

Aerobic Oxidation of Methyl Vinyl Ketone in Supercritical Carbon Dioxide[†]

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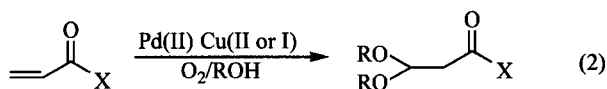
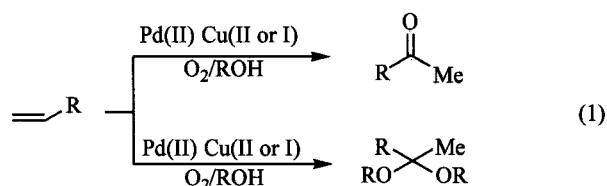
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Aerobic oxidation of methyl vinyl ketone to acetal in supercritical carbon dioxide are achieved in high conversion and high selectivity when oxygen pressure reaches to 0.5 MPa. The effects of cocatalysts, additive, pressure and temperature of the reaction are studied in detail.

Keywords aerobic oxidation, supercritical carbon dioxide, methyl vinyl ketone

The aerobic oxidation of ethylene to acetaldehyde and terminal olefins to corresponding alkan-2-ones catalyzed by palladium(II) and copper(II or I) salts are collectively known as Wacker oxidations (Scheme 1).¹ They are very important in both synthetic and industrial chemistry. Treatment of terminal olefins bearing electron-withdrawing with alcohols groups with alcohols afforded acetals at the terminal carbon.

Scheme 1



In many cases, the oxidation of olefins bearing electron-withdrawing groups gave desired product of acetals,^{2,3} but they also produced Michael addition products, which were usually not expected. So how to get a higher ratio of acetals to this kind of olefins still remains a problem.

The products, β -ketoacetals, as seen in equation 2, are useful intermediates in organic synthesis and have been used to synthesize a variety of compounds, including active cyclic enamionone derivatives,⁴ drugs for prevention and treatment of ischemic heart diseases,⁵ dyes, pharmaceuticals and auxiliary agents for textile industries.⁶ There are many ways for the preparation of 4,4-dimethoxy-2-butanone. Recently, it has been prepared via Palladium-catalyzed acetalization of olefin in the presence of PdCl₂ (0.1 equiv.) and cocatalyst CuCl (1 equiv.) in dimethylformamide (DMF) at 50 °C under an atmosphere of O₂ (0.1 MPa) by Takahiro and his co-workers.⁷ In our studies on performing different organic reactions in scCO₂, it was found that many reactions can proceed smoothly in scCO₂.⁸⁻¹⁰ The use of scCO₂ as a reaction medium is based on its special inherent properties. It is well-known that scCO₂ has many advantages such as reaction rate, higher selectivity, and facile separation of reactants, catalysts and products. It is also nontoxic, nonflammable, inexpensive and readily available in large quantities, and it provides higher dissolvability of gas in

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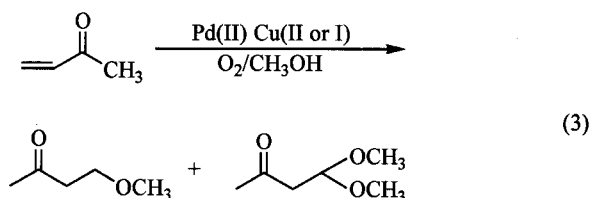
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[†]Dedicated to Professor HUANG Yao-Zeng on the occasion of his 90th birthday.

it (for example, O₂) than in conventional organic solvents. So it is expected that if this reaction (having O₂ used) conducted in scCO₂, better results could be gotten. Indeed this is what happened in our experiment. When this reaction was conducted (Scheme 2) in scCO₂ using methyl vinyl ketone (MVK) (X = CH₃) as a substrate, high conversion and high selectivity were obtained when oxygen pressure reached to 0.5 MPa. Furthermore, it required less amount of CuCl, which was added to 1 equiv. in Takahiro's. Herein we wish to report our preliminary results in detail.

Scheme 2



Since the catalyst, PdCl₂, was usually used in such small concentrations (0.1 equiv.), the catalyst cost was no longer an important factor to this kind of reaction. Hence our approach was first to investigate the effects of different cocatalysts to the conversion of MVK and to the selectivity of the acetal. We found that CuCl is superior to CuCl₂, as seen in Table 1 (Entries 1 and 2). This fact is corresponded to the literature.¹¹

It was also found that the amount of CuCl had a great effect on the conversion of MVK. When changing its amount from 0.5 to 5 mmol, the conversion decreased greatly at the beginning and then enhanced slowly from

92.7% to 78%, and then to 88.2%. Meanwhile, the selectivity for the target product (4, 4-dimethoxy-2-Butanone) increased at first and then dropped at the end, as shown in Fig. 1.

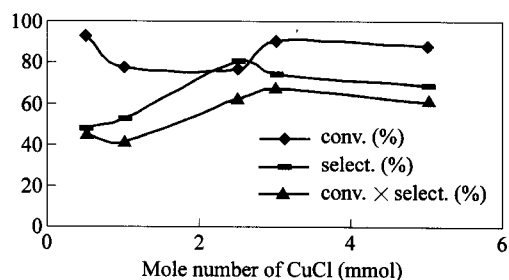


Fig. 1 Effect of different amounts of CuCl to the reaction. MVK (5 mmol) was used, the abscissa represents the consumptions of CuCl (mmol).

Takahiro *et al.*⁷ reported that the addition of Na₂HPO₄ was a key to prevent the formation of Michael adducts, and could get acetals as sole product. To our surprise, we could not get this result, although the proportion of acetal was increased when adding some amount of Na₂HPO₄. Furthermore, when some strongly anion resins (OH form) were added as additive, satisfactory results were not observed anyway (Table 2).

Table 3 shows the representative results of the reaction under different conditions. The oxygen pressure markedly affected the reaction. High oxygen pressure (0.5 MPa) gave 100% conversion of MVK and 86.7% of selectivity of acetal while lower oxygen pressure (0.1 MPa) gave 90.8% conversion and 74.19% selectivity only.

Table 1 Effect of different cocatalysts to the oxidation of MVK in scCO₂^a

Entry	Cocatalyst (mmol)	Conv. ^b (%)	Products		Select. ^c (%)	Conv. x Select. (%)
			Michael (%)	Acetal (%)		
1	CuCl ₂ (5)	A	96.8	2.7	2.7	A
2	CuCl (5)	A	53.6	46.3	46.3	A
3	CuCl ₂ (3)	97.4	94.86	B	0	0
4	CuCl (3)	90.8	22.79	65.51	74.19	67.4

^a MVK (5 mmol), PdCl₂ (0.5 mmol), Na₂HPO₄ (0.5 mmol), CH₃OH (2 mL), T = 50 °C, t = 12 h, p = 12 MPa. ^b Conversion and selectivity are determined with QP5050A-GC-MS. Column: DB-17, 30 m × 0.25 mm × 0.25 μm; injector temperature: 250 °C, from 60 °C hold for 1 min, then 12 °C/min to 260 °C; MS: ion source: 230 °C; electron energy: 70 eV. ^c Selectivity = acetal/(acetal + Michael). A: not measured, B: not detected.

Table 2 Effect of different additives to the reaction in scCO₂^a

Entry	Additive	Conv. ^b (%)	Michael (%)	Acetal (%)	Select. ^c (%)	Conv. × Select. (%)
1 ^d	no	87.9	49.28	37.18	43	37.8
2 ^d	Na ₂ HPO ₄	77.2	16.26	68.46	80.8	62.38
3 ^e	no	96.8	62.82	16.45	20.75	20
4 ^e	Na ₂ HPO ₄	90.8	22.79	65.51	74.19	67.4
5 ^f	resin	94.7	58.44	31.38	34.9	33.1
6 ^g	resin	94.4	95.75	trace	0	0

^a MVK (5 mmol), PdCl₂ (0.5 mmol), CH₃OH (2 mL), *t* = 12 h. ^{b,c} Seen in Table 1. ^d CuCl (2.5 mmol), *T* = 50 °C, *p* = 16 MPa.

^e CuCl (3 mmol), *T* = 50 °C, *p* = 12 MPa. ^f Resin 0.2 g (about 0.3 mmol OH). ^g Resin 0.4 g (about 0.6 mmol OH).

Table 3 Oxidation of MVK in different conditions under scCO₂^a

Entry	Cocatalyst [CuCl (mmol)]	Conv. ^b (%)	Products		Select. ^c (%)	Conv. × Select. (%)
			Michael (%)	Acetal (%)		
1	5.0	88.2	28.57	62.52	68.65	60.55
2	0.5	92.7	47.66	44.11	48	44.55
3	2.5	77.2	16.68	68.46	80.8	62.38
4	1.0	78.0	40.31	45.32	52.9	41.26
5	3.0	90.8	22.79	65.51	74.19	67.4
6 ^d	3.0	100	12.77	83.17	86.7	86.7
7 ^e	3.0	92.4	31.94	50.29	61.1	56.46
8 ^f	3.0	98.2	58.96	35.84	37.8	37.12

^a MVK (5 mmol), PdCl₂ (0.5 mmol), CH₃OH (2 mL), O₂: 0.1 MPa, *T* = 50 °C, *t* = 12 h, *p* = 12 MPa. ^{b,c} Seen in Table 1.

^d O₂: 0.5 MPa. ^e *p* = 18 MPa. ^f *T* = 80 °C.

The temperature and CO₂ pressure had a similar effect on the reaction. The results showed (Entries 7 and 8) that the substrate conversion was just opposite to the acetal selectivity when temperature or pressure increased (compared to Entry 3). The reason of the effect of higher pressure to this reaction is not yet clear.

In summary, the oxidation of methyl vinyl ketone can proceed smoothly in scCO₂. Of particular note is that CuCl is superior to CuCl₂ as cocatalyst in this reaction. The best amount of it is 60% equivalence of the MVK when MVK is used as 5 mmol scale. The oxygen pressure played an important role in this oxidation.

Experimental

MVK was prepared according to the reported method.¹² CuCl was prepared by traditional method. CuCl₂ was obtained by heating CuCl₂·2H₂O under the fluid of HCl gas.

General procedure The reactions were carried out in an HF-25 autoclave. PdCl₂ (10 mol% of MVK),

CuCl (0.5–5 mmol), Na₂HPO₄ (0.5 mmol), CH₃OH (2 mL) and MVK (5 mmol) were added to a 25 mL autoclave successively. O₂ and liquid CO₂ were pumped into the autoclave using a cooling pump to give the desired pressure. The autoclave was then put into an oil bath under magnetic stirring for the desired time. After the reaction was completed, the autoclave was allowed to cool to 0 °C and CO₂ was depressured. The surplus was washed with acetone and filtered. The solvent was condensed under reduced pressure. The product was analyzed by GC (quantitative analysis) and GC-MS (identification of products).

4,4-Dimethoxy-2-butanone A pale yellow oil. ¹H NMR (CDCl₃, 400 MHz) δ: 2.16 (s, 3H), 2.70 (d, *J* = 5.5 Hz, 2H), 3.34 (s, 6H), 4.77 (t, *J* = 5.5 Hz, 1H).

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