CHEMISTRY LETTERS, pp. 481-482, 1980.

THE ASYMMETRIC HYDROGENATION OF THE α-N-ACETYLAMINOCINNAMOYL DERIVATIVE OF AMINO ACIDS WITH CHIRAL BISPHOSPHINE-RHODIUM COMPLEX

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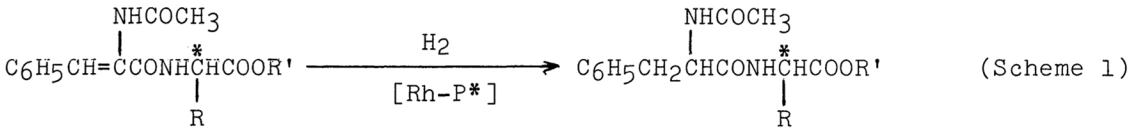
An optical yield of the dipeptide obtained in the title reaction is affected by a chiral amino acid moiety in the substrate.

Asymmetric hydrogenation of α-acylaminocinnamic acids has been successfully carried out with a rhodium complex of various chiral phosphines to give α-acylamino acids with a high optical yield. However, little is reported on application of the asymmetric hydrogenation to the α-N-acylaminocinnamoyl derivative of a chiral amino acid. The reaction gives a dipeptide as shown in the scheme 1. We have studied the effect of the amino acid on an optical yield of the dipeptide in the reaction and found that the chiral amino acid moiety in the substrate affects the optical yield significantly depending on its structure and configuration.



(Scheme 1)

R=CH_3, $CH(CH_3)_2$, R'=H, C_2H_5

α-N-Acetylaminocinnamoylalanine, its ethyl ester, and α-N-acetylaminocinnamoylvaline were hydrogenated respectively with either the neutral rhodium complex of (-)-Diop (I)[1] or the cationic complex of (1S,2S)-1,2-bis(diphenylphosphinamino)cyclohexane (II).[2] The optical yield and the conversion of the resulting dipeptide were determined by NMR.[3] The results are shown in Table 1 with those of α-N-acetylaminocinnamamide (III) as a comparison. As shown there, the optical yields and the conversion rates are affected by the structure and configuration of the amino acid moiety.

In the case of the complex I, the optical yield of the hydrogenation of the substrate containing alanine is higher than that of the hydrogenation of III regardless of the configuration of alanine. On the other hand, in the hydrogenation of α-N-acetylaminocinnamoylvaline, the optical yield is affected remarkably by the configuration of valine. This difference between alanine and valine may be due to the difference of their bulkiness.

Table 1. Asymmetric hydrogenation[a] of α-N-acetylaminocinnamoyl derivatives of amino acids and amino acid ethyl esters

Substrate[b]	Rh complex, I		Rh complex, II	
	Conv.	O.Y.[c]	Conv.	O.Y.[c]
NAcdeHPheNH$_2$	100%	71(D)%e.e.[d]	100%	92(L)%e.e.[e]
NAcdeHPhe-(L)-Ala	100	82(D)%d.e.	29	56(L)%d.e.
NAcdeHPhe-(D)-Ala	77	76(D)	4	-f)
NAcdeHPhe-(L)-AlaOEt	100	78(D)	100	91(L)
NAcdeHPhe-(D)-AlaOEt			100	85(L)
NAcdeHPhe-(L)-Val	100	50(D)	35	64(L)
NAcdeHPhe-(D)-Val	95	90(D)	100	15(L)

a) A solution of the substrate (1.0g) in the mixed solvent of ethanol and benzene (1/1, 40ml) was hydrogenated with either 0.04 mM of Rh complex I or 0.009 mM of Rh complex II.

b) NAcdeHPheNH$_2$: α-N-Acetylaminocinnamamide; NAcdeHPhe-(L)-Ala: α-N-Acetylaminocinnamoyl-(L)-alanine; NAcdeHPhe-(L)-AlaOEt: α-N-Acetylaminocinnamoyl-(L)-alanine ethyl ester; NAcdeHPhe-(L)-Val: N-Acetylaminocinnamoyl-(L)-valine.

c) Predominant configuration of the phenylalanine is shown in parenthesis.

d) Ref. 1).

e) Ref. 2).

f) The optical yield could not be measured because of a low conversion.

In the case of the complex II, the optical yields as well as the conversion rates are drastically affected by the amino acid moiety. It should be noted that both the optical yield and the chemical conversion are observed to be much higher for the ethyl ester of α-N-acetylcinnamoylalanine than for the parent acid. It was suggested that the functional groups of the substrate at a position far apart from the reaction site may play an important role on the improvement of the reaction.

Further studies on the double asymmetric synthesis are in progress.

References and Footnote

1) H.B. Kagan and T.P. Dang, J. Am. Chem. Soc., 94, 6249 (1972).

2) K. Onuma, T. Ito, and A. Nakamura, Chem. Lett., 1979, 905.

3) The diastereomeric excess and the chemical conversion are determined from an integrated value of the peak of acetyl groups in the two produced diastereomers and the substrate.

(Received February 1, 1980)