

Letter

Direct synthesis of 2-phenylethanol by hydrogenation of methyl phenylacetate using homogeneous ruthenium-phosphine catalysis under low hydrogen pressure

Kotohiro Nomura*, Hiroyuki Ogura, Yukio Imanishi

Graduate School of Materials Science, Nara Institute of Science and Technology (NAIST), 8916-5 Takayama, Ikoma, Nara 630-0101, Japan

Received 21 June 2000; accepted 3 October 2000

Abstract

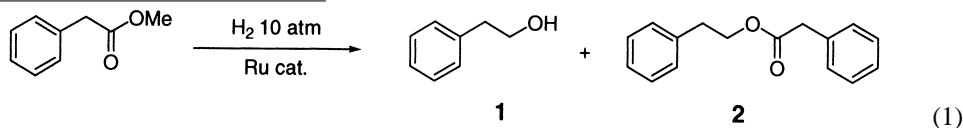
Methyl phenylacetate could be efficiently hydrogenated to yield 2-phenylethanol under lower hydrogen pressure (<10 atm) by using ruthenium-phosphine catalysis composed of $\text{Ru}(\text{acac})_3$, $\text{P}(n\text{-C}_8\text{H}_{17})_3$ in the presence of Zn. Effect of both phosphine and Zn plays an crucial role in order for this hydrogenation to proceed under mild conditions. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Hydrogenation of ester; Ruthenium; Homogeneous catalyst

Generally, direct hydrogenation of ester to afford alcohol using homogeneous transition metal catalysts requires both high reaction temperature (150 to >230°C) and high hydrogen pressure (50, 85 to >100 atm) [1–9]. Several examples for relatively efficient catalyst systems have recently been reported [6,8,9], however, these still require especially high hydrogen pressure to induce the high catalytic activity (50 and >85 atm). On the other hand, reports concerning hydrogenation of acid anhydrides to yield lactones by homogeneous ruthenium catalysts have been well-known [10–13], and one of the successful examples in this area should be the synthesis of

γ -butyrolactone by using ruthenium catalyst developed by Mitsubishi Chemical Co. [10,11].

Since we have studied ruthenium catalyzed chemoselective reduction of aromatic nitro compounds under $\text{CO}/\text{H}_2\text{O}$ conditions [14–18], also since a large number of useful reactions have been developed recently using both stoichiometric and catalytic amounts of ruthenium complexes [19], we thus, decided to explore the possibility to find a new catalyst for direct hydrogenation of ester under mild conditions [20]. In this paper, we would like to introduce our preliminary results for this reaction under low hydrogen pressure (Eq. (1)).



* Corresponding author. Tel.: +81-743-72-6041;
fax: +81-743-72-6049.
E-mail address: nomurak@ms.aist-nara.ac.jp (K. Nomura).

All manipulations were carried out under nitrogen atmosphere or in vacuo. Solvents such as

Table 1
Hydrogenation of PhCH₂CO₂Me by ruthenium-phosphine catalyst^a

Run no.	Phosphine (P/Ru) ^b	Additives (A/Ru) ^b	Solvent	Time (h)	Yield/TON ^c		Total
					1	2	
1	MeC(CH ₂ PPh ₂) ₃ (2)	NEt ₃ (20)	MeOH ^d	5	0.2	–	0.2
2	MeC(CH ₂ PPh ₂) ₃ (2)	NEt ₃ (20)	HFIP ^d	15	0.3	–	0.3
3	Ph ₂ P(CH ₂) ₂ PPh ₂ (4)	Zn (10)	Tetraglyme	15	0.4	1.7	2.1
4	Ph ₂ P(CH ₂) ₃ PPh ₂ (2)	Zn (10)	Tetraglyme	15	0.6	1.5	2.2
5	Ph ₂ P(CH ₂) ₄ PPh ₂ (2)	Zn (10)	Tetraglyme	15	1.6	3.4	5.0
6	Ph ₂ P(CH ₂) ₆ PPh ₂ (6.7)	Zn (10)	Tetraglyme	15	0.5	1.7	2.2
7	P(<i>tert</i> -Bu) ₃ (10)	Zn (10)	Tetraglyme	15	0.6	1.8	2.4
8	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	– (–)	Tetraglyme	5	0.5	0.3	0.8
9	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	Zn (10)	Tetraglyme	5	1.2	2.9	4.1
10	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	Zn (10)	Tetraglyme	15	4.4	5.3	9.6

^a Reaction conditions: Ru(acac)₃ 0.02 mmol, solvent 3 ml, PhCH₂CO₂Me 1.0 mmol, 200°C, H₂ 10 atm.

^b Molar ratio of phosphine ligand/Ru or additive/Ru.

^c TON (turnover number) = (molar amount of product)/(mol-Ru), PhCH₂CH₂OH (1) and PhCH₂CO₂CH₂CH₂Ph (2).

^d Catalyst previously reported in [9], HFIP = (CF₃)₂CHOH.

tetra(ethylene glycol) dimethyl ether (tetraglyme), 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), xylene, methanol were used as a reagent grade (Wako Chemical Co.), and stored under nitrogen in the presence of molecular sieves. Other reagents such as methyl phenylacetate, Zn, etc. were used as a reagent grade.

The catalytic reactions were typically carried out as follows: in an autoclave (20 ml) made of stainless steel was charged Ru(acac)₃ (acac = acetylacetonato), P(*n*-C₈H₁₇)₃, solvent, methyl phenylacetate, and additives such as Zn under nitrogen atmosphere. The reaction mixture was stirred under H₂ at 180 or 200°C. Reaction product was then determined by GLC using an internal standard and was identified by using GLC by co-injection with the authentic samples under different conditions. Identification was made by comparison of retention time of the chromatogram (column: DB-1 30 m, 0.25 mm ϕ \times 0.25 μ m), and GC-MS (GC-MS QP 5000, Shimadzu Co., Ltd.).

Table 1 summarizes the results for hydrogenation of methyl phenylacetate with various ruthenium-phosphine catalysts (H₂ 10 atm, 200°C, in tetraglyme). It turned out that the reaction proceeded catalytically if Zn was added into the reaction mixture (runs 3–10). The use of P(*n*-C₈H₁₇)₃ was quite effective in this catalysis, and this is the same tendency with that previously reported by Hara et al. in hydrogenation of γ -butyrolactone by ruthenium catalyst (Ru(acac)₃-phosphine catalyst, 50 atm, 200°C)

[6]. The catalyst system composed of Ru(acac)₃, MeC(CH₂PPh₂)₃, and NEt₃ (in methanol or HFIP) showed, however, low activity under these conditions (runs 1, 2).

As shown in Table 2, the use of Zn plays an important role in order for this reaction to proceed catalytically, and the absence of neither Zn nor phosphine gave extremely low activities (runs 8, 11). Since the reaction did not take place without ruthenium (run 12), it is clear that ruthenium catalyze this catalytic reaction. The use of Ti(O^{*i*}Pr)₄ or Cu in place of Zn was also found to be effective, and the use of CH₃SO₃H and *p*-toluenesulfonic acid, which have been known as the efficient reaction promoters for the synthesis of γ -butyrolactone by hydrogenation, slightly increased the activity. The exact role of these additives was, however, not so clear at this moment. Rapid decrease in the activity was not observed in this catalysis (runs 9, 10), and the yield increased for longer reaction hours.

As shown in Table 3, the choice of solvent seemed not so critical in this catalysis because the similar activity was observed between in tetraglyme and in xylene. On the other hand, noteworthy is that a significant increase in the activity was observed if the initial concentration of methyl phenylacetate into the reaction mixture was increased: this could be attained by increasing the amount of substrate charged or by reducing the amount of solvent used (runs 19–23). The

Table 2

Hydrogenation of PhCH₂CO₂Me by Ru(acac)₃-P(*n*-C₈H₁₇)₃ catalyst — effect of additives^a

Run no.	Phosphine (P/Ru) ^b	Additives (A/Ru) ^b	Time (h)	Yield/TON ^c		Total
				1	2	
11	None	—	5	—	—	—
8	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	—	5	0.5	0.3	0.8
12 ^d	P(<i>n</i> -C ₈ H ₁₇) ₃	Zn	5	—	—	—
13	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	Ti(O ^{<i>i</i>} Pr) ₄ (5)	14.5	2.9	2.8	5.7
14	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	<i>p</i> -TsOH ^e (8)	5	1.0	—	1.0
15	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	CH ₃ SO ₃ H (8)	5	1.2	—	1.2
16	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	NEt ₃ (2.5)	5	1.1	0.3	1.4
17	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	Al (10)	15	2.0	1.6	3.6
18	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	Cu (10)	15	3.5	2.0	5.5
9	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	Zn (10)	5	1.2	2.9	4.1
10	P(<i>n</i> -C ₈ H ₁₇) ₃ (10)	Zn (10)	15	4.4	5.3	9.6

^a Reaction conditions: Ru(acac)₃ 0.02 mmol, tetraglyme 3 ml, PhCH₂CO₂Me 1.0 mmol, 200°C, H₂ 10 atm.^b Molar ratio of phosphine/Ru or additive/Ru.^c TON (turnover number) = (molar amount of product)/(mol-Ru), PhCH₂CH₂OH (**1**) and PhCH₂CO₂CH₂CH₂Ph (**2**).^d Comparative experiment without Ru(acac)₃, P(*n*-C₈H₁₇)₃ 0.20 mmol, Zn 0.20 mmol.^e *p*-Toluenesulfonic acid.

Table 3

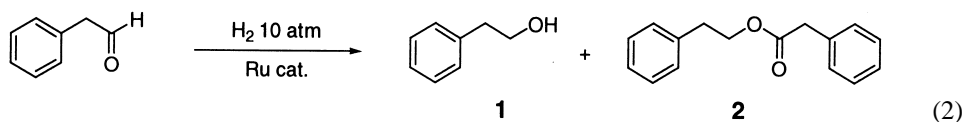
Hydrogenation of PhCH₂CO₂Me by Ru(acac)₃-P(*n*-C₈H₁₇)₃-Zn catalyst^a

Run no.	Additives (A/Ru) ^b	PhCH ₂ CO ₂ Me (mmol)	Solvent (ml)	Time (h)	Yield/TON ^c		Total
					1	2	
9	Zn (10)	1.0	Tetraglyme (3)	5	1.2	2.9	4.1
10	Zn (10)	1.0	Tetraglyme (3)	15	4.4	5.3	9.6
19	Zn (10)	4.0	Tetraglyme (3)	5	3.0	11.7	14.7
20	Zn (10)	1.0	Xylene (3)	15	2.7	8.4	11.1
21	Zn (10)	1.0	Xylene (1.25)	15	5.4	8.5	13.9
22	Zn (2.5)	1.0	Xylene (1.25)	15	7.5	11.4	19.0
23	Zn (2.5)	1.0	Xylene (0.50)	15	10.4	13.5	24.0

^a Reaction conditions: Ru(acac)₃/P(*n*-C₈H₁₇)₃ = 0.02/0.20 mmol, 200°C, H₂ 10 atm.^b Molar ratio of additive/Ru.^c TON (turnover number) = (molar amount of product)/(mol-Ru), PhCH₂CH₂OH (**1**) and PhCH₂CO₂CH₂CH₂Ph (**2**).

activity without solvent was low,¹ suggesting the suitable amount of solvent was required to promote this catalytic reaction. The amount of Zn could be reduced without the decrease in the activity (runs 21 and 22).

The reaction products in this catalytic reaction were 2-phenylethanol (**1**) and its ester with phenylacetic



¹ The activity (TON) without solvent (PhCH₂CO₂Me, 20 mmol) under the same conditions in run 19 was 14.2, and this value is smaller than that in the presence of solvent under the same conditions (TON = 20.5, tetraglyme 1.5 ml, PhCH₂CO₂Me 10 mmol).

acid (**2**). Since only a trace amount of the corresponding aldehyde could be observed on GLC chromatogram, also since the possibility to produce **2** by aldehyde coupling (Tishchenko-type) reaction was not deleted only with the above results, we examined the reaction of aldehyde under the same conditions (Eq. (2)). The results are summarized in Table 4.

The hydrogenation of aldehyde proceeded at significant rates and the yield of **1** was almost quantitative (TON => 1140, run 25). The reaction was also com-

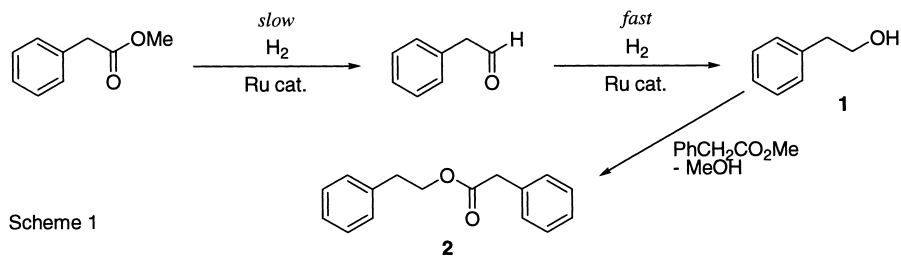
Table 4
Hydrogenation of PhCH₂CHO by Ru(acac)₃-P(*n*-C₈H₁₇)₃-Zn catalyst^a

Run no.	Ru (mmol)	Additive (A/Ru) ^b	PhCH ₂ CHO (mmol)	Temperature (°C)	Yield (%) ^c	
					1	2
24	0.02	Zn (2.5)	1.0	200	>94	0.8
25	0.005	Zn (10)	6.0	200	>95	1.8
26	0.005	Zn (10)	6.0	180	>98	1.5

^a Reaction conditions: molar ratio of Ru(acac)₃/P(*n*-C₈H₁₇)₃ = 1/10, xylene 1.25 ml, H₂ 10 atm, 5 h.

^b Molar ratio of Zn/Ru.

^c PhCH₂CH₂OH (1) and PhCH₂CO₂CH₂CH₂Ph (2).



Scheme 1

Scheme 1.

pleted at 180°C with lower ruthenium concentrations (run 26), and only a trace amount of **2** which would be generated by aldehyde coupling was also detected. These results strongly indicate that the aldehyde formed by the hydrogenation of ester quickly converted to the corresponding alcohol in this catalysis, and these results also strongly suggest that the product **2** in hydrogenation of methyl phenylacetate would be generated by ester replacement reaction (Scheme 1).

It has been reported by Hara et al. [11] that both RuH₂(PR₃)₄ and RuH₂(PR₃)₃ species (R = *n*-octyl) are generated in the reaction mixture consisted of Ru(acac)₃ and PR₃ under H₂ at >170°C, which was confirmed by ¹H, ³¹P and FD-MS analysis.² It is thus, suggested that ruthenium-hydride species plays an essential role for this catalytic reduction. It would also be suggested that the rate determining step in this catalysis would be the reaction of ester with ruthenium-hydride species, and that the role of Zn (or Zn(acac)₂, which might be generated in the reaction mixture) might be the indirect activation of substrate

by weak coordination that would promote the reaction with ruthenium-hydride species.

We have shown that hydrogenation of methyl phenylacetate could be hydrogenated to afford alcohol even under low hydrogen pressure (H₂ 10 atm), and Zn was found to be an efficient reaction promoter in order for this reaction to proceed catalytically under these rather mild conditions. We are now exploring the more detail, and these will be introduced in the near future.

Acknowledgements

K.N. would like to express his grateful acknowledgements to Mr. Mitsuhsa Tamura, and Mr. Naoki Inui (Fine Chemicals Research Laboratory, Sumitomo Chemical Co., Ltd.) for helpful discussion throughout this research. K.N. would also like to express his thanks to Sumitomo Chemical Co., Ltd. for support.

References

- [1] M. Bianchi, G. Menchi, F. Francalanci, F. Piacenti, U. Matteoli, P. Frediani, C. Botteghi, J. Organomet. Chem. 188 (1980) 109.

² It was also revealed that [(*p*-cymene)Ru₂]₂, and [(*p*-cymene)RuCl₂]₂ could also be used as the catalyst precursor in place of Ru(acac)₃ [21].

- [2] R.A. Grey, G.P. Pez, A. Wallo, *J. Am. Chem. Soc.* 103 (1981) 7536.
- [3] U. Matteoli, M. Bianchi, G. Menchi, P. Frediani, F. Piacenti, *J. Mol. Catal.* 22 (1984) 353.
- [4] U. Matteoli, G. Menchi, M. Bianchi, F. Piacenti, *J. Organomet. Chem.* 299 (1986) 233.
- [5] U. Matteoli, G. Menchi, M. Bianchi, F. Piacenti, S. Ianelli, M. Nardelli, *J. Organomet. Chem.* 498 (1995) 177.
- [6] Y. Hara, H. Inagaki, S. Nishimura, K. Wada, *Chem. Lett.* (1992) 1983.
- [7] K. Ishii, F. Mizukami, S. Niwa, M. Toba, H. Ushijima, T. Sato, *J. Am. Oil Soc.* 73 (1996) 465.
- [8] H.T. Teunissen, C.J. Elsevier, *Chem. Commun.* (1997) 667.
- [9] H.T. Teunissen, C.J. Elsevier, *Chem. Commun.* (1998) 1367.
- [10] Y. Hara, K. Wada, *Chem. Lett.* (1991) 553.
- [11] Y. Hara, C. Miyazawa, K. Takahashi, K. Wada, *Nippon Kagaku Kaishi* (1999) 567.
- [12] K. Osakada, T. Ikariya, S. Yoshikawa, *J. Organomet. Chem.* 231 (1982) 79.
- [13] T. Ikariya, K. Osakada, Y. Ishii, S. Osawa, M. Saburi, S. Yoshikawa, *Bull. Chem. Soc. Jpn.* 57 (1984) 897.
- [14] K. Nomura, *Chem. Lett.* (1991) 1679.
- [15] K. Nomura, *J. Mol. Catal.* 73 (1992) L1.
- [16] K. Nomura, *J. Mol. Catal. A* 95 (1995) 203.
- [17] K. Nomura, *J. Mol. Catal. A* 130 (1998) 1.
- [18] K. Nomura, *Catal. Surv. Jpn.* 2 (1998) 59.
- [19] T. Naota, H. Takaya, S.-I. Murahashi, *Chem. Rev.* 98 (1998) 2599.
- [20] K. Nomura, W. Sidokmai, Y. Imanishi, Our recent report concerning olefin polymerization with ruthenium catalyst, *Macromolecules* 32 (1999) 4732.
- [21] K. Nomura, unpublished results.