173. Ru-Catalyzed Oxidations with Iodosylbenzene Derivatives. Substituent Effects on Selectivity in Oxidation of Sulfides and Alcohols

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Summary

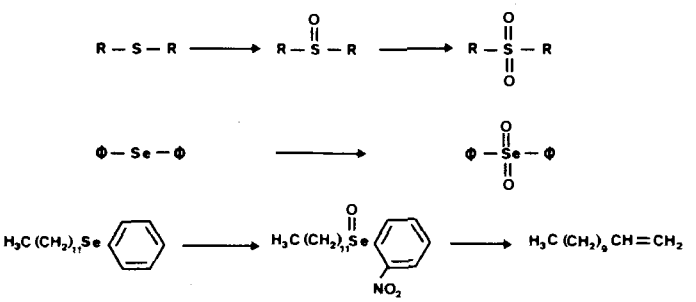
Oxidation of sulfides with PhIO/$RuCl_2(PPh_3)_3$ leads to sulfones. Electron-withdrawing substituents in the aromatic ring of PhIO reduce the reactivity and improves selectivity of the system. Thus, with *m*-iodosylbenzoic acid sulfides are converted to sulfoxide. Under the same conditions aliphatic primary alcohols are transformed to aldehydes with *m*-iodosylbenzoic acid, while PhIO affords carboxylic acids.

Introduction. – We have already reported on catalyzed oxidations with iodosylbenzene (PhIO) and alcohols [1], alkynes [2] and alkynyl ethers and amines [3]. Other investigators have since published results for oxidations with high-valent organoiodine compounds. Thus conversion of sulfides into sulfoxides was accomplished in yields of 80–90% by *Barton* [4] using *m*-iodylbenzoic acid (*m*-$HOOCPhIO_2$) in conjuction with *Lewis*-acid catalysts. Iodosylbenzene diacetate also converts sulfides to sulfoxides; the latter react further to sulfones, albeit at a much slower rate [5]. Oxidation of sulfides to sulfoxides by the action of PhIO proceeds at steam bath temperature [6], but *Ando et al.* report that the reaction is efficiently catalyzed by Fe(III) or Mn(III)-tetraphenylporphyrin (TPPM(III)Cl) complexes [7]. Diarylselenides are converted to selenoxides with iodosylbenzene dichloride [8]. A catalytic procedure for dehydrogenation of steroidal ketones, based on oxidation of diphenyl diselenide with iodylbenzene ($PhIO_2$) to benzeneselenic anhydride has been developed by *Barton et al.* [9].

This paper deals with Ru-catalyzed oxidations by PhIO to sulfides and selenides. We found that variation of substituents in the oxidant allows control of the reaction so that it can be stopped at the sulfoxide or at the sulfone stage. Similarly, oxidation of primary aliphatic alcohols can now be carried out to the aldehyde or carboxylic acid as desired, which is not possible with PhIO itself [1].

Oxidation of Sulfides and Selenides. – The reactions with sulfides were carried out on a 10-mmol scale, stirring the substrate with a slight excess of PhIO suspended in CH_2Cl_2 at r.t. *Table 1* summarizes the results. Although the sulfides react more readily than the corresponding sulfoxides, the oxidation steps cannot be neatly

Scheme 1



separated. Part of the reaction always leads to sulfone while unreacted sulfide is recovered. Use of PhIO in excess, however, results in an almost quantitative yield of sulfone. Apparently, the PhIO/Ru-system is less discriminating between sulfides and sulfoxides than iodosylbenzenediacetate [5], PhIO/TPPFe(III)Cl [7] or better investigated agents such as *tert*-butyl hydroperoxide/$VO(acac)_2$ [10] and H_2O_2/$TiCl_3$ [11]. However, there is a clear preference, as shown by phenylethynyl methyl sulfide, for oxidation of sulfide or sulfoxide to sulfone in the presence of a triple bond. Only at high excess of PhIO cleavage to benzoic acid occurs. Phenylethynyl methyl sulfide is also oxidized by *m*-chloroperbenzoic acid to yield sulfoxide and sulfone without attack at the triple bond [12].

Table 1. *Oxidation of Sulfides, Sulfoxides and Selenides with PhIO/$RuCl_2(PPh_3)_3$*[a])

Substrate	PhIO (equiv.)	Sulfoxide	Sulfone	Comment
Dibenzyl sulfide	1	71%	6%	23% of substrate (NMR)
	1.3	88%	12%	isolated
	2.5		≈ 100%	NMR
Di-*tert*-butyl sulfide	2.5	–	79%	isolated
Phenyl methyl sulfide	1.2	76%	17%	7% of substrate (NMR)
	2.5	–	≈ 100%	isolated
Phenylethynyl methyl sulfide	1.3	63%	14%	20% of substrate (NMR)
	2.5	–	≈ 100% (g.c.)	72% isolated
	5	–	–	benzoic acid
Tetramethylene sulfoxide	1.3		91%	isolated
Dimethyl sulfoxide	1.1		100%	NMR (0.5 mmol scale)
Diphenyl selenide	2.5		95%	selenone[b])
Dodecyl *o*-nitrophenyl selenide	1.5	64%		dodecene[c])

[a]) Conditions: 10 mmol of substrate in 100 ml CH_2Cl_2, 1% $RuCl_2(PPh_3)_3$. 10–15 min; isolation by column chromatography on SiO_2 or distillation (for tetramethylene sulfoxide). [b]) 1-mmol scale, isolated yield. [c]) 5 mmol, 45 min; isolated yield.

Transformation of organoselenides to selenones requires vigorous reagents [13] and is usually accomplished with ozone [14], $KMnO_4$ [15], or H_2O_2/trifluoroacetic anhydride [16]. We were therefore rather surprised to find that diphenyl selenide reacts under standard conditions with 2.4 eq of PhIO to the selenone in 95% isolated yield. The structure of the product was unambiguously established by comparison of the ^{1}H-NMR and MS data with data of an independently prepared sample [17].

Oxidation of Ph_2Se to the selenoxide was not investigated, however the system was tested to induce selenoxide elimination from alkyl aryl selenides [18]. Indeed, the dodecyl *o*-nitrophenyl selenide, available from dodecanol and *o*-nitrophenyl selenocyanate according to *Grieco et al.* [19] afforded dodecene in 64% isolated yield, which compares reasonably well with the yield of 62% reported by *Sharpless* using H_2O_2 in THF for selenide oxidation. The general usefulness of the method has yet to be established. For the time being we restrict ourselves to the observation that transformation of 1-phenylethyl *o*-nitrophenyl selenide to styrene proceeds only sluggishly and with poor yields. This may be related to the blocking effect exerted by aromatic rings or isolated double bonds during oxidation of alcohols [1].

Isolation of products (sulfoxides, sulfones, *etc.*) from the reaction mixture usually involves column chromatography to achieve separation from the iodobenzene formed during the reaction. However, if PhIO is replaced by *m*-HOOCPhIO [9] [20], the *m*-HOOCPhI formed is simply extracted with NaOH-solution. In addition, use of *m*-HOOCPhIO leads to a significant improvement in selectivity for sulfide *vs.* sulfoxide oxidation (see *Table 2*). The reactivity of the system decreases and

Table 2. *Oxidation of Sulfides and Sulfoxides by (m-HOOCPhIO[a])*

Substrate	*m*-HOOCPhIO (equiv.)	Catalyst	Time (min)	Product[b])
Dibenzyl sulfide	1.5	$RuCl_2(PPh_3)_3$	60	Sulfoxide (94%)
Phenylethynyl methyl sulfide	1.5	$RuCl_2(PPh_3)_3$	240	Sulfoxide (79%)[c])
Diphenyl sulfoxide	2	$RuCl_2(PPh_3)_3$	180	Sulfone (99%)
Diphenyl sulfoxide	2	$RuCl_3 \cdot aq$	180	Sulfone (98%)[d])

[a]) Conditions, 5 mmol of substrate in 50 ml of CH_2Cl_2, 1% of catalyst, r.t. [b]) Isolated by extraction of *m*-IPhCOOH with 2N NaOH. [c]) Extraction followed by column chromatography. [d]) In acetone.

longer reaction times are required. Although the reaction can easily be stopped at the sulfoxide stage, excess *m*-HOOCPhIO also allows conversion of sulfoxides to sulfones. During the course of the reaction the phosphine ligands of the catalyst are oxidized to Ph_3PO which contaminates the product. We therefore find it advantageous to work with $RuCl_3 \cdot aq$ in acetone whenever purification by chromatography should be avoided. In view of this substituent effect on reactivity of the oxidizing system some other iodosylbenzenes were also studied. *Table 3* shows a

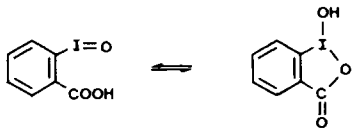
Table 3. *Oxidation of $(PhCH_2)_2S$ with Iodosyl and Iodyl Derivatives, Catalyzed by $RuCl_2(PPh_3)_3$[a])*

Oxidant	Time (min)	Sulfone[b])	Sulfoxide[b])	Sulfide[b])
Ph-IO	15	12%	88%	–
p-MeO-Ph-IO	15	18%	82%	–
p-O_2N-Ph-IO	60	2%	98%	–
o-HOOCPh-IO	60	–	–	100%
m-HOOCHPh-IO	60	–	90%	10%
m-C_5H_4N-IO	60	–	8%	92%
Ph-IO_2	60	–	10%	90%
p-O_2N-$PhIO_2$	60	–	–	100%

[a]) Conditions: 1 mmol of sulfide, 1.3 equiv. of oxidant, 1% of catalyst in 10 ml of CH_2Cl_2, r.t. [b]) by NMR.

qualitative comparison for reaction for iodosyl and iodyl derivatives with dibenzyl sulfide. Under comparable conditions the *p*-methoxy substituent increase slightly the reactivity (more sulfone) of PhIO/Ru. The comparison may not be entirely valid, since the less reactive PhIO itself consumes all the substrate present, but a more pronounced trend has been clearly demonstrated in the Fe-TTP-catalyzed oxidation of diphenyl sulfide [7]. On the other hand, a net decrease in reactivity is observed with *p*-nitro and *m*-carboxy substituents: sulfoxide is formed almost exclusively. Reaction is, however, totally suppressed by a carboxy substituent in *o*-position. The same effect has been observed by *Barton et al.* [9] for oxygen transfer from *o*-HOOCPhIO to diphenyl diselenide; it is considered to be due to blocking of the iodosyl functionality by intramolecular cyclization *(Scheme 2)*. The unique position

Scheme 2



of **1** in comparison with the corresponding *m*- and *p*-compounds has already been recognized by *Wilgerodt* [20] and *Meyer & Wachter* [21] and the cyclic structure **2** was confirmed more recently [22]. *m*-Iodosylpyridine was found to be rather inefficient as oxidant not only with sulfides, but also with alcohols. Under conditions where PhIO converts cyclododecanol quantitatively to the ketone, *m*-iodosylpyridine gives rise to only *ca.* 5% of conversion. This effect seems to be due to blocking of the catalyst by the pyridine. Indeed, addition of 5% pyridine to PhIO/1% $RuCl_2(PPh_3)_3$ reduces the reaction rate by a factor of *ca.* 3. Similarly, Et_3N has a blocking effect on the system, although less pronounced than pyridine.

According to *Barton et al.* [9] $PhIO_2$ is a far superior reagent for oxygen transfer to diphenyl diselenide than PhIO. Surprisingly, the contrary applies to Ru-catalyzed reactions. Oxidation of dibenzyl sulfide proceeds sluggishly with $PhIO_2$ and with *p*-O_2NPhIO_2 no reaction takes place.

The effect of substituents of iodosylbenzenes on the reactivity of the oxidizing system is of mechanistic significance. It implies participation of iodosylbenzene in the rate-determining step of the reaction. In the case of Fe-TPP-catalyzed reactions *Ando et al* [7] suggest rate-determining oxidation of Fe(III) to Fe(V) by PhIO. This could also apply to Ru-catalyzed oxidation. Alternatively, a mechanism where the substrate attacks Ru-complexed PhIO is also consistent with this observation. It would require that the rate of conversion depends upon the nature and concentration of the substrate. No rate measurements have been performed yet on the system; however, we know that oxidation of alcohols requires *ca.* 2 h, whereas that of sulfides or acetylenes goes to completion in less than 15 min under identical conditions. This mechanistic hypothesis, although not yet proven, must be seriously considered and it will require more detailed investigations.

Oxidation of Primary Aliphatic Alcohols. – Catalyzed oxidation of primary benzylic and allylic alcohols with PhIO leads mainly to aldehydes [1]. Primary

aliphatic alcohols afford mixtures of aldehydes and acids. The reaction can be controlled at the aldehyde stage if $PhI(OAc)_2$ is used as oxidant. Further, we now find that *m*-HOOCPhIO also converts primary aliphatic alcohols cleanly to aldehydes *(Table 4)*. Reaction times are some 3 times longer than for PhIO. Although

Table 4. *Oxidation of Primary Alcohols with Iodosylbenzenes* (at r.t.)[a])

Compound	Oxidant	Time	Aldehyde	Acid	Comment
Benzylalcohol	1.3 equiv. PhIO	0.5 h	85%	–	[1]
Octanol	1.3 equiv. PhIO	0.5 h	45%	23%	[1]
Octanol	1.3 equiv. $PhI(OAC)_2$	15 min	97%	–	[1]
Cyclododecanol	2 equiv. *m*-HOOCPhIO	3 h	98%	–	by GC
Octanol	1.5 equiv. *m*-HOOCPhIO	1.5 h	≈ 100%	–	by GC
Hexanol	1.5 equiv. *m*-HOOCPhIO	1.5 h	≈ 100%	trace	by GC
Octanol	1.5 equiv. *m*-HOOCPhIO	3 h	78%	–	isolated[b])
Hexanal	2 equiv. *m*-HOOCPhIO	4.5 h	–	≈ 100%	by GC

[a]) 0.5-mmol scale, 1% $RuCl_2(PPh_3)_3/CH_2Cl_2$. [b]) 1% $RuCl_3 \cdot aq \cdot$ acetone, 4-mmol scale.

aldehydes are also oxidized upon extended exposure to *m*-HOOCPhIO, only traces of carboxylic acids are formed during oxidation of alcohols with 1.5 equiv. of oxidant. For oxidation of alcohols or aldehydes to carboxylic acid PhIO is, however, the preferable reagent, because the desired products can be readily separated by extraction with aq. NaOH.

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Experimental Part

Synthesis of Iodosyl and Iodyl Derivatives. The iodosyl compounds were prepared by oxidation of the corresponding iodo derivatives according to published procedures: PhIO by oxidation of iodobenzene with Cl_2, followed by reaction with NaOH [23]. The same sequence was used with slight modifications to obtain *m*-HOOCPhIO [20], *p*-MeOPhIO [24], *p*-O_2NPhIO [25], *o*-HOOCPhIO [26] and *m*-C_5H_4NIO [27]. $PhIO_2$ was obtained by disproportionation of PhIO by heating [23]. *p*-O_2NPhIO_2 was similarly prepared from *p*-nitroiodobenzene dichloride [28]. The sulfides, sulfoxides and selenides used in this study are commercially available with the exception of phenylethylnyl methyl sulfide [12] which was prepared from phenylacetylene, sulfur and CH_3I [29] and of dodecyl *o*-nitrophenyl selenide following [19].

General Procedure for Ru-catalyzed Oxidation with Iodosylbenzene Derivatives. The catalyst ($RuCl_2(PPh_3)_3$, 96 mg) dissolved in 25 ml of CH_2Cl_2 was added to PhIO (5.5 g, 25 mmol) suspended in 50 ml of CH_2Cl_2. The sulfide (10 mmol) in 25 ml of CH_2Cl_2 was added at once. After 15 min of magnetic stirring the solution was transparent. The solvent was evaporated and the product was separated from PhI by column chromatography (SiO_2/CH_2Cl_2, then AcOEt). When *m*-HOOCPhIO was used as oxidant, separation of *m*-HOOCPhI was effectued by extraction of the CH_2Cl_2-solution with 2N NaOH. When product mixtures were obtained (*Tables 1, 3* and *4*) their composition was determined by NMR or GC.

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