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Preparation of an aliphatic-substituted hypervalent iodine compound, tetracoordinate 1,2-iodoxetane 1-oxide, and its application to oxidation

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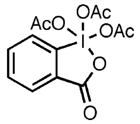
Dedicated to Professor Iwao Ojima, on the occasion of his 60th birthday

Abstract—A tetracoordinate 1,2-iodoxetane was prepared by the fluorination of a tricoordinate 1,2-iodoxetane with xenon difluoride followed by hydrolysis. The tetracoordinate 1,2-iodoxetane oxidized alcohols and a sulfide to the corresponding aldehydes and ketones, and a sulfoxide, respectively, in good to moderate yields under mild conditions.

Hypervalent iodine compounds have found wide practical application as useful reagents for oxidation of a variety of primary and secondary alcohols to carbonyl compounds.[1–4] Both the Dess–Martin periodinane (DMP) **1** and benziodoxole oxide (IBX) **2** have been widely used as hypervalent iodine oxidants. These reagents have been applied to the organic synthesis of natural products despite their potentially explosive nature and insolubility in certain common solvents. A majority of previous hypervalent iodine oxidants such as **1** and **2** are aryl-substituted iodine compounds. There are no examples of aliphatic-substituted iodinane oxides, to our knowledge, because there are limited examples of alkyliodinanes that are expected to be precursors of the alkyliodinane oxides.[5–8] On the other hand, we previously reported the synthesis and thermolysis of 1,2-iodoxetane **3** with a novel tridentate ligand.[9] On one hand oxidation of benzyl alcohol with 1,2-iodoxetane **3** resulted in an unsatisfactory benzaldehyde yield; whereas on the other hand, an iodine compound with an iodine atom in a higher oxidation state is expected to be a better oxidant. We report here the synthesis of a tetracoordinate 1,2-iodoxetane 1-oxide and its application as an oxidizing reagent. This is the first example of an iodinane oxide with an aliphatic substituent.



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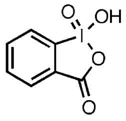

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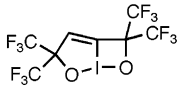

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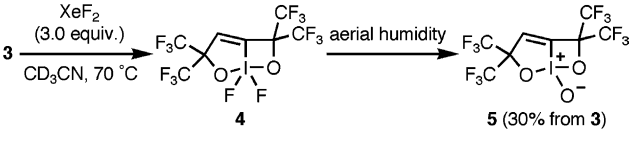
1,2-Iodoxetane **3** (30 mg, 0.062 mmol) was heated with xenon difluoride (32 mg, 0.19 mmol) in CD_3CN (0.60 mL) at 70 °C for 14 h and was monitored by ^{19}F NMR spectroscopy (Scheme 1). A set of signals [δ_F −75.32 (t, 6F, $J_{FF} = 4.9$ Hz), −74.32 (t, 6F, $J_{FF} = 8.5$ Hz), −25.45 to −25.75 (m, 2F)] increased with a decrease of the signals of **3**. The increased signals were assigned to 1,2-iodoxetane 1,1-difluoride **4**. Although an iodinane difluoride was previously synthesized by treatment of an iodinane with F_2 gas,[10] xenon difluoride is much easier to handle than fluorine gas.[11–14] The 1,2-iodoxetane 1,1-difluoride intermediate **4** was moisture sensitive and could not be isolated. The exposure of the reaction solution to aerial humidity resulted in the formation of the corresponding 1,2-iodoxetane 1-oxide



Scheme 1. Preparation of 1,2-iodoxetane 1-oxide.

Keywords: Iodine; Iodinane; 1,2-Iodoxetane; Oxidation.

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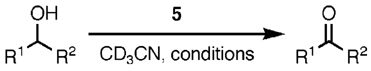
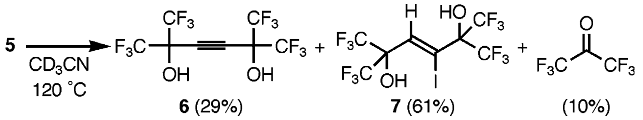
Table 1. Oxidation of primary and secondary alcohols with 1,2-iodoxetane oxide



Entry	R^1R^2CHOH	Equiv. of **5**	Temp/°C	Time/h	Conv./%	Yield/%[a]
1	$PhCH_2OH$	1.5	60	2	100	79
2	$PhCH_2OH$	1.0	60	7	96	73
3	$PhCH_2OH$	1.1	r.t.	36	87	66
4	Me_3CCH_2OH	1.0	75	15	93	23
5	PhCH(Me)OH	1.6	70	6	100	81
6	$CH_2{=}CHCH(Me)OH$	1.6	70	6	100	77

[a] The yields were determined by ^1H NMR spectroscopy using 1,3,5-tri-*tert*-butylbenzene as an internal standard.



Scheme 2. Thermolysis of 1,2-iodoxetane 1-oxide.

5 (30% from **3**) from **4**.[15] The recrystallization of the crude mixture gave the pale brown waxy solid of **5**, which contained a small amount of impurities that could not be removed.

The thermolysis of **5** at 120 °C in CD_3CN smoothly proceeded for 35 h to produce alkynediol **6** (29%), alkenediol **7** (61%), and hexafluoroacetone (10%) (Scheme 2).[16] The thermolysis of **5** proceeded under significantly milder conditions than that of **3**, which required a high temperature for thermal decomposition.[9] Compound **5** is not explosive under the thermal conditions in comparison with the potential explosiveness of **1** and **2**. Compound **5** is soluble in acetone, acetonitrile, DMF, and DMSO, and slightly soluble in dichloromethane, though it is almost insoluble in hexane, benzene, toluene, ether, and chloroform. The solubility of **5** in the former solvents and its tolerance to explosion encouraged us to explore its reactivity as an oxidant.

The oxidation of benzyl alcohol with **5** (1.5 equiv) at 60 °C for 2 h in CD_3CN had a 79% yield of benzaldehyde (Table 1, entry 1). The formation of iodoxetane was confirmed by the ^{19}F NMR spectra. The usage of an equimolar amount of **5** in this reaction resulted in an almost similar result except for the longer reaction time and recovery of a trace amount of the starting alcohol (entry 2). The reaction proceeded very slowly at room temperature (entry 3). Another primary alcohol, namely, neopentyl alcohol was similarly oxidized to produce pivalaldehyde in a low yield (23%) (entry 4). The low yield of the aldehyde is explained by the steric congestion of the neopentyl group.

Secondary alcohols are also oxidized to produce the corresponding ketones (entry 5 and 6). α-Methylbenzyl alcohol and 3-buten-2-ol were oxidized with **5** (1.6 equiv) to produce acetophenone (81%) and methyl vinyl ketone (77%) in moderate yields, respectively. The oxidation of these secondary alcohols proceeded smoothly. This is in contrast to the oxidation of 3-buten-2-ol with tricoordinate iodoxetane **3** (1.5 equiv) under more vigorous conditions (90 °C, 20 h) resulting in the corresponding ketone with a low yield (53%) and in low conversion (20%).

Although the selective formation of sulfides to sulfoxides by hypervalent reagents was previously reported in oxidation reactions with several aryliodinanes[17–22] or aryliodinane oxides,[23] oxidation reactions with alkyl- or alkenyl-iodinane have never been reported. When diphenyl sulfide was subjected to oxidation with **5** (2.4 equiv) at 70 °C for 11 h in CD_3CN, diphenyl sulfoxide was formed with a 59% yield in 59% conversion without the formation of diphenyl sulfone. Tricoordinate 1,2-iodoxetane **3**, which is formed in the reaction mixture, oxidizes neither the substrates nor the products under the reaction conditions.

In summary, we have synthesized a new iodinane oxide with an aliphatic substituent. We also demonstrate that it can be used as an oxidizing reagent because it oxidizes primary alcohols, secondary alcohols, and a sulfide under mild conditions, with good to moderate yields.

Acknowledgements

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15. Selected spectral data of **5**: ^{1}H NMR (CD_3CN, 500 MHz) δ 8.59 (s). ^{13}C NMR (CD_3CN, 125 MHz) δ 83.65 (sept, $^2J_{CF} = 33$ Hz), 97.26 (sept, $^2J_{CF} = 32$ Hz), 121.86 (q, $^1J_{CF} = 280$ Hz), 124.16 (q, $^1J_{CF} = 286$ Hz), 126.73 (s), 161.91 (s). ^{19}F NMR (CD_3CN, 500 MHz) δ −76.28 (q, $^2J_{FF} = 9.4$ Hz), −76.19 (q, $^2J_{FF} = 9.4$ Hz), −75.76 (q, $^2J_{FF} = 9.4$ Hz), −75.64 (q, $^2J_{FF} = 9.4$ Hz). HRMS (FAB) *m/z* 500.8881, calcd for $C_8H_2F_{12}IO_3$ $[M+H]^+$ 500.8857.
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