vacuo.* Silica-gel column chromatography of the crude reaction mixture yielded the products, which were characterized by spectroscopic data.

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7 (*a*) D. B. Dess and J. C. Martin, *J. Org. Chem.*, 1983, **48**, 4155; (*b*) D. B. Dess and J. C. Martin, *J. Am. Chem. Soc.*, 1991, **113**, 7277; (*c*) P. A. Grieco, J. L. Collins, E. D. Moher, T. J. Fleck and R. S. Gross, *J. Am. Chem. Soc.*, 1993, **115**, 6078; (*d*) J. M. VanderRoest and P. A. Grieco, *J. Am. Chem. Soc.*, 1993, **115**, 5841; (*e*) A. Pancrazi, C. Anies and J. Collemand, *Tetrahedron Lett.*, 1995, **36**, 7771.
8 The observed chemical shifts for the methyl groups are in agreement with those observed for a similar species in the case of DMP (see ref. 6).
9 K. C. Nicolaou, T. Montaganon and P. S. Baran, *Angew. Chem., Int. Ed.*, 2002, **41**, 993.
10 It is noteworthy that acetoxy-IBX is known to react much more rapidly than IBX itself in the oxidations of alcohols due to the fact that the displacement reaction is much faster. See: S. D. Meyer and S. L. Schreiber, *J. Org. Chem.*, 1994, **59**, 7549 and also ref. 7*b*.