Direct Conversion of Glycerol into Formic Acid via Water Stable Pd(II) Catalyzed Oxidative Carbon-Carbon Bond Cleavage

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Abstract

Using our tridentate NHC-amidate-alkoxide Pd(II) complex, we developed a catalytic method for oxidative C-C bond cleavage of glycerol. The glycerol was degraded exclusively to formic acid and CO_2. Two possible degradation pathways were proposed through ^{13}C labeled studies.

Keywords

NHC amidate ligand; Palladium catalyst; Degradation of glycerol; Formic acid; Oxidative catalysis

Glycerol, also called glycerin, is a main by-product of biodiesel production and traditional soap manufacturing processes.[1] A rapid increase in biomass conversion has produced a massive stockpile of glycerol, and its transformation to value-added chemicals has been in great demand. A number of methods have been reported to provide $C_2 \sim C_3$ chemical products such as glyceraldehyde, glyceric acid, hydroxypyruvic acid, tartronic acid, glycolic acid, and oxalic acid.[2] Because these $C_2 \sim C_3$ products have been short of practical use, the formation of C_1 products such as formic acid has attracted much attention for future energy applications.[3] There are few examples have been introduced through hydrothermal oxidation, heterogeneous catalysts, and electrocatalytic oxidation.[4]

One noteworthy application of formic acid is the DFAFC (direct formic acid fuel cell), which has been of increasing popularity compared with hydrogen and methanol based fuel cells because of their ease of refuelling, efficiency, and safety. As an emerging technology, DFAFC is currently being tested by major producers of portable electronics in phones, laptops, and computers.[5] In an effort to find a potential source of formic acid, we embarked on the development of new oxidative carbon-carbon bond cleavage methods of glycerol mainly because the previously reported conditions failed to degrade glycerol as shown in scheme 1.

Representative examples included Isbell's alkaline hydrogen peroxide and our hydrogen peroxide/ammonia water conditions.[6] Under these conditions, various aldoses were

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Supplementary Material
Supplementary material is available in a PDF format.

oxidatively transformed to formic acid whereas glycerol (**1**) barely reacted. In addition, these procedures converted ketoses to both formic and glycolic acids (**2**), while glycolic acid was resistant to further degradation. These shortcomings prompted us to undertake studies on oxidative degradation using organometallic catalysts.

Recently, we reported that NHC-palladium complexes including **4** were highly stable and still reactive enough to facilitate C-H activation of relatively unreactive hydrocarbons.[7] Their high stability in nucleophilic solvents such as water and alcohol could allow for conditions amenable to oxidative carbon-carbon bond cleavage of glycerol. These processes could provide $C_1 \sim C_2$ products encompassing carbon dioxide, formic acid (**3**), and glycolic acid (**2**). Using known palladium catalysts and our Pd(II) catalyst **4**, we evaluated the feasibility of oxidative degradation of glycerol (table 1).

Regarding oxidative degradation by hydrogen peroxide, commercially available Pd complexes including $PdCl_2$ and $Pd(OAc)_2$ didn't offer meaningful improvement over KOH or NH_4OH (entries 1 and 2).[6] However, NHC-Pd complex **4** exhibited significant consumption of glycerol at room temperature to furnish formic acid as the major product (entry 3). We also noticed that the ratio of formic acid to glycolic acid produced was much higher than that of the reaction with $Pd(OAc)_2$ despite its low yield. These results might indicate our catalyst degraded both glycerol and glycolic acid unlike other Pd salts or basic conditions. We screened other oxidants such as *tert*-butyl peroxide, oxone, $K_2S_2O_8$, and molecular oxygen, most of which were ineffective (entries 4 ~ 7). Similarly to hydrogen peroxide, oxone provided a higher ratio of formic acid to glycolic acid compared to the $Pd(OAc)_2$ case (entries 2 and 5).

In the catalytic processes using **4**, one equivalent of glycerol can produce either three equivalents of formic acid or one equivalent of formic acid and glycolic acid each. To understand how many equivalents of formic acid can be produced from glycerol, it was necessary to understand degradation pathways. In this context, we carried out the oxidative cleavage reaction using 1,3-^{13}C-labeled glycerol and 2-^{13}C-labeled glycerol in the presence of NHC-Pd complex **4** and hydrogen peroxide at 60 °C for 6 hours, under which conditions we tried to consume most of glycerol (*cf.* table 2, entry B).

As shown in figure 1, the reaction of 1,3-^{13}C-labeled glycerol (**5**) afforded both ^{13}C-labeled formic acid (**6**) and unlabeled formic acid (**3**) in a 2 to 1 ratio, as well as a small amount of ^{13}C-labeled glycolic acid on the β-carbon (**7**). In the case of 2-^{13}C-labeled glycerol (**8**), a 1 to 2.5 ratio of ^{13}C-labeled formic acid (**6**) to unlabeled formic acid (**3**), as well as 1-^{13}C-labeled glycolic acid (**9**) were observed. In addition, ^{13}C-NMR analysis further confirmed the assignment by [13]C-^{12}C coupling for ^{13}C-labeled glycolic acid (**7**) (δ= 60.6 Hz at 176.0 ppm). Therefore, these results indicated that the formic acid produced contained both the secondary and primary carbons of glycerol. On the other hand, the carbonyl carbon of glycolic acid would stem only from the secondary carbon of glycerol while the carbinol carbon would originate from the primary carbons.

Since the observed products didn't satisfy the mass balance, we suspected that we lost some carbons in the form of carbon dioxide, and examined such possibility (scheme 3). In the presence of NHC-Pd complex **4**, both acids gradually disappeared over time to form carbon dioxide. For example, glycolic acid led to formic acid in 10% yield after 3 hours while formic acid gave no detectable products except carbon dioxide. In addition, unlabeled formic acid (**3**), but no ^{13}C labeled formic acid (**6**) was detected when (1-^{13}C)glycolic acid (**9**) was reacted with hydrogen peroxide. It was evident that 2-^{12}C and 1-^{13}C in glycolic acid were incorporated into formic acid and $^{13}CO_2$, respectively. These results were consistent with the aforementioned glycol oxidation patterns.

These labeled experiments suggested two possible degradation pathways. If formic acid was derived equally from all three carbons in gylcerol, the ratio of ^{13}C-labeled formic acid (**6**) and unlabeled formic acid (**3**) should be 2 to 1 in figure 1 (A), and 1 to 2 in figure 1 (B). Even though the observed ratios were close to the theoretical ones, these ratios were still different from the expected ones by 10–25%. Thus, we assumed a major pathway would oxidize all three carbons to formic acid. Since small amounts of glycolic acid was detected, we considered that another pathway through glycolic acid was active concomitantly. In fact, both C-1 and C-3 in glycerol could be converted to formic acid whereas the C-2 would fail to give formic acid and instead furnish CO_2 as aforementioned. As a consequence, one could expect more ^{13}C-labeled formic acid than ^{12}C-formic acid in figure 1 (A) and more ^{12}C-formic acid than ^{13}C-labeled one in figure 1 (B), respectively.

Based on these results and previously reported studies, two possible degradation pathways can be proposed as in scheme 4.[3,9,10,11] One mechanistic pathway would form three equivalents of formic acid from each glycerol molecule while another mechanism would lead to two equivalents of formic acid and one part of CO_2 through the glycolic acid intermediate. As the incipient product, Pd-glycerol adducts could be generated and oxidized to aldehyde **10**, which would undergo rapid C-C bond cleavage to release formic acid and another aldedyde **11**. Further oxidative cleavage of **11** could afford the second equivalent of formic acid and formaldehyde, which eventually would generate the third equivalent of formic acid. Meanwhile, the first oxidative C-C bond cleavage product **11** can be oxidized to yield glycolic acid **2**, which subsequently can be degraded to formaldehyde and CO_2, ultimately furnishing one equivalent of formic acid. In summary, dual mechanistic pathways would contribute to our catalytic processes.

In the reaction mixture, it was unable to detect any aldehyde (**10**, **11**, or formaldehyde). This could indicate that aldehyde compound was not completely released from Pd complex but underwent C-C bond cleavage to form formic acid and another aldehyde. Even though aldehyde was released from Pd, it could be oxidized quickly by the oxidant to form acid (**2** or formic acid). Therefore the following catalytic cycle could be proposed (scheme 5). Glycerol adduct **12** could be oxidized to form **13**. Subsequently, one equivalent of H_2O_2 could generate one equivalent of formic acid and **14**. Following third oxidation, formaldehyde adduct **15** could be formed while releasing another equivalent of formic acid. The last formic acid could be produced from this formaldehyde.

To seek optimal conditions, we investigated various factors including amounts of hydrogen peroxide, reaction temperatures, and reaction times. As depicted in figure 2 (A), the formation of formic acid increased upon higher concentration of hydrogen peroxide. When we raised reaction temperatures gradually (25 to 60 °C), the amount of formic acid was increased until 40 °C, then decreased at higher temperatures (figure 2 (B)) presumably due to the overoxidation to carbon dioxide. Additionally, longer reaction times were not sufficient to enhance the formation of formic acid (figure 2 (C)). In addition, when the amount of Pd (**4**) was increased to 10 or 15% from 5%, overall yield of formic acid as well as consumption of glycerol dropped due to the degradation of formic acid and hydrogen peroxide by the catalyst.

Because excess H_2O_2 and high reaction temperatures caused the degradation of formic acid to CO_2, we decided to employ slow addition of hydrogen peroxide at mild temperatures, and evaluated the time and temperature dependence on the yields of both formic and glycolic acids using ^{1}H-NMR techniques (figure 3 and table 2). As shown in figure 3 and table 2 (entries B and C), the formation of formic and glycolic acids was increased slightly by the slow addition of hydrogen peroxide. Although glycerol was completely consumed under these conditions, glycolic acid still remained. In efforts to avert glycolic acid and maximize

the amount of formic acid, hydrogen peroxide was slowly added at 0 °C for 3 hours and stirred at room temperature over 8 hours (table 2, entry D), glycerol was not completely consumed despite higher yields of formic and glycolic acids. Finally, when we added hydrogen peroxide slowly at 0 °C for 3 hours and additional H_2O_2 at 60 °C for 3 hours, we observed exclusively formic acid in 61% yield (table 2, entry E).

In conclusion, we successfully demonstrated a method to produce formic acid as the sole product via the oxidative NHC-Pd catalyzed carbon-carbon bond cleavage of glycerol with hydrogen peroxide as an oxidizing agent. The direct conversion of glycerol into formic acid was facilitated under mild conditions. As we proposed, dual cleavage pathways were likely to be active. Based on these mechanisms, we sought optimal conditions to avoid the glycolic acid intermediate and over-oxidation of formic acid to carbon dioxide. Our catalytic conditions can be useful for the degradation of carbohydrates and biomass including starch and grass, which will be reported in due course.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

References and notes

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12. *Representative reaction*: A mixture of glycerol (10 mg, 0.1 mmol) and catalyst 4 (5 mole%) in 0.2 mL of water was placed in a rubber stoppered vial. To this mixture, 0.3 mL of 30% H_2O_2 was added for 3 hours at 0 °C by using a syringe pump. After complete addition, the reaction mixture was heated to 60 °C, then 0.2 mL of 30% H_2O_2 was added for 3 hours. Wet 1D NMR of the crude reaction mixture showed the complete conversion of glycerol to give 0.196 mmol of formic acid. Wet 1D: δ = 8.1 (s, 1H).
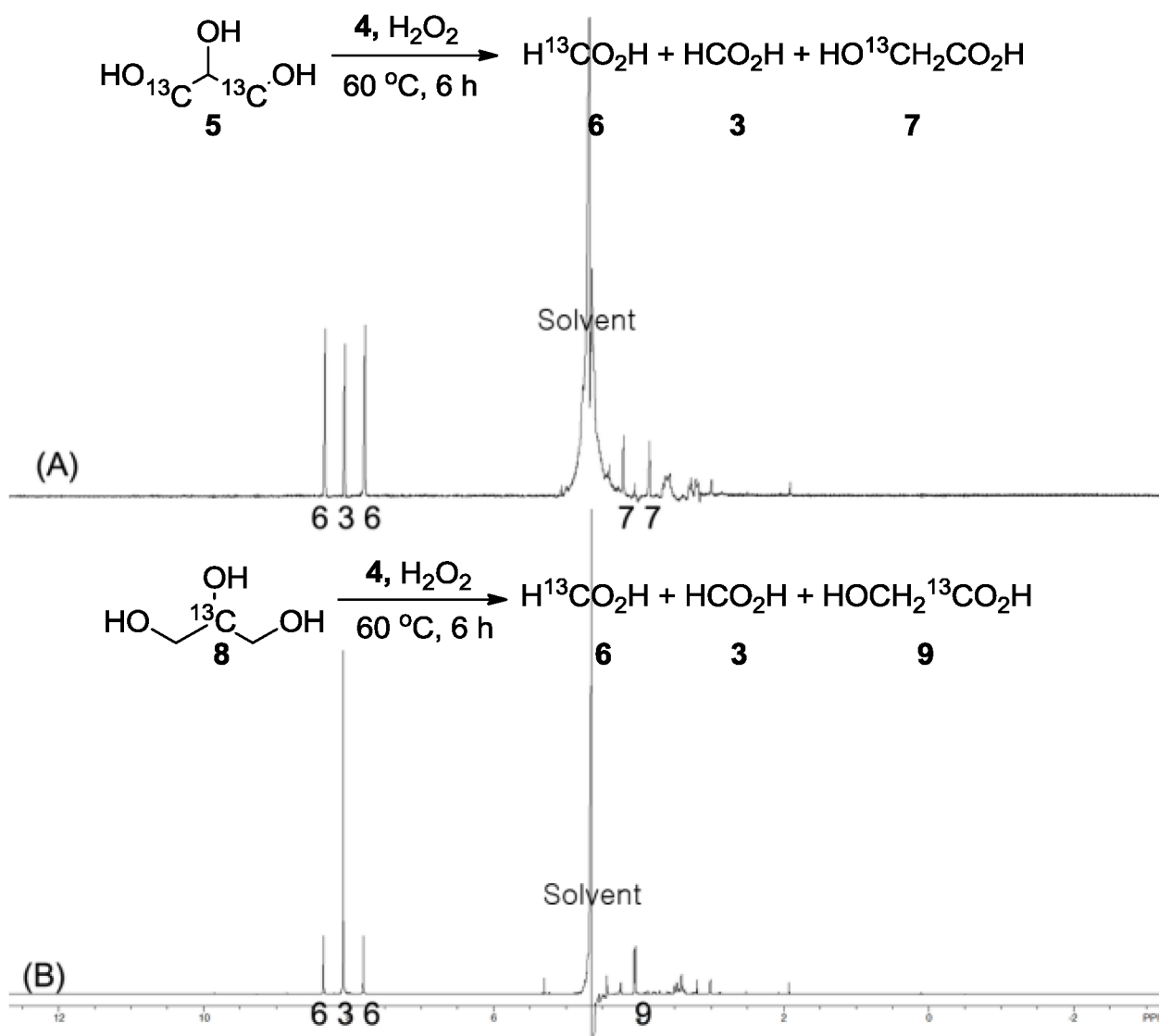
Figure 1.
^{1}H-NMR spectra for the oxidative degradation reactions of 1,3-^{13}C-glycerol (A) and 2-^{13}C-glycerol (B).
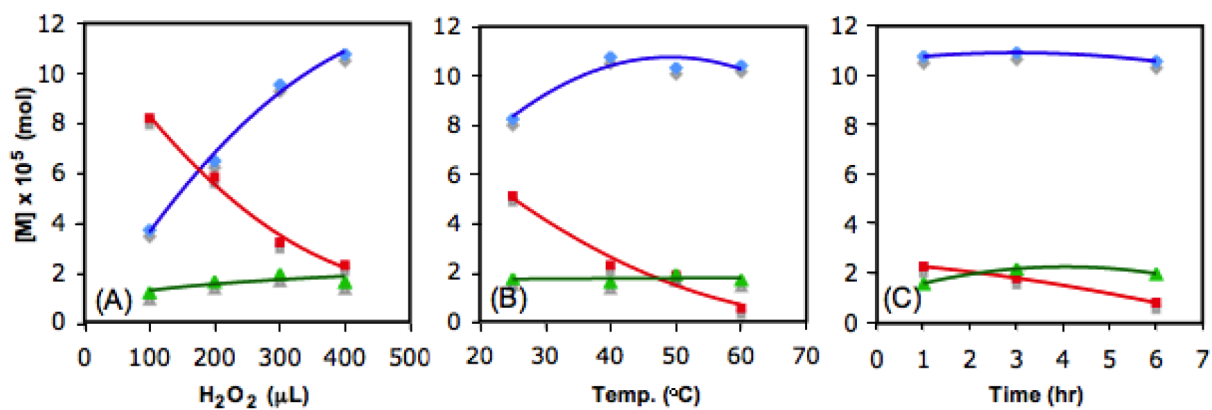
Figure 2.
Concentration changes *vs.* volume of H_2O_2 (A), reaction temperature (B), and time (C) for the oxidative degradation of glycerol: glycerol (red square), formic acid (blue diamond), and glycolic acid (green triangle).
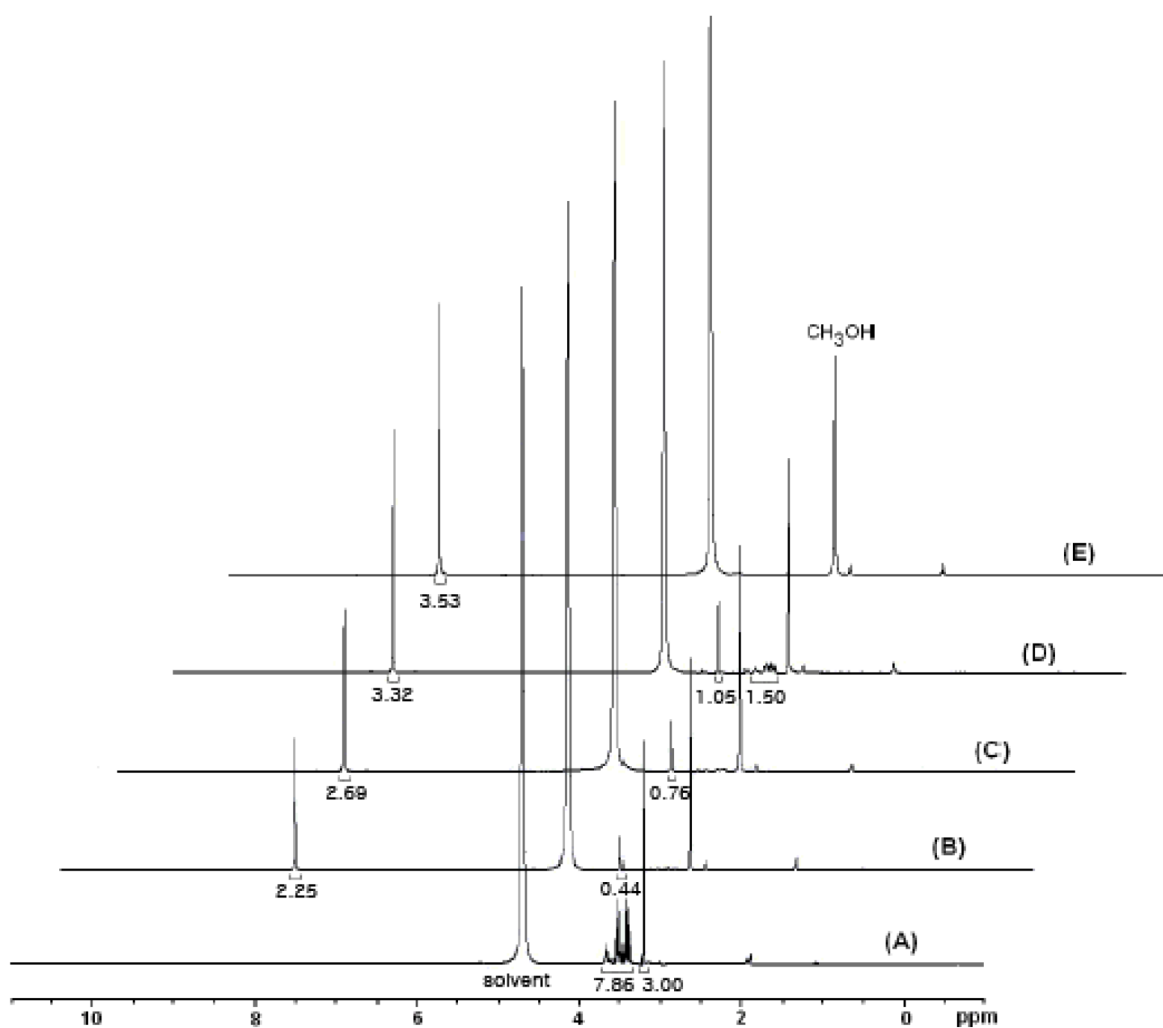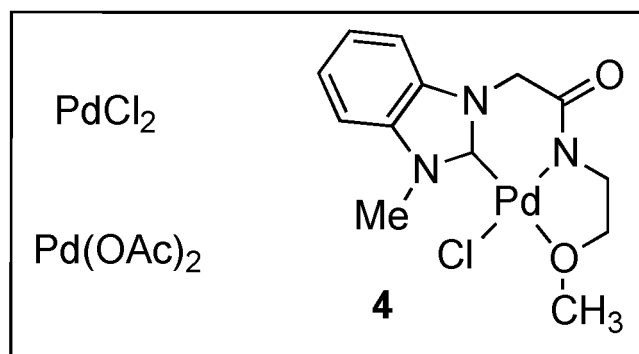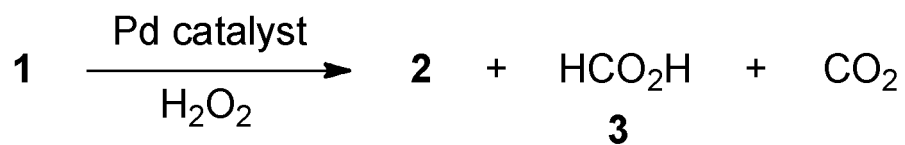
Figure 3.
^{1}H-NMR study for the degradation pathway of glycerol: (A) starting glycerol, (B) 0.4 mL
H_2O_2 for 6 hours at 60 °C, (C) 6 hour slow addition of 0.4 mL H_2O_2 at 60 °C, (D) 3 hour
slow addition of 0.4 mL H_2O_2 at 0 °C and 8 hour stirring at room temperature, (E) 3 hour
slow addition of 0.3 mL H_2O_2 at 0 °C and 3 hour slow addition of 0.2 mL H_2O_2 at 60 °C.
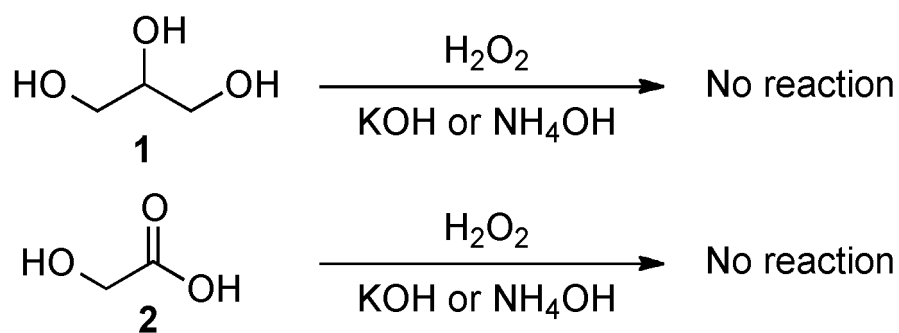
Scheme 1.
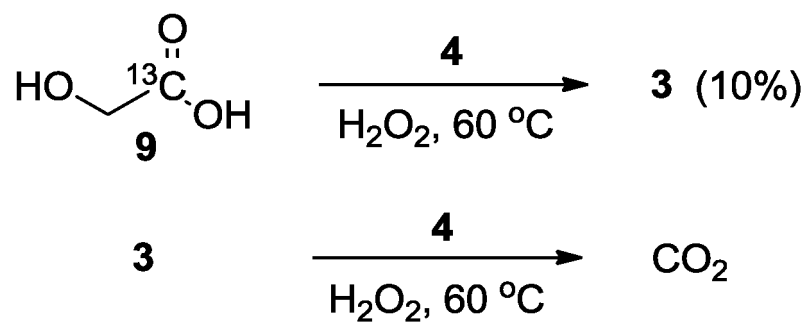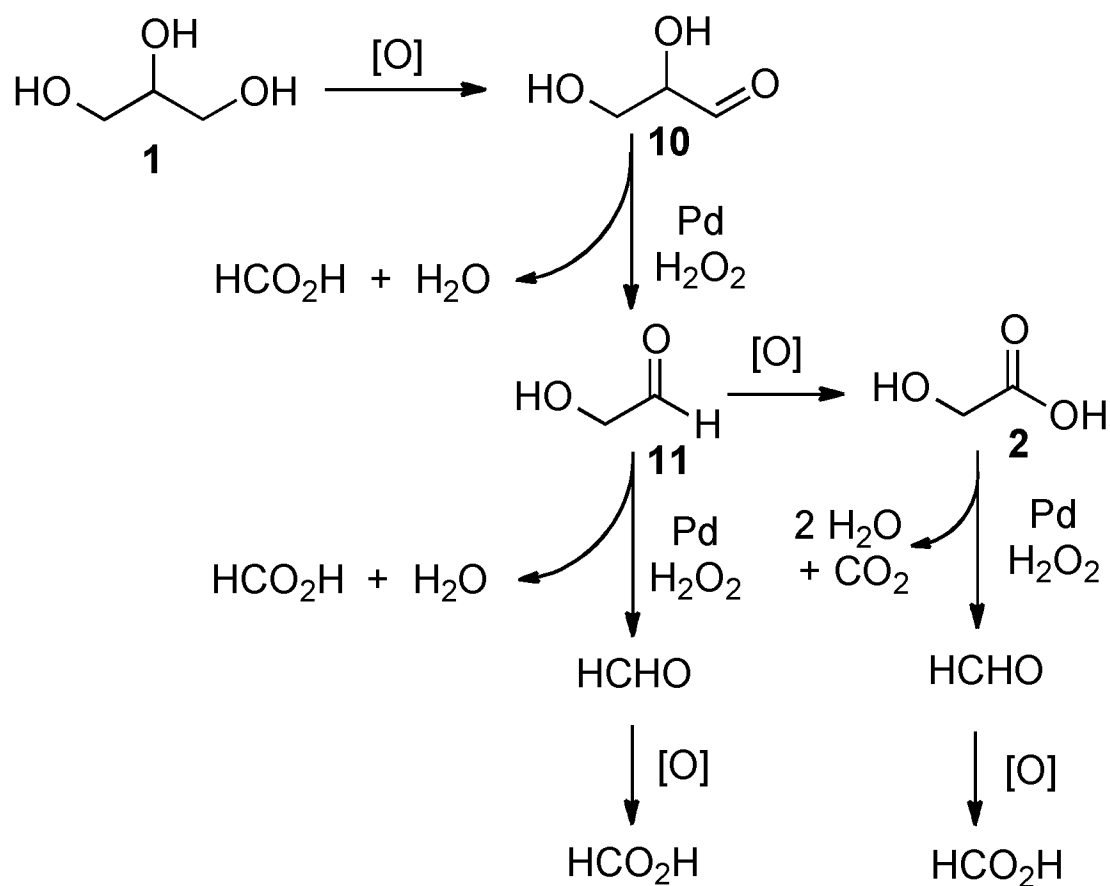Limitations of known conditions on glycerol degradation.

$$1 \xrightarrow[\text{H}_2\text{O}_2]{\text{Pd catalyst}} 2 \quad + \quad \text{HCO}_2\text{H} \quad + \quad \text{CO}_2$$
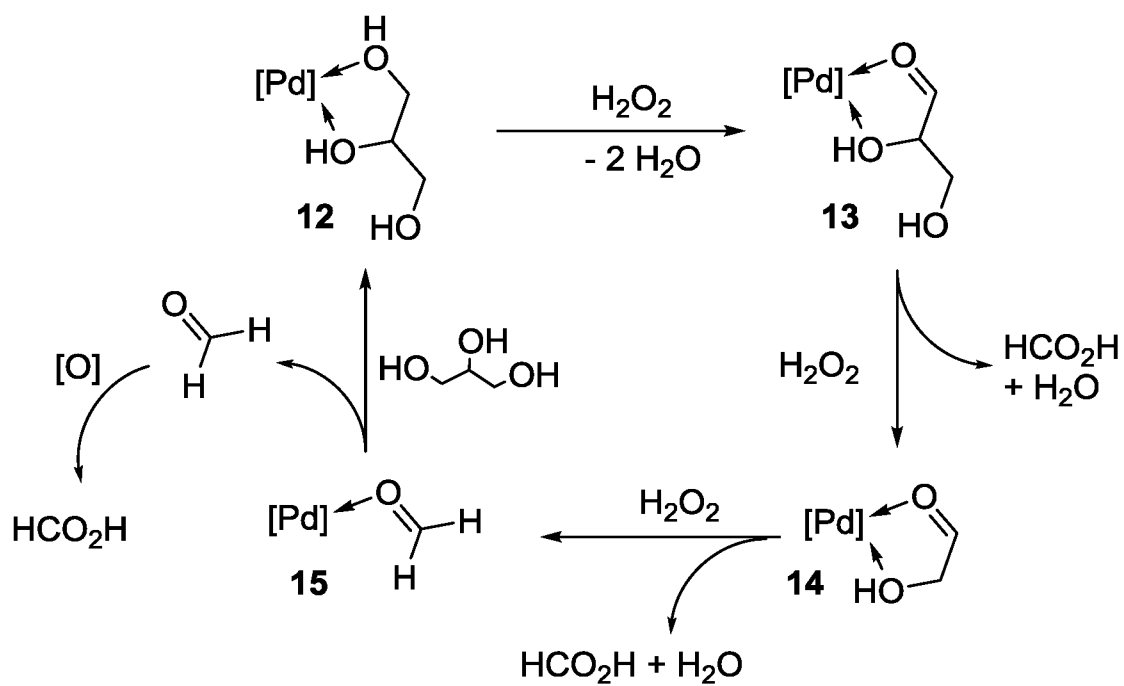
3

PdCl$_2$

Pd(OAc)$_2$

4

Scheme 2.
Glycerol degradation in the presence of Pd(II) catalysts.

Scheme 3.
Potential degradation of glycolic acid and formic acid in the presence of NHC-Pd(II) catalyst **4**.

Scheme 4.
Potential oxidative degradation pathways of glycerol.

Scheme 5.
Catalyic pathway for the formation of formic acid

Table 1

Catalytic oxidative carbon-carbon bond cleavage of glycerol with various oxidizing agents in the presence of Pd catalysts at room temperature.[a]

entry	catalyst	oxidant	yield (%)[d]	2/3 ($\times 10^{-5}$ mol)[e]
1	PdCl$_2$	H$_2$O$_2$	trace	trace/trace
2	Pd(OAc)$_2$	H$_2$O$_2$	6	0.16/0.20
3	**4**	H$_2$O$_2$	41	1.50/8.05
4	**4**	t-BuO$_2$H	trace	-/-
5[b]	**4**	Oxone	10	0.39/1.52
6	**4**	K$_2$S$_2$O$_8$	-	-/-
7[c]	**4**	O$_2$	-	-/-

[a]All reactions were performed with glycerol (10 mg, 10.8×10^{-5} mol), Pd catalyst (5 mol%). Entry 1–3: 30% H$_2$O$_2$ (0.4 mL) in H$_2$O (0.1 mL) was added. In the entry 4, tBuOOH (70% in H$_2$O, 0.4 mL) was used. Entries 5~6: 10.8×10^{-5} mol of oxidant (entry 5: oxone, entry 6: K$_2$S$_2$O$_8$) in 0.3 mL of H$_2$O was used. Entry 7: O$_2$ was bubbled in 0.3 mL of H$_2$O solution. All reactions were performed at room temperature for 6 hours..

[b]Run in H$_2$O (0.4 mL).

[c]Continuous flow with O$_2$.

[d]Conversion yield of glycerol.

[e]The amount of each product was determined by ^{1}H NMR spectral analysis using MeOH as the internal standard.[8]

Table 2

Yields of reactions in the figure 3

entry	glycerol (%)[a]	glycolic acid (%)[b]	formic acid (%)[c]
B	trace	11	39
C	trace	20	50
D	19	28	57
E	0	0	61

[a]Remaining glycerol/added glycerol × 100.

[b]Moles of glycolic acid/moles of added glycerol × 100.

[c](Moles of formic acid/moles of glycerol × 100)/3, assuming one mole of glycerol produced 3 mole of formic acid. Moles of each product were calculated by using methanol as an internal NMR reference.