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The Liquid-Phase Oxidation of *p*-Methoxytoluene to *p*-Anisaldehyde with $Co(OAc)_2/Ce(OAc)_3/Cr(OAc)_3$ Catalyst

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The liquid-phase oxidation of *p*-methoxytoluene to *p*-anisaldehyde in the presence of Co based catalysts has been studied. With $Co(OAc)_2$ alone in acetic acid as a solvent, only a trace amount of *p*-anisaldehyde could be obtained; however, upon the addition of a second metal salt (e.g., $Mn(OAc)_2$ or $Ce(OAc)_3$) a considerable improvement in the yield (up to 60%) was observed. The synergism of Co and the second component as well as the optimization of the reaction conditions were investigated. $Co(OAc)_2$–$Ce(OAc)_3$–$Cr(OAc)_3$ (3:1:2) was finally found to be the most effective catalytic system, which gave a 76% yield of *p*-anisaldehyde under 3 atm O_2 at 110° for 3 h.

The liquid-phase oxidation of substituted toluenes to the corresponding aldehydes has been receiving increasing attention from an industrial point of view[1] owing to a growing demand for these aldehydes as manufactural key intermediates for the production of medicines, perfumes, agricultural chemicals and so on. The current processes for the production of these aldehydes, based mainly on the stoichiometric chemical oxidations, have several disadvantages regarding waste treatment, small manufactural scale as well as high costs.

Although the liquid-phase oxidation of hydrocarbons has been the subject of numerous studies for many years,[2] the feature of the reaction mechanism is not simple and there is still no unified view in terms of the control of the catalytic activity and selectivity to oxidize specific substrates. In general, the aldehydes are more reactive toward oxidation than the starting substances and, thus, the selective synthesis of the aldehyde with the liquid-phase oxidation has been regarded as not being easily achieved.

p-Anisaldehyde is an useful chemical as an additive for metal plating brighteners or perfumes, as well as a source material for medicines. Recently, several attempts to produce *p*-anisaldehyde from *p*-methoxytoluene through liquid-phase oxidation have been reported. Okada and Kamiya[3] reported that only less than 10% yield of *p*-anisaldehyde can be obtained by the liquid-phase oxidation of *p*-methoxytoluene with a Co–Cu–Br catalytic system. A relatively good yield (60%) was reported by Imamura et al.[4] using a Co based catalyst under optimized reaction conditions.

In the present study, a catalytic survey for a highly selective liquid-phase oxidation of *p*-methoxytoluene to *p*-anisaldehyde was performed; multicomponent metal systems, including the most efficient system Co–Ce–Cr, have been found to give a higher yield.

Experimental

p-Methoxytoluene (purchased from Tokyo Kasei), $Co(OAc)_2\cdot 4H_2O$ (Wako), $Ce(OAc)_3\cdot H_2O$ (Wako), $Cr(OAc)_3\cdot H_2O$ (Wako) and the other reagents were used without further purification. A 50 ml stainless autoclave (SUS-316) was used for the reaction. Into the autoclave, were added the substrate, a solvent (AcOH), and metal salts with a magnetic bar. The autoclave was heated in a prewarmed oil bath with vigorous magnetic stirring at 110 °C under 3 atm of O_2. The products were isolated by TLC and the structures were assigned based on their IR, NMR, and mass spectra. Through routine procedures, these products were quantitatively analyzed by GC on SE-30 supported on Chromosorb W.

Results and Discussion

Oxidation with $Co(OAc)_2$–$Mn(OAc)_2$ Catalytic System. When 2 mmol of *p*-methoxytoluene was allowed in 10 ml of AcOH in the presence of 0.75 mmol of $Co(OAc)_2$ (generally known to be effective for a wide variety of liquid-phase oxidations of hydrocarbons) at 110 °C for 3 h under 3 atm O_2, an only trace amount of *p*-anisaldehyde was formed (although the conversion was close to 100%). As by-products, *p*-methoxybenzoic acid and *p*-anisyl acetate were formed, implying that the oxidizing capability of $Co(OAc)_2$, itself, is too high to give *p*-anisaldehyde in good yield.

The mixture of $Co(OAc)_2$ and $Mn(OAc)_2$ (known as an active catalytic system in several liquid-phase oxidation reactions[5–7]) was found to be effective for the present reaction. In Fig. 1, the yield of *p*-anisaldehyde is plotted against the Mn content per Co+Mn catalyst. The reaction was carried out at 110 °C for 3 h in the presence of 0.75 mmol of the total catalyst. The yield of *p*-anisaldehyde depended strongly on the Co–Mn ratio. $Mn(OAc)_2$, itself, showed only a limited activity toward the oxidation compared with $Co(OAc)_2$, whereas the selectivity to

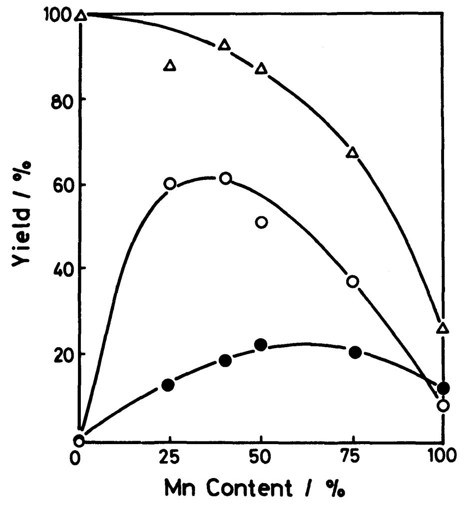


Fig. 1. The dependence of the product yield on Mn content in the oxidation of *p*-methoxytoluene with $Co(OAc)_2$–$Mn(OAc)_2$.
Total catalyst amount, 0.75 mmol; *p*-methoxytoluene, 2.0 mmol; AcOH, 10 ml; O_2, 3 atm; at 110 °C for 3 h. (△) Conversion, (○) *p*-anisaldehyde, (●) *p*-anisyl acetate.

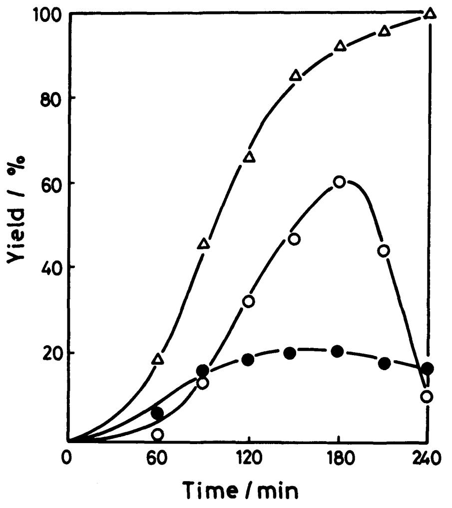
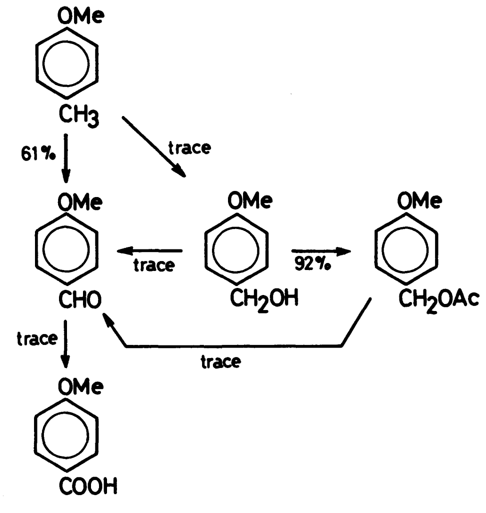


Fig. 2. The time course of *p*-methoxytoluene oxidation with $Co(OAc)_2$–$Mn(OAc)_2$ catalyst.
$Co(OAc)_2 \cdot 4H_2O$–$Mn(OAc)_2 \cdot 4H_2O$ (3:2), 0.75 mmol; O_2, 3 atm; *p*-methoxytoluene, 2.0 mmol; AcOH, 10 ml; at 110 °C.
(△) Conversion, (○) *p*-anisaldehyde, (●) *p*-anisyl acetate.



Scheme 1.

p-anisaldehyde was higher. A mixture of the two metal salts in any composition gives a higher yield of the aldehyde. A synergism is therefore evident. The highest yield (61%) was obtained when the ratio of Co:Mn was 3:2.

In Fig. 2, the change in the liquid-phase composition with the reaction time is shown. 0.75 mmol of the Co–Mn (3:2) catalyst was used for these experiments. In the initial ca. 0.5 h, the induction period was observed. The following yield of *p*-anisaldehyde increased with the reaction time and reached the highest value after 3 h. The longer reaction time resulted in a lower yield, presumably because of a subsequent oxidation of the aldehyde into undetermined polymeric by-products. Neither the increase of the catalyst concentration nor the O_2 pressure significantly affects the yield.

In order to clarify the reaction pathways for producing *p*-anisaldehyde, *p*-anisyl alcohol, *p*-anisyl acetate, and *p*-anisaldehyde were oxidized, respectively, in the presence of $Co(OAc)_2$–$Mn(OAc)_2$ (3:2) at 110 °C. The amount of the substance used was 2.0 mmol each; the other reaction conditions were the same as employed for *p*-methoxytoluene oxidation. As summarized in Scheme 1, *p*-anisaldehyde was found to be reasonably stable under the reaction conditions. The oxidation of the acetate to the aldehyde is desirable in order to obtain a higher yield of *p*-anisaldehyde. *p*-Anisyl acetate, however, was found to be stable with regard to further oxidation, giving only a trace amount of the aldehyde. *p*-Anisyl alcohol was not oxidized to *p*-anisaldehyde either, but was mainly converted to the acetate; this implies that *p*-anisaldehyde is formed directly from *p*-methoxytoluene, but not via the *p*-anisyl alcohol. Therefore, following factors seem to be the key factors for developing a more selective catalytic system: 1) the formation of alcohol should be suppressed and 2) the reaction conditions for retarding esterification is preferable. Based on these criteria, the medium oxidizing capability between $Co(OAc)_2$ and $Co(OAc)_2$–$Mn(OAc)_2$ may be suitable for the selective formation of *p*-anisaldehyde.

The Effect of Water or Anhydrous Acetic Acid. The additive effects of water[8] and anhydrous acetic

Table 1. Liquid-Phase Oxidations of *p*-Methoxytoluene with $Co(OAc)_2$–$Mn(OAc)_2$ (3:2) in the Presence of an Additive[a)]

Additive	Conv.	Ph'CHO	$Ph'CH_2OAc$	$Ph'CH_2OH$	Ph'COOH
mmol	%	%	%	%	%
H_2O, 27.8	19.4	3.4	0	0	0
H_2O, 27.8[b)]	56.1	23.6	0	0	0
Ac_2O, 17.5	100.0	49.4	0	0	0
NaBr, 0.75	100.0	19.1	0	0	0

a) Ph' denotes *p*-methoxyphenyl; O_2, 3atm; solvent (AcOH), 10 ml; *p*-methoxytoluene ($Ph'CH_3$), 2.0 mmol; temp, 110 °C; $Co(OAc)_2\cdot 4H_2O$–$Mn(OAc)_2\cdot 4H_2O$ (3:2), 0.75 mmol; reaction time, 3 h. b) Reaction time, 6 h.

Table 2. Liquid-Phase Oxidations of *p*-Methoxytoluene with $Co(OAc)_2$ in the Presence of the Second Metal Salt[a)]

Metal salt	Conv.	Ph'CHO	$Ph'CH_2OAc$	$Ph'CH_2OH$	Ph'COOH
	%	%	%	%	%
$Ni(OAc)_2\cdot 4H_2O$	100.0	0	0	Trace	Trace
$Cu(OAc)_2\cdot H_2O$	3.0	0	0	0	0
$Cr(OAc)_3\cdot H_2O$	100.0	1.6	0	3.6	Trace
$Ce(OAc)_3\cdot H_2O$	100.0	67.9	21.7	0	0

a) $Co(OAc)_2\cdot 4H_2O$, 0.56 mmol; metal salt, 0.19 mmol; O_2, 3 atm, temp, 110 °C; solvent (AcOH), 10 ml; *p*-methoxytoluene ($Ph'CH_3$), 2.0 mmol, reaction time, 3 h.

acid were examined (as summarized in Table 1). When 0.5 ml of H_2O was added to the Co–Mn catalytic system, the only obtained product was a 19.4% conversion to *p*-methoxytoluene for 3 h. When a longer reaction time was employed, a higher conversion was obtained; however, the yield of *p*-anisaldehyde was not high. Therefore, the addition of H_2O retards both the catalytic activity and the selectivity. The addition of anhydrous acetic acid or NaBr was also attempted. The addition accelerates the consumed rate of the reaction. When 0.5 ml of anhydrous acetic acid or 0.75 mmol of NaBr was added into the system, a 100% conversion of *p*-methoxytoluene was obtained in both cases. However, the yields of *p*-anisaldehyde were not very high. Anhydrous acetic acid and NaBr are known to be effective additives which can enhance the catalytic activity of the Co salt in several hydrocarbon oxidations.[2,9)] However, the use of these additives for the present reaction causes a further oxidation of the target product, *p*-anisaldehyde, and unfavorably lowers the selectivity.

The Effect of $Ce(OAc)_3$ Addition. It is generally believed that the enhancement of the catalytic activity upon the addition of the second metal component is due to the reoxidation of Co^{2+} to the catalytically active Co^{3+}. For example,[2)] the additive effect of the Mn^{2+} salt combining with the Co salt can be explained in terms of an electron transfer from the Mn^{3+} generated by the oxidation of Mn^{2+} with $RO_2\cdot$, as follows:

$$Mn^{2+} + RO_2\cdot \longrightarrow Mn^{3+} + RO_2^-$$

$$Mn^{3+} + Co^{2+} \longrightarrow Mn^{2+} + Co^{3+}$$

However, the addition of Mn in the present reaction rather lowers the oxidizing capability of the Co^{3+} species and enhances the selectivity for the production of *p*-anisaldehyde. Since the medium oxidizing capability between $Co(OAc)_2$ and $Co(OAc)_2$–$Mn(OAc)_2$ (as described above) was expected to be effective for the selective production of *p*-anisaldehyde, the other metal salt, which by itself slightly retards the oxidizing capability of the $Co(OAc)_2$ less than $Mn(OAc)_2$, seemed to be suitable as an additive for the present reaction. For these reasons the additive effects of several other metal salts, instead of $Mn(OAc)_2$, combined with $Co(OAc)_2$ were examined. The results are summarized in Table 2. In these experiments, the molar ratio of a metal salt to $Co(OAc)_2$ was fixed at 1:3. With $Co(OAc)_2$–$Ce(OAc)_3$, a considerable improvement in *p*-anisaldehyde yield was obtained, whereas the addition of $Cu(OAc)_2$ resulted in an apparent retardation of the catalytic activity. The addition of $Cr(OAc)_3$ and $Ni(OAc)_2$ also caused a further oxidation, yielding only a small amount of *p*-anisaldehyde.

The dependence of the *p*-anisaldehyde yield on the mixing ratio of $Ce(OAc)_3$ to $Co(OAc)_2$ is shown in Fig. 3. As in the Co–Mn system, a synergistic effect was evident. The highest yield (67.9%) of *p*-anisaldehyde was obtained when the molar ratio of Co:Ce was 3:1. With a smaller amount of Ce, the yield was low, although almost a complete consumption of *p*-methoxytoluene was observed. The addition of a greater amount of Ce caused a decrease in the catalytic activity, while the yield of *p*-anisyl acetate increased. The time course of the reaction in the presence of a $Co(OAc)_2$–$Ce(OAc)_3$ (3:1) catalyst is shown in Fig. 4.

The yield of *p*-anisaldehyde, as well as *p*-anisyl acetate, increased with time and reached a maximum value at 3 h. Any further reaction, however, tended to lower the yield of the aldehyde.

Oxidation with Three Components Catalysts. The additive effect of several metal salts into the effective catalytic system, $Co(OAc)_3$–$Mn(OAc)_2$ (3:2) and $Co(OAc)_2$–$Ce(OAc)_3$ (3:1), were examined (see Table 3). A slight improvement of the *p*-anisaldehyde yield was found upon the addition of $Cr(OAc)_3$ in both systems. The highest yield of *p*-anisaldehyde was obtained with a three-component catalytic system, $Co(OAc)_2$–$Ce(OAc)_3$–$Cr(OAc)_3$.

The effect of the added amount of $Cr(OAc)_3$ into a fixed amount (0.75 mmol) of $Co(OAc)_2$–$Cr(OAc)_3$ (3:1) was examined. The highest yield (72.7%) was obtained when the molar ratio of the components was 3:1:2 for Co:Mn:Cr. The change in the liquid-phase composition as a function of the reaction time

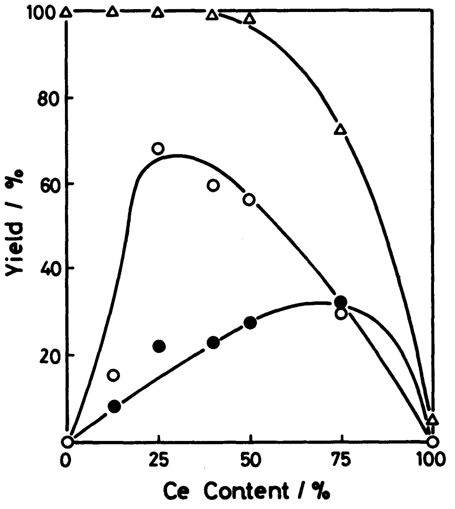


Fig. 3. The dependence of the product yield on Ce content in the oxidation of *p*-methoxytoluene with $Co(OAc)_2$–$Ce(OAc)_3$.
Total catalyst amount, 0.75 mmol; *p*-methoxytoluene, 2.0 mmol; AcOH, 10 ml; O_2, 3 atm; at 110 °C for 3 h.
(△) Conversion, (○) *p*-anisaldehyde, (●) *p*-anisyl acetate.

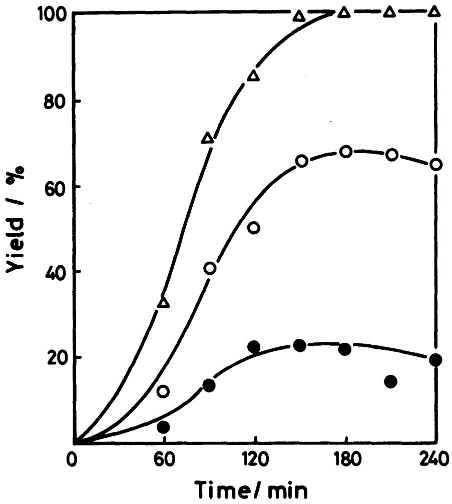


Fig. 4. The time course of *p*-methoxytoluene oxidation with $Co(OAc)_2$–$Ce(OAc)_3$ catalyst.
$Co(OAc)_2 \cdot 4H_2O$–$Ce(OAc)_3 \cdot H_2O$ (3:1), 0.75 mmol; O_2, 3 atm; *p*-methoxytoluene, 2.0 mmol; AcOH, 10 ml; at 110 °C.
(△) Conversion, (○)*p*-anisaldehyde, (●) *p*-anisyl acetate.

Table 3. Liquid-Phase Oxidations of *p*-Methoxytoluene with Three Component Metal Mixtures

Catalyst (molar ratio)	Conv. %	Ph'CHO %	$Ph'CH_2OAc$ %	$Ph'CH_2OH$ %	Ph'COOH %
$Co(OAc)_2$–$Mn(OAc)_2$–$Ni(OAc)_2$ (3) (2) (1)	93.0	53.0	0	Trace	0
$Co(OAc)_2$–$Mn(OAc)_2$–$Ce(OAc)_3$ (3) (2) (1)	98.2	63.5	0	Trace	0
$Co(OAc)_2$–$Mn(OAc)_2$–$Cr(OAc)_3$ (3) (2) (1)	98.2	64.6	0	Trace	0
$Co(OAc)_2$–$Mn(OAc)_2$–$Cu(OAc)_2$ (3) (2) (1)	99.2	63.4	0	Trace	0
$Co(OAc)_2$–$Ce(OAc)_3$–$Cu(OAc)_2$ (3) (1) (1)	99.1	62.9	0	Trace	Trace
$Co(OAc)_2$–$Ce(OAc)_3$–$Cr(OAc)_3$ (3) (1) (1)	98.5	68.7	14.4	Trace	Trace
$Co(OAc)_2$–$Ce(OAc)_3$–$Cr(OAc)_3$ (3) (1) (2)	99.9	72.7	14.1	0	0
$Co(OAc)_2$–$Ce(OAc)_3$–$Cr(OAc)_3$[a)] (3) (1) (2)	100.0	75.9	12.8	0	0

The catalyst amount of $Co(OAc)_2$–$Mn(OAc)_2$ (3:2) or $Co(OAc)_2$–$Ce(OAc)_3$ (3:1) was fixed, 0.75 mmol except the case, a) when the total catalyst amount was 1.75 mmol. O_2, 3 atm; 110 °C; *p*-methoxytoluene ($Ph'CH_3$), 2.0 mmol; solvent (AcOH), 10 ml; the reaction time, 3 h.

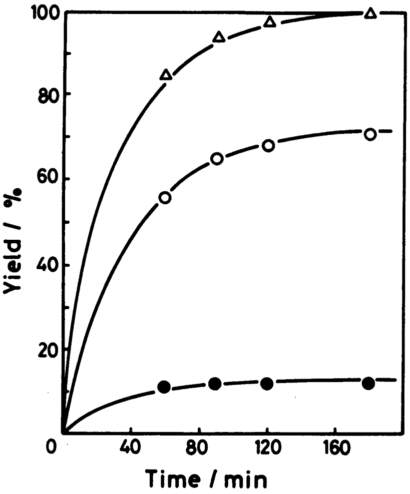


Fig. 5. The time course of *p*-methoxytoluene oxidation with $Co(OAc)_2$–$Ce(OAc)_3$–$Cr(OAc)_3$ catalyst. $Co(OAc)_2\cdot4H_2O$–$Ce(OAc)_3\cdot H_2O$–$Cr(OAc)_3\cdot H_2O$ (3:1:2), 0.75 mmol, *p*methoxytoluene, 2.0 mmol; AcOH, 10 ml; O_2, 3 atm; at 110 °C.
(△) Conversion, (○) *p*-anisaldehyde, (●) *p*-anisyl acetate.

catalyzed by this effective system is shown in Fig. 5. A similar feature of the reaction obtained in $Co(OAc)_2$–$Mn(OAc)_2$ and $Co(OAc)_2$–$Ce(OAc)_3$ systems was noted; the best reaction time for obtaining *p*-anisaldehyde was 3 h.

Finally, the dependence of the *p*-anisaldehyde yield on the catalyst concentration was examined. Reactions were performed at 110° for 3 h with $Co(OAc)_2$–$Mn(OAc)_2$–$Cr(OAc)_3$ (3:1:2). The yield slightly depended on the concentration in the range of the total amount of the catalyst, 0.5 to 2.0 mmol; the highest yield (75.9%) was obtained when 1.75 mmol of the total amount of the catalyst was used.

Okada and Kamiya reported that only a limited yield (2.7%) of *p*-anisaldehyde was obtained in the presence of $Co(OAc)_2$–$Cu(OAc)_2$–NaBr under 40 atm of air at 150 °C for 1 h.[3] Under their experimental conditions, the molar ratio of *p*-methoxytoluene:AcOH:Co was 4.2:100:0.33. Imamura et al. made a detailed investigation of suitable reaction conditions for the selective formation of *p*-anisaldehyde with a cobalt based catalytic system. They found that the highest yield (70%) of *p*-anisaldehyde was obtained with $Co(OAc)_2$ alone under 60 atm of O_2 at 120—124 °C. The molar ratio in this case was 10:100:2 for *p*-methoxytoluene:AcOH:Co. The yield was, however, significantly lower (<20%) under an ambient pressure of O_2. They examined the additive effect of several bromide additives (e.g., NaBr, HBr, $CoBr_2$) although no apparent improvement in the *p*-anisaldehyde yield was obtained. Compared with these systems, the present catalytic system is evidently more effective; a higher yield (76%) of *p*-anisaldehyde was obtainable under milder reaction conditions (at 110 °C and 3 atm of O_2, *p*-methoxytoluene:AcOH:Co was 1.1:100:0.45).

From an industrial point of view, the deactivation of the catalyst should be notable. Repeated oxidations of *p*-methoxytoluene were, thus, attempted using $Co(OAc)_2$–$Ce(OAc)_3$–$Cr(OAc)_3$. After the first reaction carried out under the same reaction conditions (described above), the catalyst was extracted with water and used for a subsequent experiment. Three repetitions of similar oxidations did not result in any deactivation, although the further repetitions caused a slight deactivation of the catalyst with a loss of the total amount of the catalyst in the extraction procedure.

References

1) J. Imamura, *J. Synth. Org. Chem. Jpn.*, **37**, 667 (1979).

2) Y. Kamiya, "Yuki Sanka Hannou," Gihōdō (1973).

3) T. Okada and Y. Kamiya, *Bull. Chem. Soc. Jpn.*, **54**, 2724 (1981).

4) K. Shimizu, K. Kizawa, T. Yoshimoto, and J. Imamura, *J. Jpn. Petrol. Inst.*, **75**, 7 (1982).

5) Y. Kamiya, "Oxidation of Organic Compounds, 2," p. 193 (1968), Am. Chem. Soc.

6) T. Taguchi, A. Naito, S. Futamura, and Y. Kamiya, Pre-prints, 19th Ann. Symp. Oxi. React., p. 7 (1985).

7) N. Kitajima, K. Takemura, Y. Moro-oka, T. Yoshikuni, M. Akada, Y. Tomotaki, and M. Taniguchi, *Bull. Chem. Soc. Jpn.*, **61**, 1035 (1988).

8) T. Taguchi, N. Naito, S. Futamura, and Y. Kamiya, Pre-prints, 20th Ann. Symp. Oxi. React., p. 7 (1986).

9) Y. Kamiya, T. Nakajima, and K. Sakota, *Bull. Chem. Soc. Jpn.*, **39**, 2211 (1966).