CHEMISTRY LETTERS, pp. 737-738, 1986.

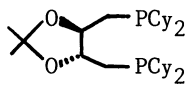
ASYMMETRIC HYDROGENATION OF N-(α-KETOACYL)-α-AMINO ESTERS

Kazuhide TANI,* Eiji TANIGAWA, Yoshitaka TATSUNO, and Sei OTSUKA
Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560

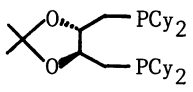
Asymmetric hydrogenation of N-(α-ketoacyl)-α-amino esters with Cydiop-rhodium(I) complex catalysts produced optically active N-(α-hydroxyacyl)-α-amino esters in high optical yields, which may be useful as building blocks of depsipeptides. Almost no influence of the chiral center of substrate was observed.

Asymmetric reduction of N-(α-ketoacyl)-α-amino esters (**1**) giving N-(α-hydroxyacyl)-α-amino esters (**2**) seems to be a useful reaction to obtain optically active depsipeptide building blocks. It is reported that the asymmetric hydrogenation of **1** using diop-rhodium(I) complex catalysts needed high pressure of H_2 (50 atm) and resulted only in simple asymmetric induction due to the chiral center of substrate. Fairly high optical induction in the asymmetric reduction of **1** has only been achieved by asymmetric hydrosilation.[1] Here we want to describe effective asymmetric hydrogenation of the ketoamides **1** using chiral peralkyldiphosphine-rhodium(I) catalysts (Eq. 1), which show a striking difference from conventional chiral diphosphine-rhodium(I) catalysts in the asymmetric hydrogenation.

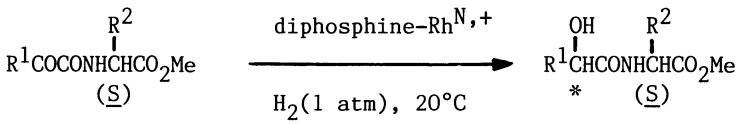
Previously we have reported that peralkyldiphosphine-rhodium(I) complexes show high catalytic activity for hydrogenation of ketones and aldehydes.[2] Subsequently we have prepared optically active peralkyldiphosphines, alkyldiop, Rdiop [2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(dialkylphosphino)butane],[3] and pyrolidine-containing peralkyldiphosphines[4] as effective chiral auxiliary ligands for asymmetric hydrogenation of prochiral ketones, especially that of α-dicarbonyl compounds.[4,5] Among these chiral peralkyldiphosphine ligands, (-)- or (+)-Cydiop



(-)-Cydiop



(+)-Cydiop Cy = cyclohexyl



(1)

1 **2**

a: R^1 = Ph; R^2 = CH_2Ph; b: R^1 = Ph; R^2 = Me; c: R^1 = Me; R^2 = CH_2Ph

is effective, in particular, for asymmetric hydrogenation of a-ketoamides. For example, with a neutral complex, (-)-Cydiop-Rh^N, $PhCOCONHCH_2Ph$ has been hydrogenated smoothly to give (+)-$PhCH(OH)CONHCH_2Ph$ in 78%ee.[5] The same catalyst system was found to be also effective for the asymmetric hydrogenation of **1**. Some representative results are summarized in Table 1. The present results form a sharp contrast to those of the hydrogenation with diop-rhodium(I) complex catalyst reported by Ojima et al.[1] The hydrogenation proceeded smoothly even under an atmospheric pressure of hydrogen. For the asymmetric hydrogenation of **1**, the neutral complex catalysts, Cy-diop-Rh^N, were much more effective compared with the cationic complex catalyst, Cydiop-Rh^+. The highest optical induction of 72% has been attained with Cydiop-Rh^N complex catalyst for hydrogenation of **1a** and almost no double asymmetric induction due to the chiral center of substrate was observed, because (+)- and (-)-Cydiop complex gave almost the same optical induction with opposite directions.

Table 1. Asymmetric hydrogenation of N-(α-ketoacyl)-α-amino esters[a]

Substrate	Catalyst[b]	Conversion/%	(R,S)/(S,S)[c]	%de
1a	(-)-Cydiop-Rh^N	100	14/86	72
	(+)-Cydiop-Rh^N	100	84/16	68
	(-)-Cydiop-Rh^+	78	41/59	18
	dipb-Rh^+	60	48/52	4
1b	(-)-Cydiop-Rh^N	100	17/83	66
	(+)-Cydiop-Rh^N	100	82/18	64
	dipb-Rh^+	57	53/47	6
1c	(-)-Cydiop-Rh^N	80	27/73	46
	(+)-Cydiop-Rh^N	72	74/26	48
	dipb-Rh^+	33	53/47	6

a) Reactions were run with [Catalyst] = 2.5 mM, [Substrate] = 0.5 M under 1 atm of H_2 at 25 °C for 20 h in MeOH (for cationic catalysts) or in THF (for neutral catalysts). b) diphosphine-Rh^N = diphosphine + $1/2[Rh(C_2H_4)_2Cl]_2$; diphosphine-Rh^+ = $[Rh(diphosphine)(nbd)]ClO_4$ (nbd = norbornadiene); dipb = $^iPr_2P(CH_2)_4P^iPr_2$. c) determined by ^{19}F NMR of the trifluoroacetate (in case of **2b**) or by HPLC (in case of **2a, 2c**).

References

1) I. Ojima, T. Tanaka, and T. Kogure, Chem. Lett., 1981, 823 .
2) K. Tani, K. Suwa, E. Tanigawa, T. Yoshida, T. Okano, and S. Otsuka, Chem. Lett., 1982, 261; K. Tani, E. Tanigawa, Y. Tatsuno, and S. Otsuka, J. Organomet. Chem., 279, 87 (1985).
3) K. Tani, K. Suwa, T. Yamagata, and S. Otsuka, Chem. Lett., 1982, 265 .
4) K. Tani, T. Ise, Y. Tatsuno, and T. Saito, J. Chem. Soc., Chem. Commun., 1984, 1641.
5) K. Tani, K. Suwa, and S. Otsuka, ACS Symposium Series, 185, 283 (1982); K. Yamamoto and S.-U.-Rehman, Chem. Lett., 1984, 1603.

(Received February 13, 1986)