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Palladium-catalyzed aerobic oxidation of terminal olefins with electron-withdrawing groups in $scCO_2$

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Abstract

Product control of palladium-catalyzed aerobic oxidation of terminal olefins with electron-withdrawing groups can be achieved through modifying reaction conditions. When the oxidant, such as $CuCl_2/O_2$, benzoquinone/O_2 or O_2, was present in $scCO_2$, aerobic oxidation of terminal olefins goes smoothly. With enough MeOH and sufficient oxygen, acetalization preponderated over cyclotrimerization, while with little MeOH as co-solvent in $scCO_2$ or no MeOH in DMF and an appropriate pressure of O_2, cyclotrimerization of terminal olefins became the dominated reaction. When oxygen is absent and triethylamine was added into the reaction system, palladium-catalyzed C–N bond formation occurs to produce β-amino acid derivatives as the sole product.

1. Introduction

Since the discovery of Wacker reaction in the late 1950s, palladium catalysis has become one of the most versatile methodologies for the synthesis of various targeted organic molecules.[1] Palladium-catalyzed reactions include two major classes: cross-coupling reactions initiated by Pd(0) and oxidation reactions initiated by Pd(II). Although the field flourished with palladium-catalyzed oxidation reactions, the catalytic systems traditionally require a stoichiometric secondary oxidant such as $CuCl_2$ or benzoquinone, which leads to the complexity of the reactions, reduces the atom economy, making product isolation complicated and toilsome.

Recently, there has been an increasing demand for environmentally friendly and sustainable chemical processes, aimed at replacing stoichiometric methods by catalytic processes. Presently, the ideal ultimate stoichiometric oxidant in these reactions turns to either molecular oxygen or hydrogen peroxide, because these oxidants are environmentally friendly and give only water as a byproduct.[2] Thus, palladium-catalyzed aerobic oxidations have received considerable attention[3] and substantial developments have been achieved. These can be linked to the discoveries of various ligands, such as DMSO,[4] pyridine,[5] 1,2-bipyridine,[6] phenanthroline,[7] bathophenanthroline disulfonate,[8] NEt_3,[9] (−)-sparteine,[10] *N*-heterocycliccarbene,[11] etc., which stabilize the reduced palladium catalyst and enable an efficient aerobic oxidation to be realized in the absence of a secondary oxidant.[12] At the same time, the choice of solvents is also critical to palladium-catalyzed aerobic oxidation because of the solubility of both palladium–ligand complexes (Pd/L) and molecular oxygen. Various solvents were employed according to different Pd/L systems, such as toluene,[13] benzene,[14] CH_2Cl_2,[15] biphasic solvents,[16] ionic liquids,[17] etc. However, a drawback is that in most cases excess ligand is needed to prevent catalyst decomposition, i.e., to prevent the Pd(0) intermediate from metal aggregation[18] and unfortunately, the excess of ligand also leads to less efficient oxidation as a result of inhibition of either substrate binding or β-hydride elimination.[19]

Pd(II)-catalyzed acetalization of terminal alkenes with alcohols, which undergo a Wacker-type process, ranks among the most important reactions for the functionalization of alkene feedstocks. Many acetals, such as alkyl 3,3-dialkoxypropanoates, β-ketoacetals, and β-cyanoacetal, are important

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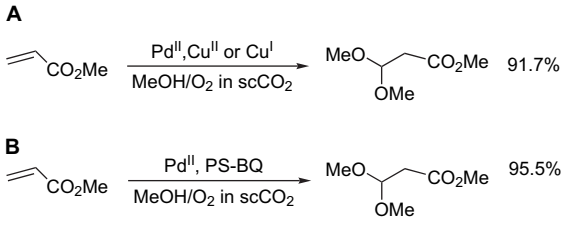
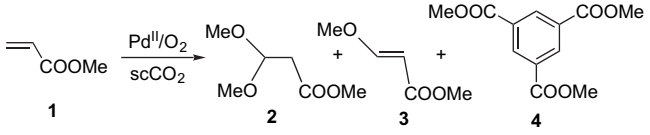
intermediates in organic synthesis and have been used to synthesize a variety of important compounds. In 1999, we first reported our investigation on the Pd(II)-catalyzed aerobic acetalization of terminal olefins with electron-withdrawing groups in supercritical carbon dioxide ($scCO_2$), using $CuCl_2$ or CuCl as cocatalyst and a yield of 91.7% was gained (Scheme 1, A). We also found that when the reaction solvent was replaced with $scCO_2$, the toxic accelerator HMPA was not necessary.[20]



Scheme 1.

Our further experimental results showed that polystyrene-supported benzoquinone (PS–BQ) was a successful substitute for the cocatalyst $CuCl_2$ (or CuCl) (Scheme 1, B).[21] Compared with small molecular cocatalysts, the separation of PS–BQ from the reaction system by simple filtration obviously made the recycling of precious palladium practical and convenient. A systemic conclusion has been made about the selective control and mechanistic study of Pd(II)-catalyzed aerobic acetalization of terminal olefins with electron-withdrawing groups using different cocatalysts in $scCO_2$.[22] When PS–BQ was used as cocatalyst, benzoquinone (BQ) might absorb HCl via Michael addition in situ, and was converted to chlorohydroquinone (CHQ), which took part in hydrogenolysis to give $PdCl_2$ and products, and then regenerated BQ. Enlightened by this, we further successfully explored polystyrene-supported phenol (PS–phenol) and polystyrene-supported hydroquinone (PS–HQ) as cocatalysts for the Pd(II)-catalyzed acetalization of terminal olefins with electron-withdrawing groups in $scCO_2$.[23]

As part of our ongoing interest in the direct utilization of molecular oxygen as the sole oxidant in the palladium-catalyzed acetalization of terminal olefins with electron-withdrawing groups in $scCO_2$, we have investigated the effects of various factors on this oxidation. Herein, we disclosed a 'ligand-free' palladium-catalyzed oxidative process using molecular oxygen as the sole oxidant in $scCO_2$ (Scheme 2). We also found that with molecular oxygen as the sole oxidant, satisfactory results can only be reached when using $scCO_2$ as reaction solvent in comparison with traditional organic solvents. It is well known that supercritical fluids are environmentally acceptable replacements for organic solvents, and as one of the most convenient of them, $scCO_2$ has also been widely studied because it is



Scheme 2.

inexpensive, inert, nontoxic, nonflammable and because its critical parameters are easily accessible (T_c=31.0 °C, P_c=7.38 MPa).[24] It is undoubtedly much more eco-friendly to bring together the very important green chemistry technologies—the use of carbon dioxide as a solvent and the use of molecular oxygen as the sole oxidant.

2. Results and discussion

2.1. The effect of different ligands on the $PdCl_2$-catalyzed acetalization

As is proved that an appropriate Pd/L system is of great help to realize an efficient palladium-catalyzed aerobic oxidation in the absence of a secondary oxidant.[11] We firstly explored the effect of various ligands on the $PdCl_2/CH_3OH/O_2/scCO_2$ system using methyl acrylate as substrate. In contrast, our study of the addition of various ligands in $scCO_2$ turned out to be not only unnecessary but also even disadvantageous. When the reaction was run ligand-free, a yield of 86.9% for **2** was obtained, with the formation of 1,3,5-benzenetricarboxylate as a byproduct. This was surprising because few examples of formation of benzene derivatives from simple olefins were reported before, and the highly regioselective manner is also novel. Traditionally, benzene derivatives were synthesized by aromatic electrophilic substitution reactions and a variety of metal-mediated coupling reactions, which generally involve multistep syntheses. Although transition-metal-catalyzed cyclotrimerization of alkynes has been greatly advanced, the regioselectivity of the process can still be troublesome.[25]

As seen in Table 1, nitrogenous ligands including pyridine, 2,2′-bipyridyl, and 1,10-phenanthroline were tried out with no good results (Table 1, entries 5–7); neither did 1,5-cyclooctadiene nor the phosphorous ligand triphenylphosphine (Table 1, entries 4 and 8); although moderate yield of acetalization product **2** was obtained in the case for some oxygenous ligands (Table 1, entries 1–3), the results were still not better than that without ligands, though the introduction of oxygenous ligands absolutely depressed the formation of byproduct **4**. When the aliphatic amine triethylamine was added in this reaction system,

Table 1
Acetalization in the presence of different ligands[a]

Entry	Ligand	Dosage of ligand/mmol	Yield of **2**/%[b]
1	None	—	86.9
2	Ethyl acetoacetate	0.3	79.2
3	Acetylacetone	0.3	53.7
4	1,5-Cyclooctadiene	0.3	Trace
5	Pyridine	0.6	Trace
6	2,2′-Bipyridyl	0.3	Trace
7	1,10-Phenanthroline	0.3	Trace
8	Triphenylphosphine	0.6	Trace

[a] Reaction was run at 50 °C for 18 h with molar ratios of 4.94 and 3% of methanol and catalyst to the substrate methyl acrylate (5 mmol), respectively, under the pressure of O_2 0.7 MPa, and the pressure of the autoclave system 14 MPa.
[b] By GC.

acetal with a yield of about 5% was obtained as a byproduct, with the β-N-addition product being predominant.[26]

2.2. Acetalization under different catalysts in $scCO_2$

Different palladium sources were evaluated and the results are presented in Table 2. Among various palladium salts, $PdCl_2$ shows the best catalytic activity for this reaction. In the presence of 3 mol % $PdCl_2$, the conversion of substrate methyl acrylate reached 99.8% and product **2** was obtained in 95.3% yield. $Pd(OAc)_2$ and anhydrous $Pd(NO_3)_2$ also exhibited high catalytic activity while $PdBr_2$ and Pd/C showed lower or no activity.

2.3. The optimization of reaction condition for aerobic acetalization in $scCO_2$

Using $PdCl_2$ as catalyst, we further optimized the reaction conditions for acetalization, including pressure of oxygen, pressure of carbon dioxide, temperature, and reaction time (Table 3). The yield of **2** exhibits a sharp dependence on the pressure of oxygen, and a higher pressure of oxygen is advantageous for the reaction. When the pressure of oxygen was as low as 0.02 MPa, the reaction cannot occur (Table 3, entry 1). A dramatic elevation of the yield of **2** can be observed with increasing the pressure of oxygen from 0.5 to 0.7 MPa (Table 3, entries 3 and 4) and it reaches a maximum value of 99.3% at 1 MPa (Table 3, entry 6). The conversion increases with increasing pressure of carbon dioxide up to 14 MPa, but it decreases thereafter probably due to the dilution effects. The value of P_{CO_2}/P_{O_2} seems to influence the yield of **4** dramatically and the increasing O_2 concentration inhabits the formation of **4** (Table 3, entries 3–5). A reaction time of 12 h cannot permit complete conversion of the substrate (Table 3, entry 14), which requires another 3 h (Table 3, entry 15). Further prolongation of the reaction time leads to no better results (Table 3, entry 16). At lower temperatures (<40 °C) (Table 3, entries 16 and 17), the results were not good. Surprisingly, the yield of **4** was dramatically elevated with an increase of reaction temperature and reached 21.6% at 80 °C (Table 3, entries 18 and 19).

Table 2
Acetalization under different catalysts[a]

Entry	Catalyst/mmol	Conversion/%[b]	Yield of **2**/%[b]
1	$PdCl_2$	99.8	95.3
2	$Pd(OAc)_2$	89.2	78.4
3	$Pd(NO_3)_2$	87.1	73.4
4	$PdBr_2$	5.3	—
5	Pd/C	—	
6	None	—	

[a] Reaction was run at 50 °C for 18 h with mole ratios of 4.94 and 3% of methanol and catalyst to the substrate methyl acrylate (5 mmol), respectively, under the pressure of O_2 0.8 MPa, and the pressure of the autoclave system 14 MPa.
[b] By GC.

2.4. Aerobic acetalization in different solvents

Why did a 'ligand-free' palladium-catalyzed aerobic acetalization of methyl acrylate in $scCO_2$ occur so smoothly with molecular oxygen as the sole oxidant? We believe that on one hand, $scCO_2$, which has a property of both liquid and gas, is so excellent a solvent and dispersant of oxygen gas that makes it more than sufficient in the reaction system and on the other hand, $scCO_2$ may serve appropriate as a 'ligand'

Table 3
Acetalization of methyl acrylate and methanol in $scCO_2$[a]

Entry	P_{Co_2}/O_2/MPa	Time/h	Temperature/°C	Conversion/%	Yield/%[b]			Selectivity for **2**[c]
					2	**3**	**4**	
1	12/0.02	15	50	Trace	—	—	—	—
2	12/0.2	15	50	9.6	8	1	0	88.8
3	12/0.5	15	50	33.7	27.6	2.5	2.1	85.7
4	12/0.7	15	50	88.2	77.9	1.7	6.3	60.6
5	12/0.8	15	50	93.4	89.5	0.6	3.0	96.1
6	12/1.0	15	50	100	99.3	0.1	0.1	99.8
7	5/1.0	15	50	60.2	55.3	3.7	0	93.7
8	8/1.0	15	50	94.1	90.4	2.1	0.3	97.4
9	14/1.0	15	50	100	99.7	0.1	0.2	99.7
10	17/1.0	15	50	98.2	90.3	0.2	6.9	92.7
11	26/1.0	15	50	88.6	73.1	2.3	12.3	83.3
12	14/1.0	6	50	30.0	23.7	5.0	0.4	71.6
13	14/1.0	9	50	56.7	49.3	4.6	0.5	90.6
14	14/1.0	12	50	84.6	82.2	0.8	0.5	98.4
15	14/1.0	24	50	100	98.2	0.1	0.7	99.2
16	14/1.0	15	20	45.6	22.3	3.4	0	86.8
17	14/1.0	15	40	99.5	85.9	1.2	0.2	98.4
18	14/1.0	15	60	100	87.6	0.3	9.5	89.9
19	14/1.0	15	80	100	72.1	0.1	21.6	76.9

[a] Reaction conditions: $PdCl_2$ 0.15 mmol, methyl acrylate 5 mmol, and the molar ratio of methanol to methyl acrylate 4.94:1.
[b] By GC.
[c] Selectivity=[**2**/(**2**+**3**+**4**)]/100.

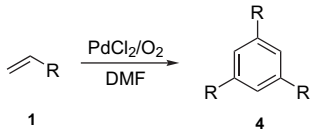
Table 4
Acetalization in different solvents[a]

Entry	Solvent	Dosage of solvent	Yield of **2**/%[b]
1	$scCO_2$	0.16 mL	98.2
2	Excess methanol	2 mL	43.4
3	Toluene	2 mL	57.8
4	CH_2Cl_2	2 mL	67.5
5	*n*-Hexane	2 mL	59.6
6	DMSO	2 mL	—
7[c]	DMF	2 mL	5.6

[a] Reaction conditions: $PdCl_2$ 0.15 mmol, methyl acrylate 5 mmol, pressure of O_2 1 MPa, 50 °C, and 24 h.
[b] By GC.
[c] Trimethyl benzene-1,3,5-tricarboxylate of 56.3% was detected.

as such, enough to stabilize the reduced palladium species but impuissant to inhibit either substrate binding or β-hydride elimination. An explanation can be further supported by the experiments in other organic solvents instead of $scCO_2$ (Table 4).

From Table 4, we can see that solvents with lower polarities seemed to favor this reaction more than polar ones (Table 4, entries 2–5). Solvents with a not so appropriate polar coordinating property such as DMSO inhibited this reaction completely. When using DMF as solvent, 56.3% of cyclotrimerization product **4** was gained. This is very interesting in comparison with that in $scCO_2$, so we further explored the cyclotrimerization of olefins with electron-withdrawing groups in the $PdCl_2/O_2$/DMF catalytic system. We found that in the absence of methanol in the $PdCl_2/O_2$/DMF system, the regioselective cyclotrimerization of both alkyl and aryl olefins with electron-withdrawing groups can occur smoothly, as previously disclosed (Scheme 3).[27]



Scheme 3.

2.5. The optimization of reaction condition for aerobic cyclotrimerization in $scCO_2$

Enlightened by the result presented in entry 19 of Table 3, we further explored the cyclotrimerization of methyl acrylate in a $PdCl_2/CH_3OH/O_2/scCO_2$ system at higher temperatures, expecting an optimized condition with the benzene derivatives **4** as major product.

As is shown in the results presented in Table 5, higher temperature favors the cyclotrimerization of methyl acrylate. Cyclotrimerization of methyl acrylate is sensitive to the concentration of molecular oxygen in $scCO_2$, which means it can neither be too high nor too low. There seemed to be a contradiction between higher reaction conversion and good selectivity to **4**. It could be concluded that lower P_{CO_2}/P_{O_2} induced higher reaction conversions with a relatively lower selectivity to **4** (Table 5, entries 1–3), while higher P_{CO_2}/P_{O_2} favored the formation of **4**, but the reaction conversion at the same time is moderate (Table 5, entries 6 and 7). Too high a pressure of carbon dioxide led to lower conversion due to its dilution effect (Table 5, entry 8). The time required for the completion of the reaction was 24 h and with an extended time period, no obvious elevation in yield is observed (Table 5, entries 9 and 10).

In order to inhabit the formation of **2**, we avoided the addition of CH_3OH and resulted in a very low conversion and trace of **4**. Because of the poor solubility of $PdCl_2$ in $scCO_2$ without methanol, we turned to other co-solvents, including 1,5-cyclooctodiene, acetone, anhydrous ethanol, distilled water, 1,4-dioxane, PEG-400, and PEG-1200, but no good results were gained.

2.6. Reactions of different terminal olefins under two typical conditions in $scCO_2$

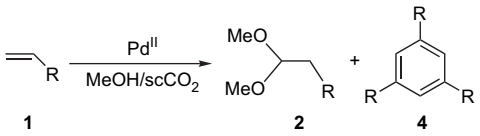
In the evaluation of other olefin substrates, each one was run under two conditions, conditions A and B, as is shown in Table 6. Terminal olefins with electron-withdrawing groups (EWG), e.g., methyl acrylate, ethyl acrylate, *n*-butyl acrylate, and methyl vinyl ketone are particularly effective under both conditions to give their acetals and 1,3,5-trisubstituted

Table 5
Cyclotrimerization of methyl acrylate in $PdCl_2/O_2/MeOH/scCO_2$ system[a]

Entry	P_{Co_2}/O_2/MPa	Time/h	Temperature/°C	Conversion/%	Yield/%[b]		Selectivity for **4**[c]
					2	**4**	
1	17/1.0	15	100	97.2	58.1	26.8	31.6
2	17/1.0	15	120	96.8	47.6	35.4	42.6
3	17/1.0	15	140	98.2	44.3	33.7	43.2
4	17/0.9	15	120	95.2	22.0	45.7	67.5
5	17/0.8	15	120	96.1	17.7	50.1	73.9
6	17/0.7	15	120	92.5	13.9	55.8	80.0
7	20/0.7	15	120	89.3	8.4	58.8	87.5
8	22/0.7	15	120	74.3	11.3	32.5	74.2
9	20/0.7	24	120	89.2	9.6	64.2	87.0
10	20/0.7	32	120	83.6	10.0	69.3	87.4

[a] Reaction conditions: $PdCl_2$ 0.25 mmol, methyl acrylate 5 mmol, and the molar ratio of methanol to methyl acrylate 2.47:1.
[b] By GC.
[c] Selectivity=[**2**/(**2**+**3**+**4**)]/100.

Table 6
Reactions of different olefins in $PdCl_2/O_2$/MeOH/$scCO_2$ system[a]



Entry	Alkene	Condition	Conversion/%[b]	Yield of **2/4**/%[b]
1	Methyl acrylate	A	100	99.7 (**2a**)
		B	93.6	69.3 (**4a**)
2	Ethyl acrylate	A	98.0	96.4 (**2b**)
		B	85.2	57.3 (**4b**)
3	*n*-Butyl acrylate	A	87.1	83.2 (**2c**)
		B	44.6	32.8 (**4c**)
4	Methyl vinyl ketone	A	99.4	88.6 (**2d**)
		B	88.5	63.4 (**4d**)
5	Methyl methacrylate	A	—	—
6	Acrylonitrile	A	80.0	77.1 (**2e**)
7	Acrylic acid	A	—	—
8	Acrylamide	A	—	—
9	Styrene	A	86.4	12.4 (**2f**)
10	4-Chlorostyrene	A	91.2	Trace
11	Cyclohexene	A	95.1	32.4 (**2g**)

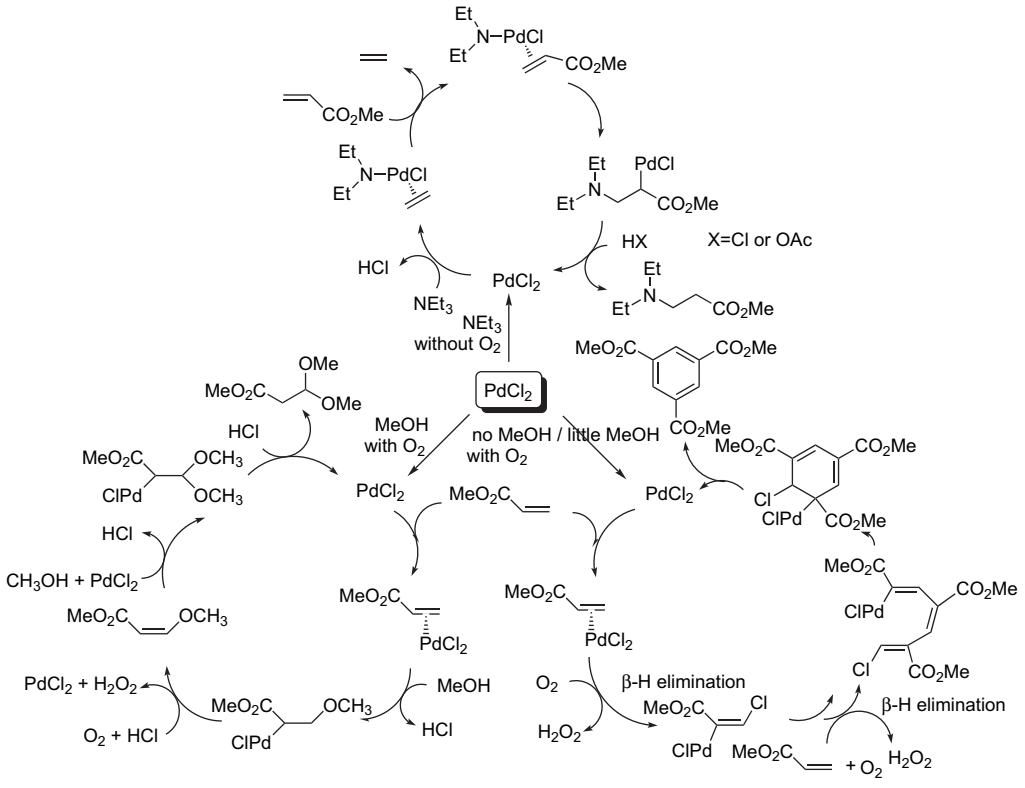
[a] Reaction was run under two conditions, respectively, condition A: $PdCl_2$ 0.15 mmol, substrate 5 mmol, methanol 1 mL, pressure of O_2 1.0 MPa, pressure of CO_2 14 MPa, 50 °C, and 15 h.; condition B: $PdCl_2$ 0.25 mmol, substrate 5 mmol, methanol 0.5 mL, pressure of O_2 0.7 MPa, pressure of CO_2 20 MPa, 120 °C, and 24 h.

[b] By GC–MS. (Condition A for yield of **2** and Condition B for yield of **4**.)

benzene derivatives (Table 6, entries 1–4). Acetalization of acrylonitrile also goes smoothly while acrylic acid, acrylamide, and the sterically encumbered methyl methacrylate gave no products (Table 6, entries 5–8). Although the conversion of styrene was fair to good, the yield of **2** was low, because most of styrene was transferred to hypnone and benzaldehyde. When 4-chlorostyrene was explored, the reaction was even more complicated than that of styrene and 4-chlorobenzoic acid (56%) was obtained as the main product. The acetalization of cyclohexene gave a mixture of its corresponding acetal and cyclohexanone (Table 6, entries 9–11). Aryl olefin phenyl acrylate was also explored and no corresponding products were gained under both conditions. Transesterification between phenyl acrylate and methanol occurred under both conditions and yielded mainly the corresponding products of methyl acrylate. This is in contrast with cyclotrimerization in DMF.[26]

2.7. Mechanism of palladium-catalyzed reactions of terminal olefins with electron-withdrawing groups under different reaction conditions

On the basis of the above results, three catalytic cycles are proposed, which represent reaction pathways of the terminal olefins with electron-withdrawing groups under different reaction conditions.[22,26,27] From Scheme 4, we can see that product control can be achieved through modifying reaction conditions.



Scheme 4.

When molecular oxygen, was present in the reaction system, aerobic oxidation of terminal olefins goes smoothly. With enough MeOH and sufficient oxygen, acetalization preponderated over cyclotrimerization, while with no MeOH or little MeOH (as co-solvent in $scCO_2$) and an appropriate pressure of O_2, cyclotrimerization of terminal olefins became the dominated reaction; when the oxygen is absent and triethylamine was added into the reaction system, palladium-catalyzed C–N bond formation occurs to produce β-amino acid derivatives as the sole product.

3. Experimental section for aerobic reaction of terminal olefins with electron-withdrawing groups in $scCO_2$

3.1. Typical experimental procedure for the synthesis of acetals

Catalyst $PdCl_2$ (0.15 mmol, 3 mol %), MeOH (1 mL, 24.7 mmol) and methyl acrylate (5 mmol) were added into a 25 mL autoclave in sequence. O_2 and CO_2 were pumped into the autoclave using a cooling pump to reach the desired pressure. Then the autoclave was put into an oil bath under magnetic stirring for the desired reaction time. After the reaction, the autoclave was allowed to cool to −30 °C. CO_2 and the surplus O_2 were then vented and the residue was extracted with *n*-hexane. The extract was filtrated and condensed under reduced pressure. The product was analyzed using GC (quantitative) and GC–MS, ^{1}H NMR, and IR analyses (identification of products: some acetals were purified by preparative TLC on silica gel using light petroleum ether/ethyl acetate as eluent before ^{1}H NMR and IR analyses).

Compound ***2a***. IR (neat, cm^{-1}): ν=2948, 2840 (CH_3, CH_2, CH), 1740 (COO), 1378, 1444 (CH_3O), 1069, 1122, 1176 (C–O–C). MS (EI): *m*/*z*=147 (M^+), 133, 117, 101, 85, 75, 59, 47, 31. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=2.62 (d, 2H, *J*=2.0 Hz, CH_2), 3.33 (s, 6H, OCH_3), 3.65 (s, 3H, OCH_3), 4.80 (s, 1H, CH).

Compound ***2b***. IR (neat, cm^{-1}): ν=2985, 2944, 2837 (CH_3, CH_2, CH); 1738 (COO), 1378, 1455 cm^{-1} (CH_3, CH_2), 1069, 1123, 1176 cm^{-1} (C–O–C). MS (EI): *m*/*z*=161 (M^+), 147, 131, 117, 103, 89, 75, 61, 43, 29; ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=1.25(t, 3H, *J*=3.2 Hz, OCH_2CH_3), 2.63 (d, 2H, *J*=6.0 Hz, CH_2CH), 3.35 (s, 6H, OCH_3), 4.15 (q, 2H, *J*=3.6 Hz, OCH_2CH_3), 4.82 (t, 1H, *J*=6.0 Hz, CH_2CH).

Compound ***2c***. IR (neat, cm^{-1}): ν=2961, 2876, 2838 (CH_3, CH_2, CH), 1737 (COO), 1461, 1402 (CH_3, CH_2), 1070, 1122, 1192 (C–O–C), 740 ($CH_2CH_2CH_2$). MS (EI): *m*/*z*=189 (M^+), 159, 117, 103, 85, 75, 57, 41, 29. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=0.92 (t, 3H, *J*=2.4 Hz, $OCH_2CH_2CH_2CH_3$), 1.34–1.38 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.57–1.64 (m, 2H, $OCH_2CH_2CH_2CH_3$), 2.63 (d, 2H, *J*=6.0 Hz, CH_2CH), 3.34 (6H, s, OCH_3), 4.09 (t, 2H, *J*=3.2 Hz, $OCH_2CH_2CH_2CH_3$), 4.82 (t, 1H, *J*=6.0 Hz, CH_2CH).

Compound ***2d***. IR (neat, cm^{-1}): ν=2937, 2839 (CH_3, CH_2, CH), 1718 (C=O), 1446 (CH_3O), 1362 (CH_3CO), 1080, 1122, 1167, 1192 (C–O–C). MS (EI): *m*/*z*=132 (M^+), 117, 101, 85, 75, 59, 31. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=2.16 (s, 3H, CH_3CO), 2.72 (d, 2H, *J*=5.2 Hz, $CHCH_2COCH_3$), 3.34 (s, 6H, OCH_3), 4.77 (t, 1H, *J*=5.6 Hz, $CHCH_2COCH_3$).

Compound ***2e***. IR (neat, cm^{-1}): ν=2936, 2845 (CH_3, CH_2, CH), 2255 (C≡N), 1455, 1417 (CH_3, CH_2), 1075, 1122 (C–O–C). MS (EI): *m*/*z*=114 (M^+), 84, 75, 56. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=2.65 (d, 2H, *J*=5.6 Hz, CH_2CH), 3.39 (s, 6H, OCH_3), 4.66 (t, 1H, *J*=5.6 Hz, CH_2CH).

4-Chlorobenzoic acid. IR (neat, cm^{-1}): ν=3179 (O–H), 1683 (C=O), 1592, 1423, 1399 (C_6H_4), 759 (C–Cl). MS (EI): *m*/*z*=156 (M^+), 139, 111, 75, 50, 38. ^{1}H NMR (400 MHz, TMS, DMSO-d_6): δ=7.9295 (d, 2H, *J*=8.2 Hz, C_2, C_6), 7.5615 (d, 2H, *J*=8.2 Hz, C_3, C_5).

3.2. Typical experimental procedure for the synthesis of polysubstituted aromatic compounds

Catalyst $PdCl_2$ (0.15 mmol, 3 mol %), MeOH (0.5 mL, 12.35 mmol), and methyl acrylate (5 mmol) were added into a 25 mL autoclave in sequence. O_2 was pumped into the autoclave using a cooling pump to reach the desired pressure. Then the autoclave was put into an oil bath under magnetic stirring for the desired reaction time. After the reaction, the autoclave was allowed to cool to −30 °C. The surplus O_2 was then vented and the residue was extracted with *n*-hexane. The extract was filtrated and condensed under reduced pressure. The product was analyzed using GC (quantitative) and GC–MS, ^{1}H NMR, and IR analyses (identification of products: the benzene derivatives were purified by preparative TLC on silica gel using light petroleum ether/ethyl acetate as eluent before ^{1}H NMR and IR analyses).

Compound ***4a***. IR (neat, cm^{-1}): ν=3091, 3007 (C_6H_3), 2956, 2847 (CH_3), 1731 (C=O), 1254 (C–O–C). MS (EI): *m*/*z*=252 (M^+), 221, 193, 147, 75, 29. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=3.953 (s, 9H, CH_3), 8.835 (s, 3H, C_6H_3).

Compound ***4b***. IR (neat, cm^{-1}): ν=3095 (C_6H_3), 2993 (CH_3), 1722 (C=O), 1240, 1024 (C–O–C). MS (EI): *m*/*z*=294 (M^+), 266, 249, 221, 193, 73, 29. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=1.412 (t, 9H, *J*=7.2 Hz, CH_3), 4.421 (q, 6H, *J*=7.2 Hz, CH_2), 8.830 (s, 3H, C_6H_3).

Compound ***4c***. IR (neat, cm^{-1}): ν=3093 (C_6H_3), 2853 (CH_3), 1728 (C=O), 1242, 1028 (C–O–C). MS (EI): *m*/*z*=378 (M^+), 323, 305, 267, 249, 211, 193, 165, 120, 56, 41, 29. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=0.971 (t, 9H, *J*=7.2 Hz, CH_3), 1.423–1.516 (m, 6H, CH_2), 1.728–1.799 (m, 6H, CH_2), 4.360 (t, 6H, *J*=6.8 Hz, CH_2), 8.817 (s, 3H, C_6H_3).

Compound ***4d***. IR (neat, cm^{-1}): ν=3064 (C_6H_3), 2922, 2852 (CH_3), 1688 (C=O), 1225, 1096 (C–O–C). MS (EI): *m*/*z*=204 (M^+), 189, 161, 119, 91, 75, 32, 28. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ=2.694 (s, 9H, CH_3), 8.684 (s, 3H, C_6H_3).

4. Conclusions

In summary, on the basis of our group's work on the aerobic acetalization of terminal olefins with electron-withdrawing groups in $scCO_2$ using $CuCl_2$ and PS-BQ as a mediated *sec*-oxidants, we for the first time, to our knowledge, disclose

a palladium-catalyzed acetalization of terminal alkenes in $scCO_2$ using molecular oxygen as the sole oxidant. We also found that product control of palladium-catalyzed aerobic oxidation of terminal olefins with electron-withdrawing groups can be achieved through modifying reaction conditions and to yield acetals and benzene derivatives differently. When the oxygen is absent and triethylamine was added into the reaction system, palladium-catalyzed C–N bond formation occurs to produce β-amino acid derivatives as the sole product.

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