PERKIN 2

Preparation of Dess–Martin periodinane—the role of the morphology of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide precursor

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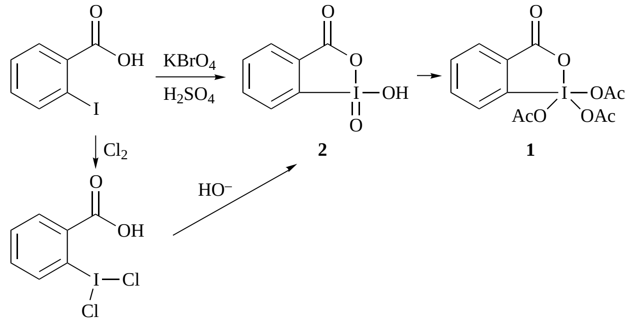
1-Hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide prepared by oxidation of *o*-iodobenzoic acid with potassium bromate forms either a microcrystalline powder, a macrocrystalline material, or a mixture of both forms. This difference in physical form is the source of the difficulty in reproducibly converting 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide to the corresponding *I*-triacetoxy derivative. A simple method is given for conversion of crystalline 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide to the more reactive powder form. The microcrystalline powder and macrocrystalline material are characterised by X-ray diffraction.

Introduction

The oxidation of primary alcohols to aldehydes is a process central in organic synthesis and many reagents have been used to effect this transformation. Three key oxidants, tetrapropylammonium perruthenate (TPAP),[1] activated dimethyl sulfoxide[2] and Dess–Martin periodinane[3] have emerged as the reagents of choice for the oxidation of sensitive alcohols to aldehydes. In terms of cost, ease of use, work up and recycleability, the Dess–Martin periodinane[3] **1** is very competitive with the other two reagents and is seeing increasing use in synthesis. Unfortunately, this reagent is no longer commercially available. We and others[4] have found that preparation of the triacetoxyperiodinane **1** from 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one 1-oxide **2** can be difficult; the yields are often not reproducible under standard reaction conditions and the oxidation activity is variable. In particular, the yield of the triacetoxyperiodinane **1** can be very dependent on the batch of the precursor **2** employed. Several modifications of the original method have been reported[4] but to date no systematic attempt has been made to identify the cause of the problem in converting **2** to **1**. We now report our findings in this area.

Results and discussions

Since yields of **1** were batch dependent it was initially suspected that the purity of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide precursor **2** was crucial. In order to check the purity of **2**, ^{1}H and ^{13}C NMR spectra in Me_2SO and ^{13}C NMR spectra in sodium hydroxide solution were recorded.† These spectra showed compound **2** to be of exceptionally high purity with no organic contaminants present regardless of batch. Alarmingly the spectra obtained were very different from those reported by Katritzky[5] but identical to those reported by Santagostino.[6] Katritzky had previously synthesised **2** by chlorination of *o*-iodobenzoic acid followed by base hydrolysis (Scheme 1) whilst Santagostino had used potassium bromate as the oxidant. An X-ray structure[7] had previously been determined on the material secured using Katritzky's route strongly indicating that the structure of the *o*-iodobenzoic acid oxidation product by potassium bromate oxidation[8] was incorrect.



Scheme 1

It was noticed that in some batches, the product of potassium bromate oxidation of *o*-iodobenzoic acid was predominantly crystalline in nature whilst in other batches it was predominantly a white microcrystalline powder. After attempting five preparations of 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one 1-oxide **2**, on a 100 g scale, we have been unable to ascertain which factors dictate the morphology of the product.[9] One of the runs gave a product which was predominantly crystalline, another run gave a product which was predominantly powder whilst three runs gave a product which was an unquantifiable mixture of both forms. In all cases severe difficulty was experienced at some stage in mechanically stirring the reaction mixture. This may be the source of the variation in morphology of the product. NMR studies showed that both solid forms were identical pure compounds in solution.

An X-ray structure on a colourless crystal produced directly from the crude aqueous reaction was therefore carried out to confirm its structure. The crystals were found to be racemic 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2r**, cell parameters $a = 7.854(1)$, $b = 11.584(2)$, $c = 8.385(2)$, $\beta = 101.29(1)°$, space group $P2_1/c$, $Z = 4$. A comparison of the unit cell parameters for this crystal with those obtained by Gougoutas[7] for 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2** showed this to be a different crystalline form; cell parameters for this sample are: $a = 8.489(3)$, $b = 11.735(5)$, $c = 8.418(3)$, $\beta = 113.67(3)°$, space group $P2_1$, $Z = 4$. The material obtained by Gougoutas was a conglomerate (each crystal contained only iodine atoms with the same absolute configuration) whereas our compound was a true racemate. Fig. 1 illustrates the molecular structure and numbering scheme for racemic 1-hydroxy-1,2-benziodoxol-

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† NMR data for 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2** (*J* in Hz).
δ_C(D_2O–NaOH 125 MHz) 172.01, 148.28, 134.55, 134.25, 131.60, 131.50, 123.02.
δ_C[$(CD_3)_2SO$ 125 MHz] 167.45, 146.60, 133.36, 132.93, 131.45, 130.06, 125.00.
δ_H[$(CD_3)_2SO$ 500 MHz] 8.14 (1 H, d, *J* 8.1), 8.02 (1 H, d, *J* 7.3), 7.98 (1 H, d, *J* 7.3), 7.83 (1 H, d, *J* 7.3).

Table 1 Iodine bond lengths (Å) and angles (°)[a]

Il–O11	1.784(2)	I1–O12	1.925(2)	I1–O81	2.263(2)
I1–C2	2.100(3)	I1–O11′	2.808(2)	I1–O82″	2.782(2)
C2–I1–O82″	162.22(10)	O11–I1–O11′	164.76(6)	O12–I1–O82″	76.84(8)
O81–I1–O11′	76.71(8)	O11–I1–O12	96.31(10)	O11–I1–C2	100.30(11)
O12–I1–C2	86.33(11)	O11–I1–O81	88.11(10)	O12–I1–O81	163.42(8)
C2–I1–O81	77.15(10)				

[a] Symmetry codes: $'x, -y+\frac{1}{2}, z-\frac{1}{2}, {}''-x+2, y-\frac{1}{2}, -z+\frac{1}{2}$.

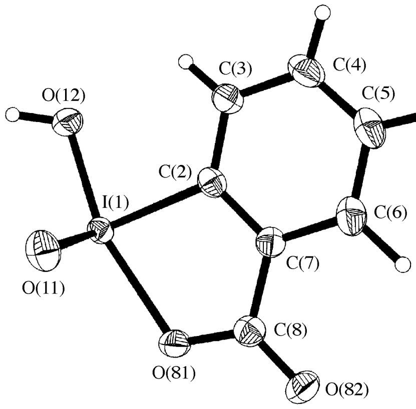

Fig. 1 Molecular structure of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2r**

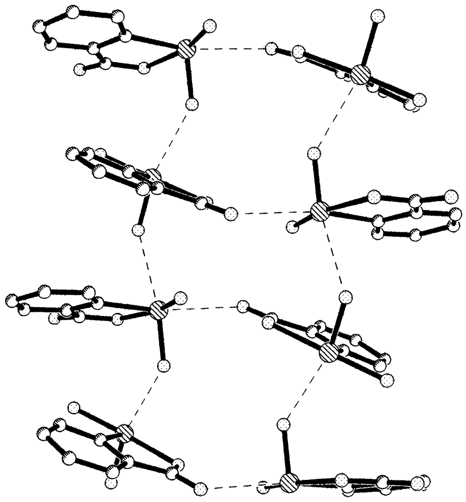

Fig. 2 Extended molecular structure, showing both enantiomers of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2r**, C–H ··· O hydrogen bonds and I ··· O bonds

Table 2 *d* values[a] for 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide[b]

2p	**2**	**2r**
7.63(100)	7.77(100)	7.70(98)
6.40(32)	6.48(94)	6.41(100)
5.82(15)	5.86(63)	5.79(55)
4.64(15)	4.68(56)	4.62(34)
4.15(22)	4.18(62)	4.25(35)
3.82(10)	3.85(45)	4.11(50)
		3.96(47)
		3.87(48)
	3.69(68)	
3.66(50)	3.66(63)	3.65(70)
		3.27(34)
2.51(17)	2.53(30)	2.50(29)

[a] Relative intensity in brackets. [b] Values for **2** and **2r** generated by CERIUS2 package from single crystal data.

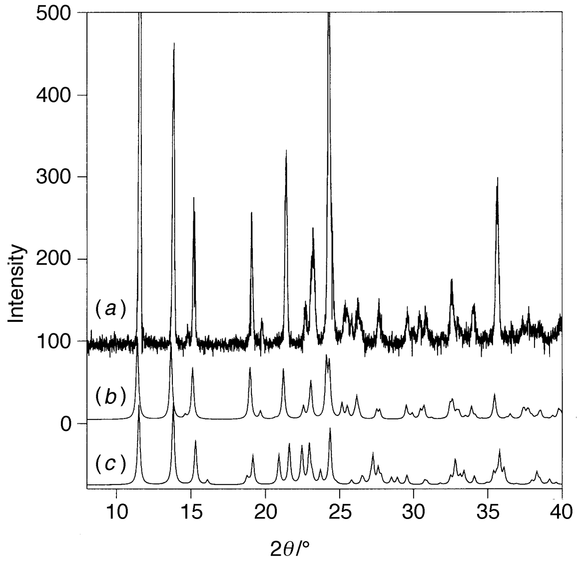

Fig. 3 Powder X-ray diffraction patterns of (*a*) reactive powder form of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2p**, (*b*) conglomerate 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2** and (*c*) racemic 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2r**

3(1*H*)-one 1-oxide **2r** and Fig. 2 illustrates the extended crystal structure.

The crystal structure of the racemic compound **2r** consists of chains of molecules linked by a hydrogen bond, O12–H120 ··· O81′, and an Il ··· O82 contact (1.98 Å). These hydrogen bonded chains contain a dimeric motif in which the two molecules are stepped at an angle of 29.8°. There is also a second iodine–oxygen contact, Il ··· O11 (2.1 Å), linking the chains to form a two-dimensional sheet. The hydrogen atoms H4 and H5 are both involved in bifurcated C–H ··· O hydrogen bonds to two other 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide molecules. Thus the 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide molecules are linked together *via* one O–H ··· O, four C–H ··· O hydrogen bonds and two I ··· O contacts to form a three-dimensional, hydrogen and iodine–oxygen bonded network in which the iodine atoms have distorted octahedral coordination (Table 1). This three-dimensional network is further stabilised by π–π stacking of the phenyl rings with C ··· C contacts of 3.2 Å, and H–ring centre contacts of 2.4 Å. The rings are staggered at an angle of 65°.

The powder form of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2p** reacts with acetic anhydride and acetic acid to give the triacetoxyperiodinane **1** as reported by Schrieber[4] (reaction time 3 h) whilst with the crystalline form the reaction had still not gone to completion after 6 h. This difference in reaction rate of the two samples is entirely due to the morphology of the material. We now report that the crystalline form of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2** can be conveniently converted to more reactive microcrystalline form by dissolving it in sodium hydroxide solution and then reprecipitating with hydrochloric acid (90% recovery for the process). A 1.2 M ratio of the Dess–Martin periodinane, produced from different batches of this powder, reproducible oxidised benzyl alcohol to benzaldehyde in quantitative yield (by NMR spectroscopy) within 10 min using dry deuteriochloroform as solvent.

The powder batch of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2p** was next examined by X-ray powder diffraction and powder patterns for **2** and **2r** were generated from the single crystal data by the CERIUS2 program (Table 2 and Fig. 3). Although the powder pattern obtained for the microcrystalline compound **2p** shows similarities with both **2** and **2r** the best match is for **2**. It therefore looks likely that the more reactive powder form of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2p** is conglomerate in nature.

Experimental

1-Hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2** was prepared by Martin's[3] modification of Greenbaum's method[8] using the same scale. **CAUTION: 1-Hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide 2 is reportedly shock sensitive.**[9] On making five batches of **2** under apparently identical conditions the sample varied from a predominantly macrocrystalline to a predominantly microcrystalline (powder) in nature.

Conversion of macrocrystalline 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide 2r to the microcrystalline 2p form

Macrocrystalline (1.0 g, 3.4 mmol) was dissolved in water (2 ml) containing sodium hydroxide (0.16 g, 4 mmol). This was rapidly ice cooled and the pH was bought to 1 by addition of hydrochloric acid. The precipitated solid was filtered off, washed with acetone (2 × 5 ml) and dried to give powdered 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide **2p** (0.9 g, 90% recovery).

X-Ray crystallography

Crystal data for 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide, $C_7H_5O_4I$, **2r**: $M = 280.1$, monoclinic, space group $P2_1/c$, $a = 7.854(1)$, $b = 11.584(2)$, $c = 8.385(2)$ Å, $\beta = 101.29(1)°$, $U = 748.1(2)$ Å^{-3}, $Z = 4$, $D_c = 2.486$ Mg m^{-3}, $F(000) = 528$, $\mu = 4.247$ mm^{-1}, crystal dimensions 0.41 × 0.18 × 0.14 mm. A total of 2011 reflections were measured for $4 < 2\theta < 50°$ and 1314 independent reflections were used in the refinement. The final parameters were $wR2 = 0.0385$ and $R1 = 0.0160$ $(I > 2\sigma I)$, S = 1.061, 109 parameters, weighting scheme $g_1 = 0.0199$, $g_2 = 0.7419$, $(\Delta/\sigma)_{\mathbf{max}} < 0.001$, $(\Delta\rho)_{\mathbf{max,min}} = 0.388$, -0.362 e Å^{-3}. An empirical absorption correction was applied using psi scans, maximum and minimum transmission range 1.00, 0.683.

Data were collected using a Siemens P4 four-circle diffractometer with graphite monochromated Mo-Kα radiation. Crystal stabilities were monitored every 100 reflections and there were no significant variations (±1%). Cell parameters were obtained from 38 accurately centred reflections in the 2θ range 10–25°. Data were collected at *ca.* 293 K and omega scans were employed for data collection. Lorentz and polarisation corrections were applied.

The structure was solved by direct methods and the non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions and a riding model with fixed thermal parameters $[U_{\mathbf{ij}} = 1.2U_{\mathbf{ij}}(\mathrm{eq})]$ was used for subsequent refinement. The function minimised was $\Sigma[w(|F_{\mathbf{o}}|^2 - |F_{\mathbf{o}}|^2)]$ with reflection weights $w^{-1} = [\sigma^2\ |F_{\mathbf{o}}|^2 + (g_1P)^2 + g_2P]$ where $P = [\max\ |F_{\mathbf{o}}|^2 + 2|F_{\mathbf{o}}|^2]/3$. The XSCANS, SHELXTL PC[10] and SHELXL-93[11] packages were used for data collection, reduction and structure solution and refinement. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 188/39.

Powder diffraction data for **2p** were collected using Siemens D5000 X-ray powder diffractometer with copper radiation in continuous mode with a step time of 10 s and step size of 0.02° for the 2θ range 4–50°.

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