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Tetrahedron

Tetrahedron 62 (2006) 9846-9854

Pd(II)-catalyzed acetalization of terminal olefins with electron-withdrawing groups in supercritical carbon dioxide: selective control and mechanism

Zhao-Yang Wang,^{a,b} Huan-Feng Jiang,^{a,*} Xiao-Yue Ouyang,^a Chao-Rong Qi^a and Shao-Rong Yang^a

^aCollege of Chemistry, South China University of Technology, Guangzhou 510640, PR China ^bDepartment of Chemistry, South China Normal University, Guangzhou 510006, PR China

> Received 5 May 2006; revised 8 August 2006; accepted 11 August 2006 Available online 1 September 2006

Abstract—Pd(II)-catalyzed acetalization of terminal olefins with electron-withdrawing groups was carried out smoothly in supercritical carbon dioxide under oxygen atmosphere when polystyrene-supported benzoquinone (PS-BQ) or Cu^{II} (Cu^{I}) chloride was employed as cocatalyst. The higher selectivity was achieved, without any chlorinated by-product detected, when using PS-BQ instead of Cu^{II} (or Cu^{I}) chloride. PS-BQ could be recycled with excellent catalytic activity remaining after each simple filtration. Chlorine ion was demonstrated to be a promoter. The different acetalization mechanisms were revealed by the subtle relationship of chlorine ion and benzoquinone (BQ) to the catalytic activity of PdCl₂/PS-BQ, Pd^{II}-CuCl₂ or Pd(OAc)₂/PS-BQ.

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1. Introduction

Since Wacker process was discovered and industrialized, many further researches and applications were developed.¹ When terminal olefins with electron-withdrawing groups, such as acrylate esters (CH₂=CH–COOR), acrylonitrile (CH₂=CH–CN), and methyl vinyl ketone (CH₂=CH– CO–CH₃), were treated with alcohols, the reaction afforded 3,3-dialkoxy acetals, which are important intermediates for organic synthesis.² For examples, alkyl 3,3-dialkoxy-propanoates, β -ketoacetals, and β -cyanoacetal were used for the synthesis of coumarins, porphyrins, spermine metabolites, loganin,³ and other practical drugs or dyes.⁴ Among the methods to prepare these acetals, the simplest one was the Pd^{II} salts catalyzed reaction of terminal olefins with electron-withdrawing groups and alcohols.

In order to improve the yield and selectivity, additives were added in the reaction. For example, hexamethylphosphoric triamide (HMPA) was an effective accelerator in the acetalization of methyl acrylate with methanol (Scheme 1),^{2b} but HMPA is expensive, toxic, and harmful to environment. Other additives, i.e., triethyl amine (NEt₃) or K₂CO₃, especially dibasic sodium phosphate (Na₂HPO₄), were used as

a proton scavenger to prevent the formation of the Michael adduct product when vinyl ketone (CH_2 =CH-CO-R) was used as the substrate (Scheme 1).^{2a}



Scheme 1.

In 1999, we first reported our investigation on the Pd^{II}catalyzed acetalization of terminal olefins with electronwithdrawing groups in supercritical carbon dioxide (scCO₂), and found that when the reaction solvent was replaced with scCO₂, the accelerator HMPA was not necessary.⁵ The further experimental results showed that polystyrene-supported benzoquinone (PS-BQ), its structure, and synthetic route (Scheme 2), was a successful substitute for the cocatalyst CuCl₂ (or CuCl).⁶

It is well-known that organic reactions in $scCO_2$ is one of the important and attractive subjects of research in green chemistry.⁷ First, carbon dioxide (CO₂) is inexpensive, non-flammable, nontoxic, and chemically inert under many conditions. Secondly, $scCO_2$ is not only a substitute

Keywords: Acetalization; Benzoquinone; Palladium; Supercritical carbon dioxide; Wacker oxidation.

^{*} Corresponding author. Tel.: +8620 22236518; fax: +8620 87112906; e-mail: jianghf@scut.edu.cn



Scheme 2.

for volatile and toxic organic solvents, but also possesses some special properties. For examples, its hybrid property of both liquid and gas is very advantageous to some reactions involving gaseous reagents; controlling of the CO_2 density by the variation of the temperature and pressure enables the solvent properties to be 'tuned' to reagents; separating of CO_2 from the reaction mixture is energy-efficient and simple.⁸ Although Pd^{II}-catalyzed acetalization^{5,6,9} and other reactions took place in scCO₂,^{7,10} it is a puzzle how to effectively control such a complicated reaction system.

In this work, we further investigate Pd^{II}-catalyzed acetalization of terminal olefins with electron-withdrawing groups in scCO₂. Our purposes here are to present detailed knowledge of catalysts and cocatalysts, reaction rate, and selectivity, solvent effects and to provide theoretical explanations about the selectivity control and the reaction mechanism based on the systematic comparison. We wish to report the conclusive discussion in this paper.¹¹

2. Results and discussion

2.1. The conditions for Pd^{II} -catalyzed acetalization of terminal olefins with electron-withdrawing groups in $scCO_2$

Based on previous reports,^{5,6} the conditions for PdCl₂/PS-BQ-catalyzed acetalization of methyl acrylate **1a** in scCO₂, especially the effect of oxygen pressure, were further investigated in Table 1. Using methyl acrylate **1a** as the typical substrate, and methanol as the typical alcohol, the appropriate conditions for Pd^{II}-catalyzed acetalization of terminal

olefins with electron-withdrawing groups in scCO₂ are summarized as the following:

- Sufficient high system pressure made the reaction go smoothly at room temperature (20–27 °C) with satisfactory results.^{5,6}
- (2) The reaction time could be shortened from 24 h to 6 h under higher total system pressure, and the excellent yield and reaction selectivity were obtained (Table 1, entry 2).
- (3) It is possible to reduce the amount of methanol to accomplish the present reaction (Table 1, entry 2).
- (4) The suitable oxygen pressure was 0.5 MPa. Once oxygen pressure was below 0.5 MPa, the conversion, yield, and selectivity were declined, even under longer reaction time and higher system pressure (Table 1, entries 3–5).

2.2. The influences of different cocatalysts on the Pd^{II}-catalyzed acetalization of methyl acrylate

It has been reported that, as cocatalyst in the acetalization of methyl acrylate **1a**, CuCl₂ was inferior to CuCl for its liability to produce chlorinated by-product **5a**.^{2a,12} When the reaction was carried out in scCO₂, CuCl₂ gave similar or better results than CuCl did,⁵ and **5a** was usually produced with yield from 0.3% to 1.6%.

When polymeric cocatalyst PS-BQ was employed, the result is satisfactory as expected without any chlorinated by-products detected (Table 1, entries 1–5). At the same time, the yield and selectivity of the major product were almost the same as that in CuCl₂ (or CuCl).⁶ And the best catalyst dosage is leading catalyst PdCl₂ 0.15 mmol (3 mol % of methyl acrylate **1a**) and PS-BQ 2 mmol (Table 1, entry 1).

Table 1. PdCl₂-catalyzed acetalization of 1a with MeOH using PS-BQ as cocatalyst in scCO₂^a

| | CH₃OC | $\frac{DC}{Pd} = \frac{C}{Pd}$ | CH ₃ OH, O ₂ | CH ₃ OOC | OMe CH OMe + a | H ₃ OOC | C + DMe | H ₃ OOC | + ℃Me | CH ₃ OOC 5a | |
|----------------|------------|--------------------------------|------------------------------------|---------------------|------------------------|--------------------|---------------|-----------------------|----------|---------------------------|---------------------|
| Entry | Cocatalyst | Temp | <i>T</i> (h) | P^{b} | Mol ratio ^c | Conv. | 1 | Yield ^d (% |) | Select. for | Yield of |
| | (mmol) | (°C) | | (MPa) | | (%) | 2a | 3a | 4a | 2a° (%) | 5a ¹ (%) |
| 1 ^g | PS-BQ (2) | 50 | 24 | 0.5/11 | 4.94:1 | 42.7 | 14.4 | 0 | 2.1 | 87.1 | 0 |
| 2 | PS-BQ (2) | 50 | 6 | 0.5/15 | 3.50:1 | 100 | 96.8 | 0 | 0 | 100 | 0 |
| 3 | PS-BQ (2) | 50 | 24 | 0.4/12 | 4.94:1 | 99.5 | 65.5 | 0 | 14.1 | 82.3 | 0 |
| 4 | PS-BQ(2) | 50 | 47 | 0.2/14 | 4.94:1 | 98.5 | 82.6 | 0 | 0 | 100 | 0 |
| 5 | PS-BQ (2) | 50 | 24 | 0.02/10 | 4.94:1 | 49.5 | 35.4 | 0 | 5.0 | 90.4 | 0 |

^a Reaction conditions: 5 mmol methyl acrylate **1a** and 0.15 mmol (3 mol %) PdCl₂.

^b O₂ pressure/total system pressure.

^c Methanol/methyl acrylate.

^d By GC spectrum.

^e Selectivity= $[2a/(2a+3a+4a)] \times 100$.

 $^{\rm f}$ When CuCl₂ (or CuCl) was used as cocatalyst, the chlorinated adduct **5a** usually was obtained with yield from 0.3% to 1.6%.

g PdCl2 0.5 mol %.

| | CH300C | CH ₃ OH, O Pd ^{II} , PS-B0 | | OC OMe + | CH300C | CH ₃ + DMe | 000C | CH ₃ C + Me | ос Соосн ₃ | CH3 |
|-------|---------------|---|------------------|------------------------|------------------------------|-----------------------------|------------------------|------------------------------|----------------------------|----------------|
| | 1a | | | 2a | 3a | | 4a | | 6 | |
| Entry | Recycle times | <i>T</i> (h) | P^{b} | Mol ratio ^c | Mol ratio ^c Conv. | | Yield ^d (%) | | Select. for | Yield of |
| | | | (MPa) | MPa) | (%) | 2a | 3a | 4a | 2a ^c (%) | 6 " (%) |
| 1 | Fresh | 24 | 0.5/10 | 4.94:1 | 99.8 | 82.8 | 1.3 | 4.8 | 93.1 | 3.5 |
| 2 | 1 | 24 | 0.5/13 | 4.94:1 | 100 | 88.7 | 0 | 7.8 | 91.9 | 1.3 |
| 3 | 2 | 24 | 0.5/12 | 4.94:1 | 99.8 | 84.3 | 0 | 7.0 | 92.3 | 6.9 |
| 4 | 3 | 24 | 0.5/14 | 4.94:1 | 100 | 80.3 | 0 | 8.4 | 90.5 | 11.2 |
| 5 | 4 | 24 | 0.5/18 | 4.94:1 | 100 | 76.7 | 0 | 1.7 | 97.8 | 21.6 |

Table 2. Recyclability of PS-BQ in PdCl₂-catalyzed acetalization of 1a with MeOH in scCO₂^a

^a Reaction conditions: 5 mmol methyl acrylate 1a, 0.15 mmol (3 mol %) PdCl₂, and 2 mmol PS-BQ. The reaction was carried out at 50 °C.

^b O₂ pressure/system pressure.

^c Methanol/methyl acrylate.

^d By GC spectrum.

^e Selectivity= $[2a/(2a+3a+4a)] \times 100$.

When PS-BQ was used as cocatalyst, its reusability was investigated as shown in Table 2. In each cycle, PS-BQ was separated easily through simple filtration, then washed with acetone, and dried in vacuo before use for the next experiment. After several runs, the selectivity for **2a** was still excellent though the yield of **2a** decreased slightly (Table 2, entries 2–5). Therefore, it is obvious that PS-BQ can be recycled after simple filtration with excellent recovery, as well as excellent catalytic activity.

To our surprise, trimethyl benzenetricarboxylate **6** was detected when PS-BQ was used as cocatalyst (Table 2, entry 1). It is very interesting that the yield of **6** increased with the cycle times of PS-BQ. As one of the useful multifunctional methyl benzoate derivatives, ¹³ **6** was usually prepared from propiolate esters, ¹⁴ including the Pd^{II}-catalyzed

trimerization of ethyl propiolate in $scCO_2^{10i}$ or organic solvent.¹⁵ Acrylate ester is cheaper and more abundant than propiolate ester. Undoubtedly, it is very valuable to synthesize **6** via the trimerization of methyl acrylate **2a** and to make the reaction mechanism clear. The further research is still in progress.

2.3. The influences of different Pd^{II} catalysts on the acetalization of methyl acrylate

PdCl₂-catalyzed acetalization of methyl acrylate **1a** with methanol was slightly faster than that of $PdCl_2(MeCN)_2$ when copper salt was employed as cocatalyst.⁵ In order to eradicate the corrosion of reactor by chlorine ion, $Pd(OAc)_2/PS$ -BQ catalytic system was further investigated, and the results are shown in Table 3.

Table 3. Acetalization of 1a with MeOH using Pd(OAc)₂ as catalyst in scCO₂ or compressed CO₂^a

| Entry | Catalyst | Temp | <i>T</i> (h) | P^{b} | Mol ratio ^c | Conv. | Yield ^d (%) | | | Select. for $2e^{e}$ (%) | Yield of |
|-------|---------------------|-----------------|--------------|------------------|------------------------|-------|------------------------|-----|------|--------------------------|------------------------------|
| | (mol %) | (°C) | | (MPa) | | (%) | 2a | 3a | 4a | $2a^{c}(\%)$ | 5a/6 ^a (%) |
| 1 | $PdCl_2$ (3) | 50 | 6 | 0.5/15 | 3.50:1 | 100 | 96.8 | 0 | 0 | 100 | 0/0 |
| 2 | $Pd(OAc)_2$ (3) | 50 | 24 | 0.2/13 | 4.94:1 | 98.2 | 77.4 | 0 | 10.6 | 88.0 | 0/0 |
| 3 | $Pd(OAc)_2$ (3) | 50 | 24 | 0.4/15 | 4.94:1 | 98.5 | 62.4 | 1.1 | 22.9 | 72.2 | 0/0 |
| 4 | $Pd(OAc)_2$ (3) | 50 | 24 | 0.4/3 | 4.94:1 | 98.5 | 76.9 | 0 | 2.1 | 97.3 | 0/0 |
| 5 | $Pd(OAc)_2$ (3) | 50 | 24 | 0.5/13 | 4.94:1 | 99.4 | 78.2 | 0 | 15.0 | 83.9 | 0/0 |
| 6 | $Pd(OAc)_2 (4)^{f}$ | 50 | 24 | 0.5/11 | 2.47:1 | 95.1 | 71.1 | 0 | 13.9 | 83.6 | 0/0 |
| 7 | $Pd(OAc)_2$ (3) | 50 | 22 | 0.5/6 | 9.88:1 | 94.6 | 54.4 | 0 | 29.7 | 64.7 | 0/0 |
| 8 | $Pd(OAc)_2$ (2) | 50 | 24 | 0.5/11 | 4.94:1 | 96.2 | 71.5 | 0 | 23.5 | 75.3 | 0/0 |
| 9 | $Pd(OAc)_{2}$ (4.5) | 50 | 24 | 0.5/3 | 4.94:1 | 98.5 | 74.3 | 0 | 20.0 | 78.8 | 0/0 |
| 10 | $Pd(OAc)_2 (3)^g$ | 50 | 24 | 0.5/15 | 4.94:1 | 91.4 | 41.4 | 0 | 0 | 100 | 0/37.8 ^h |
| 11 | $Pd(OAc)_2 (3)^f$ | 50 | 24 | 0.5/8 | 4.94:1 | 93.7 | 68.0 | 0 | 16.5 | 80.5 | 0/0 |
| 12 | $Pd(OAc)_2 (4)^f$ | 50 | 24 | 0.5/6 | 4.94:1 | 98.7 | 76.9 | 0 | 12.1 | 86.4 | 0/0 |
| 13 | $Pd(OAc)_2$ (3) | 40 | 24 | 0.5/14 | 4.94:1 | 97.7 | 69.0 | 0 | 25.4 | 73.1 | 0/0 |
| 14 | $Pd(OAc)_2$ (3) | 50 | 12 | 0.4/15 | 4.94:1 | 88.7 | 72.6 | 0 | 9.7 | 88.2 | 0/0 |
| 15 | $Pd(OAc)_2$ (3) | 50 | 12 | 0.5/10 | 4.94:1 | 88.8 | 80.1 | 0 | 6.9 | 92.1 | 0/0 |
| 16 | $Pd(OAc)_2$ (3) | 50 | 6 | 0.4/11 | 4.94:1 | 83.1 | 75.2 | 0 | 3.2 | 95.9 | 0/0 |
| 17 | $Pd(OAc)_2$ (3) | rt ⁱ | 6 | 0.5/6 | 4.94:1 | 83.3 | 73.3 | 0 | 3.9 | 94.9 | 0/0 |

^a Reaction conditions: 5 mmol methyl acrylate 1a and 2 mmol (40 mol %) PS-BQ.

^b O₂ pressure/total system pressure.

^c Methanol/methyl acrylate.

^d By GC spectrum.

^e Selectivity= $[2a/(2a+3a+4a)] \times 100$.

PS-BQ 2.67 mmol (53.3 mol %).

g PS-BQ 1.33 mmol (26.7 mol %).

^h By-product **6** was seldom obtained in other case.

ⁱ Room temperature 20–27 °C.

No adduct **5a** was detected in Pd(OAc)₂/PS-BQ catalytic system because of the absence of chlorine ion, but the catalytic activity was obviously lower than that of PdCl₂/PS-BQ catalytic system (Table 3, entry 1). In order to raise the yield of **2a**, the conditions for Pd(OAc)₂/PS-BQ-catalyzed acetalization of **1a** with MeOH were optimized.

Higher oxygen pressure was favor to the reaction catalyzed by $Pd(OAc)_2/PS-BQ$ (Table 3, entries 2–5). As $Pd(OAc)_2$ had good solubility in methanol, the system pressure showed no remarkable effect on the reaction.

Excess methanol might promote the dissolution of $Pd(OAc)_2$ in scCO₂ more effectively than that of $PdCl_2$, and the decrease of methanol amount slightly reduced the yield and selectivity of **2a** (Table 3, entry 6). However, higher molar ratio of methanol was disadvantageous to the reaction (Table 3, entry 7).

The good catalyst loading for $Pd(OAc)_2$ was 3 mol % of substrate methyl acrylate **1a** (Table 3, entries 6, 8, and 9), and for PS-BQ was 40 mol % (Table 3, entries 6, 10, and 11). When both of the loading of $Pd(OAc)_2$ and PS-BQ were increased by 33%, the yield and selectivity of **2a** were slightly raised, but the best yield was still less than 80% (Table 3, entry 12).

The appropriate reaction temperature was $50 \,^{\circ}$ C, and the lower temperature was slightly disadvantageous to the reaction (Table 3, entry 13).

Shortening the reaction time was feasible because the variation of the yield and selectivity of **2a** was not remarkable, though the conversion of methyl acrylate **1a** was slightly lowered (Table 3, entries 14–17).

2.4. Influences of different Pd^{II} catalyst system on acetalization of acrylate esters and acrylonitrile

By using different cocatalysts, the Pd^{II}-catalyzed acetalization of different types of substrates with methanol or ethanol was investigated as shown in Table 4.

It is obvious that, in different Pd^{II} catalyst system, all of the acrylate esters and acrylonitrile gave the expected acetal **2** as major product, and the chlorinated by-product **5** was produced only when copper salt was used as cocatalyst (Table 4, entries 1, 3, 4, and 10). Although substrates were different, the yield and selectivity of **2** usually had a corresponding increment in most case when PS-BQ was employed as cocatalyst instead of CuCl₂ (CuCl).

The conversion, yield, and selectivity of acetalization were affected by the hindrance of alkyl group (R' and R) in CH_2 =CH-COOR' (acrylate esters, **1a**, **1b**, and **1c**) and ROH, when either PS-BQ⁶ or copper salt was used as cocatalyst. Because of the coordination of CN with Pd^{II},^{2a} higher oxygen pressure and temperature were necessary for the acetalization of acrylonitrile **1d** (Table 4, entry 10).

According to the classical Wacker oxidation mechanism, it is inevitable to produce acidic substance (e.g., HCl) in the reaction,^{2a,16} and the transesterification between alcohol and acrylate ester may occur subsequently in acidic condition. In order to avoid the transesterification, the acetalization of

Table 4. Pd^{II}-catalyzed acetalizations of acrylate esters and acrylonitrile with alcohols using different cocatalyst in scCO₂^a

| X ROH, O ₂ | | + X OR | . X | + XCI |
|--|--|--|---|--|
| 1 | 2 | 3 | 4 | 5 |
| 1a, X = COOMe 1b, X = COOEt 1c, X = COOCH $_2$ CH $_2$ CH $_2$ CH $_3$ 1d, X = CN | 2a, X = COOM 2d, X = CN, R 2b, X = COOE 2b', X = COOE | Me, R = Me = Me Et, R = Me Et, R = Et | 2c, X = COO R = Me 2c', X = COO R = Et | CH ₂ CH ₂ CH ₂ CH ₃ CH ₂ CH ₂ CH ₂ CH ₃ |

| Entry | Cocatalyst | P^{b} | Mol ratio of substrate | Conv. | | Yield ^c (%) | | Select. for | Yield ^c of 5 (%) 1.6 0 1.8 1.4 0 0 0 0 0 0 |
|-----------------|--------------|------------------|-------------------------|-------|------|------------------------|------|---------------------------|---|
| | (mmol) | (MPa) | to alcohol | (%) | 2 | 3 | 4 | 2 ^a (%) | |
| 1 ^e | $CuCl_2$ (4) | 0.5/16 | 4.94:1 (Methanol to 1a) | 99.8 | 88.1 | 1.7 | 4.0 | 94.0 | 1.6 |
| 2 | PS-BQ (2) | 0.5/10 | 4.94:1 (Methanol to 1a) | 99.8 | 95.5 | 0.5 | 3.1 | 96.4 | 0 |
| 3^{f} | $CuCl_2$ (4) | 1.0/12 | 3.44:1 (Ethanol to 1b) | 89.0 | 68.0 | 4.8 | 13.0 | 79.3 | 1.8 |
| 4 ^g | CuCl (4) | 1.0/13 | 3.44:1 (Ethanol to 1b) | 90.0 | 75.8 | 5.6 | 6.0 | 86.7 | 1.4 |
| 5 | PS-BQ (2) | 0.5/8 | 3.44:1 (Ethanol to 1b) | 100 | 77.6 | 0 | 17.0 | 82.0 | 0 |
| 6 ^h | PS-BQ (2) | 0.5/9 | 4.94:1 (Methanol to 1b) | 99.8 | 74.2 | 0 | 10.0 | 88.1 | 0 |
| 7 | PS-BQ (2) | 0.5/10 | 4.94:1 (Methanol to 1b) | 100 | 84.5 | 0 | 9.1 | 90.3 | 0 |
| 8 | PS-BQ (2) | 0.5/8 | 4.94:1 (Methanol to 1c) | 78.9 | 77.8 | 0 | 1.1 | 98.6 | 0 |
| 9 | PS-BQ (2) | 0.5/8 | 3.44:1 (Ethanol to 1c) | 28.8 | 23.9 | 0.4 | 2.9 | 87.9 | 0 |
| 10 ⁱ | $CuCl_2(4)$ | 1.0/13 | 4.94:1 (Methanol to 1d) | 99.8 | 87.5 | 10.7 | 0.3 | 88.8 | 0.5 |
| 11 | PS-BQ (2) | 0.5/9 | 4.94:1 (Methanol to 1d) | 100 | 79.1 | 0 | 0 | 100 | 0 |

^a Reaction conditions: 5 mmol substrate 1 and 0.15 mmol (3 mol %) PdCl₂. The reaction was carried out at 50 °C for 12 h.

^b O₂ pressure/total system pressure.

^c By GC spectrum.

^d Selectivity= $[2/(2+3+4)] \times 100$.

^e Temperature 40 °C, and time 24 h.

^f Temperature 40 °C.

^g PdCl₂(MeCN)₂ 3 mol %, and temperature 40 °C.

^h Time 11 h.

ⁱ Temperature 57 °C.

methyl acrylate 1a was usually with methanol, and ethanol to ethyl acrylate 1b, especially when CuCl₂ was used as cocatalyst.2a,12

But in our experiments, when PS-BQ was used as cocatalyst in scCO₂, the transesterification did not occur in the acetalization of ethyl acrylate 1b with methanol, and ethyl 3,3dimethoxypropanoate (2b, X=COOC₂H₅, R=CH₃) was detected as the sole acetal product (Table 4, entries 6 and 7). It indicated that the prevention of transesterification was attributed to the replacement of CuCl₂ with PS-BO.⁶ This interesting phenomenon strongly suggests that some transformations in Pd^{II}/PS-BQ-catalyzed acetalization might be different from that in Pd^{II} –CuCl₂ catalytic system.

2.5. Application of different Pd^{II} catalyst system in the acetalization of other substrates

Investigation of Pd^{II}-catalyzed acetalization of other substrates showed that acrylic acid (CH₂=CH-COOH) and acrylamide (CH2=CH-CONH2) did not give the desired products whether PS-BQ⁶ or CuCl₂ (CuCl) was used as cocatalyst, and the reason is not clear yet.

For methyl methacrylate $[CH_2=C(CH_3)-COOCH_3]$, as Hosokawa's report, though the steric hindrance, its Pd^{II}catalyzed acetalization with 2,4-pentanediol still produced acetal with a lower yield (25%).^{2a} However, the acetalization of methyl methacrylate with methanol did not give the expected acetal in our reaction system, even when the reaction temperature applied was as high as that of acrylonitrile 1d. This difference may have a touch with the alcohol. 2.4-Pentanediol yielded a cyclic acetal, which was more stable than that produced by methanol.

Acrolein (CH2=CH-CHO, 7) was easily acetalized when PS-BQ⁶ or CuCl₂ (CuCl) was used as cocatalyst. After the substrate was totally converted, the acetalization of acrolein gave a mixture of anticipant acetal products (8 and 10) and Michael addition products (9 and 11) in different ratios, and the result is summarized in Table 5.

There were three methods to improve the ratio of acetals (the sum of the yield of 8, 10, and 11) when copper salt was used as cocatalyst, including the increase of oxygen pressure (Table 5, entries 1–3), the use of CuCl instead of CuCl₂ (Table 5, entries 2, 4, and 5), and the addition of Na_2HPO_4 as a proton scavenger according to the literature² (Table 5, entries 4 and 5). The maximum of the total yield was 72.1%.

When PS-BQ was employed as cocatalyst instead of copper salt, the Pd^{II}-catalyzed acetalization proceeded smoothly at mild conditions, and the yield of anticipant acetal products was 80.0% in absence of Na₂HPO₄ (Table 5, entries 5 and 6). Therefore, using of PS-BQ as cocatalyst was the best one to increase the acetal yield in the acetalization of acrolein 7.

When the acetalization of methyl vinyl ketone (CH₂=CH-CO-CH₃, 12) with methanol was catalyzed by PdCl₂/copper salt, there were many methods to improve the selectivity of acetal 13,9 including replacement of CuCl₂ with CuCl (the suitable amount of CuCl was 3 mmol), adding Na₂HPO₄ as a proton scavenger,² raising O₂ pressure and CO₂ pressure. When the conditions were optimal, the maximum selectivity for 13 was 86.7% (Table 6, entry 1), which was 1.6% higher only than that catalyzed by PdCl₂/PS-BQ catalytic system⁶ (Table 6, entry 2).

In traditional methods, basic additives, such as NEt₃ or K_2CO_3 , or Na_2HPO_4 , were used to keep the non-anticipant Michael adduct minimum.^{2a,12} Even in scCO₂, the basic additives including Na₂HPO₄ or OH type anion resin were needed to improve the selectivity of the anticipant acetal.9 However, in PS-BQ/Pd^{II} catalytic system, good selectivity could be achieved in the acetalization of methyl vinyl ketone 12 without the addition of any additives (Table 6). This indicates that different cocatalysts in Pd^{II}-catalyzed acetalization of terminal olefins with electron-withdrawing groups go through different mechanisms.

2.6. Mechanism of the Pd^{II}-catalyzed acetalization with different cocatalyst in scCO₂

Based on the above results, the mechanism of the Pd^{II}-catalyzed acetalization using copper salt as cocatalyst in scCO₂ is suggested in Scheme 3.

In this mechanism, the key step is the production of intermediate 4a,^{2a,16} which was frequently detected in our experiments. At the same time, by-product 5a was often found

Table 5. Pd^{II}-catalyzed acetalization of acrolein with MeOH using different cocatalyst in scCO₂^a

| | CH 7 | $\frac{\text{CH}_{3}\text{OH, O}_{2}}{\text{Pd}^{II}}$ | MeO MeO 8 | CHO IeO 9 | MeO OMe NeO ON | e C + MeO 11 | ОМе ОМе | | |
|-------|-------------------------|--|----------------------|-----------------|-------------------|-----------------------|------------|---------|--|
| Entry | Cocatalyst (mmol) | Time (h) | P ^b (MPa) | | | Yield ^e (% |) | | |
| | | | | 8 | 9 | 10 | 11 | 8+10+11 | |
| 1 | CuCl ₂ (0.6) | 24 | 0.2/12 | 0 | 62.5 | 2.1 | 12.7 | 14.8 | |
| 2 | $CuCl_2$ (0.6) | 24 | 0.5/12 | 0 | 56.8 | 3.2 | 24.4 | 27.6 | |
| 3 | $CuCl_2$ (0.6) | 24 | 1.0/12 | 0 | 26.3 | 6.7 | 48.9 | 55.6 | |
| 4 | CuCl (0.6) | 24 | 0.5/12 | 0 | 34.2 | 3.4 | 42.7 | 46.1 | |
| 5 | $CuCl (0.6)^d$ | 24 | 0.5/12 | 0 | 26.2 | 17.5 | 54.6 | 72.1 | |
| 6 | PS-BQ (2) | 12 | 0.5/9 | 20.4 | 3.9 | 46.7 | 12.9 | 80.0 | |

Reaction conditions: 5 mmol acrolein 7, 0.15 mmol (3 mol %) PdCl₂, and 24.7 mmol methanol. The reaction was carried out at 50 °C.

O₂ pressure/total system pressure.

^c By GC spectrum.

^d Na₂HPO₄ 0.3 mmol as additive.

Table 6. PdCl₂-catalyzed acetalization of methyl vinyl ketone 12 with MeOH using different cocatalyst in scCO₂^a

| | | | CH ₃ OH, O ₂ PdCl ₂ cocatalyst | MeO MeO 13 | COCH MeO 14 | H ₃ | | |
|----------------------------------|-----------------------|----------------------------------|---|------------------|-------------------|--------------------|-----------------|--|
| Entry | Cocatalyst | Additive | P^{b} | Conv. | Yield | d ^c (%) | Select. for | |
| | (mmol) | (mmol) | (MPa) | (%) | 13 | 14 | 13 ^u | |
| 1 ^e 2 ^f | CuCl (3) PS-BQ (2) | Na_2HPO_4 (0.5) No addition | 0.5/12 0.5/8 | 100 100 | 83.2 76.8 | 12.8 13.4 | 86.7 85.1 | |

^a Reaction conditions: 5 mmol methyl vinyl ketone 12 and 50 $^{\circ}$ C, 12 h.

^b O₂ pressure/total system pressure.

^c By GC spectrum.

^d Selectivity= $[13/(13+14)] \times 100$.

^e PdCl₂ 0.5 mmol (10 mol %), and mol ratio of methanol to **12** was 9.88:1.

 $^{\rm f}$ PdCl₂ 0.15 mmol (3 mol %), and mol ratio of methanol to **12** was 4.94:1.



Scheme 3.

when $CuCl_2$ or CuCl was used as cocatalyst because of the production of HCl.

When PS-BQ was used as cocatalyst, the basic cycle was similar to the Pd^{II} –CuCl₂ system, but benzoquinone (BQ) might absorb HCl via Michael addition¹⁷ in situ, and was converted to chlorohydroquinone (CHQ). CHQ took part in hydrogenolysis to give $PdCl_2$ and products, and then regenerated BQ (Scheme 4). Therefore, by-product **5a** was not detected.



Scheme 4.

The mechanism of $Pd(OAc)_2/PS-BQ$ catalytic system is not similar with that of $PdCl_2/PS-BQ$ system because no cycle of HCl absorption exists. And the cycle involving the oxidation

of PS-BQ was different from that of Pd^{II}–CuCl₂ system too (Scheme 5). In the absence of chlorine ion, the catalytic activity of Pd(OAc)₂/PS-BQ was lower than that of PdCl₂/ PS-BQ catalytic system. These explanation were further demonstrated by the influences of additives on Pd(OAc)₂/ PS-BQ-catalyzed acetalization (Table 7).





It is believed that the formation of $PdCl_4^{2-}$ from $PdCl_2$ may enhance the activity of $PdCl_2$.¹⁶ In order to improve the activity of $Pd(OAc)_2/PS$ -BQ and increase the yield and selectivity of **2a**, especially the yield, we tried to add anhydrous NaOAc to enhance the activity of $Pd(OAc)_2$, but the result

| Table 7. Pu(OAC) ₂ /PS-DQ-catalyzed acetalization of Ta with MeOH using different additives in sCCO ₂ of compressed C | Table 7 | 7. Pd(OAc) ₂ /PS-BO |)-catalyzed acetalization | of 1a with MeOH using | g different additives in scCO | or compressed CC |
|---|---------|--------------------------------|---------------------------|-----------------------|-------------------------------|------------------|
|---|---------|--------------------------------|---------------------------|-----------------------|-------------------------------|------------------|

| Entry | Catalyst | Additive | P^{b} | Conv. | Yield ^c (%) | | | Select. for | |
|----------------|-----------------|----------------|------------------|-------|------------------------|----|------------|---------------------|--|
| | (mol %) | (mol %) | (MPa) | (%) | 2a | 3a | 4 a | 2a ^u (%) | |
| 1 | $Pd(OAc)_2(3)$ | N ^e | 0.2/13 | 98.2 | 77.4 | 0 | 10.6 | 88.0 | |
| 2 | $Pd(OAc)_2$ (3) | N ^e | 0.4/3 | 98.5 | 76.9 | 0 | 2.1 | 97.3 | |
| 3 | $Pd(OAc)_2$ (3) | N ^e | 0.5/13 | 99.4 | 78.2 | 0 | 15.0 | 83.9 | |
| 4 | $Pd(OAc)_2$ (3) | NaOAc (3) | 0.5/16 | 92.4 | 25.5 | 0 | 57.0 | 30.9 | |
| 5 ^f | $Pd(OAc)_2$ (3) | NaOAc (3) | 0.5/6 | 89.5 | 16.0 | 0 | 61.9 | 20.5 | |
| 6 | $Pd(OAc)_2$ (3) | HOAc (3) | 0.5/8 | 98.2 | 67.6 | 0 | 22.4 | 75.1 | |
| 7 | $Pd(OAc)_2$ (3) | HOAc (15) | 0.5/16 | 99.7 | 75.6 | 0 | 19.5 | 79.5 | |
| 8 | $Pd(OAc)_2$ (3) | HOAc (30) | 0.5/6 | 98.1 | 66.5 | 0 | 23.5 | 73.9 | |
| 9 | $Pd(OAc)_2$ (3) | HOAc (90) | 0.5/10 | 94.7 | 58.3 | 0 | 23.6 | 71.2 | |
| 10 | $Pd(OAc)_2$ (3) | NaCl (3) | 0.5/13 | 99.8 | 74.8 | 0 | 13.8 | 84.4 | |
| 11 | $Pd(OAc)_2$ (3) | NaCl (6) | 0.5/5 | 99.7 | 88.4 | 0 | 6.8 | 92.9 | |
| 12 | $Pd(OAc)_2$ (3) | LiCl (3) | 0.5/20 | 99.8 | 90.8 | 0 | 5.0 | 94.8 | |

^a Reaction conditions: 5 mmol methyl acrylate **1a**, 2 mmol (40 mol %) PS-BQ, and 24.7 mmol methanol. The reaction was carried out at 50 °C for 24 h. ^b O_2 pressure/total system pressure.

^c By GC spectrum.

^d Selectivity= $[2a/(2a+3a+4a)] \times 100$.

^e No additive.

^f Room temperature 20–27 °C, 6 h.

was not satisfactory. Contrarily, the yield and selectivity were greatly decreased (Table 7, entries 4 and 5). This can be ascribed to the oxidation of reactant methanol by $Pd(OAc)_2/NaOAc$,¹⁸ as the consumption of alcohol is disadvantageous to the next conversion of the intermediate **4a** into the expected product **2a**.

Using HOAc instead of NaOAc as the additive, the yield and selectivity were not satisfied neither. Increasing the amount of acidic HOAc was not workable too (Table 7, entries 6–9). Backvall¹⁹ reported work on the application and mechanism of Pd(OAc)₂/BQ catalytic system with HOAc or NaOAc, and only PdCl₄²⁻ complex structure was mentioned. Therefore, it may be very difficult for Pd(OAc)₂ to form Pd(OAc)₄²⁻ complex structure, ¹⁶ and our experiment results were consistent with it.

When NaCl was used as an additive, $PdCl_2$ could be produced by the ion exchange of $Pd(OAc)_2$ and NaCl as shown:

 $2NaCl + Pd(OAc)_2 \rightarrow 2NaOAc + PdCl_2$

Although the simultaneously produced NaOAc was disadvantageous to the acetalization because of the oxidation of reactant methanol by $Pd(OAc)_2/NaOAc$,¹⁸ the activation property of chlorine ion could offset the side-effect caused by NaOAc. Hence, **2a** was still the major product, and its yield and selectivity remained (Table 7, entries 1–3 and 10). When the loading of NaCl was increased to 1 equiv of $Pd(OAc)_2$, the result observed was similar with the one from the catalytic system of $PdCl_2$ (Table 7, entry 11).

When LiCl was used as the additive, though its molar amount was equivalent to half of $Pd(OAc)_2$, only the activation of chlorine ion existing, the aim to enhance the activity of $Pd(OAc)_2$ was realized as expected (Table 7, entry 12). Thus, using chlorine ion and BQ to control the reaction selectivity was achieved.

3. Conclusions

Using $scCO_2$ as an environment-friendly solvent, Pd^{II} -catalyzed acetalization of terminal olefins with electron-

withdrawing groups, i.e., acrylate esters, acrylonitrile, methyl vinyl ketone, and acrolein, could be carried out smoothly under oxygen atmosphere. The effect of catalysts, cocatalysts, alcohols, system temperature, reaction time, and reactant molar ratio, is systematically investigated and summarized in this paper.

Cocatalyst PS-BQ could be recycled with excellent catalytic activity, and without any chlorinated by-product detected. The catalytic activity was slightly decreased when Pd(OAc)₂ was used as leading catalyst instead of PdCl₂. While the good yield and selectivity was achieved when the chlorine ion additive, i.e., NaCl or LiCl, was added. For different acetalization mechanism, PdCl₂/PS-BQ was a better catalytic system with higher selectivity than Pd^{II}/Cu^{II} (Cu^I) system. Especially for acrolein, and methyl vinyl ketone, basic additives were not necessary. In the Wacker oxidation cycle catalyzed by PdCl₂/PS-BQ, BQ was proposed to be initially converted to CHQ by the addition reaction with HCl and subsequently regenerated by the hydrogenolysis to give PdCl₂ and products.

Thus, the method for the synthesis of important organic intermediates, i.e., alkyl 3,3-dialkoxypropanoates, β -ketoacetals, and β -cyanoacetal, environment-friendly and high selectivity, by the acetalization reaction catalyzed by PdCl₂/PS-BQ was successfully developed. And the recycling of the precious metal palladium was feasible in a convenient manner. More importantly, the mechanism of Pd^{II}/PS-BQ catalytic system may be helpful to explain other novel phenomena, e.g., the production of tri-substituted benzene derivatives from acrylate esters, and methyl vinyl ketone.

4. Experimental

4.1. General

¹H NMR spectra were recorded on BRUKER DRX-400 spectrometer using CDCl₃ as solvent and TMS as an internal standard. GC analyses were performed on a GC-930 chromatograph (Shanghai Haixian Chromatograph Instrument Ltd. Co.) with a flame ionization detector equipped with

an OV-101 capillary column (internal diameter=0.25 mm, length=30 m). Mass spectra were recorded on a Shimadzu GCMS-QP5050A at an ionization voltage of 70 eV equipped with a DB-WAX capillary column (internal diameter= 0.25 mm, length=30 m). IR spectra were recorded on Analect RFX-65A spectrometer.

All acrylate esters, acrylonitrile, acetonitrile, acrylic acid, acrylamide, methyl methacrylate, methanol, ethanol, palladium chloride, acetone, and porous polystyrene resin, etc., were commercially purchased and used without further purification. Acrolein was distilled before use. Methyl vinyl ketone, PdCl₂(MeCN)₂, and CuCl were prepared according to the literature.^{2b,9}

4.2. Preparation of cocatalyst PS-BQ

The cocatalyst PS-BQ was prepared in three steps: chloromethylation of commercial polystyrene (PS) porous resin, alkylation of hydroquinone by chloromethylated PS, and oxidation of PS supported-hydroquinone by H_2O_2 (Scheme 2), and the composition of the product from each step was successfully confirmed with IR and elemental analyses of chlorine.⁶

4.3. Typical procedure for the acetalization

The reaction was carried out in a HF-25 autoclave. Catalyst PdCl₂ (0.15 mmol, 3 mol %), PS-BQ (2 mmol), MeOH (1 mL, 24.7 mmol), and methyl acrylate (5 mmol) were added into a 25 mL autoclave in sequence. O₂ and liquid CO₂ were pumped into the autoclave by a cooling pump to reach the desired pressure, then the autoclave was heated by oil bath under magnetic stirring for the desired reaction time. After the reaction finished, the autoclave was allowed to cool to -30 °C. CO₂ was vented and the surplus was extracted with *n*-hexane or petroleum ether. The extract was filtrated and condensed under reduced pressure. The product was purified by preparative TLC on silica gel using light petroleum ether/ethyl acetate as eluent before the test of ¹H NMR and IR.

4.3.1. Methyl 3,3-dimethoxypropanoate (acetal 2a). Oil; IR (KBr, film): ν 2948, 2840 cm⁻¹ (CH₃, CH₂, CH); 1740 cm⁻¹ (COO, very strong); 1378, 1444 cm⁻¹ (CH₃O); 1069, 1122, 1176 cm⁻¹ (C–O–C in ether or ester structure, strong). ¹H NMR (CDCl₃, TMS, ppm): δ 2.62 (2H, d, J=2.0 Hz, CH₂), 3.33 (6H, s, OCH₃), 3.65 (3H, s, OCH₃), 4.80 (1H, s, CH). GC–MS: m/z 147 (2) [M–1, C₆H₁₁O₄⁺], 133 (8) [M⁺–CH₃, C₅H₉O₄⁺], 117 (29) [M⁺–CH₃O, C₅H₉O₃⁺], 101 (8) [C₄H₅O₄⁺], 85 (5) [C₄H₅O₂⁺], 75 (100) [(CH₃O)₂CH⁺], 59 (25) [C₂H₃O₂⁺], 47 (25) [C₂H₇O⁺], 31 (16) [CH₃O⁺].

4.3.2. Ethyl 3,3-dimethoxypropanoate (acetal 2b). Oil; IR (KBr, film): ν 2985, 2944, 2837 cm⁻¹ (CH₃, CH₂, CH); 1738 cm⁻¹ (COO, very strong); 1378, 1455 cm⁻¹ (CH₃, CH₂); 1069, 1123, 1176 cm⁻¹ (C–O–C in ether or ester structure, strong). ¹H NMR (CDCl₃, TMS, ppm): δ 1.25 (3H, t, *J*=3.2 Hz, OCH₂CH₃), 2.63 (2H, d, *J*=6.0 Hz, *CH*₂CH), 3.35 (6H, s, OCH₃), 4.15 (2H, q, *J*=3.6 Hz, OCH₂CH₃), 4.82 (1H, t, *J*=6.0 Hz, CH₂CH). GC–MS: *m/z* 161 (2) [M–1, C₇H₁₃O₄⁺], 147 (7) [M⁺–CH₃, C₆H₁₁O₄⁺], 131 (25) [M⁺–CH₃O, C₆H₁₁O₃⁺], 117 (13) [M⁺–OCH₂CH₃,

 $C_5H_9O_3^+$], 103 (8) [$C_4H_7O_3^+$], 89 (26) [$C_4H_9O_2^+$], 75 (100) [($CH_3O_2CH^+$], 61 (26) [$C_2H_5O_2^+$], 43 (16) [$C_2H_3O^+$], 29 (50) [$C_2H_5^+$].

4.3.3. Ethyl 3,3-diethoxypropanoate (acetal 2b'). Oil; IR (KBr, film): ν 2980, 2933, 2893 cm⁻¹ (CH₃, CH₂, CH); 1738 cm⁻¹ (COO, very strong); 1378, 1449 cm⁻¹ (CH₃, CH₂); 1064, 1120, 1195 cm⁻¹ (C–O–C in ether or ester structure, strong). ¹H NMR (CDCl₃, TMS, ppm): δ 1.17 (6H, t, *J*=7.2 Hz, OCH₂*CH*₃), 1.25 (3H, t, *J*=3.6 Hz, COOCH₂*CH*₃), 2.64 (2H, d, *J*=5.6 Hz, *CH*₂CH), 3.50–3.55 (2H, m, O*CH*₂CH₃), 3.63–3.68 (2H, m, O*CH*₂CH₃), 4.14 (2H, q, *J*=7.2 Hz, COO*CH*₂CH₃), 4.93 (1H, t, *J*=2.4 Hz, CH₂*CH*). GC–MS: *m*/*z* 189 (2) [M–1, C₉H₁₇O₄⁺], 161 (16) [M⁺–CH₂CH₃, C₇H₁₃O₄⁺], 145 (46) [C₇H₁₃O₃⁺], 117 (38) [C₅H₉O₃⁺], 103 (100) [(CH₃CH₂O)₂CH⁺], 89 (38) [C₃H₅O₃⁺], 75 (70) [C₃H₇O₂⁺], 71 (71) [C₃H₃O₂⁺], 47 (75) [C₂H₅OH₂⁺], 29 (58) [C₂H₅⁺].

4.3.4. *n*-Butyl 3,3-dimethoxypropanoate (acetal 2c). Oil; IR (KBr, film): ν 2961, 2876, 2838 cm⁻¹ (CH₃, CH₂, CH); 1737 cm⁻¹ (COO, very strong); 1461, 1402 cm⁻¹ (CH₃, CH₂); 1070, 1122, 1192 cm⁻¹ (C–O–C in ether or ester structure, strong); 740 cm⁻¹ (CH₂CH₂CH₂, weak). ¹H NMR (CDCl₃, TMS, ppm): δ 0.92 (3H, t, *J*=2.4 Hz, OCH₂CH₂CH₂CH₃), 1.34–1.38 (2H, m, OCH₂CH₂CH₂CH₂CH₃), 1.57–1.64 (2H, m, OCH₂CH₂CH₂CH₃), 2.63 (2H, d, *J*=6.0 Hz, *CH*₂CH), 3.34 (6H, s, OCH₃), 4.09 (2H, t, *J*=3.2 Hz, OCH₂CH₂CH₂CH₃), 4.82 (1H, t, *J*=6.0 Hz, CH₂CH). GC–MS: *m*/*z* 189 (1) [M–1, C₉H₁₇O₄⁺], 159 (6) [M⁺–CH₃O, C₈H₁₅O₃⁺], 117 (8) [M⁺–C₄H₉O, C₅H₉O₃⁺], 103 (17) [C₄H₇O₃⁺], 85 (18) [C₄H₅O₂⁺], 75 (100) [(CH₃O)₂CH⁺], 57 (18) [C₄H₉⁺], 41 (24) [C₃H₅⁺], 29 (31) [C₂H₅⁺].

4.3.5. 3,3-Dimethoxypropionitrile (acetal 2d). Oil; IR (KBr, film): ν 2936, 2845 cm⁻¹ (CH₃, CH₂, CH); 2255 cm⁻¹ (C \equiv N, weak); 1455, 1417 cm⁻¹ (CH₃, CH₂); 1075, 1122 cm⁻¹ (C–O–C in ether structure, strong). ¹H NMR (CDCl₃, TMS, ppm): δ 2.65 (2H, d, *J*=5.6 Hz, *CH*₂CH), 3.39 (6H, s, OCH₃), 4.66 (1H, t, *J*=5.6 Hz, CH₂CH). GC–MS: *m/z* 114 (2) [M–1, C₅H₈NO₂⁺], 84 (92) [M⁺–CH₃O, C₄H₅NO⁺], 75 (100) [(CH₃O)₂CH⁺], 56 (46) [C₃H₄O⁺].

4.3.6. 4,4-Dimethoxy-2-butanone (acetal 13). Oil; IR (KBr, film): ν 2937, 2839 cm⁻¹ (CH₃, CH₂, CH, strong); 1718 cm⁻¹ (C=O, very strong); 1446 cm⁻¹ (CH₃O); 1362 cm⁻¹ (CH₃CO); 1080, 1122, 1167, 1192 cm⁻¹ (C–O–C in ether structure, strong). ¹H NMR (CDCl₃, TMS, ppm): δ 2.16 (3H, s, CH₃CO), 2.72 (2H, d, J=5.2 Hz, CHCH₂COCH₃), 3.34 (6H, s, OCH₃), 4.77 (1H, t, J=5.6 Hz, CHCH₂COCH₃). GC–MS: m/z 132 (3) [M⁺, C₆H₁₂O₃⁺], 117 (21) [M⁺–CH₃, C₅H₉O₃⁺], 101 (22) [M⁺–CH₃O, C₅H₉O₂⁺], 85 (12) [CH₃COCH₂CO⁺, C₄H₅O₂⁺], 75 (71) [(CH₃O)₂CH⁺], 59 (17) [CH₃OCO⁺], 43 (100) [CH₃CO⁺], 31 (10) [CH₃O⁺].

Acknowledgements

The authors thank National Natural Science Foundation of China (No. 20332030 and No. 20572027) and Young

Foundation of SCUT for the financial support of this work and Dr. Jing-Mei Huang for helpful discussion.

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