Chemoselective Oxidation of Secondary Hydroxy Groups by the Molybdenum Hexacarbonyl/Cetylpyridinium Chloride/*t*-Butyl Hydroperoxide System

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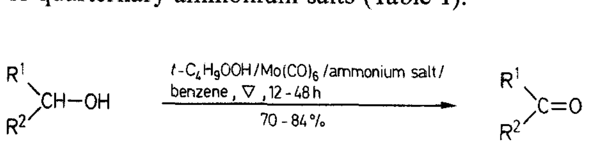
The system molybdenum hexacarbonyl/cetylpyridinium chloride/*t*-butyl hydroperoxide in benzene is used for the chemoselective oxidation of secondary hydroxy compounds to the corresponding carbonyl derivatives.

The molybdenum hexacarbonyl/*t*-butyl hydroperoxide system is known to catalyze the regioselective epoxidation of allylic alcohols[1]. In recent years, it has been reported that some molybdenum species affect the oxidation of hydroxy compounds to the corresponding carbonyl derivatives[2,3,4]. We have now found that the molybdenum hexacarbonyl/*t*-butyl hydroperoxide system catalyzes the chemoselective oxidation of secondary hydroxy compounds to the corresponding carbonyl derivatives, and that the addition of cetylpyridinium chloride to this system considerably accelerates the reaction and improves the selectivity for the oxidation[5]. In this paper, we describe the chemoselective oxidation of secondary alcohols **1a–c** and diols **3a–d** to the corresponding ketones **2a–c** and **4a–d** by the molybdenum hexacarbonyl/*t*-butyl hydroperoxide system in the presence of quarternary ammonium salts (Table 1).



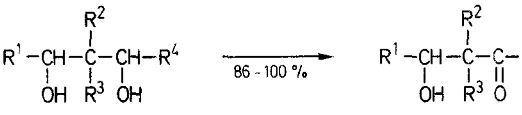
1a-c **2a-c**

1,2	R^1	R^2
a	n-C_7H_{15}	H
b	n-C_6H_{13}	CH_3
c	$-(CH_2)_5-$	

Scheme A

2-Octanol (**1b**) and cyclohexanol (**1c**) were converted into the corresponding ketones **2b, c** in good yields. However, the oxidation of 1-octanol (**1a**) under the same conditions proceeded to give only trace amounts of aldehyde **2a** (Scheme **A**).

The oxidation of diols **3a–c** containing primary and secondary hydroxy functions in their molecules occurred regioselectively at the secondary hydroxy function, affording hydroxyketones **4a–c** in fair yields. In particular, 2-ethyl-1,3-hexanediol (**3a**) was oxidized almost quantitatively to **4a** (Scheme **B**).

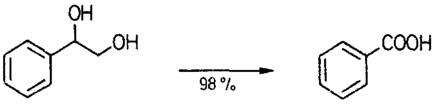


3a-c **4a-c**

3,4	R^1	R^2	R^3	R^4
a	H	C_2H_5	H	n-C_3H_7
b	H	CH_3	CH_3	i-C_3H_7
c	H	H	H	CH_3

Scheme B

Phenylethylene glycol (**3d**) was oxidized to benzoic acid (**5**), in which the carbon-carbon bond of glycol was exclusively cleaved (Schem **C**).



3d **5**

Scheme C

The influence of quaternary ammonium salts on the molybdenum hexacarbonyl/*t*-butyl hydroperoxide system for the oxidation of 2-ethyl-1,3-hexanediol (**3a**) has been studied. The quaternary ammonium salts served an essential role in this oxidation as shown in Table 2. Without the quaternary ammonium salts, the conversion for 2-ethyl-1,3-hexanediol was only 23 % after 4 h (entry 1). However, when cetylpyridinium chloride was added to the reaction system, the oxidation was completed almost quantitatively within 4 h,

Table 1. Oxidation of Alcohols and Diols by the Molydenum Hexacarbonyl/*t*-Butyl Hydroperoxide/Cetylpyridinium Chloride

Substrate	Reaction Time	Product	Conversion [%]	Selectivity [%]	I.R. (NaCl) ν[cm^{-1}]	^{13}C-N.M.R. ($CDCl_3$/TMS) δ[ppm]
1a	48 h	**2a**	trace	–	–	–
1b	24 h	**2b**	70	100	2925, 1710, 1360, 1160	207.3; 42.0; 31.0; 28.9; 28.3; 23.2; 21.9; 13.3
1c	12 h	**2c**	84	98	2900, 1705, 1440, 1330, 1240, 1130	208.8; 40.1; 25.9; 23.9
3a	4 h	**4a**	100	98	3450, 2925, 1700, 1455, 1370, 1030	214.7; 62.6; 55.4; 44.9; 21.4; 16.8; 13.7; 11.7
3b	8 h	**4b**	96	96	3450, 2950, 1685, 1460, 1370, 1020	221.2; 69.3; 49.6; 34.5; 21.1; 19.8
3c	24 h	**4c**	86	99	3350, 2950, 1700, 1360, 1180, 1050	208.8; 59.0; 45.3; 29.9
3d	6 h	**5**	98	86	3050, 1690, 1430, 1295, 710	172.3; 133.6; 130.1; 129.3; 128.3

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[a] Alcohol or diol (2 mmol), *t*-butyl hydroperoxide (6 mmol), molybdenum hexacarbonyl (0.04 mmol), cetylpyridinium chloride (0.12 mmol), magnesium sulfate (0.2 g), benzene (15 ml) at 75 °C.

Table 2. Oxidation of **3a** by Molybdenum Hexacarbonyl/*t*-Butyl Hydroperoxide in the Presence of Various Quaternary Ammonium Salts[a]

Entry	Ammonium Salt (mmol)	Reaction Time	Conversion [%]	Selectivity [%]
1	none	4 h	23	88
2	cetylpyridinium chloride (0.04)	4 h	50	97
3	cetylpyridinium chloride (0.12)	4 h	100	98
4	*N*-benzylpicolinium chloride (0.12)	24 h	81	94
5	trioctylmethylammonium chloride (0.12)	24 h	53	93
6	tetra-*n*-butylammonium iodide (0.12)	7 h	34	85

[a] Diol **3a** (2 mmol), *t*-butyl hydroperoxide (6 mmol), molybdenum hexacarbonyl (0.04 mmol), benzene (15 ml) at 75 °C.

giving 2-ethyl-1-hydroxy-3-hexanone (**4a**) with a chemoselectivity above 98 % (entries 2 and 3).

A similar effect was also observed when *N*-benzylpicolinium chloride was used (entry 4), although the oxidation proceeded more slowly than with cetylpyridinium chloride. With trioctylmethylammonium chloride (entry 5) or tetra-*n*-butylammonium iodide (entry 6), however, the reactions stopped at 53 % and 34 % conversion, respectively, because of decomposition of *t*-butyl hydroperoxide during the reaction.

From these results, the molybdenum hexacarbonyl/cetylpyridinium chloride/*t*-butyl hydroperoxide system was found to be efficient for the oxidation of secondary hydroxy compounds to the corresponding carbonyl derivatives. The chemoselectivity of the present oxidation was superior to those by vanadyl acetylacetonate/*t*-butyl hydroperoxide[6] or tetraalkylammonium tetrabromomolybdate/*t*-butyl peroxide[7] oxidations. We believe that this catalytic oxidation may proceed through the coordination of secondary hydroxy group to a molybdenum species, followed by abstraction of hydrogen from the carbon to which the hydroxy function is bonded to give ketone.

Oxidation of Secondary Alcohols and Diols; General Procedure:

To a solution of 70 % *t*-butyl hydroperoxide (771 mg, 6 mmol) and benzene (15 ml), which is dehydrated with anhydrous magnesium sulfate prior to use, is added molybdenum hexacarbonyl (11 mg, 0.04 mmol), cetylpyridinium chloride (41 mg, 0.12 mmol), magnesium sulfate (200 mg), and the alcohol or diol (2 mmol). After the stirring for 24 h under reflux (75 °C), the mixture is worked up by addition of sodium hydrogen sulfite, acidification, extraction, drying of the organic layer, and then removal of the benzene on a rotary evaporator. The oxidation products are purified by chromatography and identified by comparison of their spectral data with those reported in the literature[8, 9].

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