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CATALYZED OXIDATION OF ALCOHOLS AND ALDEHYDES WITH IODOSYLBENZENE

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Summary. $RuCl_2(PPh_3)_3$ catalyzes oxidation of alcohols to carbonyl compounds by iodosylbenzene and that of aldehydes to carboxylic acids. Catalyzed oxidation of primary alcohols with phenyliodosodiacetate affords aldehydes.

Oxidations of organic substrates by iodosylbenzene with transition metal catalysis have been investigated in connection with model studies for cytochrome P-450. Thus several catalyzed oxidations such as epoxidation of alkenes,[1,2] oxidation of alcohols[2] and hydroxylation of alkanes[1,3] have been reported, although none of these reactions is applicable for preparative purposes. We recently discovered that iodosylbenzene in conjunction with Ru-catalysts is an efficient oxidant for conversion of alcohols to aldehydes, ketones or acids (Table 1). The procedure consists in stirring the alcohol in methylene chloride or aceton containing 1% of $RuCl_2(PPh_3)_3$ with a 1.3-2 fold excess of suspended iodosylbenzene at room temperature. The endpoint is usually attained when the solution becomes transparent (0.5-2 h for reactions on a 10 mmol scale). Scope and limitations of this system are similar to the Ru-catalyzed alcohol oxidation with N-methylmorpholin-N-oxide reported by Sharpless,[4] with two major exceptions. Primary aliphatic alcohols afford mixtures of aldehydes and carboxylic acids. With excess iodosylbenzene complete transformation to acids is observed. However, reaction can be stopped at the aldehyde stage when iodosylbenzene is substituted by phenyliodosodiacetate. Benzylic alcohols react readily to aldehydes and ketones respectively. The former are oxidized slowly with excess oxidant to carboxylic acids. In general, the situation is very complex with unsaturated alcohols. For example, cinnamyl alcohol affords the aldehyde together with almost 50% benzaldehyde; geraniol gives 62% citral and 12% unreacted alcohol. Under the reaction

Table 1. Oxidation of Alcohols and Aldehydes with Iodosylbenzene/RuCl$_2$(PPh$_3$)$_3$ a)

No	Substrate	Scale (mmol)	eq. PhJO	Time	Carbonyl cpd (GC)	Isolated Yield
1	Cyclohexanol	2	2	3h	78%	
2	Cyclododecanol	10	2	2h		90%
3	5α-Cholestan-3β-ol	2	2	10h		85%
4	Borneol	10	2	2h		84%
5	Isoborneol	2	2	2h	86%	
6	Octanol	10	1.3	0.5h		45% aldehyde + 23% acid
7	"	10	3	1h		88% acid
8	"	2	1.3 PhJ(OAc)$_2$	15 min	97% aldehyde	
9	Hexanal	2	2	0.5h		88% acid
10	Benzylalcohol	10	1.3	0.5h		85% aldehyde
11	Benzaldehyde	10	2	24h		96% acid
12	1-Phenylethanol	2	2	1h	91%	
13	Cinnamylalcohol	2	2.5	5 min	50% aldehyde + 48% benzaldehyde	
14	Geraniol	2	2.5	15 min	62% aldehyde + 12% alcohol	
15	Citronellol	2	2.5	2.5h/reflux	70% aldehyde	
16	Hexin-3-ol	2	2.5	5 min	66%	
17	Cholesterol				-	decomposition of substrate
18	3-Phenylpropanol				-	
19	3-Butinol				-	
20	β-3-Indolylethanol				-	

a) In methylene chloride (8 ml/mmol of alcohol) at RT, unless indicated otherwise

conditions cinnamaldehyde is cleaved to benzaldehyde. With cholesterol as substrate a complex untractable mixture of products is formed. Alcohols with double bonds further removed from the OH group react sluggishly at RT. Further, addition of cyclohexene to the reaction results in decrease of the rate of production formation. These observations suggest nonproductive association of the substrate to the Ru-complex, resulting in a lower concentration of free catalyst, as originally proposed by Sharpless. Interestingly, cyclohexene itself is unreactive towards PhJO/RuCl$_2$(PPh$_3$)$_3$. As entry 15 shows, the problem can be overcome by carrying out the reaction at reflux. However, in some cases (entries 18-20), the method fails completely for unknown reasons.

Uncatalyzed oxidation of alcohols to aldehydes or ketones with iodosylbenzene has been known for some time.[5] It requires heating of the reagents in dioxane for 12 h. Several complexes of Fe, Rh, Ir, Co, Mo and W catalyze the reaction, but Ru-catalysts proved to be most efficient. Table 2 shows the yield for reaction of 1-phenylethanol under standard conditions with several Ru-complexes. With the exception of RuO_2 the variations are not very important

Table 2. Oxidation of 1-Phenylethanol with PhJO with various catalysts[a)]

Catalyst	Yield of Acetophenone
$RuCl_2(PPh_3)_3$	91%
$Ru_3(CO)_{12}$	86%
$RuCl_2(CO)_2(PPh_3)_2$	57%
$RuCl_3$ aq.[b)]	85%
Ruthenocene[c)]	80%
RuO_2	10%

[a)] Conditions: 2 mmol of alcohol in 16 ml of solvent, 2 eq. of PhJO, 1% catalyst, 1h, RT, [b)] in acetone, [c)] ref. 6.

At the present time it seems unwise to provide a mechanistic rationale for the reaction. The intervention of Ru-alkoxides seems unlikely in the light of the recent observation that their dehydrogenation requires temperatures in the range of 180-210°.[7] Benzylic alcohols have been dehydrogenated at RT with $RuCl_2(PPh_3)_3$ under phase-transfer conditions,[8] presumably *via ortho*-metalated complexes. Obviously, such intermediates cannot be formed with aliphatic alcohols. Finally, we note that ketone reduction with formic acid and $RuCl_2(PPh_3)_3$ catalysis occurs at 125°.[9]

Preliminary results indicate that the PhJO/$RuCl_2(PPh_3)_3$ system is also reactive towards several other functional groups. We hope that these reactions, as well as the recently reported uncatalyzed oxidations with iodosylbenzene[10] will contribute to the understanding of the mechanism of action of this rediscovered oxidant.

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