

SELECTIVE OXIDATION OF A PRIMARY HYDROXYL
 IN THE PRESENCE OF SECONDARY ONE

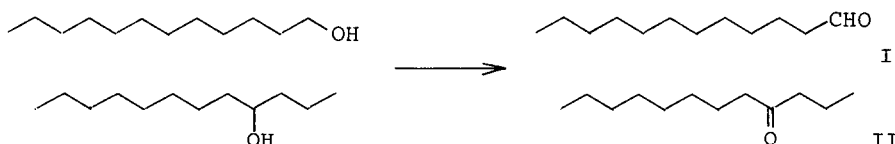
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Abstract: $\text{RuCl}_2(\text{PPh}_3)_3$ -benzene system has been found to be highly effective for the title selective oxidation providing 10-hydroxyundecanal in 89% yield from 1,10-undecanediol.

Reagents which are sufficiently selective to distinguish between functional groups of the same class are exceedingly valuable in syntheses. Recently a couple of methods have been reported that permit the oxidation of secondary alcohols in the presence of primary ones.¹ In contrast, there are few efficient methods for the preferential oxidation of primary over secondary hydroxyls.²

In an attempt to find such a selective oxidant, we have examined the relative rates of oxidation between 1-dodecanol and 4-dodecanol with various systems.

Table 1. Relative oxidation rates of 1-dodecanol and 4-dodecanol^a



Oxidant	Product Ratio (I/II)	Oxidant	Product Ratio (I/II)
$\text{CrO}_3 \cdot 2\text{py} \cdot \text{CH}_2\text{Cl}_2$ ³	1/1.6	$\text{Al}(\text{O}^t\text{Bu})_3 - ^t\text{BuOOH} \cdot \text{PhH}$ ⁷	1/9
$\text{PCC} \cdot \text{CH}_2\text{Cl}_2$ ⁴	3/1	$\text{MoO}(\text{O}_2)(\text{PhCONPhO})_2 \cdot \text{ClCH}_2\text{CH}_2\text{Cl}$ ⁸	1/9
$\text{DMSO} \cdot \text{DCC} \cdot \text{PhH}$ ⁵	1/1	$\text{Pd}(\text{OAc})_2 \cdot \text{DMF}$ ⁹	1/1
$\text{Me}_2\text{S} \cdot \text{NCS} \cdot \text{Et}_3\text{N} \cdot \text{CH}_2\text{Cl}_2$ ⁶	1/2	$\text{RuCl}_2(\text{PPh}_3)_3 \cdot \text{PhH}$	50/1

^aThe rates were determined by monitoring the appearance of dodecanal and 4-dodecanone by glpc (PEG 20M 5% on Celite 545, 1.5 m, 120°C) at the stage of 5% completion of the reaction.

Most popular reagents oxidized the primary and secondary alcohol at comparable rates with preference, if any, for the secondary one. In sharp contrast, $\text{RuCl}_2(\text{PPh}_3)_3$ ¹⁰ dissolved in benzene was found to be highly effective for the selective oxidation in the opposite sense: 1-dodecanol was oxidized fifty times faster than 4-dodecanol.

A mixture of the two hydroxy compounds was added to a brown homogeneous solution of $\text{RuCl}_2(\text{PPh}_3)_3$ in benzene. After stirring for a couple of hours at 25°C, the solution turned black and precipitates came out. The resulting mixture was diluted with ether and passed through a short silica gel column to remove black solids to give the crude product which was analyzed. Table 2 illustrates the selectivity that can be achieved by this system. The secondary alcohol is recovered practically unchanged, while the primary one is oxidized to the aldehyde in high yield. With aliphatic and acyclic hydroxy compounds this selectivity is excellent. An equimolar mixture of (*E*)-2-hexen-1-ol and 1-octanol gave 55% yield of (*E*)-2-hexenal and 40% of octanal.

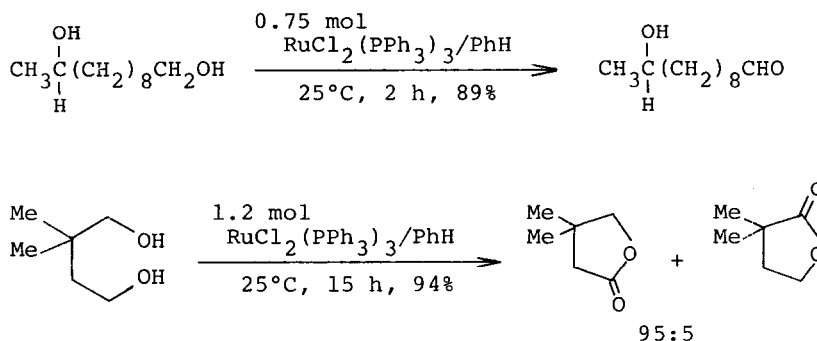
Table 2. Oxidation of primary alcohols in the presence of secondary ones^a

Starting Mixtures of Alcohols	Yields ^b of Aldehyde/Ketone
1-dodecanol/4-dodecanol	90/2
(<i>E</i>)-2-hexen-1-ol/2-heptanol	91/2
benzyl alcohol/1-phenylethanol	100/7
cyclohexylmethanol/2-heptanol	95/3
1-dodecanol/cyclohexanol	86/10
(<i>E</i>)-2-hexen-1-ol/(<i>E</i>)-3-hepten-2-ol	83/6

^aThe two hydroxy compounds (0.1 mmol each) and $\text{RuCl}_2(\text{PPh}_3)_3$ (77 mg, 0.08 mmol, 60 mol% excess) were dissolved in benzene (2 ml) and the mixture was stirred for 2-4 h (ref. 11) at 25°C. ^bIdentification of oxidation products was made by comparison with authentic samples. Olefinic alcohols were oxidized to the corresponding aldehydes or ketones. No epoxidized products could be observed. Yields were calculated by glpc (PEG 20M 5% on Celite 545, 1.5 m).

The solvent was found to be critical. Acetonitrile, tetrahydrofuran, and dimethylformamide were unsatisfactory since little or no reaction occurred. Acetone and dichloromethane did provide oxidation products with preference for primary alcohols, but the reaction rates were inconveniently low (2 days for the completion of the reaction).

Treatment of 1,10-undecanediol with the system gave 10-hydroxyundecanal in 89% glpc yield (75% isolated yield). As exemplified below, the selective oxidation of a primary, primary-diol, 2,2-dimethyl-1,4-butanediol,¹² has been observed.



The oxidation presumably involves formation of a ruthenium alkoxide which undergoes β -elimination to produce the carbonyl compound and hydrido-chlorotris(triphenylphosphine)ruthenium.^{13,14} The oxidation of alcohols was completed with half mol of $\text{RuCl}_2(\text{PPh}_3)_3$, so that this hydrido-chloro complex is supposedly capable to oxidize another mol of the alcohol to the carbonyl compound.^{15,16}

References and Notes

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- $\text{PtO}_2\text{-O}_2$ system has been used for the selective oxidation (P. T. Lansbury, D. G. Hangauer, Jr., and J. P. Vacca, *J. Am. Chem. Soc.*, **102**, 3964 (1980); R. A. Kretchmer and W. J. Thompson, *ibid.*, **98**, 3379 (1976); J. Fried and J. C. Sih, *Tetrahedron Lett.*, **1973**, 3899) and the system ($\text{PtO}_2\text{-O}_2$ /heptane) showed a similar high selectivity (40/1) as $\text{RuCl}_2(\text{PPh}_3)_3$ for 1-dodecanol/4-dodecanol combination. The latter is preferred because of the generality and reproducibility of the reaction, as the former heterogeneous system can be capricious. Recently selective reductions of ketones in the presence of aldehydes have been reported that are another approach to the same target. J. L. Luche and A. L. Gemal, *J. Am. Chem. Soc.*, **101**, 5848 (1979); M. P. Paradisi, G. P. Zecchini, and G. Ortar, *Tetrahedron Lett.*, **21**, 5085 (1980).

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10. $\text{RuCl}_2(\text{PPh}_3)_3$ was purchased from Alfa Ventron Corporation.
11. The reaction was monitored by tlc.
12. M. P. Doyle, R. L. Dow, V. Bagheri, and W. J. Patrie, *Tetrahedron Lett.*, 21, 2795 (1980). The reaction proceeded *via* lactols.
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14. The coexistence of the base such as CaCO_3 or Na_2CO_3 was found to be effective to trap HCl for the compound sensitive to acid. Et_3N was less effective since the reaction was retarded considerably.
15. Treatment of a mixture of 1-dodecanol and 4-dodecanol (1.0 mmol each) with preformed $\text{HRuCl}(\text{PPh}_3)_3$ (P. S. Hallman, B. R. McGarvey, and G. Wilkinson, *J. Chem. Soc.*, (A), 1968, 3143) (1.0 mmol) in benzene provided dodecanal in 75% yield along with a trace of 4-dodecanone (<2%).
16. Attempt to complete the oxidation reaction with a catalytic amount of $\text{RuCl}_2(\text{PPh}_3)_3$ ¹⁷ resulted in loss of selectivity. For instance, heating a mixture of 1,10-undecanediol (0.19 g, 1.0 mmol), benzoquinone (0.65 g, 6.0 mmol), $\text{RuCl}_2(\text{PPh}_3)_3$ (98 mg, 0.1 mmol), and benzene (20 ml) to reflux resulted in a formation of a mixture of 10-hydroxyundecanal (50%), 10-oxo-1-undecanol (10%), and the starting diol (30%).
17. N-Methylmorpholine-N-oxide has been reported to be a good oxidant for the ruthenium catalyzed oxidation of alcohols (K. B. Sharpless, K. Akashi, and K. Oshima, *Tetrahedron Lett.*, 1976, 2503). Under this condition 1-dodecanol reacts at only three times the rate of 4-dodecanol.

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