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Oxovanadium complex-catalyzed oxidation of propargylic alcohols using molecular oxygen

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Abstract—Oxovanadium complexes work as useful catalysts for the oxidation of propargylic alcohols to the corresponding carbonyl compounds in the presence of 3 Å molecular sieves under an atmospheric pressure of molecular oxygen. © 2001 Elsevier Science Ltd. All rights reserved.

α,β-Acetylenic carbonyl compounds (ynones) are the useful precursor for various heterocycles, α,β-unsaturated ketones and DNA-cleavage agents[1] and many methods for the preparation of ynones have been reported.[2] The oxidation of propargylic alcohols, which can be easily prepared by the coupling reaction of lithium acetylides with aldehydes, is one of the useful methods for obtaining them. Various oxidation methods of propargylic alcohols have so far been developed using stoichiometric oxidants such as MnO_2, chromium salts, a combination of dimethyl sulfoxide and oxalyl chloride (Swern oxidation), $TiCl_4$ and Dess–Martin reagent.[3] Recently, there appeared two reports of transition metal-catalyzed aerobic oxidation of such alcohols to the corresponding ynones, but the substrate employed was limited to only one alcohol in each case: Ishii and co-workers have used $Cu(acac)_2$-NHPI (NHPI = *N*-hydroxyphthalimide) and Katsuki and co-workers have used (nitroso)(salen)Ru as catalysts.[4] We have now found that some oxovanadium compounds worked as effective and more general catalysts for this purpose (Fig. 1).

Recently, we reported that the catalytic system composed of $Pd(OAc)_2$, pyridine and 3 Å molecular sieves was quite efficient for the aerobic oxidation of alcohols under an atmospheric pressure of molecular oxygen.[5] Although it was revealed that the catalytic system could be applied for the oxidation of a wide variety of alcohols, there were some limitations for substrates to be oxidized, one of which is propargylic alcohols. Their oxidation gave many unidentified products under this catalytic system. In the course of our continuing studies, we found that some oxovanadium compounds worked as effective catalysts for the aerobic oxidation of such alcohols to the corresponding carbonyl compounds under an atmospheric pressure of molecular oxygen.[6,7]

First, 1-phenyl-2-propyn-1-ol (**1a**) was chosen as a substrate. Treatment of **1a** in acetonitrile in the presence of a catalytic amount of $VO(acac)_2$ at 50°C under 1 atm O_2 gave 1-phenyl-2-propyn-1-one (**2a**) in 10% yield after 7 h (Table 1, entry 1). Interestingly, when 3 Å molecular sieves (500 mg) was added to the reaction mixture, the yield of **2a** increased dramatically (95% yield) (entry 2).[8] When the oxidation was performed at 80°C in acetonitrile (0.2 M), **1a** was smoothly and

1 **2**

a X = Ph, Y = H
b X = α-Naphthyl, Y = H
c X = β-Naphthyl, Y = H
d X = Ph, Y = Ph
e X = Ph, Y= *n*-C_6H_{13}
f X = *trans*-PhCH=CH, Y = H
g X = PhC≡C, Y = Ph
h X = H, Y = *n*-C_6H_{13}
i X = Me, Y = Ph
j X = *n*-C_5H_{11}, Y = H
k X = Cyclohexyl, Y = H

Figure 1.

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Table 1. Optimization of $VO(acac)_2$-catalyzed oxidation of **1a** to **2a** under O_2[a]

Entry	Solvent (mL)	Catalyst (mol%)	Temp. (°C)	Time (h)	Conversion (%)	GLC yield (%)
1[b]	MeCN (10)	5	50	7	19	10
2	MeCN (10)	5	50	7	95	95
3	MeCN (5)	5	80	3	98	98
4	PhCN (5)	5	80	3	86	83
5	toluene (5)	5	80	3	50	41
6	THF (5)	5	80	3	31	25
7	$(ClCH_2)_2$ (5)	5	80	3	70	46
8[c]	MeCN (5)	5	80	3	79	79
9[d]	MeCN (5)	5	80	3	48	48
10[e]	MeCN (2)	1	80	3	20	18
11	MeCN (5)	1	80	3	99	99
12	MeCN (2)	1	80	3	$\sim$100	Quant.

[a] Reaction conditions: **1a** (1 mmol), $VO(acac)_2$ (0.01–0.1 mmol), solvent (2–10 mL), 3 Å molecular sieves (500 mg), O_2 (1 atm).

[b] In the absence of 3 Å molecular sieves.

[c] 3 Å molecular sieves (250 mg).

[d] 3 Å molecular sieves (100 mg).

[e] 4 Å molecular sieves (500 mg).

selectively converted to **2a** within 3 h (entry 3). Other solvents such as benzonitrile, toluene, tetrahydrofuran and 1,2-dichloroethane less effective for this oxidation (entries 4–7). It should be noted that the product yield was much affected by the amount of 3 Å molecular sieves and the kind of molecular sieves as well as substrate concentration. Thus, when the amount of 3 Å molecular sieves was reduced, the yield of **2a** decreased (entries 8 and 9; compare also with entries 1 and 3). The use of 4 Å molecular sieves instead of 3 Å molecular sieves gave much less amount of **2a** (entry 10). The amount of the catalyst could be reduced to 1 mol% (entry 11) and when the oxidation was carried out in a higher substrate concentration, **2a** was obtained in excellent yield (entry 12).

Other oxovanadium compounds such as $VOCl_3$, $VO(OEt)_3$, $VO(hfac)_2$ (hfac = hexafluoroacetylacetonate) and V_2O_5 were examined as catalysts for this aerobic oxidation using **1a** as a substrate. Although every compound worked effectively except for V_2O_5, $VO(acac)_2$ was chosen as a suitable catalyst considering the ease of handling and an economical reason.

The oxidation of some other propargylic alcohols was examined. Typical results are listed in Table 2. The alcohols having an aryl substituent at the α-position (**1a–e**) were converted to the corresponding carbonyl compounds in high yields (entries 1–5). Similarly, propargylic alcohols having a vinylic substituent (**1f**) and an acetylenic substituent (**1g**) gave the corresponding carbonyl compounds in good yields (entries 6 and 7). The alcohol having no substituent at the α-position (**1h**) was converted to the corresponding aldehyde (**2h**) in low yield (entry 8), but when the oxidation was performed using 5 mol% $VO(acac)_2$, the yield of **2h** much improved (entry 9). The alcohols having an alkyl substituent at the α-position (α-acetylenic alkanols) (**1i–**

Table 2. $VO(acac)_2$-catalyzed oxidation of various propargylic alcohols under O_2[a]

Entry	Alcohol **1**	X	Y	Product **2**	Conversion (%)	Yield (%)[b]
1	**1a**	Ph	H	**2a**	$\sim$100	Quant.[c]
2	**1b**	α-Naphthyl	H	**2b**	80	70
3	**1c**	β-Naphthyl	H	**2c**	98	86
4	**1d**	Ph	Ph	**2d**	96	81
5	**1e**	Ph	n-C_6H_{13}	**2e**	99	98
6	**1f**	*trans*-PhCH=CH	H	**2f**	90	65
7	**1g**	PhC≡C	Ph	**2g**	83	76
8	**1h**	H	n-C_6H_{13}	**2h**	36	25
9[d]	**1h**	H	n-C_6H_{13}	**2h**	91	62
10	**1i**	Me	Ph	**2i**	33	33
11	**1j**	n-C_5H_{11}	H	**2j**	68	52
12[d,e]	**1j**	n-C_5H_{11}	H	**2j**	90	65
13	**1k**	Cyclohexyl	H	**2k**	71	41

[a] Reaction conditions: propargylic alcohol (1 mmol), $VO(acac)_2$ (0.01 mmol), MeCN (2 mL), 3 Å molecular sieves (500 mg), 80°C, 3 h, O_2 (1 atm).

[b] Based on the alcohol employed (%).

[c] GLC yield.

[d] 5 mol% catalyst.

[e] At 60°C for 36 h.

k) gave the corresponding ketones in low yields (entries 10–13).

The present catalytic system was found to be ineffective to the oxidation of such alcohols as benzyl alcohol and 1-dodecanol; 13 and 11% yields of the corresponding aldehydes were obtained, respectively, under the same conditions.

The reaction mechanism is not yet clear, but the main reaction course should be an ionic one, because the oxidation was not much influenced by the addition of a radical inhibitor such as 2,6-di-*tert*-butylphenol.

In summary, we found that the oxidation of some propargylic alcohols to the corresponding carbonyl compounds proceeded efficiently using VO(acac)$_2$ as a catalyst and in the presence of 3 Å molecular sieves in acetonitrile under an atmospheric pressure of molecular oxygen. Further study to find the effective catalytic oxidation system for α-acetylenic alkanols such as **1i**–**k** is in progress.

General procedure for the oxidation of propargylic alcohols using molecular oxygen: To a solution of VO(acac)$_2$ (2.65 mg, 0.01 mmol) in acetonitrile (1.5 mL) in a 10 mL two-necked round-bottomed flask was added 3 Å molecular sieves (500 mg, powder). Next, a solution of propargylic alcohol (1 mmol) in acetonitrile (0.5 mL) was added and the resulting mixture was stirred. Oxygen gas was then introduced into the flask from an O$_2$ balloon under atmospheric pressure and then the mixture was stirred vigorously for 3 h at 80°C under oxygen. After the reaction, the mixture was cooled to room temperature and 3 Å molecular sieves was separated by filtration through a glass filter. The amount of the product was determined by GLC analysis using bibenzyl as an internal standard. For isolation of the product the solvent was evaporated and the residue was purified by column chromatography (Merck silica gel 60; hexane–diethyl ether as an eluent) to give the product.

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