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

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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 H₂ (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 peralkyldiphosphinerhodium(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 [2,3-0isopropylidene-2,3-dihydroxy-1,4-bis(dialkylphosphino)butane],³⁾ and pyrolidinecontaining peralkyldiphosphines⁴⁾ 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

$$R^{1}COCONHCHCO_{2}Me \xrightarrow{H_{2}(1 \text{ atm}), 20^{\circ}C} H_{2}(1 \text{ atm}), 20^{\circ}C \xrightarrow{(S)} H_{2}(1 \text{ at$$

is effective, in particular, for asymmetric hydrogenation of a-ketoamides. For example, with a neutral complex, (-)-Cydiop-Rh^N, PhCOCONHCH₂Ph has been hydrogenated smoothly to give (+)-PhCH(OH)CONHCH₂Ph 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.

Substrate	Catalyst ^{b)}	Conversion/%	(<u>R,S</u>)/(<u>S,S</u>) ^{c)}	%de
la	(-)-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
lc	(-)-Cydiop-Rh ^N	80	27/73	46
	(+)-Cydiop-Rh ^N	72	74/26	48
	dipb-Rh ⁺	33	53/47	6

Table 1. Asymmetric hydrogenation of N-(α -ketoacy1)- α -amino esters^a)

a) Reactions were run with [Catalyst] = 2.5 mM, [Substrate] = 0.5 M under 1 atm of H₂ at 25 °C for 20 h in MeOH (for cationic catalysts) or in THF (for neutral catalysts). b) diphosphine-Rh^N = diphosphine + $1/2[Rh(C_2H_4)_2C1]_2$; diphosphine-Rh⁺ = [Rh(diphosphine)(nbd)]C10₄ (nbd = norborna-diene); dipb = ${}^{i}Pr_2P(CH_2)_4P^{i}Pr_2$. c) determined by ${}^{19}F$ NMR of the trifluoroacetate (in case of 2b) or by HPLC (in case of 2a, 2c).

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