Direct hydroxylation of methyl benzoate to methyl salicylate by using new Pd membrane reactor

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The direct hydroxylation of methyl benzoate was carried out using a newly developed Pd membrane reactor in which the active oxygen species is formed on the surface of Pd by the reaction between oxygen gas and the active hydrogen atoms that permeate through the Pd membrane from the opposite side. By using this Pd membrane reactor system, methyl salicylate showed a 4.7% yield at 423 K. The reaction mechanism was clarified based on the distribution of by-products.

KEY WORDS: Pd membrane; methyl benzoate; methyl salicylate; direct hydroxylation; active oxygen.

1. Introduction

Significant research effort has been expended on direct hydroxylation of aromatic compounds to manufacture the fine chemicals, such as conversion of benzene to phenol. Direct hydroxylation of benzene using oxygen gas, however, has not been achieved at satisfactory conversion and selectivity. The problem is difficulty in properly forming the active oxygen species for the direct hydroxylation and in suppressing the successive oxidation due to the higher reactivity of phenol than that of benzene.

To overcome these two difficulties, N_2O has been used as the oxidizing reagent for last two decades [1–4]. N_2O is decomposed on the catalyst surface, and can supply the active oxygen species, such as hydroxyl radical or "α-oxygen" [3,5,6]. Ribera *et al.* [7] reported phenol selectivity of 99% at a benzene conversion of 27% for the N_2O oxidation at 623 K using Fe-ZSM5 catalyst. In a similar attempt, H_2O_2 has also been used as the oxidizing reagent [8–11]. The high cost of these two oxidizing reagents, however, limits their practical application. Although formation of active oxygen species has been achieved on the surfaces of catalysts by mixing the reductive reagents, such as carbon oxide and hydrogen, with oxygen, the yield has been inadequate for practical use [12–15]. In addition, hydrogen mixing carries serious risk of explosion.

For a more effective supply of active oxygen species, we developed a Pd membrane reactor through which hydrogen permeates to be activated to the atoms [16]. In this reactor, hydrogen and oxygen are separately supplied on the respective sides of the membrane. The active hydrogen species formed by permeation from one side of the Pd membrane safely produces active oxygen species on the opposite side by reacting with oxygen gas. The active oxygen species reacts with the adsorbed benzene on Pd and the benzene directly converts into phenol. By using this Pd membrane reactor system, a selectivity of 85% for phenol formation was achieved at a benzene conversion of about 13% at 423 K [16]. The quite recent results showed a selectivity of 77% at a conversion of 20% at 473 K [17]. This reactor system overcomes the two difficulties discussed above in that it does not need expensive oxidizing reagents such as N_2O and H_2O_2, and it eliminates the risk of explosion because of the separative supply of hydrogen and oxygen.

In this study, first, direct hydroxylation of methyl benzoate using a Pd membrane reactor was performed for apply to various aromatic compounds. Although the preferable product of this reaction is methyl salicylate, carboxyl can work as a meta-detector (inactive substitute) in the electrophilic substitution mechanism. On the other hand, the active oxygen species in this reactor system is considered the neutral or radical oxygen species based on a previous report [16]. Then, by varying the reaction conditions, the reaction mechanism and the reactivity of active oxygen species were discussed.

2. Experimental

2.1. Preparation of Pd membrane

Figure 1 shows a schematic of the Pd membrane reactor system. The Pd membrane tube was prepared by

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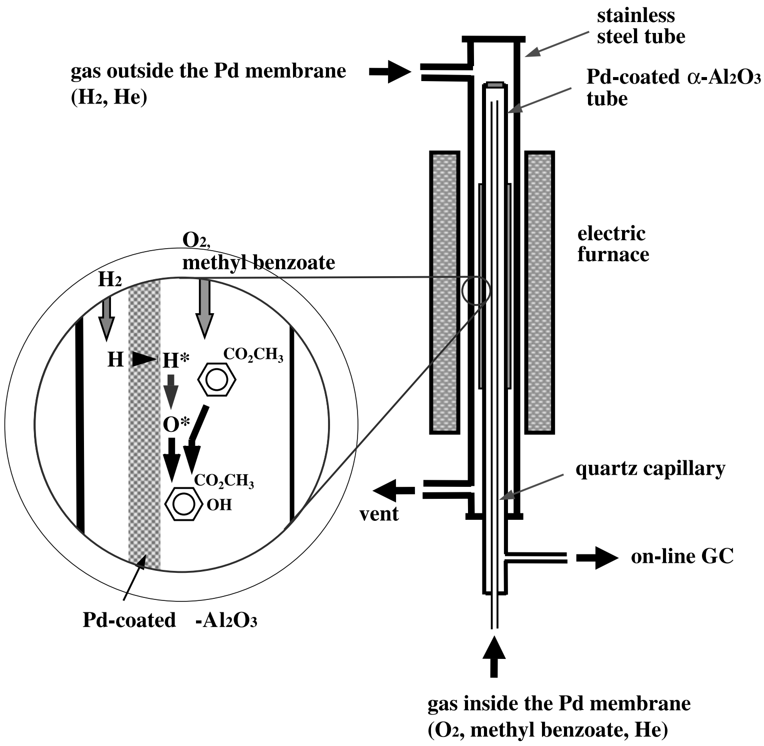

Figure 1. Schematic of direct hydroxylation using Pd membrane reactor.

coating of Pd layer on a porous α-Al_2O_3 tube (NOK Corporation) whose outer diameter was 2.0 mm and inner diameter was 1.6 mm and average pore size was 0.15 μm. The Pd coating was deposited along 100 mm with ca. 1 μm thick on the α-Al_2O_3 tube using a metallorganic chemical vapor deposition method [18] with $Pd(COOCH_3)_2$ as the source of Pd. The remainder of the surface of the α-Al_2O_3 tube was coated with glass paste to prevent gas permeation. One end of the tube was sealed with epoxyde resin.

2.2. *Reactor construction*

The Pd membrane tube was placed inside a stainless steel tube whose outer diameter was 19.1 mm (figure 1). A quartz capillary with 0.7 mm of outer diameter was then inserted inside this Pd membrane tube. A ternary mixture gas of He, O_2, and methyl benzoate was introduced into the inside of the Pd membrane *via* the quartz capillary, while H_2 diluted with He was introduced to the outside of the membrane. The gas flow rates were controlled by a mass flow controller as follows: 2–40 mL/min for H_2, 10 mL for He in outside, 2 mL/min for O_2, and 5 mL/min for He in the inside of the membrane. Methyl benzoate was introduced with He gas (5 mL/min) through the gas bubbler at 333 K. The molar ratio of O_2 to methyl benzoate was constant at 50. The reactor was heated to a preset temperature, between 423 and 493 K, by an electric furnace. All the gas lines were heated to avoid condensation of the products. The whole reactions in this study were performed by using the sole Pd membrane tube. Between the reactions, the reactor was kept at the reaction temperature with He flow both the inside and outside of the membrane to avoid the damage of membrane by the rapid change of temperature. The significant deactivation was not observed during the series of reactions.

The products were analyzed using two on-line gas chromatographs (Shimazu GC-14A), one equipped with a TCD detector (TCD-GC) and the other with an FID detector (FID-GC). The TCD-GC had packed columns (Molecular sieve 13×, 2 m, and Gasukuropak 54, 2 m) for the analysis of inorganic gases, and the FID-GC had a Supel-Q plot capillary column (SUPELCO, 30 m) for the analysis of organic compounds. For the products identification, GC-MASS (Varian Saturn 2000) was employed.

3. Results and discussion

3.1. *Combination of reaction gases*

As the preliminary reaction, the effect of reaction temperature between 423 and 493 K was investigated. The production of methyl salicylate by using the Pd membrane reactor was confirmed as shown in figure 2a. Although hydroxylation using the Pd membrane was attained for the aromatic compounds as well as benzene, the formation rate decreased with increasing reaction temperature. At 493 K, the reaction rate was low due to

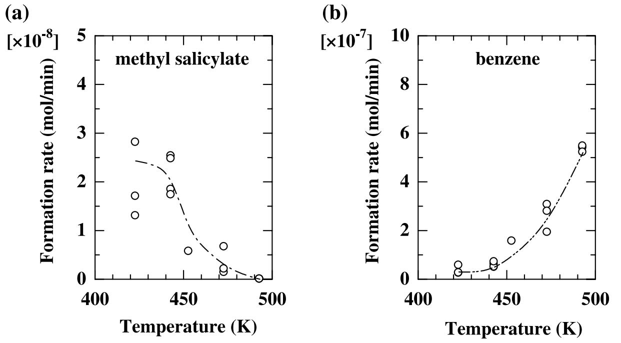

Figure 2. Effect of reaction temperature on formation rate of methyl salicylate and benzene at an H_2 flow rate of 10 mL/min ($H_2/O_2 = 5$).

the decrease in methyl benzoate caused by the formation of benzene induced by the decarboxylation of methyl benzoate (figure 2b). To ensure a sufficient reaction rate, all reactions reported here were carried out at the optimal reaction temperature of 423 K.

Table 1 summarizes the formation rate under various reaction-gas compositions at 423 K. Under the coexistence of methyl benzoate, oxygen and permeated hydrogen with $H_2/O_2 = 5$, methyl salicylate was confirmed as a product (table 1a), although it was not the most dominant product. The estimated yield of methyl salicylate was ca. 4.7% for a methyl benzoate conversion of 45.9%. In contrast to phenol synthesis from benzene [16,17], the selectivity was not high due to the many kinds of by-products. The major by-products were benzene, toluene, cyclohexanone, phenol, hydrogenated methyl benzoate (mainly, methyl cyclohexane carboxylate), and carbondioxide, and the trace by-products were methanol, methyl acetate, cyclohexane, and methyl cyclohexanone 2-carboxylate (and its isomers). The formation of many kinds of by-products was responsible for the high reactivity of methyl benzoate in comparison with benzene. In addition, by-products from methyl benzoate underwent further consecutive reactions. For instance, phenol was formed by the hydroxylation of benzene or an intermediate species from methyl benzoate to benzene. Cyclohexanone and methyl cyclohexanone 2-carboxylate were generated by the hydrogenation of phenol and methyl salicylate, respectively. The hydrogenation of carboxylate to form the alcohol and aldehyde did not occur. No reaction of the side chain is similar to previously reported results for toluene hydroxylation using a Pd membrane [16].

Table 1
Formation rate of principal products under various gas combinations at 423 K

Gas combination	a[a]	B	C
Inside membrane	Feed, O_2	Feed	Feed, O_2
Outside membrane	H_2	H_2	–
Product (mol/min)			
Benzene	7.0×10^{-8}	2.2×10^{-8}	0
Toluene	6.1×10^{-9}	6.1×10^{-8}	0
Cyclohexanone	1.7×10^{-8}	0	0
Phenol	6.6×10^{-9}	0	0
Hydrogenated methyl benzoate	4.4×10^{-8}	1.6×10^{-7}	0
Methyl salicylate	2.8×10^{-8}	0	0
3-Hydroxy methyl benzoate	0	0	0
4-Hydroxy methyl benzoate	0	0	0
Carbondioxide	8.1×10^{-7}	0	2.1×10^{-6}

[a] H_2: 10 mL/min, $H_2 / O_2 = 5$.

It is noteworthy that isomers of methyl salicylate, i.e., 3-hydroxy methyl benzoate and 4-hydroxy methyl benzoate, were not detected. Assuming the electrophilic substitution mechanism, methyl carboxylate works as a meta-director. Hence, this result suggests that the active oxygen species generated by the permeated hydrogen species for direct hydroxylation were not the ionically activated species, such as O^-, O^{2-} and O_2^-. It is corresponded to the report that negative oxygen species indicate low activity for the hydroxylation [19]. The active oxygen species might be neutral oxygen or radical oxygen species, such as $HO^{\cdot}$ or $HOO^{\cdot}$ [16]. The reaction between oxygen and permeated hydrogen can also form $HOO^{\cdot}$ and H_2O_2, and H_2O_2 is then decomposed to atomic oxygen, $HO^{\cdot}$, and water. Indeed, most of the permeated hydrogen species reacted oxygen and formed water. In the present reaction, the high selectivity for the formation of methyl salicylate among three isomers might be related to the form of methyl benzoate adsorbed. The steric hindrance of methyl carboxylate on Pd inhibited the direct hydroxylation to the meta and para positions.

The oxidation and hydrogenation of methyl benzoate were, respectively, carried out using the Pd membrane reactor system to confirm the advantage of co-feeding of three kinds of gases, i.e, permeated hydrogen, oxygen, and methyl benzoate. The reaction of permeated hydrogen and methyl benzoate without oxygen mainly produced hydrogenated methyl benzoate and decomposed compounds, such as benzene and toluene, but no oxidized products (column b in table 1). In contrast, the reaction of methyl benzoate and oxygen on Pd without hydrogen caused complete oxidation, and produced carbondioxide (column c in table 1). These results suggest that the direct hydroxylation only occurred under the coexistence of ternary gases.

3.2. *Effects of H_2/O_2 ratio on direct hydroxylation*

The reaction products shown in column a in table 1 were classified into three categories: hydrogenated products, such as hydrogenated methyl benzoate; oxidized products, such as carbondioxide; and hydroxylated products, such as methyl salicylate and phenol. As suggested in section 3.1, hydrogenated products were obtained under the reductive condition with permeated hydrogen (column b in table 1), and oxidized products under the oxidative condition with oxygen gas (column c in table 1). The coexistence of the three kinds of products, therefore, indicates that each reaction might occur at different sections of the Pd membrane depending on the surface state at that section. The surface state should strongly depend on the atmospheric gas. To investigate this phenomenon, the effect of H_2/O_2 ratio on the products selectivity was examined by changing the H_2 flow rate.

Figure 3 shows the formation rates of the principal products as a function of H_2/O_2 ratio. The maximum formation rate of methyl salicylate, ca. 2.5×10^{-8} mol/min, was obtained at $H_2/O_2 = 5$ (figure 3a). Note that methyl salicylate was not formed when $H_2/O_2 < 2.5$. The maximum formation rate of phenol was also obtained at $H_2/O_2 = 5$ (figure 3b). These formation rates of hydroxylated products differ from those of hydrogenated and oxidized products. For example, hydrogenated methyl benzoate was not formed (figure 3c) until $H_2/O_2 > 2.5$, and then the formation rate increased with increasing H_2/O_2, finally reaching 1.0×10^{-7} mol/min at $H_2/O_2 = 20$. The formation rate of cyclohexanone, which was produced by the hydrogenation of phenol, showed a similar trend (figure 3d). In contrast, low H_2/O_2 favored the formation of carbondioxide, which is the main oxidized product (figure 3e). These trends in formation rates of the hydrogenated and oxidized products correspond to the concentrations of hydrogen gas and oxygen inside the membrane (figure 3f). When $H_2/O_2 < 2.5$, the permeated hydrogen was completely consumed mostly by the reaction with oxygen, and the unreacted oxygen remained in the exhaust gas. When $H_2/O_2 > 2.5$, oxygen in the reactor was completely consumed by the permeated hydrogen. The almost constant formation rate of water when $H_2/O_2 > 2.5$ confirms this complete consumption. The excess hydrogen species were re-combined on Pd, and consequently desorbed into the gas phase. Hydrogen gas increased with increasing H_2/O_2 ratio.

The presence of oxygen or the formation of water enhanced the hydrogen permeation. Figure 4 shows the flow rate of non-permeated hydrogen as a function of initial H_2 flow rate for different gas compositions inside the Pd membrane. When only He was the gas inside the membrane, the hydrogen permeation rate was linearly proportional to the set flow rate of H_2. In contrast, the addition of oxygen and methyl benzoate inside the membrane enhanced the hydrogen permeation when $H_2 < 10$ mL/min (i.e., $H_2/O_2 < 5$). This enhancement is due to the ease at which water is

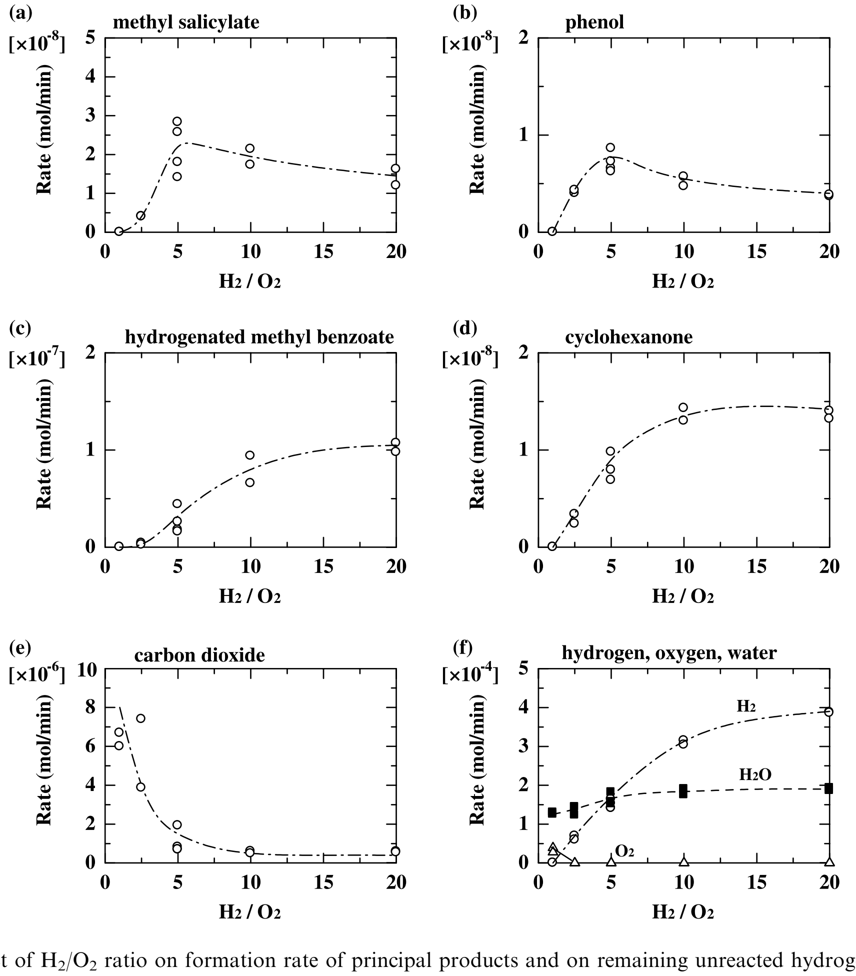

Figure 3. Effect of H_2/O_2 ratio on formation rate of principal products and on remaining unreacted hydrogen and oxygen.

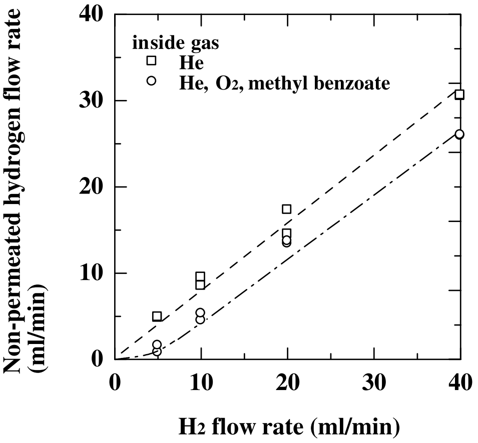

Figure 4. Effect of initial H_2 flow rate on non-permeated hydrogen. (10 mL/min of He was mixed. it is not plotted on figure).

formed by the reaction between hydrogen and oxygen compared with the re-combination of hydrogen atoms to the molecules in the inert gas, such as He [20]. When $H_2 > 10$ mL/min (i.e., $H_2/O_2 > 5$), the hydrogen permeation rate linearly increased with increasing H_2 flow rate, because the amount of water formed was constant (figure 3f).

Figure 5 schematically summarizes the gas concentration inside the Pd membrane. The atmosphere on the Pd membrane is controlled by the oxygen consumption with the formation of water. At low H_2 flow ($H_2/O_2 < 2$), even if all of the hydrogen permeates through the Pd membrane, it is not enough to react with all of oxygen molecules (figure 5a), and thus the exhaust gas contains unreacted oxygen and the entire surface of Pd is exposed to an oxidative atmosphere. Under this condition, the supply of oxygen on the surface from the gas phase might be sufficient. The adsorbed oxygen that cannot react with the hydrogen dissociated on the Pd membrane changes to an ionically active oxygen species, which favors complete oxidation. This mechanism corresponds to the observed reaction of oxygen and methyl salicylate (column c in table 1). If the neutral or radical active oxygen species for the hydroxylation is formed during the water formation, then the intermediate species from methyl benzoate to methyl salicylate must be easily oxidized into carbondioxide by the abundant negatively charged oxygen species on the Pd surface.

With increasing H_2 concentration ($2 < H_2/O_2 < 10$), oxygen gas is completely consumed by the reaction with the permeated hydrogen at the upper region of the Pd membrane (figure 5b). The oxidative region is shortened by the acceleration of hydrogen permeation, as exhibited in figure 4. After the consumption of oxygen, the bottom region of the membrane is exposed to a reductive atmosphere due to the hydrogen gas, which is formed by the re-combination of the permeated species. In the absence of oxygen, hydroxylation does not occur, as shown in column b in table 1.

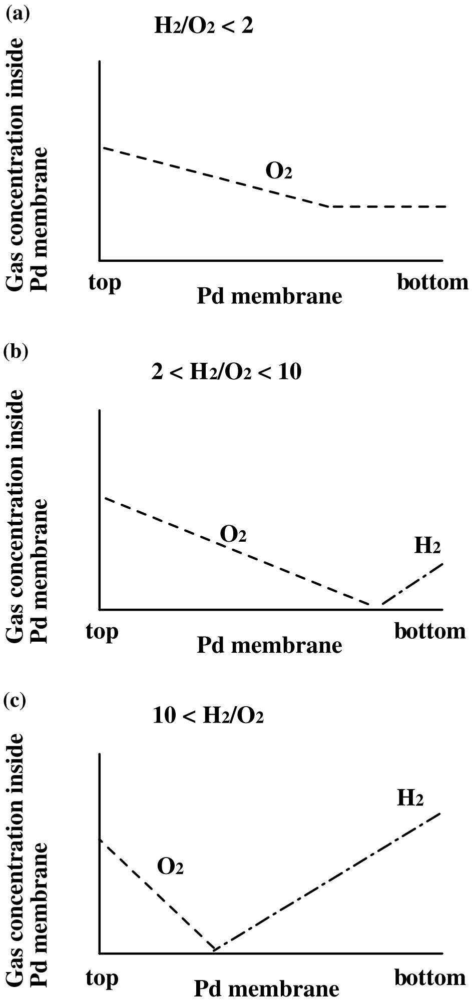

Figure 5. Schematic of gas concentration inside the Pd membrane for various H_2/O_2 ratios.

Therefore, the above-mentioned indicates that the direct hydroxylation occurs within a very limited region of the Pd membrane in which the oxygen concentration is very low. In this region, the low oxygen concentration restricts the formation of ionically active oxygen species for further oxidation.

When $H_2/O_2 > 10$, the upper region of the Pd membrane is exposed to an oxidative atmosphere and is further shortened by increasing the hydrogen permeation (figure 5c). Therefore, the region with low oxygen concentration favoring the hydroxylation might be shortened, which in turn decreases the formation rate of methyl salicylate (figure 3a). Thus, most of the Pd membrane is exposed to a reductive atmosphere due to the recombination of permeated hydrogen. Under these conditions, hydrogenation reactions are dominant, such as methyl benzoate to hydrogenated methyl benzoate, phenol to cyclohexane, and methyl salicylate to methyl cyclohexanone 2-carboxylate (column b in table 1). These hydrogenation reactions are also responsible for the decrease in the yield of hydroxylated products.

These phenomena observed in the hydroxylation of methyl benzoate might be inapplicable to the direct hydroxylation of benzene because the reactivity of benzene is lower than that of methyl benzoate. However, improvement in direct hydroxylation by using the Pd membrane is possible for all of the aromatic compounds for the following two reasons. First, the hydrogen and oxygen concentration can be controlled, which is crucial for increasing the yield of hydroxylated products. Second, the Pd membrane can be optimized for the formation of active species. In the current Pd membrane reactor system, the efficiency of hydrogen utilization is quite low due to the high formation rate of water.

4. Conclusion

The direct hydroxylation of methyl benzoate to methyl salicylate was achieved using the Pd membrane reaction system. The yield of methyl salicylate reached to ca. 4.7% at 423 K. Direct hydroxylation using the Pd membrane was successfully applied to various aromatic compounds. Isomers of methyl salicylate, such as 3-hydroxy methyl benzoate and 4-hydroxy methyl benzoate, were not detected, suggesting that direct hydroxylation using the Pd membrane does not proceed *via* the electrophilic substitution mechanism

The reactions under different compositions of reaction gases (i.e., different H_2/O_2 ratios) suggest that respective oxidation and hydrogenation occur at different sections of same membrane. The oxidation to carbondioxide is dominant in the upper region, whereas hydrogenation is favored in the lower region of the membrane. Hydroxylation occurs in only a limited area near the end of upper region where the oxygen concentration is low.

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